Descriptive analysis of the use of long- and intermediate-acting insulin, and key safety outcomes in adults with diabetes mellitus

**INTRODUCTION**

Real-world safety and effectiveness is based on real-world data (RWD). The Biologics and Biosimilars Collective Intelligence Consortium (BBCIC) was convened by the Academy of Managed Care Pharmacy (AMCP) in 2015 to provide real-world, post-marketed evidence generation for innovator biologics and corresponding biosimilars in the US.1,2

BBCIC leverages the FDA Sentinel system data and analytic infrastructure: BBCIC Distributed Research Network (DRN). The BBCIC DRN uses the Sentinel Common Data Model for data standardization and Sentinel-based analytic tools for distributed analyses and examining medical product risk and benefit.3

Four BBCIC research teams formed to describe the biologics of the first-to-market biosimilars. The purpose was to learn about the RWD in the BBCIC DRN. Insulins were among the four descriptive analyses.

An estimated 29.1 million people in the United States have Type 1 (T1DM) or Type 2 (T2DM) diabetes, representing 9.3% of the total population.4

**Objective**

The insulin analysis objective was to describe adults with diabetes who use long-acting (LAI) or intermediate-acting (NPH) insulin, insulin episodes, diabetic outcomes, and potential confounders in the BBCIC DRN.

**METHODS**

This retrospective, observational study evaluated data from 6 BBCIC DRN data partners that contributed a population of over 57 million people currently covered by Commercial or Medicare-Advantage health insurance. We identified adults with prevalent T2DM or T2DM and medical and drug coverage during January 1, 2011 and September 30, 2015. The population criteria included people 18 years or older, with at least one drug claim for long- and intermediate-acting insulin (LAI, NPH) alone or with either rapid/short-acting insulin (R) or sulfonurea (Suf), at least 183-days of medical and drug enrollment pre-insulin claim, and no claim evidence of insulin pumps or related supplies, gestational diabetes, liver disease, dialysis, end-stage renal disease, amputations, homologous/bioyouth, hemolytic anemia, sickle cell anemia, and blood transfusion, modified major adverse cardiac events (MACE), ED visit or hospitalization (excluded mortality), or hypoglycemia ED visit.

Insulin episodes was the unit of analysis and data was presented in either 4 subgroups: 1) T1DM w LAI 2) T1DM w NPH 3) T2DM with LAI 4) T2DM w NPH: or 6 sub-groups per diabetes type: 3) LAI only 2) LAI plus R, 3) LAI plus Suf, 4) NPH only, 5) NPH plus R, and 6) NPH plus Suf. Episodes were followed through the earliest of health plan disenrollment, medical-attended hypoglycemia or MACE (study outcomes), insulin regimen switch, current regimen discontinuation, or study end. Study outcomes included medical-attended severe hypoglycemic events, modified MACE, and hemoglobin A1C lab results.

Covariates included Combined Comorbidity Score (CCS) – a measure of probability of 1-year mortality.5 7 diagnoses, healthcare utilization, and Metformin use.

**RESULTS**

**Study population.** The BBCIC DRN had 4,591 T1DM and 103,951 T2DM unique patients who met the study criteria.

**Diabetic Outcomes**

- **Modified MACE.** The unadjusted MACE rates were 40.2% (T1DM) and 67.6% (T2DM) users per 10,000 person years at risk (10kPYR).
- **Hypoglycemia.** The unadjusted severe hypoglycemic event rates were 34.9 (T1DM) and 96.9 (T2DM) 10kPYR.
- **A1C.** Only 53% of T1DM and 38% of T2DM patients had a baseline A1C and less than 50% had a follow-up A1C result.

**Conclusions.** T2DM: The most frequent comorbidity was hypertension and the CI was low at 0.1 due to the clinical exclusions. Patients with a LAI episodes had 3 ambulatory visits and 8 prescriptions filled in 3 drug classes. Patients with NPH episodes had 3 ambulatory visits and 7 prescriptions filled in 3 drug classes.

T1DM: The most frequent comorbidity was hypertension, with CI’s less than 1% mortality probability. For LAI episodes, patients had 5 ambulatory visits and 13 prescriptions filled in 7 drug classes.

**Acknowledgements.**

With the BBCIC DRN we are able to reliably identify and characterize exposures, outcomes, and potential confounders for a large population of people with diabetes.

- Unadjusted MACE and severe hypoglycemic rates were consistent with other clinical and observational studies.
- The limited number of baseline and follow-up A1C values will require consistency demonstration in data sources and de novo programming for numeric lab values.
- Significant diabetic diagnosis inconsistence, variation in days supply and use of rapid acting insulin and sulfonureas adherence requires additional methods development.
- Careful study design, including attention to length of episode gap and use of algorithms to accurately identify patients with Type 1 and Type 2 diabetes, is essential in observational studies using large administrative claims data.

**References**


**Table**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LAI group (%)</th>
<th>NPH group (%)</th>
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<tbody>
<tr>
<td>Age group: 79 years</td>
<td>34.9%</td>
<td>96.9%</td>
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<tr>
<td>Age group: 49 years</td>
<td>74.1%</td>
<td>34.9%</td>
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<tr>
<td>Average dispensings per User per Insulin Episode</td>
<td>3.4</td>
<td>2.5</td>
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**Figure**

- Distribution of A1C levels in T1DM and T2DM patients.
- Comparison of diabetic outcomes between LAI and NPH groups.

**Figure 1**

- Distribution of A1C levels in T1DM and T2DM patients.
- Comparison of diabetic outcomes between LAI and NPH groups.

**Figure 2**

- Distribution of A1C levels in T1DM and T2DM patients.
- Comparison of diabetic outcomes between LAI and NPH groups.