Welcome

FDA Public Workshop
Reducing the Risk of Preventable Adverse Drug Events Associated with Hypoglycemia in the Older Population

September 12, 2017
8:00am - 4:30pm
WO Building 31, Room 1503

Hosted By:
Professional Affairs and Stakeholder Engagement (PASE)
Safe Use Initiative

Keynote Speaker:
Don Wright, MD, MPH
Acting Assistant Secretary for Health HHS
Office of the Secretary
Scott K. Winiecki, MD

Team Lead, FDA Safe Use Initiative, Professional Affairs and Stakeholder Engagement Staff (PASE)
FDA Public Workshop: Reducing the Risk of Adverse Drug Events Associated with Hypoglycemia in the Older Population

Scott K. Winiecki, MD
Team Lead, Safe Use Initiative
Professional Affairs and Stakeholder Engagement
Center For Drug Evaluation and Research (CDER)
U.S. Food and Drug Administration

September 12, 2017
Disclosures

• I have nothing to disclose.
Disclaimer

This presentation reflects the views of the author and should not be construed to represent FDA’s views or policies.
Welcome

• Wi-Fi Network: FDA-Public
  – Passcode is “publicaccess”

• Opportunities for lunch are limited
  – Consider purchasing lunch from the kiosk to avoid lines at lunchtime
Safe Use Initiative

• **Mission:** Create and facilitate public and private collaborations within the healthcare community.

• **Goal:** Reduce *preventable harm* by developing, implementing, and evaluating cross sector interventions with partners committed to safe and appropriate medication use.
How do you Reduce Preventable Harm?

- Identify patients at highest risk
- Provider and facility feedback and/or self-assessment
- Make meds easier to use
- Patient education
- Improve communication

➢ There is no “one size fits all” solution
Safe Use Partners

- Federal agencies
- Healthcare professionals and professional societies
- Pharmacies, hospitals, and other health care entities
- Patients, caregivers, consumers, and their representative organizations

= Almost anyone
Drugs with Active Safe Use Projects

Safe Use has 16 current projects. These involve a wide variety of drugs and potential adverse events.

- Opioids
- Antibiotics
- Anti-hyperglycemic agents
- Stimulants
- Pediatric cough and cold medications
- Appearance and Performance Enhancing Substances
- NSAIDS

https://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/ucm277720.htm
Themes for Today

• Bring everyone to the table
  – Patients, family and professionals who care for patients with diabetes, advocacy groups, professional organizations, industry, healthcare administrators, others

• Moving from ideas to action is challenging

• Individualizing care and evaluating medications
  – takes time and energy
  – Barriers exist at multiple levels
  – Inertia
FDA Safe Use Team Contact Information

Scott K. Winiecki, MD

• Email: scott.winiecki@fda.hhs.gov or CDERSafeUseInitiative@fda.hhs.gov
Welcome

FDA Public Workshop
Reducing the Risk of Preventable Adverse Drug Events Associated with Hypoglycemia in the Older Population

September 12, 2017
8:00am - 4:30pm
WO Building 31, Room 1503

Keynote Speaker:
Don Wright, MD, MPH
Acting Assistant Secretary for Health HHS
Office of the Secretary

Hosted By:
Professional Affairs and Stakeholder Engagement (PASE)
Safe Use Initiative
Disclaimer

This presentation reflects the views of the author and should not be construed to represent FDA’s views or policies.
Why are we here today?
Focused Outpatient Medication Safety Efforts

"Of the thousands of drugs available to older adults, it is a really small group of medications that creates most of the hospitalizations."

Among older adults (65 years and older), three drug classes were implicated in an estimated 60 percent of ED visits for adverse drug events; 1. anticoagulants, 2. diabetes agents, and 3. opioid analgesics

Hypoglycemia

Increasing healthcare burden of hypoglycemia in the United States from 1999-2010. Rates of hospital admissions for hypoglycemia among Medicare beneficiaries increased by 22.3% (94 to 115 per 100,000 person years) compared to a 39.5% decrease in the rate of hyperglycemia admission (114 to 69 per 100,000 person-years) (ref: Lipska KJ, Ross JS, Wang Y et al. National trends in US hospital admissions for hyperglycemia and hypoglycemia among Medicare beneficiaries, 1999 to 2011. JAMA Intern Med 2014;174:1116-1124.)


Severe hypoglycemia may result in serious consequences like coma, seizures, and even death. (ref: Bonds DE, Miller ME, Bergenstal RM et al. The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study. BMJ 2010;340:b4909.)

Even mild hypoglycemic events have consequences, including lower health related quality of life, higher mortality, increased risk for cardiovascular disease, serious fracture related to falls, automobile crashes, and even a higher risk for dementia (ref: Bonds DE, Miller ME, Bergenstal RM et al. The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study. BMJ 2010;340:b4909.)
Why are we here today?

“Targeting adverse drug events common among specific patient populations, such as among the youngest (age 19 years or less) and oldest (age 65 years and older), may help further focus outpatient medication safety efforts” Shehab 2016

“The question remains how to best leverage the existing system to improve the safety of the process of starting, monitoring, and discontinuing medications,” Chad Kessler, M.D., M.H.P.E

“Collaboration is needed among physicians and other health professionals in primary care, specialty care, pharmacy, and emergency medicine to answer these questions in the quest for safer models of patient care. Furthermore, this collaboration across health care locations and the continuum of care will affect how much benefit or harm patients receive from prescribed medications. Integrated health care systems can help lead the way through improved care coordination and transition of care models. The work by Shehab et al shines a spotlight on the problem of adverse drug events and highlights the need to address this important clinical issue in a more systematic and organized fashion.” Chad Kessler, M.D., M.H.P.E

Call to Action!

Dissemination

Implementation
Leveraging FDA Safe USE partnerships in ACTION
Dissemination efforts

Amplification of message

- FDA public workshop
- ODPHP Listening session
- Partnership with professional societies, health care professionals, patients, caregivers, etc
- Conference oral and poster presentations
- VA patient videos
- Audience specific Key messages
Implementation efforts

- FDA Hypoglycemia CME/CE
- FDA Safe Use Initiative
- Social media project
- ODPHP: Individualizing Glycemic Targets eLearning
- CMS TCPI
- Partnerships with professional organizations, private organizations, patients, etc.
- VA Hypoglycemia Safety Initiative (HSI)
Patient Voice and Engagement

Shared Decision Making

Social Needs/Comorbidities

Individualizing Glycemic Goals
Thank you
PUBLIC HEALTH BURDEN
Don Wright, MD, MPH

Keynote Speaker

Acting Assistant Secretary for Health
FDA Public Workshop
Reducing the Risk of Preventable Adverse Drug Events Associated with Hypoglycemia in the Older Population

September 12, 2017
8:00am - 4:30pm
WO Building 31, Room 1503

Keynote Speaker:
Don Wright, MD, MPH
Acting Assistant Secretary for Health HHS
Office of the Secretary

Hosted By:
Professional Affairs and Stakeholder Engagement (PASE) Safe Use Initiative
Mary Julius RDN, CDE

Department of Veterans Affairs
HYPOGLYCEMIA AND FOOD INSUFFICIENCY

MARY M. JULIUS, RDN, CDE, PWD
OBJECTIVES

- Encourage individuals with diabetes to seek support to lower the risk of hypoglycemia.

- Enable all clinicians to recognize the importance of improving safety for food insecure patients at risk for hypoglycemia,
ARE YOU FOOD SECURE?

• During the last year, did you ever worry whether the food in your house would run out before there was money to get more?

• During the last year, was there ever a time when the food in the house just didn’t last and there wasn’t money to get more?

Do you know someone who would answer yes to either of these?

Does that person have diabetes?
• Cyclic and episodic phenomenon
• The average food-insecure household in the United States completes the above cycle 7 times each year.

May result from:
• High seasonal expenditures
  • Heat cost & holiday spending in winter
• Divorce ($35 per pay for food)
• Loss of benefits (COBRA)
• Unforeseen expenditures (car, home, toilet, broken appliance, etc)
• Time away from work due to illness or injury
• “Pay cycle” phenomenon
  • Depleted funds by the end of month
  • SNAP, SSI, once a month retirement
SPOTTED ----- WAKE UP

No Napping in Traffic
• Low-income households with incomes **below 185% of the poverty threshold**
  • The Federal poverty line was only $24,036 for a family of 4 in 2015.

• Households with children headed by a **single woman**

• Households with children headed by single man

• Black, non-Hispanic households

• Hispanic households

• Households with children under age 6

• All **households with children**

• Women living alone

• Men living alone
No Napping at Work!
The ADE Action Plan suggests a four-pronged approach to reduce patient harms:

- **Surveillance**
  - We have an ICD-10 code Food Insufficiency ICD-10 59.3
  - We have validated questions. Social Service and Nutrition.

- **Prevention**
  - #1 cause of Hypoglycemia = missed or insufficient meal
    - MARKET; create risk mitigation education

- **Incentives**

- **Oversight, and Research**
REFERENCES


Andy Geller, MD

Centers for Disease Control and Prevention
Hypoglycemia Adverse Drug Events: Translating Data into Prevention

September 12, 2017

Andrew Geller, MD, LCDR USPHS
Medical Officer, CDC Medication Safety Program
Disclosures

- None

**Disclaimer:** The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention (CDC). Moreover, any use of trade names is for identification purposes only and does not imply endorsement by CDC or the U.S. Department of Health and Human Services.
Objectives – Hypoglycemic Adverse Drug Events (ADEs)

- What is the national burden?
  - Who are the patients at risk?
  - How serious/severe are these events?

- Why do these events happen?
  - Precipitating factors
  - Products involved

- Important gaps?
  - Surveillance
  - Best Practice
Objectives – Hypoglycemic Adverse Drug Events (ADEs)

- What is the **national burden**?
  - Who are the patients at risk?
  - How serious/severe are these events?

- **Why** do these events happen?
  - Precipitating factors
  - Products involved

- Important **gaps**?
  - Surveillance
  - Best Practice
How often do inpatients experience diabetes agent ADEs (hypoglycemia)?

- **Hospitals:**
  - 3rd most common ADE in a nationally-representative sample of hospitalized Medicare beneficiaries (2008)
  - 5 of 12 deaths due to all adverse events (drug and non-drug related) involved hypoglycemia

- **Skilled Nursing Facilities (SNFs):**
  - 1st most common ADE in a nationally-representative sample of SNF resident Medicare beneficiaries (2011)
How often do outpatients seek care for all ADEs?

- 4 per 1,000 population (ED Visits)
- Older adults have highest rate

![Diagram showing the number of visits and admissions annually]

Shehab N et al. *JAMA* 2016;316:2115-25
Budnitz DS et al. *JAMA* 2006;296:1858-66
How often do outpatients seek care for diabetes agent ADEs?

- Diabetes agents:
  - ~13% ADE ED Visits (170,000/yr) in 2013-2014
    - ~1/3 resulted in hospitalization

![Diagram showing office visits, ED visits, admissions, and annually for diabetes agents]

**Insulin:** second most commonly implicated drug in ADE ED visits

<table>
<thead>
<tr>
<th>Drug Product</th>
<th>ED Visits for ADEs</th>
<th>National Estimate, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients (N = 42 585)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>6179</td>
<td>15.1 (12.3-17.9)</td>
</tr>
<tr>
<td>Insulin</td>
<td>4859</td>
<td>10.7 (8.6-12.7)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>1778</td>
<td>4.4 (2.9-5.9)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>1780</td>
<td>3.8 (3.3-4.3)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1518</td>
<td>3.5 (2.2-4.9)</td>
</tr>
<tr>
<td>Sulfamethoxazole-trimethoprim</td>
<td>1152</td>
<td>3.2 (2.7-3.7)</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>1096</td>
<td>2.4 (1.8-3.0)</td>
</tr>
<tr>
<td>Metformin</td>
<td>766</td>
<td>1.7 (1.4-2.1)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>722</td>
<td>1.6 (1.3-2.0)</td>
</tr>
</tbody>
</table>

How serious are insulin ADEs?

- Severe hypoglycemic sequelae
  - ~61% ADE ED visits (~56,000 ADE ED visits) in 2007-11
  - ~1/3 resulted in hospitalization

How serious are insulin ADEs?

- **Severe hypoglycemic sequelae**
  - ~61% ADE ED visits (~56,000 ADE ED visits) in 2007-11
  - ~1/3 resulted in hospitalization

- **Oldest adults (aged ≥80 years):**
  - ~2.5x as likely to visit ED (as age 45-64)
  - ~Five times more likely to be hospitalized

---

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Persons With DM Receiving Insulin Treatment With or Without Oral Antidiabetic Agents, No. (%)</th>
<th>ED Visits per 1000 Persons With DM Receiving Insulin Treatment With or Without Oral Antidiabetic Agents, Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18y</td>
<td>152,555 (2.8)</td>
<td>13.7 (4.9-22.5)</td>
</tr>
<tr>
<td>18-44</td>
<td>871,150 (15.9)</td>
<td>24.3 (15.0-33.6)</td>
</tr>
<tr>
<td>45-64</td>
<td>2,492,704 (45.5)</td>
<td>13.7 (9.1-18.3)</td>
</tr>
<tr>
<td>65-79</td>
<td>1,515,077 (27.7)</td>
<td>16.3 (10.7-21.9)</td>
</tr>
<tr>
<td>≥80</td>
<td>443,497 (8.1)</td>
<td>34.9 (20.5-49.3)</td>
</tr>
<tr>
<td>Total</td>
<td>5,474,983 (100.0)</td>
<td>17.8 (11.8-23.8)</td>
</tr>
</tbody>
</table>

Why do insulin ADEs happen?

- Precipitating factors documented in 21% of ED visits for hypoglycemia:
  - Meal-related (45.9%)
  - Wrong insulin (22.1%)
  - Wrong dose / confused units (12.2%)
  - Additional (“extra”) dose (6.0%)
  - Pump misadventure (1.5%)
  - Other (13.4%)

- 75-year-old male with syncope, EMS found patient with blood glucose in the 20s. Per wife, patient has been having low blood glucose and it has been difficult to keep elevated. ... has not been eating enough. Diagnosis: hypoglycemia.
Why do insulin ADEs happen?

- Precipitating factors for ED visits:
  - Meal-related (45.9%)
  - Wrong insulin (22.1%)
  - Wrong dose / confused units (12.2%)
  - Additional (“extra”) dose (6.0%)
  - Pump misadventure (1.5%)
  - Other (13.4%)

In one-half* of these ED visits, took rapid-acting instead of long-acting:

- 51-year-old male, per spouse she injected patient with 50 units of NovoLog instead of 50 units of Lantus, blood glucose 33 at time of arrival. Diagnosis: hypoglycemia.

Why do insulin ADEs happen?

- Precipitating factors for ED visits:
  - Meal-related (45.9%)
  - Wrong insulin (22.1%)
  - Wrong dose / confused units (12.2%)
  - Additional (“extra”) dose (6.0%)
  - Pump misadventure (1.5%)
  - Other (13.4%)

Other cases involved mixups of other insulin types:
Prevention gaps: Surveillance

- Gap: National estimates of hypoglycemia underestimate the problem
  - Surveillance/research need: Identify frequency of self-reported hypoglycemia
  - Validate methods of asking about hypo episodes not presenting to ED or leading to hospitalization

- Gap: Knowledge of hypoglycemia precipitating factors that are most modifiable
  - Identify modifiable factors
  - Focus prevention efforts
Prevention gaps: Interventions

- Reduce errors that cause harm:
  - Design and test insulin delivery systems that prevent mixups
    - Packaging to distinguish rapid- and long-acting products
      - Differences in shape, color, and texture to improve product distinction?
      - Audible (electronic voice instructions) or visible cues (LED lights)?
Prevention gaps: Interventions

- Reduce errors that cause harm:
  - Design and test insulin delivery systems that prevent mixups
    - Packaging to distinguish rapid- and long-acting products
      - Differences in shape, color, and texture to improve product distinction?
      - Audible (electronic voice instructions) or visible cues (LED lights)?
Prevention gaps: Interventions

- Increase uptake of Best Practices
  - Toolkits for older adults
    - Example: VA *Clinicians’ Toolkit*
  - Toolkits for patients in nursing homes
    - *Example: CDC Core Elements of Outpatient Antibiotic Stewardship for Nursing Homes*

- Are they effective for outcomes that matter to patients?
Prevention gaps: Interventions

- Increase uptake of Best Practices
  - Toolkits for older adults
    - Example: VA Clinicians’ Toolkit
  - Toolkits for patients in nursing homes
    - Example: CDC Core Elements of Outpatient Antibiotic Stewardship for Nursing Homes

- Are they effective for outcomes that matter to patients?
Thank you

- CDC Medication Safety Program:
  - CAPT Dan Budnitz, MD, MPH
  - Nadine Shehab, PharmD, MPH
  - Maribeth Lovegrove, MPH
  - Katie Rose, BSN
  - Sandra Goring, RN
  - Nina Weidle, PharmD
  - Arati Baral, MS
  - Alex Tocitu, BS, MBA
  - Dee Slaughter
Evidence based guidelines:
importance of individualized
glycemic control targets for older patients with diabetes
Gerardo Moreno, MD

American Geriatric Society
Len Pogach MD, MPH

Department of Veterans Affairs
The Veterans Administration/Department of Defense 2017 Guidelines for Management of Type 2 Diabetes Implementing Evidence to Prevent Hypoglycemia

Presented by Leonard Pogach MD, MBA, FACP
National Director Medicine
Office of Specialty Care Services
Office of Policy and Services
Veterans Health Administration
Collaborators

David Aron MD  VA/Cleveland
Rachel Brophy   VACO
Brian Burke MD VA/Dayton
Jeff Colburn MD DoD/USAF
Paul Conlin MD  VA/Boston
Alaina Fournier PhD  AHRQ
Carol Greenlee MD CMS/TCPi
Chester Bernie Good VA/Pittsburgh
Laurie Haughey  HRSA

Sandra Hedin, PharmD VA/Chicago
Mary Julius RD, LD VA/VISN 10
Christine Lee PharmD FDA
Mark McConnell VA/UPMI
Storm Morgan VACO
Rose Mary Pries VHA NCP
Jim Warner VHA EES
Sharon Watts PhD VA/Cleveland
Samantha Wright PharmD VA/Chicago
VA/DoD  Guideline Working Group
• The target **value for an individual patient** considers the approximate risk-to-benefit ratio of the treatment necessary to achieve it.

• Health care providers and their patients to establish individually negotiated targets based on **personal preferences** and **individually appraised risks and benefits**.

• **Intensive glycemic control** is known to **increase** the incidence and severity of **hypoglycemia**.
At-Risk Veterans - FY 2017

1 in 4 Veterans (1.6 million) receiving care in the VA has diabetes

70% of Veterans with diabetes are 65 and older

About 30% of older Veterans receive insulin

60% have serious co-morbid conditions

Provided by: VHA Support Service Center (VSSC in the office of Organizational Excellence. April 2017)
Process: Evidence Review Conducted by ECRI Institute, Lewin Group Project Management

- Interdisciplinary group of Guideline Champions and Workgroup Members
- Peer-Reviewed by FDA, CMS, HHS, NIH, Academy of Nutrition and Dietetics

Target Audience

- Physicians, nurse practitioners, nurses, physician assistants, dietitians/nutritionists, diabetes educators, pharmacists, and others
- Primary Care Setting

KEY RECOMMENDATIONS:

- Emphasize shared decision-making
- Assess the patient factors and establish individual glycemic goals
- Glycemic Goals should be a range, not a number.
- Understand interpretation of the HbA1c test, including racial differences
**Risk Stratification Tool for Hypoglycemia and Action Steps**

<table>
<thead>
<tr>
<th>Identify risk factors and patient preferences:</th>
<th>Determine prior hypoglycemia events:</th>
<th>Develop and individualized action plan:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cognitive impairment/dementia</td>
<td>Hypoglycemia requiring paramedics, emergency dept. visit or inpatient evaluation/care</td>
<td>Case management, specialty care if available, urgent review of medication regimen</td>
</tr>
<tr>
<td>• Clinically significant Chronic Kidney Disease</td>
<td>Any episode(s) of hypoglycemia requiring bystander assistance</td>
<td>Urgent review of medication regimen, self-management, target goals, patient education to identify cause of lows and course of action</td>
</tr>
<tr>
<td>• Social factors (homelessness, live alone/socially isolated)</td>
<td>Self-reported hypoglycemia</td>
<td>Review of medication regimen, self-management, target goals, patient education to identify cause of lows and course of action</td>
</tr>
<tr>
<td>• History of or risk for falls</td>
<td>No prior events but high risk and/or patient fears and concerns</td>
<td>Telephone/remote monitoring; individualized risk reduction strategies/education, discuss patient goals and preferences</td>
</tr>
<tr>
<td>• Difficulty in self-management (poor dexterity, mental health issues)</td>
<td>No major issues identified</td>
<td>Routine management and continued surveillance</td>
</tr>
<tr>
<td>• Food insufficiency (Do you ever skip meals? Do you ever go to bed hungry?)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Patient fears and quality of life</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This tool will assist clinicians to assess and address patients' risk for hypoglycemic events of any severity while using oral hypoglycemic prone medications or insulin. Use this tool to increase your awareness of hypoglycemia as a common and important, yet potentially preventable, complication of therapy. It should not be used as a clinical guideline.

Developed in collaboration with the Federal Interagency Work Group-Diabetes Agents/Department of Health and Human Services (5/2017)
Food insecurity Screening Algorithm. **In the 3 months, were there times when the food for you just did not last and there was no money to buy more?**

**Screening question**
(at intake and every 3 months)
(Administered by anyone on team)

- **YES**
  - PCP: Medication management/dose adjustments
  - Social Work: Assistance with food stamp application, Identification of alternative food sources (soup kitchens, food pantries)
  - Nutrition: Counseling/education on food intake, meal strategies
  - RN Case Manager: Pt. education, Case management, f/u for recurrent symptoms

- **NO**
  - No further action

Local registry assignment:
Data tracking and follow-up
Key Recommendations of 2017 VA/DoD Diabetes Guidelines- Shared Decision Making

<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Strength</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B. Shared Decision Making</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>SDM should be included, at a minimum, at the time of diagnosis, during difficulties with management, and at times of transition or development of complications</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
</tr>
</tbody>
</table>

- Greater knowledge of medications and understanding of risks.
- Decrease patient anxiety, increase trust in clinicians, and improve treatment adherence
To share decisions about treatment options, patients need information that they can understand about their condition and treatment choices. To quickly find out how well the patient understood what you discussed, use Teach Back. You can find out in 1-2 minutes using questions like this:

- “We talked about two ways that you might be able to treat your diabetes: either starting medicine right away to lower your blood sugar or increasing your physical activity and following a Mediterranean diet to try to lose a little weight. I want to make sure I explained each option clearly. Would you please tell me how you would explain the two choices to a member of your family?”
- “I want to make sure I was clear about the risks and benefits of taking insulin to control your diabetes. Could you tell me about insulin’s possible side effects and how it might impact your life on a day-to-day basis?”
- If the patient did not understand, say “I must not have done a good job explaining. Let me try again.” And use a different approach.
Glycemic Targets – VA/DoD 2017

• “We recommend setting an HbA1c target **RANGE** based on absolute risk reduction of significant microvascular complications, life expectancy, patient preferences and social determinants of health.” – Strong for

<table>
<thead>
<tr>
<th>Major Comorbidities or Physiologic Age</th>
<th>Microvascular Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent or Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Absent</td>
<td>6.0-7.0%</td>
</tr>
<tr>
<td>&gt;10-15 years life expectancy</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>7.0-8.0%</td>
</tr>
<tr>
<td>5-10 years of life expectancy</td>
<td></td>
</tr>
<tr>
<td>Marked</td>
<td>8.0-9.0%</td>
</tr>
<tr>
<td>&lt;5 years of life expectancy</td>
<td></td>
</tr>
</tbody>
</table>
Goal 7.5-8.5%

- “…7.5-8.5% is appropriate for most individuals with established microvascular or macrovascular disease, comorbid conditions, or 5-10 years life expectancy, if it can be safely achieved” – Strong for
  - No evidence that A1c <8.5% lowers mortality
  - A1c <7% shows no benefit with CVD and may increase mortality
  - Individual benefits of glycemic control must be balanced against risks of medication therapy
Definitions: Microvascular Comorbidities

Mild
- Early retinopathy, and/or microalbuminuria, and/or mild neuropathy

Moderate
- pre-proliferative retinopathy or persistent, fixed proteinuria (macroalbuminuria), and/or demonstrable peripheral neuropathy (sensory loss)

Advanced
- severe non-proliferative or proliferative retinopathy and/or renal insufficiency (Stage 3b CKD), and/or insensate extremities or autonomic neuropathy (e.g., gastroparesis, impaired sweating, orthostatic hypotension)
Goal: 8.0-9.0%

• “...8.0-9.0% for patients with type 2 diabetes with life expectancy < 5 years, significant comorbid conditions, advanced complications of diabetes or difficulties in self-management” – Weak for

  – 8.0%-9.0% is appropriate for life expectancy <5 years
  – Surrogate markers for life expectancy can include:
    • Functional status
    • Multiple recent hospitalizations
    • Organ failure
    • Cancer diagnosis/treatment plans
    • Advanced medical directives
### Key Recommendations of 2017 VA/DoD Diabetes Guidelines - MAGNITUDE OF BENEFIT

<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Strength</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B. Glycemic Control Targets and Monitoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>We recommend setting an HbA1c target range based on <strong>absolute risk reduction (ARR)</strong> of significant microvascular complications, life expectancy, patient preferences and social determinants of health.</td>
<td>Strong for Reviewed, New-added</td>
<td></td>
</tr>
</tbody>
</table>

- Using data from systematic reviews to calculate the number needed to treat (NNT) and number needed to harm (NNH) carries high risk for bias. This can lead to over- or under-estimation of risk.
- For example, in UKPDS, there was a 37% RRR for microvascular complications that was continuous and without a threshold. However, the ARR for any microvascular complication was 5.0/100 and the number needed to treat over 10 years was 19.6.
The United Kingdom Prospective Study (UKPDS), conducted from the mid-1980s to late 1990s with patients whose average A1c was 9% at time of diagnosis, provides the primary evidence base for tight control of type 2 diabetes from onset of disease for individuals with a life expectancy of around 10 years - UKPDS 33 (sulfonylurea/insulin therapy compared to conventional therapy – Lancet 1998); Use of metformin may confer additional benefit; UKPDS 34 (metformin vs. conventional therapy Lancet 1988).

For new onset diabetes, if A1c levels are targeted to be around 7% for the first 10 years
82 alive with diabetes without microvascular disease
8 alive with diabetes and microvascular disease
10 dead from diabetes

For new onset diabetes, if A1c levels are targeted to be around 8% for the first 10 years
78 alive with diabetes without microvascular disease
11 alive with diabetes and microvascular disease
11 dead from diabetes

Microvascular complications include retinopathy, nephropathy, and neuropathy
### Key Recommendation- A1C Range

<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Strength</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Glycemic Control Targets and Monitoring</td>
<td>6. We recommend assessing patient characteristics such as race, ethnicity, chronic kidney disease, and non-glycemic factors (e.g., laboratory methodology and assay variability) when interpreting HbA1c, fructosamine and other glycemic biomarker results.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
</tr>
</tbody>
</table>

- A single HbA1c measurement, even from a high quality laboratory, has a margin of error. Its true value is within a range defined by the coefficient of variation.
- Many factors affect HbA1c measurement besides the level of glycemia such as anemia, CKD, hemoglobin variants.
- The evidence is strong that African Americans have higher A1c values than Whites for a given level of glycemia.
An A1c Test Result is Within a Range Dependent Upon the Assay
A result of 8.0% is within a 7.84 to 8.16 range from a high quality laboratory (intra-assay coefficient of variation [CV]=2.0%) and between 7.68% and 8.32% if the CV is 3.0%). A CV of 2% will produce a 95% probability that a difference of about 0.5% HbA1c between successive patient samples is a true difference 95 out of 100 times for a A1c value of 8.0%. 
Evidence – Any A1c test result is in a range dependent upon individual factors

• Decrease unnecessary medication adjustments and risk for hypoglycemia from treating numbers, not patients

• Racial differences between HbA1c values and assessment of glycemia
  – African Americans have 0.4% higher A1c than Whites without differences in glycemic measures at time of entry in DPP study and ADOPT Study
  – VA/DoD recommends against use of estimated average glucose which is derived from A1c values using a formula.
Encourage Numeracy, Not Measures
VHA Laboratory Result Comment

- In support of the VHA Choosing Wisely-Hypoglycemic Safety Initiative, the Pathology and Laboratory Medicine Services was asked to append the following comments to A1c reports (including both lab and POC tests):
  - Citing performance measures or target values is not consistent with the individualized target approach advocated by the VA/DOD Guidelines.

```plaintext
Specimen: BLOOD. SC 1124 484
Specimen Collection Date: Nov 24, 2015@12:55
<table>
<thead>
<tr>
<th>Test name</th>
<th>Result</th>
<th>units</th>
<th>Ref. range</th>
<th>Site Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLYCATED HEMOGLOBIN</td>
<td>9.8 H</td>
<td>%</td>
<td>4.0 - 6.0</td>
<td>[578]</td>
</tr>
</tbody>
</table>

Comment: Target A1C values should be individualized. Better understanding of A1C test result accuracy is essential if clinicians are to interpret results for Veterans, and discuss treatment options through the process of Shared Decision Making. Contact your laboratory for performance characteristics of this assay.
```
Challenges in Prevention of Hypoglycemia

Measures
• <8% HbA1c measure applies to all older adults 65-75 years
• DHHS NAP (8/2014):
  • Does not reflect latest evidence
  • Does not stratify by medications
  • Does not exclude high risk patients
  • Does not address overtreatment

SDM Knowledge Gap
• Evidence: Clinicians and Patients
• Legacy of <7% measures and guidelines
• Delivery Mechanism
• Tools
• Trainers

EMR: Failure to Identify at Risk Patients
• Risk
• Severity
• Social Determinants
• Patient Preferences
• Patient Individualized Goal
• Prior Hypoglycemic Events

Lack Coordinated Message for Public Health Campaign for Clinicians and Patients
Consumer magazines
• Professional Organizations
• Lay Leadership
• Provider Bias
Challenges in Reducing Glycemic Over-treatment

Response to a vignette of a 77 y/o male with long-standing T2DM, severe kidney disease, HbA1c 6.5%, receiving glipizide 10mg BID (Cavanaugh et al, JAMA Internal Medicine 2015)

<table>
<thead>
<tr>
<th>Statement</th>
<th>Disagree</th>
<th>Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>I think this patient would benefit if his HbA1c is maintained below 7%</td>
<td>61.4%</td>
<td>38.6%</td>
</tr>
<tr>
<td>I worry that this patient would be harmed if his HbA1c is maintained below 7%</td>
<td>44.9%</td>
<td>55.1%</td>
</tr>
<tr>
<td>I would worry that reducing his diabetes medication would lead to an HbA1c that falls outside of current performance measures</td>
<td>57.9%</td>
<td>42.1%</td>
</tr>
<tr>
<td>It would be helpful to have a clinical decision-support tool that would help me determine whether this patient would benefit from reducing his diabetes medications</td>
<td>30.8%</td>
<td>69.2%</td>
</tr>
<tr>
<td>It would be helpful to have patient education materials to discuss reducing diabetes medication</td>
<td>14.6%</td>
<td>85.4%</td>
</tr>
</tbody>
</table>
A Brief History of VA Hypoglycemia Safety Initiative

2010’s

- 2003-2010 VA/DoD guidelines support individualized targets and targets up to 8.5% for complex medical/mental health conditions or limited life expectancy
- ABIM’s Choosing Wisely Campaign: AGS (2012) “Avoid using medications other than metformin to achieve hemoglobin A1c<7.5% in MOST older adults; moderate control is generally better”
- VISN 12 Great Lakes Hypoglycemia Safety Initiative 2012
- VHA-Choosing Wisely Hypoglycemia Safety Initiative 2014
VHA Choosing Wisely: Hypoglycemia Safety Initiative (HSI) Goals

- Foster Shared Decision Making
- Inform Best Available Evidence
- Reduce Unnecessary Care
- Improve Safety
Identification of Patients – EMR tools

High risk cohort

- HbA1c < 7%
- Insulin or Sulfonylurea
- Age ≥ 75 or Dementia / Cognitive Impairment or SCr > 1.7 mg/dL

Integrated Approach

- Multi-Professional Education
- EMR Tools
- Online Panel Reports
EMR Tools, cont.

Clinical Alert - Point-of-care patient identification

<table>
<thead>
<tr>
<th>Active Problems</th>
<th>Active/Susp</th>
<th>Clinical Reminders</th>
<th>Due Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroesophageal Reflux Disease (SCT)</td>
<td>Active/Susp</td>
<td>*** HOW TO RESOLVE A REMINDER ***</td>
<td>DUE NOW</td>
</tr>
<tr>
<td>Hyperlipidemia (SCT 55822004)</td>
<td></td>
<td>D: Advance Directive</td>
<td>DUE NOW</td>
</tr>
<tr>
<td>Type 2 Diabetes Mellitus Without Compl.</td>
<td></td>
<td>BPM PhrecO Pharmatherapy Ren VZ</td>
<td>DUE NOW</td>
</tr>
<tr>
<td>Chronic Atrial Fibrillation (SCT 42674900)</td>
<td></td>
<td>D: Diabetes Hypoglycemia Screen</td>
<td>DUE NOW</td>
</tr>
<tr>
<td>Visual Impairment (SCT 397540003)</td>
<td></td>
<td>D: Prevention · Non VA Meds</td>
<td>Oct 10,16</td>
</tr>
<tr>
<td>Simvastatin</td>
<td></td>
<td>N: Braden Scale (OPT/Non Acute)</td>
<td>Jun 23,16</td>
</tr>
<tr>
<td>Niacin [Niaspan Starter Pack]</td>
<td></td>
<td>N: ID Screen/Influenza (Off Season)</td>
<td>DUE NOW</td>
</tr>
<tr>
<td>Colestipol</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Allergies / Adverse Reactions                         |                      |                                          |             |
| Simvastatin                                           |                      |                                          |             |
| Niacin [Niaspan Starter Pack]                         |                      |                                          |             |

| Active Medications                                    |                      |                                          |             |
| Precision Xtra (glucose) 50 Test Strip                | Active/Susp          |                                          |             |
| Fluticasone Prop 50mcg 120d Nasal Inh                 | Active               |                                          |             |
| Lancet Lite Touch                                     | Active               |                                          |             |
| Insulin Glargine 100 Unit/ml 3ml Solostar             | Active               |                                          |             |
| Needle Pen 31g, 8mm                                   | Active/Susp          |                                          |             |
| Non-Va Ranitidine HCl 150mg Tab                       | Active               |                                          |             |
| Non-Va Diltiazem (tiazac) 180mg Sa Cap                | Active               |                                          |             |
| Non-Va Rosuvastatin Ca 20mg Tab                       | Active               |                                          |             |
| Non-Va Multivitamins Cap/Tab                          | Active               |                                          |             |
| Non-Va Metformin Hcl 1000mg Tab                       | Active               |                                          |             |
| Non-Va Warfarin (coumadin) Na 4mg Tab                 | Active               |                                          |             |
| Non-Va Insulin Glargine Solostar Inj                  | Active               |                                          |             |
| Non-Va Tamsulosin Hcl 0.4mg Cap                       | Active               |                                          |             |
EMR tools, cont.

1. Questions
2. Care Plan
3. Data Capture
Each of these also includes a lower section allowing for test ordering and allowing for documentation of any change in a shared decision about intensifying or relaxing management.

- Patient/Caregiver agrees to an A1C goal of < 7%
- Patient/Caregiver agrees to an A1C goal of < 8%
- Patient/Caregiver agrees to an A1C goal of <= 9%
- A1c goal discussed. Goal under consideration by patient/caregiver.

Order A1C

Enter Outside (A1C) *
Location: 
Enter Lab Value: *

Shared Patient Centered Plan
- No change in glycemic management at this time.
- Relax glycemic treatment
- Intensify glycemic treatment
### Online Panel Reports

#### Proactive Patient Identification

<table>
<thead>
<tr>
<th>Patient Name</th>
<th>Age</th>
<th>Dementia or Cog Impair</th>
<th>HbA1c Value</th>
<th>HbA1c Date</th>
<th>Prior HbA1c (months, yr)</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Johnson</td>
<td>87</td>
<td>N</td>
<td>7.5</td>
<td>04/17/15</td>
<td>6.9 (07/14/14)</td>
<td>INSULIN N</td>
</tr>
<tr>
<td>B. Smith</td>
<td>89</td>
<td>N</td>
<td>7.2</td>
<td>04/26/16</td>
<td>9.2 (06/15/15)</td>
<td>INSULIN GL</td>
</tr>
<tr>
<td>C. Wilson</td>
<td>72</td>
<td>N</td>
<td>6.9</td>
<td>02/26/15</td>
<td>6.7 (06/15/14)</td>
<td>INSULIN GL</td>
</tr>
<tr>
<td>D. Peterson</td>
<td>88</td>
<td>N</td>
<td>6.2</td>
<td>12/17/15</td>
<td>6.7 (06/14/15)</td>
<td>INSULIN, DETEMIR, HUMAN 100 UNIM INJ, FLEXTOUCH, 3ML</td>
</tr>
<tr>
<td>E. Davis</td>
<td>86</td>
<td>Y</td>
<td>7.8</td>
<td>01/21/15</td>
<td>6.3 (03/04/15)</td>
<td>DEXTROSE 15G/37 5GM SQUEEZE TUBE 1 TUBE ONCE PRN</td>
</tr>
<tr>
<td>F. Rodriguez</td>
<td>93</td>
<td>N</td>
<td>6.0</td>
<td>05/10/16</td>
<td>6.5 (03/16/15)</td>
<td>GLIMEPIRADE 2MG TAB (non/A)</td>
</tr>
<tr>
<td>G. Gonzalez</td>
<td>69</td>
<td>Y</td>
<td>6.7</td>
<td>03/13/16</td>
<td>6.7 (03/15/16)</td>
<td>IN SULIN, ASPAR T, HUMAN 100 UNIM, NOVOLUM, FLEXEN</td>
</tr>
</tbody>
</table>

**Parameters**

- ** Facility:**
  - **Division:**
  - **Team:**
  - **Primary Provider:**
  - **Associate Provider:**

**Cohort/Evaluation Status** (Evaluated) means use of the Hypoglycemia Screening (CGS Test)
- Not Currently in Risk Cohort, Prevalent
- Currently in Risk Cohort, Never Evaluated
- Currently in Risk Cohort, Evaluated Within 1 Year
- Currently in Risk Cohort, Evaluated > 1 Year
National Results (8/2017)

Evaluation: Nearly 30,000 patients have been evaluated using the EMR template.

Occurrence: Hypoglycemia has been reported by 21% of those evaluated.

Action: Of all patients evaluated, 86% have documented shared decision making. Of those reporting hypoglycemia, 53% have made a shared decision with their provider to relax treatment.
Ask about Low Blood Sugars
Ask About Low Blood Sugars to inform patients and their family members and clinicians about asking about the low blood sugars.

Below you will find links to the July Monthly Topic resources from the National Center For Health Promotion and Disease Prevention (NCP). Please use this month’s materials and supporting file links to promote awareness about low blood sugars to Veterans and clinicians.

VA Virtual Medical Center Pilot

• Health Professional Education: Shared Decision Making Decision-Simulation based on 3 clinical scenarios addressing Hypoglycemic Safety

• Synchronous Diabetes Self-Management Education employing flipped classroom pedagogy (planned)

• Synchronous and Asynchronous Health Professional training for Shared Medical (Group) Medical Appointment implementation (planned)
Tom’s Story: Be Aware
Ask About Low Blood Sugar

Tom’s Story: Be Aware
Ask About Low Blood Sugar

Current hypoglycemia medication safety efforts
Andy Karter, PhD

Kaiser Permanente
Development and Validation of a Practical Tool to Identify Patients with Type 2 Diabetes at High Risk of Hypoglycemia-Related Utilization

Andrew Karter, PhD
Kaiser Permanente Northern California
“Diabetes agents were implicated in 1 of 5 ED visits for adverse drug events among older adults” - Shehab et al. JAMA 2017

Hypoglycemia-related utilization is only the tip of the iceberg

- 0.5% annually experience “hypoglycemia-related utilization” (ED visits or hospitalization with primary/principal discharge diagnosis of hypoglycemia)
- 11% annually self-reported “severe hypoglycemia”
- 95% of severe hypoglycemia episodes are not clinically recognized
Motivation

- Misconception that hypoglycemia is not a serious concern for T2D
  - Clinicians suffer from their own form of “hypoglycemic unawareness”
  - Clinician messaging has primarily focused on achieving glycemic control (“lower-is-better” myth)
  - Little attention paid toward hypoglycemia prevention

- Lack population management strategies to address this public health problem
Risk Stratification

The presence of an effective but costly intervention to prevent hypoglycemia makes “targeting” high risk patients for population management particularly compelling.
Risk Stratification

The presence of an effective but costly intervention to prevent hypoglycemia makes “targeting” high risk patients for population management particularly compelling

→ Identify higher risk patients
Risk Stratification

The presence of an effective but costly intervention to prevent hypoglycemia makes “targeting” high risk patients for population management particularly compelling.

→ Identify higher risk patients

→ Intervene
Risk Stratification

The presence of an effective but costly intervention to prevent hypoglycemia makes “targeting” high risk patients for population management particularly compelling.

→ Identify higher risk patients

→ Intervene

→ Prevent
Over-arching goal

Develop a pragmatic, risk-stratification tool to identify type 2 diabetes patients at elevated risk for short-term hypoglycemia-related utilization
Development and Validation of a Tool to Identify Patients With Type 2 Diabetes at High Risk of Hypoglycemia-Related Emergency Department or Hospital Use

Andrew J. Karter, PhD; E. Margaret Warton, MPH; Kasla J. Lipska, MD, MHS; James D. Ralston, MD, MPH; Howard H. Moffet, MPH; Geoffrey G. Jackson, MHA; Elbert S. Huang, MD; Donald R. Miller, ScD
Methods

Internal Sample: 206,435 adult with type 2 diabetes (T2D) from Kaiser Permanente Northern California (KPNC)

Outcome: Hypoglycemia-related utilization (HU): ≥1 ED visits with primary or hospitalization with principal discharge diagnosis of hypoglycemia (2014)

Model-Building: Machine-learning (recursive partitioning) using 156 EMR-based variables (from literature)

External Validation: Tested in 2 fully-independent populations: 1,245,352 VA and 15,108 Group Health
Dominant predictors of hypoglycemia-related utilization (annual rate=0.5%)*

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014.
Classification Tree

Derivation Sample (n=165,148)

- ≥3 prior HU events (14.9%)
  - Insulin (5.1%)
  - No insulin (2.0%)

- 1-2 prior HU events
  - No insulin

- No previous HU events
  - No Insulin
  - Sulfonylurea (0.1%)
  - Insulin

Risk stratification:
- High risk (>5%)
- Intermediate risk (1-5%)
- Low risk (<1%)

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Classification Tree

Derivation Sample (n=165,148)

≥3 prior HU events (14.9%)
- Insulin (5.1%)
- No insulin (2.0%)

1-2 prior HU events
- No insulin

No previous HU events
- No Insulin

≥2 ED visits prior yr (2.1%)
- Sulfonylurea
- >2 ED visits prior yr

<2 ED visits prior yr
- Age ≥77 (1.1%)
- Age <77 (0.7%)

Risk stratification:

- High risk (>5%)
- Intermediate risk (1-5%)
- Low risk (<1%)

87% Low risk
11% Intermediate risk
2% High risk

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Discrimination: tool distinguishes between those with vs. without HU

Area under the receiver operator characteristic (ROC) curve (C-statistic) = 83%
Annual Incidence of Hypoglycemia-related ED visit or hospitalization

Risk Strata

Low: 0.21% 0.21%
Intermediate: 1.40% 1.60%
High: 6.73% 6.49%

Calibration: Good agreement between observed vs expected

Pearson’s Chi-Square Goodness of Fit p-value = 0.68
Clinical utility: 35-fold higher rate of HU in high vs. low risk strata

OR =34.6*

*p<0.0001
Clinical utility: 5-fold higher rate of HU in high vs. intermediate strata

Annual Incidence of Hypoglycemia-related ED visit or hospitalization

OR = 5.1*

*p < 0.0001
Clinical utility: 7-fold higher rate of HU in intermediate vs. low strata

Annual Incidence of Hypoglycemia-related ED visit or hospitalization

Risk Strata

Low
Intermediate
High

OR =6.8*

*p<0.0001
Hypoglycemia Risk Stratification Tool

**Tool Inputs**

- How many times has the patient ever had hypoglycemia-related utilization in an emergency department (primary diagnosis of hypoglycemia*) or hospital (principal diagnosis of hypoglycemia*) (0, 1-2, ≥3 times)?
- How many times has the patient gone to an emergency department for any reason in the prior 12 months (<2, ≥2 times)?
- Does the patient use insulin (yes/no)?
- Does the patient use sulfonylurea (yes/no)?
- Does the patient have severe or end-stage kidney disease (CKD stage 4 or 5) (yes/no)?
- Is the patient <77 years old (yes/no)?

**Instructions:** The 6 inputs above are used to identify one of the mutually-exclusive exposure groups and the corresponding risk category (high, low or intermediate) for hypoglycemia-related emergency department or hospital utilization* in the following 12 months. The first five options are defined by unique combinations of predictor variables, while the sixth option is indicated only after ruling out the first five options.

<table>
<thead>
<tr>
<th>Option</th>
<th>Risk Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥3 prior hypoglycemia-related emergency department or hospital utilization</td>
<td>High risk (&gt;5%)</td>
</tr>
<tr>
<td>1-2 prior hypoglycemia-related emergency department or hospital utilization AND Insulin user</td>
<td></td>
</tr>
<tr>
<td>No prior hypoglycemia-related emergency department or hospital utilization AND No insulin AND No sulfonylurea</td>
<td>Low risk (&lt;1%)</td>
</tr>
<tr>
<td>No prior hypoglycemia-related emergency department or hospital utilization AND No insulin AND Uses sulfonylurea AND Age &lt;77 years old AND Does not have severe or end-stage kidney disease</td>
<td></td>
</tr>
<tr>
<td>No prior hypoglycemia-related emergency department or hospital utilization AND Uses insulin AND Age &lt;77 years old AND &lt;2 ED visits in prior year</td>
<td>Intermediate risk (1-5%)</td>
</tr>
<tr>
<td>All other risk factor combinations</td>
<td></td>
</tr>
</tbody>
</table>
External validation

Annual Incidence of Hypoglycemia-related ED visit or hospitalization (%)

Group Health (n=15,108)
- Low: 0.17%
- Int.: 0.95%
- High: 3.48%

Veterans Admin (n=1,245,352)
- Low: 0.25%
- Int.: 1.07%
- High: 5.42%

*p<0.0001 for odds ratios
**External validation: Good discrimination**

Annual Incidence of Hypoglycemia-related ED visit or hospitalization (%)

**Group Health (n=15,108)**
- Low: 0.17%
- Int.: 0.95%
- High: 3.48%

**Veterans Admin (n=1,245,352)**
- Low: 0.25%
- Int.: 1.07%
- High: 5.42%

C-statistic=0.79

C-statistic=0.81

*p<0.0001 for odds ratios*
External validation: Good clinical utility

Annual Incidence of Hypoglycemia-related ED visit or hospitalization (%)

Group Health (n=15,108)
- Low: 0.17%
- Int.: 0.95%
- High: 3.48%

Veterans Admin (n=1,245,352)
- Low: 0.25%
- Int.: 1.07%
- High: 5.42%

20-fold higher* for Low Group Health vs. High Group Health
22-fold higher for Low Veterans Admin vs. High Veterans Admin

*p<0.0001 for odds ratios
Ecological validity: 54% of patients classified as high risk self-reported experiencing severe hypoglycemia in following 12 months.

Risk stratification of DISTANCE respondents based on EMR data:

- **Low** (OR = 1.0)
- **Intermediate** (OR = 3.6*)
- **High** (OR = 11.1*)

*P<0.0001; Based on logistic regression of any self-reported severe hypoglycemia (last 12 months) among 14,897 survey responders to the Diabetes Study of Northern California (DISTANCE) (2005-6).
Limitations

- Hypoglycemic utilization is only the tip of the iceberg
- All inputs are EMR-based
  - Patient-reported behaviors (e.g., skipping meals) and social factors (e.g., health literacy, food insecurity) are not factored into the model
- Inappropriate for quantifying individual risk
  - Estimating the probability of rare events is unreliable
- Not optimized for T1D patients
- Does not include utilization due to injuries caused by hypoglycemia (if coded as secondary)
  - <2% of hypoglycemia-related ED encounters fall into this category
Strengths

- Developed in a large sample of ethnically-diverse T2D patients with uniform access to care
- Validated in over 1 million T2D patients from two external populations
- Simplicity: needs only 6 input variables
- Meaningful use: leverages EMR data for decision support
- Robust across validation sites, after including T1D, with varying length of medical history, and calendar year
- Risk strata predicts self-reported severe hypoglycemia and mortality
Summary

- ~20-fold greater rates of HU among patients categorized as high vs low risk
- Over half of patients categorized as high risk self-reported having a severe hypoglycemic episode in the subsequent 12 months
Now that we have a tool to identify higher risk patients, what do we do?
Now that we have a tool to identify higher risk patients, what do we do?

The answer depends on **why** the patient is at increased risk.
Hypoglycemia risk factors

- **Medication mismatch** – Overly intensive regimen
- **Clinical vulnerability** – impaired hypoglycemic awareness, glucose counterregulatory failure, renal failure, acute GI illness
- **Behavioral** – Missed meals, alcohol use
- **Psychosocial and cognitive** – depression, dementia
- **Social determinants** – food insecurity
- **Limited health literacy** – not understanding insulin management or recognizing symptoms of hypoglycemia
Potential workflow response

Hypoglycemia Risk Tool → List of high risk patients

Triage

Automated alerts, problem list update, patient messaging

Identify the cause

Medication mismatch/clinical vulnerability
Psychosocial Cognitive
Behavioral
Social determinant
Health Literacy

Make referral

Primary Care Provider
Clinical Pharmacist
Accountable population manager
Endocrinologist
Health Educator
Conclusion

• This risk stratification tool facilitates targeting interventions at high and intermediate risk patients (2% and 11% respectively)

• Given the heterogeneity of causes and risk level, tailoring interventions and resources should be tested as a strategy to lower hypoglycemia rates, improve patient safety and reduce hospital readmissions
Acknowledgements

COAUTHORS:
Margaret Warton, MPH; Jennifer Liu, MPH; Melissa Parker, MS; Howard Moffet, MPH; Kaiser Permanente Northern California, Oakland, CA
James D. Ralston, MD, MPH and Geoffrey G. Jackson, MHA; Kaiser Permanente Washington Health Research Institute, Seattle, WA.
Kasia J. Lipska, MD, MHS; Yale School of Medicine, Department of Internal Medicine, Section of Endocrinology, New Haven, CT
Elbert S. Huang, MD; University of Chicago, Department of Medical, Section of General Internal Medicine, Chicago, IL
Donald R. Miller, ScD; Center for Healthcare Organization and Implementation Research, Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA.

FUNDING:
Food & Drug Administration (FDA-BAA-13-00119)
National Institutes of Health (NIDDK R01 DK103721; P30 DK092924-06)
Reasons EHR-based surveillance underestimates true incidence

- ~95% of all SH events are cared for outside of the medical system and do not result in an ED visit or hospitalization
  - In 2005-6, 11% of KPNC diabetes patients self-report SH vs. only 0.7% utilized ED or were hospitalized for SH\(^1\)
  - *EMS also care for and release ~1% SH episodes (~15% of Alameda Co. 911 calls are not transported to ED)\(^2\)

• Inadequate patient-provider communication about hypoglycemia
  - 16% of T1D and 26% of insulin treated T2D reported not being asked by their provider about hypoglycemia\(^3\)
  - 82% and 69% of T1D and T2D patients did not inform their general practitioner/specialist about their hypoglycemia\(^4\)

\(^1\)Lipska et al. Diabetes Care, 2013;36:3535-42
\(^2\)Moffet et al, in press
\(^3\)Diabet Med 2014: 31, 92-101
\(^4\)Diabet Med 2016;33:1125-1132
Focus on primary/principal Dx

- Secondary diagnoses of hypoglycemia are common:
  - Aggressive insulin management in ED or hospital
  - Acute non-metabolic conditions, e.g., sepsis, acute renal failure, nausea/vomiting/diarrhea, and congestive heart failure

- Ignored in model development because:
  - Our objective was to identify T2D patients at elevated risk of hypoglycemia events which were potentially preventable via outpatient interventions (e.g., de-intensified therapy or self-management)
  - Secondary hypoglycemia is poorly aligned with this objective
**Potential workflow response**

**Hypoglycemia Risk Stratification Tool** ➔ **List of high risk patients** ➔ **Population Management**

- **Individual level**
  - Triage team
  - Identify possible cause(s)
  - Refer to appropriate provider*
  - Intervene

- **System level**
  - Automated updating of alerts, problem lists, patient messaging

*Depending on the situation, could refer to clinical pharmacist, PCP, endocrinologist, accountable population manager, health educator, or social worker.
Soft touch (low cost) system-level interventions

- Automated updates of EMR
  - Clinical alert flags
  - Include “hypoglycemia” in problem list

- Guidelines modification
  - Automated stratification of glucose targets and step-care algorithm

- Patient messaging
  - Secure message, eLetter, or printed health education flyer
Learning About Low Blood Sugar (Hypoglycemia) in Diabetes

Your Kaiser Permanente Care Instructions

Hypoglycemia means that your blood sugar is low and your body (especially your brain) is not getting enough fuel. If you have diabetes, your blood sugar can go too low if you take too much of some diabetes medicines. It can also go too low if you miss a meal. And it can happen if you exercise too hard without eating enough food. Some medicines used to treat other health problems can cause low blood sugar too.

What are the symptoms?

Symptoms of low blood sugar can start quickly. It may take just 10 to 15 minutes. If you have had diabetes for many years, you may not realize that your blood sugar is low until it drops very low.

- If your blood sugar level drops below 70 (mild low blood sugar), you may feel tired, anxious, dizzy, weak, shaky, or sweaty. You may have a fast heartbeat or blurry vision.
- If your blood sugar level continues to drop (usually below 40), your behavior may change. You may feel more irritable. You may find it hard to concentrate or talk. And you may feel unsteady when you stand or walk. You may become too weak or confused to eat something with sugar to raise your blood sugar level.
- If your blood sugar level drops very low (usually below 20), you may pass out (lose consciousness). Or you may have a seizure or stroke. If you have symptoms of severe low blood sugar, you need to get medical care right away.

If you had a low blood sugar level during the night, you may wake up tired or with a headache. Or you may sweat so much during the night that your pajamas or sheets are damp when you wake up.
Intensive (higher cost) interventions

- Monitoring
  - Continuous Glucose Monitors; Flash Glucose Monitors

- Medication management
  - De-intensification Rx: Discontinue, lower dose, or switch
  - Insulin pump with threshold suspend
  - Intervention (raise GLU target) for impaired hypoglycemic awareness

- Health education programs
  - Teach recognition of symptoms (e.g., HypoAware, Youtube video)
  - Diet/lifestyle and self-management (e.g., avoid meal-skipping)
  - Teach “Rule of 15”: take 15 gm of rapid-acting carbs, wait 15 minutes, then retest blood sugar.
Intensive interventions- cont.

- **Rescue**
  - Glucagon kit

- **Screening**
  - Take hypoglycemia history at each visit
  - Screen for impaired hypoglycemic awareness (Clarke score)

- **Hypoglycemia specialty clinic**

- **Care management to address psychosocial risk factors** (e.g., health literacy, food insecurity, depression, impaired cognitive function)

Patients with Diabetes

Prevalence (% of total membership)
Calibration Plots

Figure 3. Calibration Plots Comparing the Expected vs Observed 12-Month Rate of Having Any Hypoglycemia-Related Utilization for the Interval Derivation Sample From Kaiser Permanente Northern California (KPNC) (n = 165,148), the KPNC Internal Validation Sample (n = 41,287), the External Validation Sample From Group Health (GH) (n = 14,972), and the External Validation Sample From the Veterans Administration (VA) (n = 1,335,966).

---

Hypoglycemic-related utilization was defined by having any emergency department visit with a primary diagnosis of hypoglycemia or a hospitalization with a principal diagnosis of hypoglycemia. Hypoglycemia cases were ascertained with any of the following International Classification of Diseases, Ninth Revision, codes: 251.0, 251.1, 251.2, 962.3, or 250.8, without concurrent 259.8, 272.7, 681.2x, 682.2x, 686.9x, 707.3-707.9, 709.3, 730.0-730.2, or 731.8 codes.27
SCIENCE
Hypoglycemia-related utilization (HU) risk classification tree*

Derivation Sample (n=165,148)

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Hypoglycemia-related utilization (HU) risk classification tree*

Derivation Sample (n=165,148)

≥3 prior HU events (14.9%)

1-2 prior HU events

No previous HU events

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Hypoglycemia-related utilization (HU) risk classification tree*

Derivation Sample (n=165,148)

≥3 prior HU events (14.9%)

Insulin (5.1%)

1-2 prior HU events

No insulin (2.0%)

No previous HU events

≥2 ED visits prior yr (2.1%)

<2 ED visits prior yr

Age ≥77 (1.7%)

Age <77 (0.7%)

Stage 4 or 5 CKD (2.8%)

Stage 1-3 CKD (0.3%)

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Hypoglycemia-related utilization (HU) risk classification tree*

Derivation Sample (n=165,148)

≥3 prior HU events (14.9%)
  - Insulin (5.1%)
  - No insulin (2.0%)

1-2 prior HU events
  - No insulin

No previous HU events
  - No Insulin
  - Insulin

No Insulin

≥2 ED visits prior yr (2.1%)
  - Age ≥77 (1.7%)
  - Age <77 (0.7%)

<2 ED visits prior yr
  - Age ≥77 (1.1%)
  - Age <77 (0.3%)

Stage 4 or 5 CKD (2.8%)
  - Insulin
  - No Insulin

Stage 1-3 CKD (0.3%)
  - No Insulin

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Hypoglycemia-related utilization (HU) risk classification tree*

- Derivation Sample (n=165,148)
  - ≥3 prior HU events (14.9%)
    - Insulin (5.1%)
    - No insulin (2.0%)
  - 1-2 prior HU events
  - No previous HU events
    - No Insulin
  - Insulin
    - ≥2 ED visits prior yr (2.1%)
    - <2 ED visits prior yr

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Hypoglycemia-related utilization (HU) risk classification tree*

Derivation Sample
(n=165,148)

≥3 prior HU events (14.9%)
- Insulin (5.1%)
- No insulin (2.0%)

1-2 prior HU events
- No insulin

No previous HU events
- No Insulin

Insulin

≥2 ED visits prior yr (2.1%)
- Age <77 (0.7%)
- Age ≥77 (1.7%)

<2 ED visits prior yr

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Hypoglycemia-related utilization (HU) risk classification tree*

Derivation Sample (n=165,148)

≥3 prior HU events (14.9%)
- Insulin (5.1%)
- No insulin (2.0%)

1-2 prior HU events
- No insulin

No previous HU events
- No Insulin
- Insulin

≥2 ED visits prior yr (2.1%)
- Sulfonylurea

<2 ED visits prior yr
- Age <77 (0.7%)
- Age ≥77 (1.7%)

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Hypoglycemia-related utilization (HU) risk classification tree*

Derivation Sample (n=165,148)

≥3 prior HU events (14.9%)

Insulin (5.1%)

No insulin (2.0%)

1-2 prior HU events

No Insulin

No Sulfonylurea (0.1%)

Sulfonylurea

≥2 ED visits prior yr (2.1%)

<2 ED visits prior yr

No previous HU events

Insulin

Age ≥77 (1.1%)

Age <77 (0.7%)

Stage 4 or 5 CKD (2.8%)

Stage 1-3CKD (0.3%)

≥2 ED visits prior yr (2.1%)

<2 ED visits prior yr

Age ≥77 (1.7%)

Age <77 (0.7%)

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Hypoglycemia-related utilization (HU) risk classification tree*

Derivation Sample (n=165,148)

≥3 prior HU events (14.9%)
- Insulin (5.1%)
- No insulin (2.0%)

1-2 prior HU events
- No insulin
  - No Sulfonylurea (0.1%)
  - Sulfonylurea
    - Age ≥77 (1.1%)
    - Age <77
      - Stage 1-3 CKD (0.3%)
      - Stage 4 or 5 CKD (2.8%)

No previous HU events
- Insulin
  - >2 ED visits prior yr (2.1%)
  - <2 ED visits prior yr
    - Age ≥77 (1.7%)
    - Age <77 (0.7%)

*Based on 156 candidate variables linked to 808 HU events (any primary diagnosis in ED or principal diagnosis in hospital for hypoglycemia) occurring in 165,148 T2D adults from Kaiser Permanente (4.9 events per 1000 person years) in 2014; HU risk for each leaf node (solid boxes) in parentheses.
Calibration Plots

Figure 3. Calibration Plots Comparing the Expected vs Observed 12-Month Rate of Having Any Hypoglycemia-Related Utilization* for the Interval Derivation Sample From Kaiser Permanente Northern California (KPNC) (n = 165,148), the KPNC Internal Validation Sample (n = 41,287), the External Validation Sample From Group Health (GH) (n = 14,972), and the External Validation Sample From the Veterans Administration (VA) (n = 1,335,966)

(A) KPNC derivation
(B) KPNC internal validation
(C) GH external validation
(D) VA external validation

* Hypoglycemic-related utilization was defined by having any emergency department visit with a primary diagnosis of hypoglycemia or a hospitalization with a principal diagnosis of hypoglycemia. Hypoglycemia cases were ascertained with any of the following International Classification of Diseases, Ninth Revision, codes: 251.0, 251.1, 251.2, 962.3, or 250.8, without concurrent 259.8, 272.7, 681.2X, 682.2X, 686.9X, 707.1-707.9, 709.3, 730.0-730.2, or 731.8 codes.27
Robert Flemming, PhD

Centers for Medicare/Medicaid - Transforming Clinical Practice Initiative
Transforming Clinical Practice Initiative (TCPI)

Robert Flemming, PhD
Director, Transforming Clinical Practice Initiative
Centers for Medicare and Medicaid Services

Sep 2017
TCPI – Background & Overview

- Launched in September 2015
- Practice/clinician based
- Leading technical assistance track for the Quality Payment Program (QPP).
- Provides assistance for 100% participation in QPP (MIPs or APMs)
- > 75% of practices to join APMs.
TCPI Supports Quality Payment Program (QPP) in 3 Ways

1. Prepare practices for participation in APMs and Advanced APMs.

2. Provide technical assistance and support to clinicians participating in MIPs.

3. Demonstrate meaningful, impactful, and sustainable transformation of outpatient practices.
Rogers Adoption/Innovation Curve

- Innovators: 2.5%
- Early Adopters: 13.5%
- Early Majority: 34%
- Late Majority: 34%
- Laggards: 16%
The TCPI Aims

1. Support more than 140,000 clinicians in their practice transformation work
2. Improve health outcomes for millions of Medicare, Medicaid and CHIP beneficiaries and other patients
3. Reduce unnecessary hospitalizations for 5 million patients
4. Generate $1 to $4 billion in savings to the federal government and commercial payers
5. Sustain efficient care delivery by reducing unnecessary testing and procedures
6. Transition 75% of practices completing the program to participate in Alternative Payment Models
7. Build the evidence base on practice transformation so that effective solutions can be scaled
## TCPI Change Package: Goals and Drivers

<table>
<thead>
<tr>
<th>Primary Drivers</th>
<th>Secondary Drivers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient and Family-Centered Care Design</strong></td>
<td>1.1 Patient &amp; family engagement</td>
</tr>
<tr>
<td></td>
<td>1.2 Team-based relationships</td>
</tr>
<tr>
<td></td>
<td>1.3 Population management</td>
</tr>
<tr>
<td></td>
<td>1.4 Practice as a community partner</td>
</tr>
<tr>
<td></td>
<td>1.5 Coordinated care delivery</td>
</tr>
<tr>
<td></td>
<td>1.6 Organized, evidence based care</td>
</tr>
<tr>
<td></td>
<td>1.7 Enhanced Access</td>
</tr>
<tr>
<td><strong>Continuous, Data-Driven Quality Improvement</strong></td>
<td>2.1 Engaged and committed leadership</td>
</tr>
<tr>
<td></td>
<td>2.2 Quality improvement strategy supporting a culture of quality and safety</td>
</tr>
<tr>
<td></td>
<td>2.3 Transparent measurement and monitoring</td>
</tr>
<tr>
<td></td>
<td>2.4 Optimal use of HIT</td>
</tr>
<tr>
<td><strong>Sustainable Business Operations</strong></td>
<td>3.1 Strategic use of practice revenue</td>
</tr>
<tr>
<td></td>
<td>3.2 Staff vitality and joy in work</td>
</tr>
<tr>
<td></td>
<td>3.3 Capability to analyze and document value</td>
</tr>
<tr>
<td></td>
<td>3.4 Efficiency of operation</td>
</tr>
</tbody>
</table>
The 5 Phases of TCPI

1. Set Aims
2. Use Data to Drive Care
3. Achieve Progress on Aims
4. Achieve Benchmark Status
5. Thrive as a Business via Value Approaches
Transforming Clinical Practice Initiative:
Practice Transformation Networks (PTNs)

- Arizona Health-e Connection
- Baptist Health System, Inc.
- Children's Hospital of Orange County
- Colorado Department of Health Care Policy & Financing,
- Community Care of North Carolina, Inc.
- Community Health Center Association of Connecticut, Inc.
- Consortium for Southeastern Hypertension Control
- Health Partners Delmarva, LLC
- Iowa Healthcare Collaborative
- Local Initiative Health Authority of Los Angeles County
- Maine Quality Counts
- Mayo Clinic
- National Council for Behavioral Health
- National Rural Accountable Care Consortium
- New Jersey Innovation Institute
- New Jersey Medical & Health Associates dba CarePoint Health
- New York eHealth Collaborative
- New York University School of Medicine
- Pacific Business Group on Health
- PeaceHealth Ketchikan Medical Center
- Rhode Island Quality Institute
- The Trustees of Indiana University
- VHA/UHC Alliance Newco, Inc.
- University of Massachusetts Medical School
- University of Washington
- Vanderbilt University Medical Center
- HQI
- VHS Valley Health Systems, LLC
- Washington State Department of Health
Transforming Clinical Practice Initiative: Support & Alignment Networks (SANs)

- American College of Emergency Physicians (ACEP)
- American College of Physicians, Inc. (ACP)
- American College of Radiology (ACR)
- American Medical Association (AMA)
- American Psychiatric Association (APA)
- HCD International, Inc. (HCDI)
- National Nursing Centers Consortium (NNCC)
- Network for Regional Healthcare Improvement (NRHI)
- Patient Centered Primary Care Foundation (PCPCF)
- The American Board of Family Medicine, Inc. (ABFM)
- Virginia Cardiac Services Quality Initiative (VCSQI)
- American Psychological Association (APA)
## Examples of Ongoing Interventions, Measures, and Aims

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Clinical Intervention</th>
<th>Measure</th>
<th>Aims</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>Optimizing medication management and safety processes</td>
<td>ED Visits Hospitalizations</td>
<td>Improve Outcomes Reduce Admissions Decrease Cost</td>
</tr>
<tr>
<td>Headache</td>
<td>Practice guidelines reviewed with clinicians and patients to reduce testing</td>
<td>CT scans MRIs</td>
<td>Improve Outcomes Unnecessary Tests Decrease Cost</td>
</tr>
<tr>
<td>Depression</td>
<td>Primary care clinician calls psychiatrist in real time for clinical guidance</td>
<td>Depression score</td>
<td>Improve Outcomes Decrease Cost</td>
</tr>
<tr>
<td>Low Back Pain</td>
<td>Choosing Wisely program implemented</td>
<td>X-ray</td>
<td>Improve Outcomes Unnecessary Tests Decrease cost</td>
</tr>
</tbody>
</table>
What Participants Are Saying

• “Working on TCPI has been the most rewarding experience of my entire career.”

• “We are sitting on all this data; we need to figure out how to unleash it to help our patients.”

• “I have been working on behavioral health-primary care integration for over a decade; now we have the ability to finally do it!”
Helpful Links

TCPI: https://innovation.cms.gov/initiatives/Transforming-Clinical-Practices/
Healthcare Communities: http://www.healthcarecommunities.org/
Quality Payment Program: https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/MACRA-MIPS-and-APMs/Quality-Payment-Program.html
Value Modifier: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeedbackProgram/ValueBasedPaymentModifier.html
Healthcare Payment Learning and Action Network (HCP-LAN): https://hcp-lan.org
Implementing the Hypoglycemia Risk Tool: Case Study within the Mayo Clinic Practice Transformation Network (PTN)

Nilay Shah
Division of Health Care Policy and Research
Knowledge and Evaluation Research Unit
Center for the Science of Health Care Delivery
Mayo Clinic
The colors on the map represent locations which operate under the same regional management structure.
Overview – Mayo PTN

MAYO CLINIC in the MIDWEST

Academic Medical Center
Rochester, Minn.
• 500,000 patients/year
• 2,000 physicians
• 125 primary care providers

Community and Regional Health System
75 communities in Minn., Iowa and Wis.
• 4 regions
• 18 hospitals
• 525,000 patients/year
• 1,000+ physicians

Primary care
At full risk for PC

Cerner EMR

Primary care
At risk for PC

MAYO CLINIC in the SOUTHWEST

Arizona
• 90,000 patients/year
• Approx. 400 physicians

Primary care
At full risk for PC

MAYO CLINIC in the SOUTHEAST

Florida
• 90,000 patients/year
• Approx. 400 physicians

Primary care
At full risk for PC

Separate Cerner EMR
TCPI Aims

- Support more than 140,000 clinicians in their practice transformation work
- Improve health outcomes for millions of Medicare, Medicaid and CHIP beneficiaries and other patients
- Reduce unnecessary hospitalizations for 5 million patients
- Generate $1 to $4 billion in savings to the federal government and commercial payers
- Sustain efficient care delivery by reducing unnecessary testing and procedures
- Transition 75% of practices completing the program to participate in Alternative Payment Models
- Build the evidence base on practice transformation so that effective solutions can be scaled
Preventing Adverse Drug Events

• Opioids
• Anticoagulation
• Beers Criteria Related Medications
• Diabetes medications/insulins
  – hypoglycemia
# Increased Mortality of Patients With Diabetes Reporting Severe Hypoglycemia

Rozalina G. McCoy, MD\textsuperscript{1}  
Holly K. Van Houten, BA\textsuperscript{2}  
Jeanette Y. Ziegenfuss, PhD\textsuperscript{2}  
Nilay D. Shah, PhD\textsuperscript{2}  
Robert A. Wermers, MD\textsuperscript{1,3}  
Steven A. Smith, MD\textsuperscript{1,2,3}

Hypoglycemia did have significantly higher rates of death (11,12) as well as micro-, macro-, and nonvascular complications (12). The cause of increased fatal and nonfatal adverse events among pa-

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Alive</th>
<th>Deceased</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients (%)</strong></td>
<td>1,013</td>
<td>873 (86.2)</td>
<td>140 (13.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at baseline (years), mean (SD)</strong></td>
<td>60.5 (15.2)</td>
<td>59.2 (15.0)</td>
<td>68.1 (13.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Men, n (%)</strong></td>
<td>555 (54.8)</td>
<td>462 (52.9)</td>
<td>93 (66.4)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Type 1 diabetes, n (%)</strong></td>
<td>216 (21.3)</td>
<td>195 (22.3)</td>
<td>21 (15.0)</td>
<td>0.049</td>
</tr>
<tr>
<td><strong>Diabetes duration (years), mean (SD)</strong></td>
<td>13.6 (11.4)</td>
<td>13.3 (11.3)</td>
<td>15.6 (11.6)</td>
<td>0.025</td>
</tr>
<tr>
<td><strong>HbA\textsubscript{1c} (%)</strong>, mean (SD)</td>
<td>7.2 (1.4)</td>
<td>7.2 (1.3)</td>
<td>7.2 (1.6)</td>
<td>0.792</td>
</tr>
<tr>
<td><strong>CCI, mean (SD)</strong></td>
<td>1.9 (1.9)</td>
<td>1.6 (1.5)</td>
<td>3.6 (3.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hypoglycemia, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>388 (38.3)</td>
<td>342 (39.2)</td>
<td>46 (32.9)</td>
<td>0.153</td>
</tr>
<tr>
<td>Mild</td>
<td>549 (54.2)</td>
<td>473 (54.2)</td>
<td>76 (54.3)</td>
<td>0.982</td>
</tr>
<tr>
<td>Severe</td>
<td>76 (7.5)</td>
<td>58 (6.6)</td>
<td>18 (12.9)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Mortality data were obtained from the SSDI after 5 years of follow-up. P value compares those alive vs. deceased at time of follow-up. Unless otherwise specified, all values refer to baseline measurements.
Increased Mortality of Patients With Diabetes Reporting Severe Hypoglycemia

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.047</td>
<td>1.027–1.066</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.716</td>
<td>1.135–2.596</td>
<td>0.011</td>
</tr>
<tr>
<td>Type 1 diabetes</td>
<td>0.836</td>
<td>0.410–1.706</td>
<td>0.623</td>
</tr>
<tr>
<td>Diabetes duration</td>
<td>1.006</td>
<td>0.985–1.027</td>
<td>0.595</td>
</tr>
<tr>
<td>HbA\textsubscript{1c}</td>
<td>1.127</td>
<td>0.965–1.316</td>
<td>0.131</td>
</tr>
<tr>
<td>CCI</td>
<td>1.437</td>
<td>1.323–1.561</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>1.564</td>
<td>0.986–2.481</td>
<td>0.468</td>
</tr>
<tr>
<td>Severe</td>
<td>3.381</td>
<td>1.547–7.388</td>
<td>0.005</td>
</tr>
</tbody>
</table>

OR for 5-year mortality was adjusted for age, sex, diabetes type and duration, HbA\textsubscript{1c}, CCI, and hypoglycemia history. Unless otherwise specified, all measures were obtained at baseline.
<table>
<thead>
<tr>
<th></th>
<th>None/Mild (n=337)</th>
<th>Severe (n=81)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Rating, %</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Excellent</td>
<td>4.5</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Very Good/Good</td>
<td>77.2</td>
<td>62.9</td>
<td></td>
</tr>
<tr>
<td>Fair/Poor</td>
<td>18.4</td>
<td>35.8</td>
<td></td>
</tr>
<tr>
<td>EQ-5D scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-care</td>
<td>1.0</td>
<td>1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Usual activities</td>
<td>1.3</td>
<td>1.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Utility index</td>
<td>0.85</td>
<td>0.77</td>
<td>0.002</td>
</tr>
<tr>
<td>HFS score: worry/behavior</td>
<td>17.4</td>
<td>31.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Original Investigation | LESS IS MORE

Intensive Treatment and Severe Hypoglycemia Among Adults With Type 2 Diabetes

Rozalina G. McCoy, MD, MS; Kasia J. Lipska, MD, MHS; Xiaoxi Yao, PhD, MHS; Joseph S. Ross, MD, MHS; Victor M. Montori, MD, MS; Nilay D. Shah, PhD

Figure 2. Risk-Adjusted Probability of Hypoglycemia as a Function of Patient Clinical Complexity and Treatment Intensity

<table>
<thead>
<tr>
<th>Source</th>
<th>Adjusted Probability of Severe Hypoglycemia (95% CI)</th>
<th>Difference of Probabilities (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low complexity with standard treatment</td>
<td>1.02 (0.87 to 1.17)</td>
<td>0.28 (-0.10 to 0.66)</td>
</tr>
</tbody>
</table>
| Low complexity with intensive treatment          | 1.30 (0.98 to 1.62)                                 | vs low complexity with standard treatment  
|                                                  |                                                     | \( P = .15 \)                        |
| High complexity with standard treatment          | 1.74 (1.28 to 2.20)                                 | vs low complexity with standard treatment  
|                                                  |                                                     | \( P < .01 \)                        |
| High complexity with intensive treatment         | 3.04 (1.91 to 4.18)                                 | vs high complexity with standard treatment  
|                                                  |                                                     | \( P = .03 \)                        |

High clinical complexity was defined as a composite measure of age of 75 years or older or high comorbidity burden defined by presence of end-stage renal disease, dementia, or 3 or more chronic conditions (myocardial infarction, congestive heart failure, pulmonary disease, non-end-stage chronic renal disease, or cancer). Intensive treatment was defined as a composite measure of intensive baseline regimen (use of greater number of medications than recommended for a given index hemoglobin \( A_1c \) \( (HbA_1c) \) level) and treatment intensification despite a low index \( HbA_1c \) result. Risk-adjusted probabilities are adjusted for patient sex, race, household income, residency region, index \( HbA_1c \) year, and specialty of treating health care professional. Error bars indicate 95% CIs.
Hypoglycemia Risk Prediction Tool

**Tool Inputs**
- How many times has the patient ever had hypoglycemia-related utilization in an ED (primary diagnosis of hypoglycemia) or hospital (principal diagnosis of hypoglycemia) (0, 1–2, ≥3 times)?
- How many times has the patient gone to an ED for any reason in the prior 12 months (<2, ≥2 times)?
- Does the patient use Insulin (yes/no)?
- Does the patient use sulfonylurea (yes/no)?
- Does the patient have severe or end-stage kidney disease (CKD stage 4 or 5) (yes/no)?
- Is the patient <77 years old (yes/no)?

**Instructions:** The 6 inputs above are used to identify one of the mutually exclusive exposure groups and the corresponding risk category (high, low, or intermediate) for hypoglycemia-related ED or hospital utilization in the following 12 months. The first 5 options are defined by unique combinations of predictor variables, while the sixth option is indicated only after ruling out the first 5 options.

<table>
<thead>
<tr>
<th>Risk Factor Combinations</th>
<th>Risk Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥3 Prior hypoglycemia-related ED or hospital utilization</td>
<td>High risk (&gt;5%)</td>
</tr>
<tr>
<td>1–2 Prior hypoglycemia-related ED or hospital utilization AND Insulin user</td>
<td>Low risk (&lt;1%)</td>
</tr>
<tr>
<td>No prior hypoglycemia-related ED or hospital utilization AND No insulin AND No sulfonylurea use</td>
<td>Low risk (&lt;1%)</td>
</tr>
<tr>
<td>No prior hypoglycemia-related ED or hospital utilization AND No insulin AND Uses sulfonylurea AND Age &lt;77 years AND Does not have severe or end-stage kidney disease</td>
<td>Low risk (&lt;1%)</td>
</tr>
<tr>
<td>No prior hypoglycemia-related ED or hospital utilization AND Uses insulin AND Age &lt;77 years AND &lt;2 ED visits in prior year</td>
<td>Intermediate risk (1%-5%)</td>
</tr>
<tr>
<td>All other risk factor combinations</td>
<td>Intermediate risk (1%-5%)</td>
</tr>
</tbody>
</table>
Implementing the Hypoglycemia Risk Prediction Tool

90 primary care clinics – Mayo Clinic PTN
Patients attributed to clinicians, care teams and clinics
Patients identified with a diagnosis of type 2 diabetes – n= 52,633
Implement risk prediction tool
Considerations for Implementing the Risk Prediction Tool

Right population
Challenges with observation period
Completeness of medication data
Completeness of utilization data
Hypoglycemia Risk across Mayo Clinic PTN

- 1 or 2 prior SH events, Insulin: 1.35%
- >=3 prior SH events: 1.35%
- 1 - 2 prior SH events, No Insulin: 12.2%
- No previous SH events, Insulin, <2 ED visits prior year, Age >= 77: 12.2%
- No previous SH events, Insulin, >=2 ED visits prior year: 12.2%
- No previous SH events, No Insulin, Sulfonylurea, Age < 77, ESRD: 12.2%
- No previous SH events, No Insulin, No Sulfonylurea, Age > 77: 12.2%
- No previous SH events, No Insulin, No Sulfonylurea, Age < 77, No ESRD: 12.2%

Counts:
- 661
- 49
- 100
- 3,375
- 1,290
- 10
- 1,622
- 13,720
- 24,706
- 7,100
### Risk of Hypoglycemia by Age

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Age (mean)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (n=698)</td>
<td>59.2 (17.7)</td>
<td>18-99</td>
</tr>
<tr>
<td>Intermediate (n=6,281)</td>
<td>79.9 (10.7)</td>
<td>18-104</td>
</tr>
<tr>
<td>Low (n=45,637)</td>
<td>63.5 (13.4)</td>
<td>18-87</td>
</tr>
</tbody>
</table>

![Age Group Distribution of High Risk Group](image)
Distribution of Risk by Marital Status

- **High**
  - Married or Life Partner: 41.7%
  - Not Married or Legally Separated: 58.2%

- **Intermediate**
  - Married or Life Partner: 54.9%
  - Not Married or Legally Separated: 44.9%

- **Low**
  - Married or Life Partner: 64.8%
  - Not Married or Legally Separated: 34.8%
## Distribution of Risk Across Clinics

<table>
<thead>
<tr>
<th>Range of Patients per Clinic (n)</th>
<th>60-4,924</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range of Risk</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>0.0-4.2%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>5.4-20.8%</td>
</tr>
</tbody>
</table>
Now what?

Two pilot approaches to intervene:
Shared Decision Making

Low Blood Sugar (Hypoglycemia)

Metformin
- No Severe Risk
- Minor = 0 - 1%

Insulin
- Severe = 1 - 3%
- Minor = 30 - 40%

Glitazones
- No Severe Risk
- Minor = 1 - 2%

Exenatide
- No Severe Risk
- Minor = 0 - 1%

Sulfonylureas
- Severe = Less than 1%
- Minor = 21%

Gliptins
- No Severe Risk
- Minor = 0 - 1%

Mullan RJ et al. Archives of Internal Medicine 2009

http://shareddecisions.mayoclinic.org
Medication Therapy Management Pilot

- Pharmacists part of primary care teams
- Identify patients at high risk
- Proactively contact them and identify self reported experiences and approaches to decrease risk
- Outcomes over time
Real time knowledge delivery at right time, right format, right contest and to right person.
### Generic Disease Management System

#### Summary for diseases and preventive services

<table>
<thead>
<tr>
<th>Patient summary</th>
<th>Labs for past 6 years</th>
<th>Recommended actions</th>
<th>Educational links &amp; forms</th>
<th>Alerts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient summary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refresh data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic #</td>
<td>Clinic Id.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Name</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth date</td>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre. Phys.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has DM1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has DM2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has CAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has Asth. Depr.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has Myeloma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has Gamopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last blood pressure</td>
<td>99/55</td>
<td>Date: 02/10/2011</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last height</td>
<td>cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last weight</td>
<td>kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH2.9 score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last Asthma Action Plan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current tobacco use</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last advance directive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last MAGE screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last echo</td>
<td>Date: 11/09/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last ECG</td>
<td>Date: 07/15/2009</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last nuclear study</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EIA Score</td>
<td>25%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Preventive services</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza vaccine</td>
<td>11/04/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Td vaccine</td>
<td>03/02/2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella vaccine</td>
<td>09/22/2003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal vaccine</td>
<td>12/20/2005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon X-ray</td>
<td>11/02/2003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mammogram</td>
<td>11/09/2005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone density screening</td>
<td>04/17/2003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Labs for past 6 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Normal value: 12.0-15.5</td>
<td>Most recent value: 15.4</td>
<td>Date: 07/15/2009</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>Normal value: 135-145</td>
<td>Most recent value: 141</td>
<td>Date: 07/15/2009</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>Normal value: 3.6-5.2</td>
<td>Most recent value: 3.9</td>
<td>Date: 07/15/2009</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>Normal value: 70-100</td>
<td>Most recent value: 156</td>
<td>Date: 07/15/2009</td>
<td></td>
</tr>
<tr>
<td>HbA1c</td>
<td>Normal value: 4.0-6.0</td>
<td>Most recent value: 8.3</td>
<td>Date: 07/15/2009</td>
<td></td>
</tr>
<tr>
<td>ALT (SGPT)</td>
<td>Normal value: 8-43</td>
<td>Most recent value: 21</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>AST (SGOT)</td>
<td>Normal value: 8-43</td>
<td>Most recent value: 21</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>Normal value: 0.6-1.1</td>
<td>Most recent value: 1.0</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>eGFR</td>
<td>Normal value: 80</td>
<td>Most recent value: 80</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>Normal value: 265</td>
<td>Most recent value: 265</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>Normal value: 285</td>
<td>Most recent value: 275</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>Normal value: 39</td>
<td>Most recent value: 39</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>Normal value: 191</td>
<td>Most recent value: 191</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>hsCRP</td>
<td>Normal value: 0.0</td>
<td>Most recent value: 0.0</td>
<td>Date: 03/02/2010</td>
<td></td>
</tr>
<tr>
<td>Lipoprotein(a)</td>
<td>Normal value: 0.9-1.2</td>
<td>Most recent value: 2.7</td>
<td>Date: 12/30/2010</td>
<td></td>
</tr>
<tr>
<td>INR</td>
<td>Normal value: 0.9-1.2</td>
<td>Most recent value: 2.7</td>
<td>Date: 12/30/2010</td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>Normal value: 0.3-5.0</td>
<td>Most recent value: 1.8</td>
<td>Date: 11/13/2009</td>
<td></td>
</tr>
<tr>
<td>TSH</td>
<td>Normal value: 0.05</td>
<td>Most recent value: 0.05</td>
<td>Date: 09/20/2009</td>
<td></td>
</tr>
</tbody>
</table>

#### Recommended actions

- Colon cancer screening due.
- LDL should be < 100.
- Eye exam due.
- HbA1c should be < 8.
- Creatinine due.
- Microalbumin due.
- Lipid panel due.
- INR due.

#### Rec. actions next 90 days


#### Alerts

- Consider beta blocker therapy.
- Recommend ACE or ARB.
- Consider cardiac device (AICD) consult.
- Diastolic level due.
Hypertension

- BP should be < 140/90.

- Hemoglobin: Normal value 12.0-15.5 g/dL, Most recent value 15.6 g/dL
- Sodium: Normal value 135-145 mmol/L, Most recent value 142 mmol/L
- Potassium: Normal value 3.6-5.2 mmol/L, Most recent value 4.1 mmol/L
- Glucose: Normal value 70-100 mg/dL, Most recent value 261 mg/dL
- HbA1c: Normal value 4.0-6.0 %, Most recent value 9.9 %
- AST (SGOT): Normal value 8-43 U/L, Most recent value 46 U/L

- Blood pressure: 169/90

- Height: 161 cm
- Weight: 94.8 kg
- BMI: 38.6

- Q Score: 1
- Action Fraction: 20%

- Date for tests and assessments:
  - X-ray: 09/07/1999
  - ECG: 11/09/2010
  - Bone density screening: 01/14/2011
  - PSA: 01/16/2011
  - Influenza vaccine: 10/23/2010
  - Pneumococcal vaccine: 11/07/2006
  - Zoster vaccine: 09/21/2006

- Ask Mayo Expert: Hypertension
  - Why focus on hypertension?
  - Why should this approach be implemented?
  - What are the objectives from a work up for a patient with hypertension?
Summary

- Implementation of hypoglycemia risk prediction tool is feasible
- Significant variation in risk across clinics and care teams
- Pilot low-cost approaches may decrease risk, improve health outcomes, and decrease preventable utilization
- Potential benefit from collecting self-reported risk of hypoglycemia
Acknowledgments

Parvez Rahman, MS
Jordan Haag, PharmD
Kari Bunkers, MD
Rob Stroebel, MD
Rozalina McCoy, MD, MS
Open discussion
Reducing the risk of preventable adverse drug events associated with hypoglycemia in older adults

Medha Munshi, M.D.

Associate Professor, Harvard Medical School
Director, Joslin Geriatric Diabetes Program
Beth Israel Deaconess Medical Center
3 major points

• Hypoglycemia – frequently unrecognized – are common in older adults

• A1c levels do not correlate with risk of hypoglycemia in older adults

• De-intensification of insulin regimen can reduce the risk of hypoglycemia without compromising glycemic control
Unrecognized hypoglycemic episodes are frequent in older adults on insulin, age > 70 yrs; A1C > 8%; n=40

Patients with hypoglycemia n = 26 (65 %)

Patients with A1C 8-9 % 14 (54 %)
Patients with A1C > 9 % 12 (46 %)

Severity of hypoglycemic episodes

60-69 mg/dl 100 %
50-59 mg/dl 73 %
< 50 mg/dl 46 %

Munshi et al; Arch Intern Med. 2011;171(4):362-364
### Lack of association between A1c levels and hypoglycemia risk

<table>
<thead>
<tr>
<th>Baseline A1C (multiple insulin injections)</th>
<th>≤ 7% (N=17)</th>
<th>7.1-8 % (N=27)</th>
<th>8.1-9 % (N=14)</th>
<th>&gt;9% (N=7)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypo Duration (mins/5 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70 mg/dL</td>
<td>292 ± 306</td>
<td>292 ± 244</td>
<td>280 ± 260</td>
<td>246 ± 222</td>
<td>0.9</td>
</tr>
<tr>
<td>&lt;60 mg/dL</td>
<td>146 ± 225</td>
<td>157 ± 183</td>
<td>160 ± 174</td>
<td>162 ± 168</td>
<td>0.9</td>
</tr>
<tr>
<td>&lt; 50 mg/dL</td>
<td>76 ± 184</td>
<td>91 ± 139</td>
<td>74 ± 115</td>
<td>56 ± 70</td>
<td>0.7</td>
</tr>
<tr>
<td>Nocturnal Hypo (10 pm-6 am)</td>
<td>119 ± 207</td>
<td>132 ± 205</td>
<td>147 ±144</td>
<td>175 ± 201</td>
<td>0.6</td>
</tr>
<tr>
<td>8-month A1C (once/day bBasal insulin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 7% (N=12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypo duration (mins/5 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70 mg/dL</td>
<td>34 ± 63</td>
<td>167 ± 216</td>
<td>46 ± 99</td>
<td>104 ± 75</td>
<td>0.09</td>
</tr>
<tr>
<td>&lt;60 mg/dL</td>
<td>21 ± 43</td>
<td>87 ± 131</td>
<td>27 ± 72</td>
<td>86 ± 61</td>
<td>0.1</td>
</tr>
<tr>
<td>&lt; 50 mg/dL</td>
<td>14 ± 31</td>
<td>43 ± 65</td>
<td>10 ± 35</td>
<td>48 ± 47</td>
<td>0.1</td>
</tr>
<tr>
<td>Nocturnal Hypo (10 pm-6 am)</td>
<td>13 ± 34</td>
<td>95 ± 127</td>
<td>26 ± 67</td>
<td>41 ± 83</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Munshi MN et al; Journal of dia and its compli, june 2017
Simplification of Regimen


Primary outcome: Duration of hypoglycemia by CGM
Secondary outcome: A1C

- Age >70 yrs
- ≥ 1 insulin injection/day
- High stimulated c-peptide
- ≥ 1 episode of glucose <70

Active Intervention (5 months)

Independent Period (3 months)

Simplification of Regimen to Once a day Glargine ± Non-insulin agents

No Active Contact
Deintensification of insulin regimen improve hypoglycemia without worsening glycemic control

Next steps

• Identify better outcome measure without sole dependence on A1C

• Larger studies and more education regarding “reversed” algorithm to de-intensify complex regimen in vulnerable population
Break for lunch

12 PM-1 PM
Research readiness for implementation and dissemination
William Lee, D.Ph, MPA, FASCP

Carilion New River Valley Medical Center
Carilion Medical Center
Roanoke, Virginia
Reducing the Risk of Hypoglycemic events in the Older Population through Patient Engagement and Feedback

William T. Lee  D.Ph, MPA, FASCP
Senior Director, Pharmacy System
wtlee@carilionclinic.org
540-267-6416
Hypoglycemia in Older Patients

- Challenge for provider
- Challenge for patient
- Too many medications or not enough
- Too tight of Control with Insulin
- A1c Metrics - is that enough
- Are we treating numbers or the Patient
The Diabetic Patient

- Hypoglycemic agents increases risk
- Inaccurate Medication reconciliation
- Comorbidities - hypertension- masking of symptoms with beta blockers.
The Elderly Patient

- Changes in ADME - drug absorption, drug distribution, drug metabolism and drug elimination
- Changes in Cognitive Function and Physical Function can significantly impact medication outcomes
- Changes in Nutritional Status- malnutrition, access to balanced meals, and increased risk of GI problems in this population can impact diabetic care.
- Need for regular and increased monitoring in this population
Life style and More medications

- Appropriate timing and composition of meals.
- Drug - Drug interactions:
  - Diuretics, Steroids, Phenytoin, beta blockers, antipsychotics.
IHARP

Improving the health of patients at risk in the rural community
IHARP: Connecting the Dots

- Focus: At Risk Patients in Rural Areas

- Diabetes: One of top three Diseases with Medication Errors Reported

- Major Challenges:
  - Recognition of Signs and Symptoms
  - Optimize medication therapy to prevent therapeutic duplication and/or effect therapeutic de-escalation
  - Development of Individualized Medication Reminders
  - Engage caregivers and Family members
  - Increase patient monitoring/awareness of signs and symptoms of hypo-/hyperglycemia
  - Ensure patient has an emergency plan to treat hypo-/hyperglycemia.
  - Development of tool to track and monitor patient.
Patient Engagement and Feedback

- Opportunities: New Transitional care model
  - Connect with the clinician in the clinic and pharmacist in the community

- Management plan when the patient cannot eat
  - (test, surgery, GI illness)

- Medication titration - challenges
  - Dose changes, medication addition and removal
  - Medication timing
Pharmacists

- Pharmacists are essential to the care team in getting the medications right.

- Pharmacists have the ability to recognize scenarios in which elderly patients are vulnerable to ADE (adverse drug events) and can take action to correct potential problems.

- Counseling is key: Utilizing the teach back method with patients and caregivers to review: Drug Names, Dosages, Route of Administration, Timing, Duration, Storage and Handling, what to expect, common side effects, adherence, what to do if you miss a dose or meal, contact information in the event additional information is needed.
## Clinical Efficacy of Pharmacy

<table>
<thead>
<tr>
<th>Article</th>
<th>Service</th>
<th>Clinical Outcomes</th>
</tr>
</thead>
</table>
| Spence et al.      | Outpatient clinical pharmacy service on adherence and clinical outcomes in DM and CAD | 1. Higher adherence rates for DM  
2. Lower mean and greater reduction in HbA1c  
3. Lower mean LDL-C |
| Polgreen et al.    | Collaboration Among Pharmacists and Physicians to Improve BP Now (CAPTION) | 1. Average systolic BP was 6.1 mmHg lower and diastolic was 2.9 mmHg lower in intervention group  
2. Hypertension control was 43% in intervention vs. 34% in control |
| Bunting et al.     | Community-based MTM program for patients with asthma                    | 1. ER visits decreased 9.9% to 1.3%  
2. Hospitalization decreased 4% to 1.9%  
3. 55% patients had improvement in severity classification |
| Cranor et al.      | Community-based MTM program for patients with diabetes                   | 1. >50% patients showed A1c improvements at each visit  
2. > 50% patients showed improvement in lipid levels |
| Bunting et al.     | Community-based MTM program for patients with hypertension and/or dyslipidemia | 1. Significant improvements in systolic and diastolic BP  
2. Significant improvements in % patients meet BP goal  
3. Change in annual lipid measure significantly lower  
4. Statistically decreased risk of CV event |
# Clinical Efficacy of Pharmacy

## Project ImPACT

<table>
<thead>
<tr>
<th>Article</th>
<th>Service</th>
<th>Clinical Outcomes</th>
</tr>
</thead>
</table>
| **ImPACT: Depression** | Patients with depressive symptoms met with a pharmacist for 2 or more visits over 1 year | 1. Significant improvements in PHQ-9 (80% of patients had improvements)  
2. 68% of patients had ≥ 50% reduction in PHQ-9  
3. Clinical improvements and outcomes superior for patients with severe depression at baseline |
| **ImPACT: Osteoporosis** | Patients with 1 or more known risk factors for osteoporosis met with a pharmacist for disease prevention and management if necessary | 1. Patients given risk for future fracture (78% of patients had no prior knowledge of risk)  
2. 70% of patients screened were at moderate or high risk  
3. 29% of patients scheduled physician visit after screening (19% initiated on medications) |
| **ImPACT: Hyperlipidemia** | Patients with newly diagnosed dyslipidemia and poorly controlled dyslipidemia followed with pharmacist | 1. 93.6% of patients achieved medication persistence  
2. 90.1% of patients achieved medication compliance  
3. 62.5% of patients achieved lipid goal |
| **ImPACT: Diabetes** | 25 communities in 17 states disproportionally affected by diabetes Patients seen by interdisciplinary care teams including pharmacists | At 1 year:  
1. Significant decrease in A1c (-0.8%)  
2. 51.7% received eye examinations  
3. 72% received foot examinations  
4. 41.7% received influenza vaccine  
5. 92% of the communities intend to sustain pharmacy services |
IHARP and Beyond

- Face to Face interactions preferred
  - Building of patient rapport
  - Support effective patient education
  - Use of glucose meter, disease state, insulin administration

- Long standing relationship as well as Longitudinal relationship
Technology and Apps

- Remote access
- Medical devices- Remote monitoring.
  - Blood pressure and blood glucose machines
- Apps on Tablets, iPhone, Android phones
- Tools for the Healthcare Team
- Screening tools for potentially inappropriate prescribing
- Open Source Platform-sharing of Data
Precision Medicine: Role of Pharmacogenomics

- CRADLE to GRAVE
- Drug-Drug Interaction
- Drug-Gene Interaction
- Drug-drug-gene-interaction
- “Fine tuning” medication regimen
References


THANK YOU
David Aron, MD

Department of Veterans Affairs
Clinic
REDUCING THE RISK OF PREVENTABLE ADVERSE DRUG EVENTS ASSOCIATED WITH HYPOGLYCEMIA IN THE OLDER POPULATION

RESEARCH READINESS CHALLENGES FOR IMPLEMENTATION AND DISSEMINATION

David C. Aron, MD, MS
Louis Stokes Cleveland VAMC
School of Medicine and Weatherhead School of Management,
Case Western Reserve University

David.aron@va.gov
Research Challenges for Implementation and Dissemination

- Complexity of the problem
  - Multiple targets (each with their own interests/issues)
    - Clinicians, both prescribers and non-prescribers
    - Patients and care givers
    - Organizations – healthcare systems, payors, pharma, interest groups
  - Interactions among targets
- Context-dependence and the limitations of research itself
• Goal: pin your partner as many times as possible in 15 seconds. I will tell you when to start.
Model of Unlearning

Patients and care givers

Agree to

Doctors act upon

Patients aware of

Adhere to

Outcomes

- Data Collection Issues

- Education Issues (health literacy and numeracy)
- Competition from other messages (DTC)
- Patients’ competing priorities

Shared Decision Making
Organizations – healthcare systems, payors, pharma, interest groups

<table>
<thead>
<tr>
<th>Levels</th>
<th>A1C Levels</th>
<th>Glucose Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severely Elevated</td>
<td>13</td>
<td>380</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>345</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>310</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>275</td>
</tr>
<tr>
<td>Elevated and Poorly</td>
<td>9</td>
<td>240</td>
</tr>
<tr>
<td>Controlled levels</td>
<td>8</td>
<td>205</td>
</tr>
<tr>
<td></td>
<td>*7</td>
<td>170</td>
</tr>
<tr>
<td>Normal Levels</td>
<td>*6</td>
<td>135</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>65</td>
</tr>
</tbody>
</table>

An A1C Diabetes test above 5.9 is considered Pre-Diabetic.

Under 7 is considered normal or "GOOD" if you already have Diabetes.

Stay under 5.9 to play safe to avoid Prediabetes and under 7 if you already have a Diabetic.

If you are in Elevated or Severely Elevated Levels above, or getting close to 5.9 Prediabetics level, it is extremely important that you Lose weight, Exercise, and see a Doctor and Nutritionist!

National Diabetes Call to Action and Blueprint for Change

Situation Analysis

Of the 11 million Americans with diabetes, more than half are not achieving their target blood sugar levels, defined as hemoglobin (Hb) A1C of <7 percent. As a result, these individuals remain at a higher risk for serious complications, such as blindness, kidney disease, heart disease, stroke, and amputation. Although insulin therapy is one of the most effective methods for achieving target A1C levels, treatment is often delayed or dosed inadequately for fear of hypoglycemia (low blood sugar) and weight gain. Yet, research shows that a new generation of insulin treatments can significantly reduce these problems.

Aventis wanted to create an initiative to address the growing epidemic of uncontrolled diabetes. Through a host of educational efforts, the company sought to encourage people to know their A1C level, to be aware of the target for good control, and to work with their healthcare provider to learn about the available treatment options (including insulin) that could help them achieve and maintain an A1C<7%.

Strategy & Implementation

In response, Burson-Marsteller (B-M) designed and implemented a national
Complexity – Interactions among Targets

“Remember that what the rest of us call health care costs, they call income.”
Paul Krugman, NYTimes 5/10/09

The health care "quality problem" is widely recognized, generally accepted and (reasonably) well-understood.

The problem is also the focus of considerable effort.

Yet effective "evidence-based" solutions (and success) remain elusive; a common answer to why we have failed:

- We lack sufficient evidence and knowledge regarding effective quality improvement (practice change) strategies (intervention/problem matching, effect modifiers, etc.)

Adapted from B. Mittman
An alternative answer:

- We have the knowledge, but lack the will and/or ability to act on that knowledge
- We fail to act on the evidence and advice we receive (and produce)
  - we repeatedly initiate new efforts without attending to barriers, or including elements, previously found to be important
  - we discount evidence and advice that fail to have universal, total effectiveness
- We continue to seek--and believe in—(non-existent) simple solutions ("the answer")

Adapted from B. Mittman
Traditional Improvement of Healthcare

Professional (scientific) knowledge

Patient with Need ➔ Knowledge ➔ Operationalize Knowledge ➔ Patient Need Met Well

Adapted from Paul Batalden MD
QI – the linear Ramp of Complexity
The reality of the (non)linear ramp of complexity.

Legend:
P=Plan      D= Do                            = Barrier                                                          = Direct flow of impact
S=Study    A=Act                             = Lingering background impact         Arrowhead = Feedback or feedforward
Different Sizes of letters and cycles and bolding of letters = denotes differences in importance/impact

Tomolo, Lawrence, and Aron, QSHC.
Integrated Conceptual Framework based on Greenhalgh et al. Model of Innovation dissemination/diffusion (rounded boxes); Theory of Healthcare Professionals’ Behavior and Intention (square boxes) is nested and impacts Adoption/Assimilation

- Finding 1: Practice change disturbs the status quo equilibrium. Establishing a new equilibrium that incorporates the change may be a struggle.

- Finding 2: Part of the struggle to establish a new equilibrium incorporating a practice change involves both the "evidence" itself and tensions between evidence and context.

Change in Overtreatment Rate (A1c<7%) vs Change in Undertreatment Rate (A1c>9%)

R = -0.653  p<0.001
Equifinality

*Explanatory factors rarely operate alone
*Multiple configurations of different explanatory conditions can explain the same outcome – therefore QCA (Qualitative Comparative Analysis)

Kurt Richardson.
http://jasss.soc.surrey.ac.uk/5/2/6.html
Aron’s Heuristics of Implementation and Sustainability

**Implementation** = f(\text{Intervention} \times \text{CONTEXT})
- Intervention = Evidence plus Method and Cost of Implementation
  (although this bears resemblance to the PARIHS model, I place the emphasis on the interaction.)

**Sustainability** = f(\text{CinOteNroTenEtiXonT})
- Sustainability = the degree to which the intervention becomes part of the context - just the way we do business)

Greenhalgh et al.'s conceptual framework for the spread of innovations in service organizations.

"Let it happen"  "Help it happen"  "Make it happen"

**Defining Features**

- Unpredictable, unprogrammed, uncertain, emergent, adaptive, self-organizing
- Negotiated, influenced, enabled
- Scientific, orderly, planned, regulated, programmed, systems “properly managed”

**Assumed Mechanism**

- Natural, emergent
- Social
- Technical
- Managerial

**Metaphor for Spread**

- Emergence, adaptation
- Knowledge construction, making sense
- Diffusion, Negotiation, Knowledge transfer
- Dissemination, Recascading, Engineering

It is one thing to say with the prophet Amos, “Let justice roll down like mighty waters,” and quite another to work out the irrigation system.

~ Rev. William Sloane Coffin

But *let justice* well up as waters, and righteousness as a mighty stream. Amos 5:24, JPS
Sustaining success –
Moving research into practice;
private & public
Partnerships
Preventing Hypoglycemia: A Public Health Priority

Clydette Powell, MD, MPH, FAAP
Director, Division of Health Care Quality
Office of Disease Prevention and Health Promotion
Office of the Assistant Secretary for Health
Clydette.Powell@hhs.gov
• The increasing burden of serious hypoglycemic events has been recognized as an important public health issue

• Diabetic agents including insulin and secretagogues are common causes of hypoglycemic events across inpatient and outpatient health care settings

• Among adults diagnosed with either type 1 or type 2 diabetes, 18% take insulin only, 13% take both insulin and oral medication, 50% take oral medication only, and 18% do not take either insulin or oral medication
• The National Action Plan for Adverse Drug Event Prevention defines severe hypoglycemia as:
  o Requiring third party assistance (e.g., from a family member and/or medical personnel?)
  o Leading to an emergency department visit or hospital admissions
  o Blood glucose lower than 40 mg/dl

• While the National Action Plan for Adverse Drug Event Prevention focuses on adverse events from diabetic agents, it recognizes that not all diabetes agents are associated with severe hypoglycemia (e.g., metformin monotherapy)
Persons with diagnosed diabetes whose A1c value is greater than 9% (age adjusted, percent, 18+ years) By Total


Data Source: National Health and Nutrition Examination Survey (NHANES); Centers for Disease Control and Prevention, National Center for Health Statistics (CDC/NCHS)
Error Bar (I) represents the 95% confidence interval
Additional footnotes may apply to these data. Please refer to footnotes below the data table for further information.
• HP2020 Baseline: In 2005–08, 18.0% of adults aged 18 years and over with diagnosed diabetes had poor glycemic control (age adjusted).

• HP2020 Target: 16.2%, a 10% improvement over the baseline.

• Most Recent: In 2011–14, 20.5% of adults aged 18 years and over with diagnosed diabetes had poor glycemic control (age adjusted).
Among racial and ethnic groups in 2011–14, the white non-Hispanic population had the lowest (best) rate of poor glycemic control, 14.6% of adults aged 18 years and over with diagnosed diabetes (age adjusted). The rate for the Hispanic population (30.2%, age adjusted) was more than twice the rate of the white non-Hispanic population.

Rates (age adjusted) for other race/ethnicity groups were:
- 25.5% among the black non-Hispanic population
- 17.3% among the Asian non-Hispanic population (not significantly different than the best group rate)
Disparities

- Persons with diagnosed diabetes aged 65 years and over had the lowest rate of poor glycemic control among age groups, 9.2% in 2011–14. Rates for the other age groups were:
  - 17.8% among persons aged 45–64 years
  - 26.4% among persons aged 18–44 years; more than 2.5 times the best group rate
Hypoglycemic Adverse Drug Events

• Diabetes agents are implicated in **13% of ED visits** for adverse drug events
  - **90%** of cases are associated with **hypoglycemia**
  - **39%** of cases result in **hospitalization**
• Real-world incidence of hypoglycemia is likely much higher
  - Insulin users experience **23** mild/moderate episodes and **1** severe episode per person-year

---

Older and more complex patients are at greatest risk of hypoglycemia
  - Diabetes agents are implicated in >18% of cases
  - More than half of older adults may be over treated

Despite availability of newer agents, hypoglycemia remains a significant problem

Anticoagulants

primary ADE of concern: bleeding

Diabetes agents

primary ADE of concern: hypoglycemia

Opioids

primary ADE of concern: accidental overdoses/oversedation/respiratory depression

☑️ Common
☑️ Clinically significant
☑️ Preventable
☑️ Measurable
ADE Action Plan: Approach

- Surveillance
  - Health IT
- Evidence-Based Prevention Tools
  - Health IT
- Incentives & Oversight
  - Health IT
- Research/Unanswered Questions
  - Health IT
Federal Interagency Workgroup: Diabetes Work

Surveillance
- FDA’s FAERS tracks self reported ADEs

Prevention Tools
- ODPHP’s Individualizing Glycemic Targets Training

Incentives & Oversights
- CMS’ Transforming Clinical Practice Initiative (TCPI) is working with Practice Transformation Networks all over the US to make hypoglycemia a number 1 medication safety issue

Research
- FDA’s Safe Use program funds research in preventing adverse drug events : Kaiser Risk Stratification Tool
ADE Action Plan: Partners
Development of National Targets and Measures

AUG 2014
Release of the ADE Action Plan

OCT 2014

SEP 2014
Release of the diabetes eLearning

MAR 2015
Steering Committee Meeting #7

Drug Class-Specific Workgroups Develop Targets and Measures

AUG 2016
Steering Committee Meeting #8
Drug Class Lead(s) Present Proposed Targets and Measures

2016-2017
Finalize Targets and Measures
## National Targets and Measures

<table>
<thead>
<tr>
<th>Setting</th>
<th>Measure</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Data Source</th>
<th>Baseline Year</th>
<th>Target Reduction</th>
<th>Departmental Measure Alignment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inpatient</strong></td>
<td>Rates of adverse events from hypoglycemic agents among U.S. inpatient stays</td>
<td>Number of U.S. hospital discharges with adverse events from hypoglycemic agents</td>
<td>Number of U.S. hospital discharges in which hypoglycemic agents were administered</td>
<td>MPSMS, QSRS</td>
<td>2014</td>
<td>10%</td>
<td>Partnership for Patients</td>
</tr>
<tr>
<td><strong>Outpatient</strong></td>
<td>Rate of visits to U.S. hospital EDs for adverse events from insulin</td>
<td>Number of visits to U.S. hospital EDs for adverse events from insulin</td>
<td>Number of patients receiving dispensed insulin in U.S. retail outpatient settings</td>
<td>NEISS-CADES, IMS TPT</td>
<td>2014</td>
<td>10%</td>
<td>Healthy People 2020 Medical Product Safety Objective 5.2³</td>
</tr>
</tbody>
</table>
Inpatient

• **Goals:** Reduce ADEs from diabetes agents among inpatient stays

• **Data sources:** MPSMS and QSRS
  • Both use reviews of medical records from U.S. hospitals
  • As of 2016, QSRS is replacing MPSMS
Outpatient

• **Goals:** Reduce ED visits due to ADEs from diabetes agents

• **Data sources:** NEISS-CADES (numerator) and IMS Total Patient Tracker (denominator)
  - NEISS-CADES use reviews of medical records
  - IMS TPT uses data from U.S. retail pharmacies
  - IMS data agreement secured through FDA in Dec 2016
• Raising awareness about hypoglycemia is imperative.
  o Education for patients, families, and clinicians about risk factors, symptoms, and treatment
• Clinicians need tools to recognize risk factors and suggest appropriate treatment options.
  o Diabetes care is more than just reducing hyperglycemia
    ▪ Risk stratification tools
  o Risks and benefits of treatment options must be balanced
    ▪ Shared decision making
Shared Decision Making (SDM)
  - Engaging patients in collaborative goal setting and problem solving
  - Setting individualized glycemic goals can help prevent hypoglycemia

SDM is endorsed by federal and non-federal organizations.
  - VA/DoD Clinical Practice Guidelines
  - IHS Standards of Care
  - ADA Standards of Care
ADEs: Diabetes Agents

Preventing Adverse Drug Events: Individualizing Glycemic Targets Using Health Literacy Strategies is an eLearning course that teaches health care providers how to reduce hypoglycemic adverse drug events (ADEs) in patients with diabetes.

https://health.gov/hcq/training-prevent-ADE.asp
Since September 2014, 441 individuals have received CME, CNE, CEU, or CPE for taking Individualizing Glycemic Targets

<table>
<thead>
<tr>
<th>Credit Type</th>
<th>Registered</th>
<th>Completed</th>
<th>% Completed</th>
<th>Passed</th>
<th>% Passed</th>
</tr>
</thead>
<tbody>
<tr>
<td>CME (physicians)</td>
<td>23</td>
<td>18</td>
<td>78.26%</td>
<td>18</td>
<td>100%</td>
</tr>
<tr>
<td>CME (non-physicians)</td>
<td>49</td>
<td>42</td>
<td>85.71%</td>
<td>42</td>
<td>100%</td>
</tr>
<tr>
<td>CNE</td>
<td>327</td>
<td>282</td>
<td>86.24%</td>
<td>281</td>
<td>99.65%</td>
</tr>
<tr>
<td>CEU</td>
<td>53</td>
<td>44</td>
<td>83.02%</td>
<td>43</td>
<td>97.73%</td>
</tr>
<tr>
<td>CPE</td>
<td>65</td>
<td>57</td>
<td>87.69%</td>
<td>57</td>
<td>100%</td>
</tr>
<tr>
<td>Audit</td>
<td>16</td>
<td>13</td>
<td>81.25%</td>
<td>13</td>
<td>100%</td>
</tr>
<tr>
<td>Totals</td>
<td>533</td>
<td>456</td>
<td>85.55%</td>
<td>454</td>
<td>99.56%</td>
</tr>
</tbody>
</table>

Preventing Hypoglycemic ADEs
Questions?

Thank you

Clydette Powell, MD, MPH, FAAP
Director, Division of Health Care Quality
Office of Disease Prevention and Health Promotion
Office of the Assistant Secretary for Health
Clydette.Powell@hhs.gov
Matthew Pickering, PharmD

Pharmacy Quality Alliance
Measuring What Matters: Turning Data into Action

September 12, 2017

Matthew K. Pickering, PharmD, RPh
Associate Director, Research & Quality Strategies
Pharmacy Quality Alliance
If you cannot measure it…
  you cannot monitor it.

If you cannot monitor it…
  you cannot manage it.

If you cannot manage it…
  you cannot improve it.

Dr. H. James Harrington
About the Pharmacy Quality Alliance (PQA)

Mission Statement:
Optimizing patient health by improving the quality of medication use.
## PQA Measures within Medicare Part D Star Ratings

<table>
<thead>
<tr>
<th>Measure ID</th>
<th>Measure</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>D11</td>
<td>High Risk Medication</td>
<td>3</td>
</tr>
<tr>
<td>D12</td>
<td>Medication Adherence for Diabetes Medications</td>
<td>3</td>
</tr>
<tr>
<td>D13</td>
<td>Medication Adherence for Hypertension (RAS antagonists)</td>
<td>3</td>
</tr>
<tr>
<td>D14</td>
<td>Medication Adherence for Cholesterol (Statins)</td>
<td>3</td>
</tr>
<tr>
<td>D15</td>
<td>MTM Program Completion Rate for CMR</td>
<td>1</td>
</tr>
</tbody>
</table>

Due to heavy weighting by CMS on intermediate outcome measures, PQA measures make up almost half of a plan’s Star rating.
## CMS Quality Programs: A 10,000ft View

<table>
<thead>
<tr>
<th>Hospital Quality</th>
<th>Physician Quality</th>
<th>PAC Quality</th>
<th>Payment Models</th>
<th>Population Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meaningful use EHR incentive</td>
<td>Merit-based Incentive Payment System (MIPS)</td>
<td>Inpatient rehabilitation facility quality reporting</td>
<td>Medicare Shared Savings Program (ACOs)</td>
<td>Medicare Part C</td>
</tr>
<tr>
<td>Inpatient quality reporting</td>
<td>Maintenance of certification</td>
<td>Nursing Home Compare measures</td>
<td>Hospital value-based purchasing</td>
<td>Medicare Part D</td>
</tr>
<tr>
<td>Outpatient quality reporting</td>
<td></td>
<td>LTCH quality reporting</td>
<td>Physician Feedback</td>
<td>Medicaid Adult Core Measures</td>
</tr>
<tr>
<td>Ambulatory surgical centers</td>
<td></td>
<td>Hospice quality reporting</td>
<td>ESRD QIP</td>
<td>Medicaid Child Core Measures</td>
</tr>
<tr>
<td>Readmission reduction program</td>
<td></td>
<td>Home health quality reporting</td>
<td>Innovations Pilots</td>
<td>Health Insurance Exchange Quality Reporting System (QRS)</td>
</tr>
<tr>
<td>HAC payment reduction program</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPS-exempt cancer hospitals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient psychiatric facilities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Quality Improvement: A Continuous, Evidence-based Process

Adapted from: Richardson, S, McBride, T, Herr, A, Mitchell, K. Avalere Health, LLC. "New Approaches to Performance Measurement Post Health Reform." Poster session presented at: AcademyHealth Annual Research Meeting; 2011 June 12-14; Seattle, WA.

P4R: Pay-for-reporting
P4P: Pay-for-performance
VBP: Value-based purchasing
PQA’s Measure Development Process

I. Measure Concept

II. Development

III. Member Comment

IV. Measure Testing

V. Endorsement

VI. Evaluation

Deep Thought

1. How do we know what to measure?

2. How do we know what is measured is patient-centered?

3. How do we know that which is patient-centered [in measurement], truly matters to patients?
Deep Thought

1. How do we know what to measure?

2. How do we know what is measured is patient-centered?

3. How do we know that which is patient-centered \textit{in measurement}, truly matters to patients?
Deep Thought

1. How do we know what to measure?

2. How do we know what is measured is patient-centered?

3. How do we know that which is patient-centered [in measurement], truly matters to patients?
Choosing What to Measure

The Triple Aim and priority areas set the agenda for measure development, endorsement and implementation.

Priorities

- Health and Well-Being
- Prevention and Treatment of Leading Causes of Mortality
- Person- and Family-centered Care
- Effective Communication and Care Coordination
- Patient Safety
- Affordable Care

Healthy People
Healthy Communities

Better Care

Affordable Care

Quality Improvement: A Continuous, Evidence-based Process

Diabetes Guidelines

- Hemoglobin A1c (HbA1c) goals
- 10-year cardiovascular risk
Deep Thought

Diabetes Outcome Measures Beyond A1c

1. How do we know what to measure?

2. *How do we know what is measured is patient-centered?*

3. How do we know that which is patient-centered [*in measurement*], truly matters to patients?
The three initial targets of the Adverse Drug Event (ADE) Action Plan are:

- Anticoagulants (primary ADE of concern: bleeding)
- Diabetes agents (primary ADE of concern: hypoglycemia)
- Opioids (primary ADE of concern: accidental overdoses/oversedation/respiratory depression)
Responding to the ADE National Action Plan

Development of a Suite of ADE Measures:
1. Bleeding Events
2. Hypoglycemic Events
3. Opioid Overdose Events
PQA ADE Hypoglycemic Measure

Title: Hypoglycemic Events Requiring Hospital Admission or Emergency Department (ED) Visit Associated with Anti-hyperglycemic Medications

Description: The rate of events among adults receiving anti-hyperglycemic medications that have evidence of a hospitalization or ED visit related to a hypoglycemic event.

Level of Accountability: Health plan

Status: Working with stakeholders for valid ICD-10 codes, at which point, we will test the measure for reliability and validity
Lamppost Measures

This is where you lost your wallet?

No, I lost it in the park, but this is where the light is.
Deep Thought

1. How do we know what to measure?

2. How do we know what is measured is patient-centered?

3. How do we know that which is patient-centered [in measurement], truly matters to patients?
Patient-Reported Outcome Measures

**PRO** → **PROM** → **PRO-PM**

<table>
<thead>
<tr>
<th>PRO</th>
<th>PROM</th>
<th>PRO-PM</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>patient-reported outcomes</em></td>
<td><em>instrument, tool, single-item measure</em></td>
<td><em>PRO-based performance measure</em></td>
</tr>
<tr>
<td>Information on the patient, told by the patient, without interpretation</td>
<td>Means to collect information told by the patient without interpretation</td>
<td>Means to aggregate information shared by the patient and collected into a reliable, valid measure of performance</td>
</tr>
</tbody>
</table>

**Research is needed to determine what matters to patients, and how to prioritize identified gaps in care.**

**EXAMPLE:** Patient with clinical depression

**Symptom:** depression

**Patient Health Questionnaire (PHQ-9©), a standardized tool to assess depression**

**Percentage of patients with diagnosis of major depression or dysthymia and initial PHQ-9 score >9 with a follow-up PHQ-9 score <5 at 6 months (NQF #0711)**
PQA’s Measure Development Process

I. Measure Concept

II. Development

III. Member Comment

IV. Measure Testing

V. Endorsement

VI. Evaluation

Patient & Caregiver Advisory Panel

The Pharmacy Quality Alliance. PQA’s Measure Development Process. Accessed February 2017 at:
FDA Safe Use – Hypoglycemia

- Increasing awareness of hypoglycemia through targeted messaging
- Increasing awareness of the need for measures that matter to patients
- Collaborating with stakeholders to educate and promote proper care coordination
Summary

- Quality measures continue to shape healthcare delivery

- Measures should not only be evidence-based, but they should *matter* to patients

- Improving patient care is a multi-stakeholder effort
Measuring What Matters: Turning Data into Action

September 12, 2017

Matthew K. Pickering, PharmD, RPh
Associate Director, Research & Quality Strategies
Pharmacy Quality Alliance
e: mpickering@pqaalliance.org
Deb Pasko, PharmD

American Society of Health -System Pharmacists
Reducing the Risk of Preventable Adverse Drug Events associated with Hypoglycemia in the Older Population: ASHP Perspective

Deborah A Pasko, Pharm.D., MHA
September 12th, 2017
FDA Symposium
Topic Outline

• **ASHP and Quality**
  – Quality Measures
  – Glycemic Control Measures

• **Current state of medication usage and antidiabetic medications**

• **Polypharmacy**

• **Hospitals and the risk for hypoglycemia**
  – Why is it so complex?

• **Deprescribing**

• **Best practices**

• **Next steps**
ASHP Commitment to Quality

**Commitment in Strategic Plan**

- Our Patients and Their Care
  - Goal 1: Optimize medication outcomes in all settings of care
A suite of inpatient and outpatient clinical measures for pharmacy accountability: Recommendations from the Pharmacy Accountability Measures Work Group

Mary A. Andrawis and Jannet Carmichael

Am J Health-Syst Pharm. 2014; 71:1669-78
ASHP Quality Goals

- Identify pharmacy-sensitive measures
- Support member education
- Pharmacy school curriculum changes
- Nominate members to measure development
- Respond to proposed measures
- Revise existing measures
- Evaluate pharmacist value in quality improvement
- Provide feedback on deployed measures
- Member resources
- Highlight process improvements
- Demonstrate
- Shape
- Support Member Implementation
- Raise Awareness

Identify pharmacy-sensitive measures
Support member education
Pharmacy school curriculum changes
Nominate members to measure development
Respond to proposed measures
Revise existing measures
Evaluate pharmacist value in quality improvement
Provide feedback on deployed measures
Member resources
Highlight process improvements
Pharmacy-Sensitive Accountability Measures

• **Goals**
  – Increase pharmacist awareness of measures that they can be accountable for in a team-based manner;
  – Promote the use of measures in pharmacy department dashboards; and
  – Identify gaps in measurement

• **Process**
  – Identify medication-related measures that address preventable harm in the inpatient and outpatient setting
    • Measure databases: NQF, PQA, AHRQ, HHS
Pharmacy-Sensitive Accountability Measures

• **Results**
  – 4 high-risk clinical topic areas
    • Glycemic control
    • Anticoagulant safety
    • Pain management
    • Antimicrobial stewardship

• **Findings related to glycemic control**
  – Measures focused on screening, adherence, co-morbid condition, disease state management; however, no measure of harm
    • A few measure incidence of hyper/hypoglycemia
  – MIPS quality measures
    • 8 focused on diabetes but no measurement of risk or preventable harm
<table>
<thead>
<tr>
<th>Measure Title</th>
<th>Measure Type</th>
<th>Federal Reporting Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Kidney Disease, Diabetes Mellitus, Hypertension and Medication Possession Ratio for ACEI/ARB Therapy</td>
<td>Process</td>
<td></td>
</tr>
<tr>
<td>PDC with RAS antagonists, DM, Statins</td>
<td>Process</td>
<td>Y</td>
</tr>
<tr>
<td>DM: Treatment of hypertension</td>
<td>Process</td>
<td></td>
</tr>
<tr>
<td>Adult(s) taking insulin with evidence of self-monitoring blood glucose testing</td>
<td>Process</td>
<td></td>
</tr>
<tr>
<td>Diabetes and Elevated HbA1C – Use of Diabetes Medications</td>
<td>Process</td>
<td></td>
</tr>
<tr>
<td>Glycemic Control - Hyperglycemia</td>
<td>Outcome</td>
<td></td>
</tr>
<tr>
<td>Glycemic Control - Hypoglycemia</td>
<td>Outcome</td>
<td></td>
</tr>
<tr>
<td>Adherence to Oral Diabetes Agents for Individuals with Diabetes Mellitus</td>
<td>Process</td>
<td></td>
</tr>
</tbody>
</table>
Usage of Diabetic Agents 25-50% Increases

Original Investigation

Trends in Prescription Drug Use Among Adults in the United States From 1999-2012

Elizabeth D. Kantor, PhD, MPH; Colin D. Rehm, PhD, MPH; Jennifer S. Haas, MD, MSc; Andrew T. Chan, MD, MPH; Edward L. Giovannucci, MD, ScD

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidiabetic agents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biguanides</td>
<td>2.0 (1.5-2.6)</td>
<td>2.5 (2.0-3.1)</td>
<td>3.6 (3.0-4.3)</td>
<td>3.6 (2.9-4.5)</td>
<td>4.7 (3.9-5.7)</td>
<td>4.9 (4.3-5.7)</td>
<td>5.5 (4.7-6.4)</td>
<td>&lt;.001</td>
<td>3.6 (2.3 to 5.0)</td>
<td>1.8 (1.4 to 2.2)</td>
</tr>
<tr>
<td>Insulin</td>
<td>1.1 (0.8-1.6)</td>
<td>1.3 (0.9-1.8)</td>
<td>1.5 (1.2-1.9)</td>
<td>1.6 (1.4-1.9)</td>
<td>2.1 (1.6-2.7)</td>
<td>2.1 (1.6-2.7)</td>
<td>2.6 (2.2-3.1)</td>
<td>&lt;.001</td>
<td>1.5 (0.9 to 2.1)</td>
<td>2.3 (1.6 to 3.3)</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>2.6 (2.1-3.2)</td>
<td>2.7 (2.3-3.1)</td>
<td>2.3 (2.6-4.1)</td>
<td>2.9 (2.3-3.6)</td>
<td>3.3 (2.8-3.8)</td>
<td>3.0 (2.6-3.5)</td>
<td>3.2 (2.5-4.2)</td>
<td>&lt;.001</td>
<td>0.6 (-0.4 to 1.5)</td>
<td>1.2 (0.88 to 1.7)</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>0.5 (0.3-0.8)</td>
<td>0.9 (0.7-1.2)</td>
<td>2.0 (1.7-2.4)</td>
<td>2.0 (1.5-1.6)</td>
<td>1.9 (1.4-2.4)</td>
<td>1.2 (1.0-1.6)</td>
<td>0.8 (0.6-1.1)</td>
<td>.17</td>
<td>0.3 (-0.1 to 0.7)</td>
<td>1.6 (0.86 to 2.9)</td>
</tr>
</tbody>
</table>

JAMA. 2015;314(17):1818-1831
The opioid epidemic has become a national crisis. The number of overdose deaths involving opioids has quadrupled since 1999. Indeed, the United States, with 5% of the global population, consumes 80% of the global opioid supply. This epidemic has rightly entered the national consciousness as America's major drug problem. The nation also has another persistent drug problem, however—polypharmacy.

As the number of medications an individual uses increases, the risks of drug-drug interactions, adverse drug events, and nonadherence also increase. Polypharmacy is especially prevalent among older adults, who are more likely to be living with multiple chronic conditions. Prescribing cascade (i.e., use of a newly prescribed drug to counter adverse effects of another prescribed drug) and poor-quality prescribing among the elderly are common. More than 35.8% of older U.S. adults are prescribed 5 or more medications, and 15% of those patients are taking medications in combinations that pose a risk of major drug-drug interactions. A recent study found that 4 emergency department visits per 1,000 individuals occur secondary to adverse drug reactions annually in the United States, with 27.3% of visits resulting in hospitalization; patients 65 or older accounted for approximately 34.6% of these visits and the highest hospitalization rate (43.6%). One half of patients are not adherent to prescribed medications; only 35.6% of pharmacists reported participation in discharge planning, a serious gap that is corroborated by other studies. Results of another recent survey indicated that pharmacists complete medication histories in only one third of hospital stays; results of a study conducted in the Veterans Affair system revealed that 45% of patients had at least 1 unnecessary medication at discharge. These gaps are serious and threaten our nation’s health.

Recently, ASHP submitted 5 recommendations to the Choosing Wisely campaign, an initiative of the American Board of Internal Medicine Foundation, working in partnership with the testing and rating organization Consumer Reports and more than 80 national specialty societies. These recommendations focus attention on the need to reduce unnecessary treatment, prevent adverse events, and enhance patient safety, as follows:

- Do not initiate medications to treat symptoms, adverse events, or adverse effects without determining the cause.
- Do not prescribe medications for patients taking 5 or more medications, or continue medications indefinitely without a comprehensive review, including nonprescription medications and dietary supplements.
- Do not continue medications based solely on past use unless a reason for use is verified.
- Do not prescribe medications at discharge that the patient was taking prior to admission without verifying the need.
- Use only metric units when prescribing liquid forms.
Polypharmacy: Geriatrics

- Currently defined as 5 medications or more
- Geriatric patients
  - Inappropriate prescribing and polypharmacy in older persons are associated with increased risks of falls, adverse drug events, hospital admissions, and death\(^1,2\)

Medication Induced Hypoglycemia

- **Obviously glycemic control agents:**
  - Insulin, oral agents, etc.
- **Non-diabetic hypoglycemia**
  - Reactive hypoglycemia
  - Fasting hypoglycemia
    - Aspirin, sulfa agents, pentamidine, quinine, beta-blockers, quinolones, ACE-I’s, dietary supplements
    - Alcohol
    - Tumors
    - Hormone imbalances
- **Systematic review, 2009 found 164 medications**

Glycemic Agents and Medication Use Cycle: Opportunity for Errors

- **Medication use cycle**
  - Inventory
  - FDA approvals: [https://www.fda.gov/forpatients/illness/diabetes/ucm408682.htm](https://www.fda.gov/forpatients/illness/diabetes/ucm408682.htm)
    - All insulins and orals up to 2002
    - 2013-2016 (15 total, 5 insulin)
    - 2000-2012 (22 total, 5 insulin)
    - Before 1999 (10 all insulin)
  - Types of products
    - Injection, oral, inhalation
    - Vials (3 mL & 10 mL)
      - Standard 100 units/mL
      - Concentrated
        » U-500 still in vial
  - So complicated for P & T

<table>
<thead>
<tr>
<th>Name/Concentration</th>
<th>Insulin/Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humulin Regular U-500</td>
<td>Regular \ Bolus / Basal</td>
</tr>
<tr>
<td>500 units insulin/mL</td>
<td></td>
</tr>
<tr>
<td>KwikPen or Vial</td>
<td></td>
</tr>
<tr>
<td>Humalog KwikPen U-200</td>
<td>Lispro (Humalog) \ Bolus</td>
</tr>
<tr>
<td>200 units insulin/mL</td>
<td></td>
</tr>
<tr>
<td>Toujeo Solostar U-300 Pen</td>
<td>Glargine (Lantus) \ Basal</td>
</tr>
<tr>
<td>300 units insulin/mL</td>
<td></td>
</tr>
<tr>
<td>Tresiba FlexTouch U-200 Pen</td>
<td>Degludec (Tresiba) \ Ultra basal</td>
</tr>
<tr>
<td>200 units insulin/mL</td>
<td></td>
</tr>
</tbody>
</table>

Complexities within Hospitals and Health Systems

- **Inventory (both in large stock areas and satellites)**
  - Selection, storage (where in the fridge, labeling), vials, pens
  - Floorstock vs. patient specific

- **Ordering**
  - Order-sets, number of products to choose from
  - DKA, Non-ketotic hyperglycemia, Type I, Type II
    - Weight-based vs. non-weight base
  - Automatic nurse driven protocols for hypoglycemic events
  - Diet protocols – what happens when NPO, feeding tube comes out or clogged
  - Surgical procedures (before, during, after OR)
  - Pumps!!

- **Dispensing**
  - Again, storage
  - Infusions (large risk potential here)
    - More than one concentration? New standard 1 unit/mL
  - Patient specific and insulin syringes vs. 1 mL standard syringe
  - Vials – need to have expiration labeling – TJC!!

- **Administering**
  - Nurse administered vs. patient or parent/caregiver
  - Second checks – yes or no?
  - Anything special for concentrated
  - BCMA
Medication Errors Associated with Transition from Insulin Pens to Vials

• 450 bed community hospitals transitioning from pens to vials

• 3 major insulin administration errors
  – Nurse administered whole vial (10 mL) instead of 1 mL (thought the whole vial was 100 units instead of 1000 units)
  – Patient was ordered 1 unit and nurse gave 100 units instead (thought the vial was the same as the infusion of 1 unit/mL)
  – Nurse confused the furosemide dose 20 mg (2 mL) and gave 2 mL of insulin (200 units) instead of the 1 unit ordered

• RCA and interventions:
  – Education to nurses
  – Revising appearance in EHR and MAR
  – Emphasized use of insulin syringes instead of standard IV syringes
  – Performing daily safety rounds
  – Implementation of daily huddles and information/”show and tell” at during the huddle

Polypharmacy: When to Deprescribe

• More than 90% of patients are willing to stop a medication if their doctor says it is possible”

• Canada: Caden
  – www.deprescribing.org
  – Antihyperglycemic agent discontinuation and video

American Board of Internal Medicine (ABIM)

Started in 2012 with goal of decreasing wasteful diagnostics and reducing harm

Currently over 101 medication related topics on the list

ABIM asked ASHP to get involved

International efforts:
- Australia, Brazil, Canada, Italy, Japan, UK, Wales

ASHP has contributed 5 topics that are medication focused

http://www.choosingwisely.org/
https://choosingwiselycanada.org/campaign/international/
The Time Is Now

BEST PRACTICES AND WHERE WE NEED TO GO
Multifaceted Approach to Reducing Occurrence of Severe Hypoglycemia in a Large Healthcare System

- **Paul E. Milligan et al, St. Louis-based BJC Healthcare**
- **Pharmacist led task force**
  - Automated event detection and dashboards amongst 11 hospitals
  - Implementation of best practices in the network
  - “Hypoglycemic Event Analysis Tool” (HEAT)
  - Assembly of targeted interventions on intranet site: “Hypoglycemia Facility Tracking” (H-FaST)
- **System-wide rate 6.45/1000 patient days in 2009 to 1.32/1000 patient days in 2014**
- **Overall reduction of in hypoglycemia of 80% and severe hypoglycemia of 70-100%**
Interventions Over Time and Impact

Baseline 6-Month Average
153 events/month

Recent 6-Month Average
31 events/month

2011 Q3
HEAT implemented; collection of data on causative factors initiated

2010 Q3
Hypoglycemia Task Force and dashboards created

2010 Q1
Identified severe hypoglycemia as #1 drug-related harm event

2011 Q2
Best practices implemented

2012 Q1
High-risk sulfonylurea alert implemented

2012 Q2
H-FaST implemented

2013 Q2
High-risk admission alert pilot tested

2013 Q1 & Q2
Hypoglycemia risk alert implemented

2014
All interventions continue to be active
We Know Pharmacists Make a Difference, but Now What?

• Need to connect the hospital, clinic, outpatient pharmacy and home environments

• Heightened awareness around hypoglycemia and stratify high-risk patients
  – ED and other hospital pharmacists critical to close the loop for the community
  – Better communication and transitions of care
  – How can technology be used
  – Continuous monitoring and electronic warnings to MD/pharmacist

• Pharmacists can do comprehensive care
  – We aren’t just about medications
  – Referrals to others: diabetic educators, dietician, social work, etc.
  – Exercise, diet, foot care, eye care

• Need pharmacists as providers
The Ambulatory Diabetic Care Team

- Patient
- Pharmacist
- Care Manager
- Social Worker
- Behavioral Health
- Registered Nurse
- Physician/Specialist
- Mid-Level Practitioner
- Diabetes Educator & Dietician
- Care Manager
- Pharmacist

Diagram showing the relationships and interactions between the different roles in the ambulatory diabetic care team.
Summary

- **WE WANT TO HELP!**
- Pharmacists have proven ourselves but why are we still having to fight the good fight?
- It takes a team, everyone can play a role
- Pharmacists aren’t just about medications and can help identify problems such as hypoglycemia
Questions?

• Deborah Pasko: dpasko@ashp.org
• Anna Dopp: adopp@ashp.org
Impacting the Incidence of Hypoglycemia

Robert W. Lash, MD
Chair, Hypoglycemia Quality Improvement Project Steering Committee
Professor of Internal Medicine, University of Michigan
The Substantial Burden of Hypoglycemia

$600M
Estimated spending on ED visits for therapy-associated hypoglycemia between 2007 and 2011

Hypoglycemia is the largest single barrier to achieving glycemic control in Type 1 and Type 2 diabetes

The prevalence and impact of hypoglycemia is substantially underappreciated in both Type 1 and Type 2, and improved surveillance is urgently needed, especially approaches that leverage electronic health records (EHR)

Multi-Year Effort to Impact Incidence of Hypoglycemia

- **ACA Implementation: Impact on Patients with Diabetes** Summit - 2014
- Hypoglycemia Roundtable - 2015
- Hypoglycemia Quality Collaborative (HQC) – 2016
- Hypoglycemia Quality Improvement Project (HQuIP) - 2017
History of Recent Hypoglycemia Focused Initiatives

- JDRF launches multi-stakeholder T1D Outcomes Program to better define clinically meaningful T1D outcomes beyond hemoglobin A1c (HbA1c). Gaining consensus on the definition for hypoglycemia is one of the topics.

- Endocrine Society hosts a multi-stakeholder roundtable discussion re: challenges in preventing and managing hypoglycemia among people with diabetes, and potential solutions.

- Endocrine Society launches the Hypoglycemia Quality Collaborative (HQC) project.

- After the formation of the HQC, Endocrine Society creates the HQC Blueprint.

- T1D Outcomes Program publishes Draft Consensus Statement with a public comment period.

- Endocrine Society begins work on the Hypoglycemia Quality Improvement Project (HQuIP).

- T1D Outcomes Program will publish Final Consensus Statement.


**Endocrine Society Prioritizes Hypoglycemia Prevention**

**Challenge:** Endocrine Society was interested in learning how to increase national awareness of hypoglycemia and facilitate joint action by stakeholders to reduce its incidence.

<table>
<thead>
<tr>
<th><strong>Establish the Hypoglycemia Quality Collaborative (HQC)</strong></th>
<th><strong>Develop the HQC Strategic Blueprint</strong></th>
<th><strong>Develop Tactical Plans to Support Hypoglycemia Strategic Activities</strong></th>
<th><strong>Partner with Federal Agencies to Raise Awareness</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A coalition of diabetes stakeholders including medical specialty societies, payers, industry, patient advocates, diabetes educators, and research organizations</td>
<td>An actionable document and evergreen resource for stakeholders to identify strategic activities and contextualize how the activity contributes to reducing the incidence of hypoglycemia</td>
<td>A high-level overview of specific tasks, rationale, and timing of tasks to advance Endocrine Society’s visibility as a leader in diabetes quality with the ultimate goal of improving patient outcomes and reimbursement for its members</td>
<td>A collaborative of Federal agencies, including FDA, CMS, VA, HHS, Endocrine Society, and quality improvement organizations the common goal of raising awareness, improving surveillance, and improving quality of care</td>
</tr>
</tbody>
</table>
Hypoglycemia Quality Collaborative

The Endocrine Society established the **Hypoglycemia Quality Collaborative (HQC)** in January 2016 to increase national awareness of hypoglycemia and facilitate joint action by stakeholders to reduce its incidence.

### Organizations Participating in the Hypoglycemia Quality Collaborative

- Abbott Diabetes Care Inc.
- Aetna
- American Association of Clinical Endocrinologists
- American Association of Diabetes Educators
- American College of Physicians
- American Diabetes Association
- Astrazeneca
- Close Concerns
- Dexcom
- Johnson & Johnson
- Joslin Diabetes Center
- Juvenile Diabetes Research Foundation
- Lilly
- Medtronic Diabetes
- Merck & Co
- Novo Nordisk
- Pharmacy Quality Alliance
- T1D Exchange
The HQC released a **Strategic Blueprint in November 2016** to articulate its recommendations for action and serve as a key source of information to stakeholders seeking to reduce the incidence of hypoglycemia.

**Blueprint Domain Recommendations**
1. Define and Describe Hypoglycemia to Support Standards of Care
2. Advance Hypoglycemia Evidence to Reduce Gaps in Care
3. Measure and Improve Quality of Care
4. Advocate for Increased Focus on Hypoglycemia
5. Deliver Hypoglycemia Prevention and Management Education
6. Recognize Hypoglycemia as a Public Health Issue

**Goals to Advance Hypoglycemia Quality**
1. Improve Hypoglycemia Surveillance and Risk Assessment
2. Improve Management of Patients on Insulins and Sulfonylureas
3. Improve Reimbursement for Endocrinologists

HQC Strategic Blueprint: [www.endocrine.org/hypoglycemia](http://www.endocrine.org/hypoglycemia)
Key Strategies to Define and Describe Hypoglycemia

Domain: Define and Describe Hypoglycemia to Support Standards of Care

- Define Clinical Features
- Release Consensus Statements
- Disseminate Publications
- Establish Data Standards
- Evaluate Claims Coding
- Facilitate Electronic Capture
- Develop Validated Survey Tools
- Establish Consensus Body
- Conduct Evidence Review
- Update Publications

Key Strategies

- Create the Definition
- Implement the Definition
- Maintain the Definition
Endocrine Society Prioritizes Hypoglycemia Prevention

**Challenge:** Endocrine Society was interested in learning how to increase national awareness of hypoglycemia and facilitate joint action by stakeholders to reduce its incidence.

<table>
<thead>
<tr>
<th>Establish the Hypoglycemia Quality Collaborative (HQC)</th>
<th>Develop the HQC Strategic Blueprint</th>
<th>Develop Tactical Plans to Support Hypoglycemia Strategic Activities</th>
<th>Partner with Federal Agencies to Raise Awareness</th>
</tr>
</thead>
<tbody>
<tr>
<td>A coalition of diabetes stakeholders including medical specialty societies, payers, industry, patient advocates, diabetes educators, and research organizations</td>
<td>An actionable document and evergreen resource for stakeholders to identify strategic activities and contextualize how the activity contributes to reducing the incidence of hypoglycemia</td>
<td>A high-level overview of specific tasks, rationale, and timing of tasks to advance Endocrine Society’s goal of improving patient outcomes and reimbursement for providers who meet standards of care</td>
<td>A collaborative of Federal agencies, including FDA, CMS, VA, HHS, Endocrine Society, and quality improvement organizations the common goal of raising awareness, improving surveillance, and improving quality of care</td>
</tr>
</tbody>
</table>
Hypoglycemia Quality Improvement Project Goals

Improve outcomes of patients with T2D by:

- **Decreasing** the frequency and severity of episodes of hypoglycemia
- **Identifying** patients at high risk for hypoglycemia in a timely manner
- **Supporting** appropriate clinical interventions for patients in outpatient settings
## Hypoglycemia Quality Improvement Project Objectives

<table>
<thead>
<tr>
<th>1. Improve Hypoglycemia Surveillance and Risk Assessment</th>
<th>2. Improve Management of Patients on Insulin and Sulfonylureas</th>
<th>3. Align Provider Reimbursement to Promote Prevention and Management of Hypoglycemia</th>
<th>4. Enhance the Current Understanding of the Overall Assessment and Treatment of Hypoglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>The program seeks to understand the rate of hypoglycemia and reduce the economic burden of the condition by implementing strategies that lead to better prevention and surveillance</td>
<td>Create and pilot a toolkit, which will support providers in assessing and managing patients at-risk for hypoglycemia. This toolkit can be used to meet quality measure requirements in private and public payer value-based programs</td>
<td>Develop reliable measures that can be adopted into existing and future incentive programs to increase the use of support tools for the prevention and management of hypoglycemia</td>
<td>Provide evidence that can be used to understand the epidemiology of hypoglycemia, the pattern in which it occurs, and evidence-based strategies that can be implemented for prevention</td>
</tr>
</tbody>
</table>
HQuIP Yearly Milestones 2017 Onwards

- Conduct Environmental Scan
- Develop Study Protocol and Toolkit
- Publish Scan Findings
- Finalize Study Protocol and Toolkit
- Submit Abstracts for Presentations
- Establish Technical Expert Panel and Patient Panel
- Design Study Protocol
- Begin Measure Development
- Recruit Pilot Sites
- Test Toolkit
- Train Pilot Sites
- Launch Pilot
- Test Measures
- Complete Measure Testing
- Analyze Pilot Data
- Publish Pilot Results
- Submit Toolkit for CPIA Consideration Under MIPS
- Potential Inclusion of Measures in CMS MUC List

Note: Additional ongoing milestones will include: 1) continuous engagement with stakeholders such as CMS and FDA to ensure alignment of activities to support overall goal to decrease incidence and/or severity of hypoglycemia through measure adoption and quality improvement, and 2) presentations at key annual meetings.
Environmental Scan Will Support Development of the HQuIP

**THE OBJECTIVES OF THE ENVIRONMENTAL SCAN ARE TO IDENTIFY:**

| Risk assessment tools that can be considered while designing the HQuIP protocol | Current and planned outpatient-based quality improvement initiatives focused on hypoglycemia | Quality measure concepts focused on improving hypoglycemia in outpatient settings that are currently being explored by stakeholders |
# Three-Pronged Approach to Environmental Scan

RESULTS OF THE SCAN WILL BE USED TO INFORM RECOMMENDATIONS FOR DESIGNING THE HQUIP PROTOCOL

<table>
<thead>
<tr>
<th>Survey HQC Members</th>
<th>Literature Search</th>
<th>Stakeholder Interviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Create a 10 to 15-question online survey to be sent to HQC members. The intent of this survey is to gather preliminary information on currently existing diabetes-related initiatives.</td>
<td>• Conduct a white and grey literature search that will identify risk assessment tools, existing payment and delivery programs that incentivize providers to participate in a program such as HQuIP, quality measure concepts focused on improving hypoglycemia, and current and planned outpatient-based quality improvement initiatives focused on hypoglycemia.</td>
<td>• Conduct 8 to 10 one-hour interviews with key experts identified through the literature search.</td>
</tr>
</tbody>
</table>

HQC: Hypoglycemia Quality Collaborative
A Wide Variety of Sources Are Being Evaluated as Part of the HQuIP Environmental Scan*

800+ Articles in the white literature were identified

60+ Sources in the grey literature were analyzed

30+ Quality measures and measure concepts related to hypoglycemia identified

We used structured search strings in PubMed

Sources reviewed include:
• Health Plans Programs
• Professional Societies’ Reports and Programs
• Government Agency Reports

Sources reviewed include:
• National Action Plan
• Government agency programs
• Professional Societies
• Qualified Clinical Data Registries

These figures are based on most recent research findings as of September 1, 2017
Review of Clinical Guidance Documents in Diabetes Care

- ADA 2017: ADA Standards of Medical Care in Diabetes
- AACE/ACE 2015: Clinical Practice Guidelines for Developing a Diabetes Mellitus Comprehensive Care Plan
- ADA/EASD 2016: Glucose Concentrations of Less Than 3.0 mmol/L (54 mg/dL) Should Be Reported in Clinical Trials: A Joint Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes
- ADA/ES 2013: Hypoglycemia and Diabetes: A Report of a Workgroup of the American Diabetes Association and The Endocrine Society
- Joslin 2013: Joslin Diabetes Center and Joslin Clinic Guideline for Specialty Consultation/Referral
- VA/DoD 2017: VA/DoD Clinical Practice Guideline for the Management of Type 2 Diabetes Mellitus in Primary Care
Endocrine Society Prioritizes Hypoglycemia Prevention

**Challenge:** Endocrine Society was interested in learning how to increase national awareness of hypoglycemia and facilitate joint action by stakeholders to reduce its incidence.

<table>
<thead>
<tr>
<th>Establish the Hypoglycemia Quality Collaborative (HQC)</th>
<th>Develop the HQC Strategic Blueprint</th>
<th>Develop Tactical Plans to Support Hypoglycemia Strategic Activities</th>
<th>Partner with Federal Agencies to Raise Awareness</th>
</tr>
</thead>
<tbody>
<tr>
<td>A coalition of diabetes stakeholders including medical specialty societies, payers, industry, patient advocates, diabetes educators, and research organizations</td>
<td>An actionable document and evergreen resource for stakeholders to identify strategic activities and contextualize how the activity contributes to reducing the incidence of hypoglycemia</td>
<td>A high-level overview of specific tasks, rationale, and timing of tasks to advance Endocrine Society's visibility as a leader in diabetes quality with the ultimate goal of improving patient outcomes and reimbursement for its members</td>
<td>A collaborative of Federal agencies, including FDA, CMS, VA, HHS, provider organizations, and quality improvement organizations with the common goal of raising awareness, increasing surveillance, and improving quality of care</td>
</tr>
</tbody>
</table>
Opportunities Beyond HQuIP

Engagement with Federal Agencies, Provider Organizations, and Quality Improvement Organizations

Endocrine Society is a member of a multi-stakeholder group involved in FDA’s Safe Use Initiative focused on decreasing hypoglycemic adverse drug events in patients with diabetes.

Conversations have centered around the implementation of hypoglycemia risk assessment tools in the outpatient setting, raising awareness among target audiences, and developing quality measures.

Identifying common messages and target audiences is the first priority. Opportunities to employ these messages are being pursued for Diabetes Awareness Month.
Opportunities Beyond HQuIP

Application for CMS Measure Development Grant

CMS recently announced it will award up to $30 million in grant funding for measure development to entities engaged in developing quality measures for use in the Quality Payment Program.

To support the goals of the HQuIP, the Endocrine Society is currently developing measure concepts related to Type 2 Diabetes and hypoglycemia in preparation to submit a grant application.
Thank you!

www.endocrine.org/hypoglycemia
Public comments/ Discussion
Reducing the Risk of Preventable Harm Associated with Hypoglycemia in the Older Population

Paul B. Madden, M.Ed.
Managing Director Diabetes
American Diabetes Association
Living a Bold Life with Type 1 Diabetes for 55+ Years

Significant Contributions to this Presentation:
Pearl Lee, MD; Irl B. Hirsch, MD; Ruth Weinstock, MD; Len Pogach MD, MPH, Priscilla White, MD and several thousand patients ≥60 yrs. old, my mother, and diabetes specialists I have worked with over the last 42 years.
Older Adults are Achieving Lower A1c Levels

Data Source: CDC's Behavioral Risk Factor Surveillance System, 2010

Mean A1c: 7.7%  7.4%  6.4%

A1c<7%  A1c>9%

Age (years)  20-44  45-64  65+

Percentage of adults with diabetes

80
70
60
50
40
30
20
10
0
National Trends in US Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries, 1999 to 2011

Figure Legend:
Rates of Estimated Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries With Diabetes Mellitus, 1999 to 2010. The circles and diamonds indicate observed values; the lines represent the smoothed trend over time.
How Do We Compromise on Glycemic Targets Given All of these Risks?

A reasonable generic glycemic goal is the lowest A1C that 1) does not cause severe hypoglycemia, 2) preserves awareness of hypoglycemia, and 3) causes an acceptable number of episodes of symptomatic hypoglycemia at a given stage of the evolution of the individual’s diabetes.

Reasonable, but misleading when reviewing the newer evidence...

For Multiple Reasons Seniors Require Additional Considerations as Therapy is Tailored to Their Lives.

Risk Factors for Hypoglycemia in Older Adults with Diabetes Mellitus

Physiological
- Cognitive impairment
- Impaired autonomic nervous system function
- Diminished glucagon secretion
- Kidney or liver failure
- Sensory impairment (vision, hearing)
- Functional impairment (mobility, hand dexterity)

Behavioral
- Unhealthy choices, (poorly understood) or irregular, unbalanced nutrition and/or calories
  - Irregular, poorly planned (misunderstood) exercise
- Over Use of alcohol or other sedating agents
- Limited support village (family, diabetes experts, friends) available for senior
- Others: Polypharmacy (use of multiple drugs to treat one or more conditions).

The Population of Older Adults with Diabetes is Heterogeneous

<table>
<thead>
<tr>
<th>RELATIVELY HEALTHY</th>
</tr>
</thead>
<tbody>
<tr>
<td>• &lt; 3 chronic diseases</td>
</tr>
<tr>
<td>• No cognitive or significant visual impairment</td>
</tr>
<tr>
<td>• 0 or 1 instrumental activities of daily living (IADL) dependencies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COMPLEX/INTERMEDIATE HEALTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ≥ 3 chronic diseases</td>
</tr>
<tr>
<td>• Mild cognitive impairment</td>
</tr>
<tr>
<td>• Severe vision impairment</td>
</tr>
<tr>
<td>• ≥ 2 IADL dependencies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VERY COMPLEX / POOR HEALTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Moderate to severe cognitive impairment</td>
</tr>
<tr>
<td>• ≥ 2 ADL dependencies</td>
</tr>
<tr>
<td>• Residence in a long-term nursing facility</td>
</tr>
</tbody>
</table>

*ADL: routine activities people do everyday without needing assistance; eating, bathing, dressing, toileting, walking, continence.

Current diabetes care goals for these patients are:
- Likely to benefit
- Difficult to implement
- Limited benefit


HEALTH AND RETIREMENT STUDY
A Longitudinal Study of Health, Retirement, and Aging
Sponsored by the National Institute on Aging
Recommendations (guidance)

Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM

- **Patient / Disease Features**
- Risks potentially associated with hypoglycemia and other drug adverse effects
- Disease Duration
- Life Expectancy
- Important Comorbidities
- Established Vascular Complications
- Patient attitude and expected treatment efforts
- Resources and support system

Therapy Considerations; MUST Be Based on best science and the individual’s needs and abilities
Hypoglycemia in Older Adults with T1D

• Cases and controls had similar mean glucose and HbA1c

• Cases had
  • increased hypoglycemia unawareness
  • increased CGM glucose variability
  • trend towards more CGM hypoglycemia
  • greater fear of hypoglycemia (quality of life)
  • slightly higher daily frequency of blood glucose monitoring
  • greater use of beta blockers

Secondary Analysis

Percentage of Time Spent in Hypoglycemia (<70 mg/dl) by HbA1c

- HbA1c <7%
  - 9.7%
- HbA1c ≥7%
  - 5.1%

p<0.001

Hypoglycemia In Adult vs Elderly Type 2 Diabetes Mellitus Patients: Risks, Costs, and Impact on Treatment Persistence

Difference in both all-cause and diabetes-related annual healthcare costs between patients with and without hypoglycemia were greater in elderly ($20,264 vs. $11,897 vs. $11,829 vs. $4,190, respectively than adults ($14,031 vs $9,007 and $7,012 vs. $3,265, respectively,

Compared to adults, elderly T2DM patients exhibit higher risks of treatment- associated hypoglycemia In most treatment groups.


American Diabetes Association.
So What Are Our Current And Future Strategies to Better Address Hypoglycemia in Diabetes?

- Insulin analogues: becoming unaffordable for many in U.S. This must be addressed by all.
- CGM: growing evidence of improvements in hypoglycemic exposure
- Movement to “smarter” insulin pumps: hybrid closed-loop to complete closed loop
- Encapsulated islets
- Glucose responsive insulins
- Preventions and Cures
Resources; Working Together to Improve Lives of Seniors with Diabetes.

Seniors Living with Diabetes and their loved ones. Colleagues and Associations focused on DM Care
NIH, NIDDK, FDA
American Diabetes Standards of Medical Care
Best Research on Seniors Living with Diabetes

We invite your suggestions on other best research, clinical experiences and information that will benefit this important focus to improve the lives of seniors with diabetes.
Lixisenatide Therapy in Older Patients With Type 2 Diabetes Inadequately Controlled on Their Current Antidiabetic Treatment: The GetGoal-O Randomized Trial


Management of Inpatient Hyperglycemia and Diabetes in Older Adults

G.E. Umpierrez and F.J. Pasquel

Extracellular RNAs Are Associated With Insulin Resistance and Metabolic Phenotypes


Proinflammatory Cytokines Predict the Incidence and Progression of Distal Sensorimotor Polyneuropathy: KORA F4/FF4 Study


SPECIAL ARTICLE COLLECTION: Emerging Science and Concepts for Management of Diabetes and Aging
Systematic Risk Assessment of Hypoglycemia in the Older Population Associated with Anti-Hyperglycemics using the DERISK System

Stephen Sun, MD, MPH
Head of Quality Risk Management Group
qrm@inventivhealth.com

September 12, 2017
Development of a Safe Use Initiative Risk Repository
As part of a 3-year Research Collaboration Agreement with the FDA

1. Build organizational structure (framework)
2. Harvest non-proprietary info from Source X
3. Deposit content into framework gaps
4. Expand the repository framework
5A. Briefing book background for stakeholder meetings
5B. Training resource or primer for new team members
5C. Map and pinpoint when new crisis and issues occur
5D. Leadership and conference presentations
5E. Manuscript and other publications

Sources are Agnostic:
1. Public meeting
2. Stakeholder association
3. SME testimony
4. Press release
5. New safety news
6. Manuscript
7. Guidelines
8. Scientific findings
Codified Risk Library that Grows Smarter With Every Project Using Systematic and Heuristic Methods

1. Multi-stakeholder journey
2. Learning repository
3. Source-agnostic
4. Web-based
5. Uses engineering FMEA
6. Risk-based score ready
7. Mapped for targeting
8. Designed for “new” info
9. Minimal maintenance
10. Database report outputs
Systematic Risk Assessment for a Patient’s Journey in Diabetes and Hypoglycemia Management

(Part 1: Diabetes Management)

1. BEFORE DIAGNOSIS OF HYPERGLYCEMIA
   1. GENERAL WELLNESS
2. OUTPATIENT MANAGEMENT OF DIABETES
   1. INITIAL OUTPATIENT MANAGEMENT
   2. FOLLOW-UP OUTPATIENT MANAGEMENT
   3. SERVICES FOR PATIENTS: DIABETES EDUCATOR
   4. SERVICES FOR PATIENTS: DIETITIAN
   5. OUTPATIENT INCIDENTAL FINDING OF DIABETES
3. FIELD MANAGEMENT OF HYPERGLYCEMIA
   1. INITIAL PRESENTATION
   2. EMERGENCY DEPARTMENT MANAGEMENT
4. INPATIENT MANAGEMENT OF DIABETES
   1. INPATIENT MANAGEMENT
   2. SURGERY AND DIABETES
   3. LONG-TERM CARE AND DIABETES
   4. INPATIENT INCIDENTAL FINDING
5. SPECIAL POPULATIONS WITH DIABETES
   1. SENIORS
   2. CHILDREN
   3. HISPANIC AMERICANS
   4. AFRICAN-AMERICANS
   5. ASIAN OR ASIAN-AMERICANS
   6. NATIVE-AMERICANS
   7. NON-INSURED POPULATION
   8. PREGNANT WITH DIABETES
   9. FEMALES WITH GESTATIONAL DIABETES
6. PATIENT SELF-MANAGEMENT OF DIABETES

(Part 2: Hypoglycemia Management)

7. BEFORE DIAGNOSIS OF HYPOGLYCEMIA
8. PATIENT SELF-MANAGEMENT OF HYPOGLYCEMIA
   1. PATIENT SELF-MANAGEMENT OF HYPOGLYCEMIA
9. FIELD MANAGEMENT OF HYPOGLYCEMIA
   1. EMERGENCY PRESENTATION
   2. EMERGENCY DEPARTMENT MANAGEMENT
A. PRODUCTS FOR THE MANAGEMENT OF HYPOGLYCEMIA
   1. ANTI-HYPERGLYCEMICS
   2. INSULIN PENS
   3. INSULIN VIAL INJECTIONS
   4. INSULIN PUMP AND ARTIFICIAL PANCREAS
   5. GLUCOSE METER
B. PRODUCTS FOR THE MANAGEMENT OF DIABETES
   1. PHARMACY ACCESS
   2. AT HOME PATIENT MANAGEMENT OF DIABETES

Powered by INC Research/InVentiv Health / DERISK System outputs. We gratefully acknowledge: Bullock A, Pogach L, Julius MM, Moran J, Pries RM, Watts S. Private communications. Aug 2, 2017. As part of a Research Collaboration Agreement with the FDA; we welcome any comments and access to this early version of a systematic risk assessment; join the collaboration: grm@inventivhealth.com

© 2017 All Rights Reserved | Confidential – for INC Research/inVentiv Health use only
Systematic Risk Assessment of Hypoglycemia in the Older Population Associated with Anti-Hyperglycemics Using the DERISK System

OLDER POPULATION RISKS:
1. Additional comorbid conditions besides diabetes
2. More prescribed and non-prescribed medications
3. Difficult time understanding and retaining treatment-related instructions
4. Dependence on caregivers
5. Resources such as an elderly support organization
6. More travel limitations
7. Limited income and conserves medications
8. Discontinue use of insulin from hypoglycemia

ANTI-HYPERGLYCEMIC RISKS:
1. Metformin
2. Sulfonylureas
3. Thiazolidinediones
4. Dipeptidyl peptidase iv
5. SGLT2 inhibitors
6. Alpha-glucosidase inhibitors
7. Bromocriptine mesylate
8. Colesevelam
9. Meglitinide analogs
10. GLP1 receptor agonists
11. Amylin analogs
12. Insulin pen
13. Insulin with vial and syringes

*A Systematic Risk Assessment (SRA) Report will be updated in the DERISK repository and a report will be generated in real-time and be made available to the FDA after any additional learnings are incorporated.
Reducing the Risk of Hypoglycemia in the Older Population

FDA Patient Panel, September 12, 2017
Alan C Moses, MD
Global Chief Medical Officer, Novo Nordisk A/S
Disclosures

ACM is a full-time employee of Novo Nordisk and, as such, is compensated by salary and share options.
Hypoglycemia is a Major Healthcare Burden for American Citizens

Hypoglycemia is a risk factor for mortality and adverse cardiovascular (CV) events\(^1\):

- Mild hypoglycemia: 68% increased risk of death and adverse cardiovascular events (p<0.001)
- Severe hypoglycemia: 133% increased risk of death and adverse cardiovascular events (p<0.001)

Severe hypoglycemia often requires hospitalisation and inpatient care\(^2\)

\(~\text{USD} 7,317\) is the total cost of one severe hypoglycemic episode if a patient is admitted to hospital directly\(^3\)

---

1. Systematic review, Yeh et al. *Acta Diabetol* 2016;53:377–92 (hazard ratio 1.68 [95 % CI 1.25–2.26] for mild and 2.33 [95 % CI 2.07–2.61] for severe)
2. Based on 8655 patients with diabetes experiencing 244 episodes requiring help from healthcare professionals (Leese et al. *Diabetes Care* 2003;26:1176–80)
DEVOTE: A CVOT that also Assessed Risk of Severe Hypoglycemia

7637 people with type 2 diabetes

- High CV risk profile
- Appropriate for basal insulin initiation or switch
- Current therapy with oral or injectable diabetes therapy

Randomised 1:1

IDeg OD (blinded vial) + standard of care

IGlar OD (blinded vial) + standard of care

Interim analysis at 150 primary events

Final analysis at 633 primary events

**Primary endpoint**
The time from randomisation to first occurrence of a 3-component MACE: cardiovascular death, non-fatal heart attack or non-fatal stroke

**Key secondary endpoint**
Number of severe hypoglycemic episodes*, including nocturnal severe hypoglycemia

*An episode requiring assistance of another person to actively administer carbohydrate, glucagon or take other corrective actions (ADA definition, 2013)

MACE: Major adverse cardiac event; OD: Once daily

Source: Marso SP et al. Am Heart J. 2016 Sep;179:175-83
DEVOTE Included a High Percentage of Older Patients

DEVOTE baseline characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>IDeg</th>
<th>IGlar</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>64.9</td>
<td>65.0</td>
</tr>
<tr>
<td><strong>Subjects aged ≥75 years, %</strong></td>
<td>10.0</td>
<td>11.5</td>
</tr>
<tr>
<td><strong>Sex, Male, %</strong></td>
<td>62.8</td>
<td>62.4</td>
</tr>
<tr>
<td><strong>HbA$_{1c}$, %</strong></td>
<td>8.4</td>
<td>8.4</td>
</tr>
<tr>
<td><strong>FPG, mg/dL</strong></td>
<td>169.8</td>
<td>173.5</td>
</tr>
<tr>
<td><strong>[mmol/L]</strong></td>
<td>[9.4]</td>
<td>[9.6]</td>
</tr>
<tr>
<td><strong>Duration of diabetes, years</strong></td>
<td>16.6</td>
<td>16.2</td>
</tr>
<tr>
<td><strong>Insulin treated, %</strong></td>
<td>84.8</td>
<td>84.3</td>
</tr>
<tr>
<td><strong>Body weight, kg</strong></td>
<td>96.1</td>
<td>96.1</td>
</tr>
<tr>
<td><strong>BMI, kg/m$^2$</strong></td>
<td>33.6</td>
<td>33.6</td>
</tr>
</tbody>
</table>

*Mean value
HbA$_{1c}$ and FPG measured at randomisation. All other parameters measured at the screening visit.
BMI: body mass index; FPG: fasting plasma glucose; IDeg: insulin degludec; IGlar: insulin glargine
Source: Marso SP et al. Am Heart J. 2016 Sep;179:175-83
Risk for Severe Hypoglycemia Increased with Age for people with Insulin Treated T2D

Post-hoc analysis of data from DEVOTE

*Hazard ratios for patients ≥65 years, 1.288 [95% CI 1.065; 1.556], and for patients ≥75 years, 1.549 [95% CI 1.196; 2.006], estimated in a Cox proportional hazard model adjusted for treatment and age-group.

Severe hypoglycemia: an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions (ADA definition (2013); CI: confidence interval)
Severe Hypoglycemia in LEADER: 31% reduction in the Liraglutide Group

*Estimated rate ratio 0.69 [95% confidence interval 0.51–0.93] from analysis using a negative binomial regression model.
Severe hypoglycemia was defined as hypoglycemia for which the patient required assistance from a third party (ADA definition, 2013).
IDegLira Reduced Risk of Hypoglycemia by 89% Compared to Basal/Bolus Insulin Treatment

Data from DUAL VII

Mean observed HbA$_{1c}$ +/- standard error of mean based on full analysis set (left slide). Mean cumulative function of hypoglycemia based on safety analysis set (right side).

*Estimated rate ratio 0.11 [95% confidence interval 0.08–0.17] from analysis using a negative binomial regression model.

Severe or symptomatic hypoglycemia: an episode that is severe according to the ADA classification or blood glucose -confirmed by plasma glucose value <3.1 mmol/L (<56 mg/dL) with symptoms; IAsp: insulin aspart; IDegLira: insulin degludec/liraglutide combination; IGlar: insulin glargine 100 units/mL; n: number of patients

Source: Billings et al. ADA 2017;136-OR.
Conclusions

All individuals with diabetes deserve to be treated to the lowest average glucose level possible without increasing their risk of hypoglycemia.

- **Individualization** of diabetes therapy is essential to achieve medically appropriate goals for each patient.
- Goals should be set within the context of the overall health status of an individual and the available medications.
- Protection against the risk of hypoglycemia should be a major part of the decision making process by clinician and patient together.

New molecules have been and will continue to be developed with the goal to achieve glucose targets with a very low risk of hypoglycemia.
Summary,
Next Steps,
FDA’s Role