

Intensive Treatment and Severe Hypoglycemia Among Adults with Type 2 Diabetes

What is the association between intensive treatment, clinical complexity, and incidence of severe hypoglycemia among adults with type 2 diabetes not using insulin?

Evidence and practice landscape



Clinical guidelines recommend targeting HbA1c <7% for most non-pregnant adults with type 2 diabetes, although personalized treatment is encouraged based on age, medical conditions, and risk of hypoglycemia. Despite this caveat, tight glycemic control is common among patients who are at increased risk for complications: those who are older or have serious chronic health conditions.

Prior studies have not assessed the prevalence or impact of intensive treatment among

younger patients or those using medications other than insulin or sulfonylureas. Moreover, little is known about treatment practices and outcomes among patients once they achieve tight glycemic targets.

This study quantifies the prevalence of intensive treatment, specifically among clinically complex patients with controlled type 2 diabetes; and estimates the degree to which intensive treatment is associated with hypoglycemia.

Concepts to know

HbA1c: the percentage of hemoglobin protein in red blood cells that is coated in sugar. A HbA1C measure (6.5% +) indicates high blood sugar levels that are diagnostic of diabetes. HbA1c above 7% may increase risk of long-term diabetes complications.

Hypoglycemia: a serious potential complication of diabetes treatment characterized by an abnormally low blood sugar level. It worsens quality of life and has been associated with cardiovascular events, cognitive impairment, and even death.

Study Population

31,542 non-pregnant adults age ≥18 years with type 2 diabetes who achieved and maintained HbA1c <7% without use of insulin, and had no episodes of severe hypoglycemia or hyperglycemia in the prior 12 months – 3910 (12%) were *clinically complex* (see appendix).

Intensive treatment was defined as being treated with more glucose-lowering medications than clinical guidelines consider necessary given the patient's HbA1c level (see appendix).

Key findings

Intensive glucose-lowering treatment is quite common, even among patients with high clinical complexity.

1 in 4
patients were treated intensively overall.

- 26.5% low complexity patients
 - 18.7% high complexity patients
- Patients cared for by endocrinologists were more likely to be intensively treated (OR 1.66; 95% CI 1.53-1.79).

Intensive treatment nearly doubled the risk of severe hypoglycemia in older patients and patients with serious chronic health conditions.

Severe hypoglycemia treatment burden:

- 73% of patients went to a doctor's office.
- 18% of patients visited the emergency room.
- 9% of patients were admitted to the hospital.

Severe hypoglycemia was significantly more frequent in complex patients, increasing with intensive treatment.

- Low complexity: risk-adjusted probability of severe hypoglycemia did not increase; 1.02% (95% CI, 0.87-1.17) with standard treatment, 1.30% (95% CI, 0.98-1.62) with intensive treatment.
- High complexity: risk-adjusted probability of severe hypoglycemia increased from 1.74% (95% CI, 1.28-2.20) with standard treatment to 3.04% (95% CI, 1.91-4.18) with intensive treatment; absolute difference 1.30% (95% CI, 0.10-2.50).

Translation potential

This study addresses issues of importance to:

- **Patients** who are sometimes overtreated and thus at risk for severe hypoglycemia,
- **Providers** who may prescribe intensive glucose lowering therapy,
- **Professional societies** who draft clinical practice guidelines to inform high quality care, and
- **Payers and policy makers** who currently prioritize HbA1c reduction over hypoglycemia and patient quality of life based on national standard quality measures.

Implications for practice:

- Overtreatment is a manifestation of clinical inertia.
- Performance metrics have potential to address overtreatment and undertreatment.
- Rates of intensive treatment decreased after 2009, which may reflect recent campaigns that caution overuse in healthcare.
- Specialists may be prone to overtreatment.
- Intensive treatment with any medication, not just sulfonylurea and insulin, increases hypoglycemia risk.

Project mechanics

Objectives

Estimate the prevalence of intensive treatment and the association between intensive treatment, clinical complexity, and incidence of severe hypoglycemia among adults with type 2 diabetes not using insulin.

Methods

- First, multivariable logistic regression separately examined the risk-adjusted probabilities of intensive treatment and severe hypoglycemia. Adjustment variables were set to the sample means of sex, race (white, non-white, unknown), household income, U.S. region, index HbA1c year, and provider specialty.
- Then, the risk-adjusted probabilities for intensive treatment were calculated for low and high complexity patients, adjusting for the aforementioned variables.
- The association between intensive treatment and severe hypoglycemia was examined in a second logistic regression model where the main predictor was a four level measure of patient complexity and treatment intensity: (1) low complexity with standard treatment; (2) low complexity with intensive treatment; (3) high complexity with standard treatment; and (4) high complexity with intensive treatment.

Study limitations

- Stringent inclusion criteria that restricted the population to patients with type 2 diabetes who achieved and maintained glycemic control without use of insulin.
- Because the study cohort was derived from a dataset of privately-insured and Medicare Advantage beneficiaries, the unadjusted rates of intensive treatment and severe hypoglycemia may not be directly generalizable to the broader US or international population. The association between intensive treatment and severe hypoglycemia, however, is likely comparable once pertinent covariates are accounted for.
- We considered treatment change that occurred within 120 days of the HbA1c test, but measured rates of severe hypoglycemia during two years of follow-up, which may miss patients who received standard treatment at time of cohort entry but were intensified later, causing hypoglycemia. Conversely, patients who were intensively treated at baseline and de-intensified later may have avoided hypoglycemia, thereby decreasing the measured association between intensive treatment and severe hypoglycemia.
- Individuals who may have died during follow-up were excluded due to lack of continuous enrollment.
- Not all hypoglycemic events culminate in a clinical encounter, which would underestimate the incidence of severe hypoglycemia, particularly among younger and healthier patients, since sicker and elderly patients, and those without readily available support, are more likely to require medical attention for severe hypoglycemia.

Driving discovery

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Appendix

Defining intensive treatment:

For the purposes of this study, “intensive treatment” was defined as being treated with more glucose-lowering medications than clinical guidelines consider to be necessary given their HbA1C level. Patients whose HbA1C was less than 5.6% (diabetes is defined by HbA1C 6.5% or higher) were considered intensively treated if they were taking any medications. Patients with HbA1C in the “pre-diabetes” range, 5.7-6.4%, were considered to be intensively treated if using two or more medications at the time of the test, or if started on additional medications after the test, because current guidelines consider patients with HbA1C less than 6.5 percent to already be optimally controlled. For patients with HbA1C of 6.5-6.9% the sole criteria for intensive treatment was treatment intensification with two or more drugs or insulin.

Defining clinical complexity:

This study focused specifically on patients with high clinical complexity due to either advanced age ≥ 75 years, presence of life-limiting conditions (e.g., dementia, end-stage kidney disease), or presence of at least three serious chronic health conditions (e.g., heart disease, stroke, non-end stage chronic kidney disease).

Sources

McCoy RG, Lipska KJ, Yao X, Ross JS, Montori VM, Shah ND. [Intensive treatment and severe hypoglycemia among adults with type 2 diabetes](#). *JAMA Intern Med.* Epub ahead of print June 6, 2016.

Mayo Clinic. Patient Care & Health Information website <http://www.mayoclinic.org/tests-procedures/a1c-test/home/ovc-20167930>. Updated January 7, 2016. Accessed June 2016.

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