

Study Designs

Brod et al:

A 20-minute Internet survey (N=1404) assessing how non-severe hypoglycemic events (NSHEs) in working type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) populations in the United States, the United Kingdom, Germany, and France affect productivity and behaviors.

Among individuals reporting an NSHE at work (n=972), 18% missed work for an average of 10 hours; lost productivity was estimated to range from \$15.26 to \$93.47 per NSHE, representing 8 to 16 hours of lost work time per month. A key limitation of this study includes the potential for recall bias, which can impact results. It is also possible that data collection via Internet surveys can introduce selection bias. In addition, there was an incentive for survey respondents, which could impact the accuracy of the data. Last, this study may have underestimated the complete burden of NSHEs on work productivity from the patient perspective because NSHEs affect absenteeism and the ability to be productive while at work, which were not fully captured in the study design.

Heller et al:

An analysis evaluating resource utilization incurred during 536 severe hypoglycemic events across 3 insulin groups in a phase 3a clinical program (people with T1DM on basal-bolus therapy, people with T2DM on multiple injections, and people with T2DM on basal + orals)

The analysis documented the use of ambulance/emergency teams, a hospital/emergency room visit ≤ 24 hours, or a hospital visit > 24 hours. 157 events (29.3%) involved an ambulance/emergency team, 64 (11.9%) led to a hospital/emergency room visit ≤ 24 hours, and 36 (6.7%) required hospital admission > 24 hours. Rates of hypoglycemia may have been underestimated because people who are at high risk for severe hypoglycemia or hypoglycemia unawareness were excluded from the clinical trials. Due to the global nature of the clinical trials, variation in health care utilization and local procedures is to be expected. In addition, underreporting or inconsistent reporting of ambulance use could have occurred. Information about how patients arrived at the hospital was not consistently recorded; only the resource was included in the analysis. Finally, only direct resources relating to the involvement of emergency services and hospital treatment were reported; additional measurements and costs were not quantified or included.

Ward et al:

Costs of managing macrovascular/microvascular complications, hypoglycemic episodes, and infections were estimated using direct data analysis and micro-costing. Data were obtained from inpatient and emergency department databases, national physician and laboratory fee schedules, government reports, and literature.

Event-year costs reflect the resource use during an acute care episode (initial management in an inpatient or outpatient setting) and any subsequent care provided in the first year. The costs were estimated from the perspective of a US health care payer and expressed in 2012 US dollars. Costs for managing hypoglycemic episodes were \$176 to \$16,478, depending on the treatment required. One limitation of this study is that it did not reflect true economic implications related to diabetes management because lost productivity and care provided by an unpaid caregiver were not taken into account. Also, cost estimates available in other published studies cannot be directly compared with the estimates from this study. Last, cost data available before 2012 were inflated and reported in 2012 US dollars.



Study Designs (cont'd)

Johnston et al:

This retrospective, observational study examined the association between ICD-9-CM–coded outpatient hypoglycemic events and fall-related fractures in Medicare-covered patients with T2DM. The data originated from health care claims for individuals with employer-sponsored Medicare supplemental insurance.

Patients included were ≥ 65 years of age with evidence of T2DM as identified using a Healthcare Effectiveness Data and Information Set algorithm or by ≥ 2 prescription claims for oral antidiabetic drugs. Logistic regression was used to examine the association between hypoglycemic events and fall-related fractures, adjusting for patient demographics and clinical characteristics. Patients with hypoglycemic events had 70% higher regression-adjusted odds of fall-related fractures than patients without hypoglycemic events (hypoglycemic events odds ratio, 1.70; 95% confidence interval, 1.58–1.83). Limitations of the study include that it was based on administrative claims data, meaning that the true validity of the measured variables cannot be known with certainty. In addition, there was no randomization, creating the possibility of residual confounding. Last, the administrative claims data source lacked important information such as a direct measure of the duration and severity of diabetes, and measures of patient frailty and bone mineral density.

Khunti et al:

A retrospective cohort study evaluating the association between hypoglycemia, the risk of cardiovascular events (CVEs), and all-cause mortality in insulin-treated patients ≥ 30 years of age, utilizing data from the Clinical Practice Research Datalink database and Hospital Episode Statistics data.

Among patients (N=13,682) without a history of cardiovascular disease, patients who experienced an episode of hypoglycemia had a 92% and 50% significantly increased risk, respectively, of composite CVEs in T1DM and T2DM cohorts. Limitations of the analysis include that the selection criteria applied to the cohort could have potentially affected its representative quality, not all relevant confounding factors were captured so predicting causality was not possible, and underreporting of hypoglycemia could potentially affect the analysis because patients may self-manage an episode and not present to a physician.

Nunes et al:

A cohort study assessing the incidence of serious and mild-to-moderate hypoglycemia in T2DM patients (N=844,683) in the Humedica electronic health record (EHR) database. Estimates of the occurrence of hypoglycemia derived from diagnostic codes were compared to those recorded within clinical notes and classified via natural language processing.

The identification of hypoglycemic events from clinical notes in the EHR relative to measures from structured data such as diagnostic codes increased capture of nonserious events more than 20-fold. A key limitation of this study is that EHR systems are unable to completely capture measures of health and utilization due to providers not recording patient-reported hypoglycemic episodes, patients not reporting self-treated hypoglycemic episodes, or the fact that patients might receive care from providers external to Humedica-contributing groups.