# Association between glucagon-like peptide 1 receptor agonist (GLP1-RA) and sodium glucose co-transporter 2 inhibitor (SGLT2i) use and COVID-19 outcomes: A national retrospective cohort study

**First published:** 01/11/2020

**Last updated:** 23/04/2024

Study Planned

## Administrative details

**EU PAS number**

EUPAS37860

**Study ID**

40044

**DARWIN EU® study**

No

**Study countries**

United States

**Study description**

Emerging evidence from the COVID-19 pandemic suggest that patients with type 2 diabetes comprise a significant portion of the affected population and are at higher risk for severe outcomes including hospitalization and death, yet it remains largely unknown how pre-morbid medication may impact outcomes of COVID-19 in patients with type 2 diabetes. Several medications have biologically plausible mechanisms with relevance for patients with diabetes among others including ACE inhibitors, metformin, and DPP4-inhibitors. Recent large cardiovascular outcome trials and subsequent metanalyses have demonstrated that some glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium-glucose-linked cotransporter 2 inhibitors (SGLT2i) are associated with a reduction of cardiovascular events and all-cause mortality among the same high-risk populations who show higher susceptibility to severe COVID-19 and increased mortality. Yet, no studies have examined the class effect of these newer anti-hyperglycemic of mortality and other outcomes in the setting of COVID-19 infection. These data are critical because therapeutics represent a highly actionable intervention point to improve outcomes from both the inpatient and outpatient setting for a large population of patients with inherently high risk for COVID-19 associated mortality. To address this gap and inform evolving care guidelines for patients with medication-managed type 2 diabetes during the COVID-19 pandemic, this study aims to characterize the association of use of GLP1-RA and SLGT2i with COVID-19 outcomes using real world data from the National COVID Cohort Collaborative (N3C). We will consider the well-studied and commonly used class of dipeptidyl peptidase-4 inhibitors (DPP4i) as the active comparator drug to avoid confounding by indication.

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**Study status**

Planned

## Research institutions and networks

## Institutions

### University of North Carolina at Chapel Hill

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution

## Networks

### National COVID Cohort Collaborative (N3C)

## Contact details


**Study institution contact**

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Study contact

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**Primary lead investigator**

John Buse

Primary lead investigator


## Study timelines

**Date when funding contract was signed**
Planned: 01/06/2020

**Study start date**
Planned: 01/06/2020

**Date of final study report**
Planned: 01/04/2020

## Sources of funding

- Other

## More details on funding

National Institutes of Health (National Center for Advancing Translational Sciences)

## Study protocol

N3C_DM_Meds_Covid_Outcomes_Protocol_301020_Locked.pdf (166.17 KB)

## Regulatory

**Was the study required by a regulatory body?**

No

**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

# Methodological aspects

## Study type

**Study type:**

Non-interventional study

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**Scope of the study:**

Disease epidemiology

**Main study objective:**

This study aims to characterize the association of use of GLP1-RA and SLGT2i with COVID-19 outcomes among adults with diabetes and COVID-19 infection, using real world data from the National COVID Cohort Collaborative (N3C).

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(A10BJ) Glucagon-like peptide-1 (GLP-1) analogues

Glucagon-like peptide-1 (GLP-1) analogues

(A10BK) Sodium-glucose co-transporter 2 (SGLT2) inhibitors

Sodium-glucose co-transporter 2 (SGLT2) inhibitors

(A10BH) Dipeptidyl peptidase 4 (DPP-4) inhibitors

Dipeptidyl peptidase 4 (DPP-4) inhibitors

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**Medical condition to be studied**

Diabetes mellitus

COVID-19

## Population studied

**Age groups**

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

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**Estimated number of subjects**

5.000

## Study design details

**Outcomes**

The outcome is 60-day mortality following a COVID-19 diagnosis. Secondary outcomes will include markers of illness severity including hospital admission and level of respiratory support required.

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**Data analysis plan**

The aim of the analysis is to estimate the relative odds of mortality 60 days following a COVID-19 diagnosis for patients with type 2 diabetes and a history of SGLT2i/GLP1-RA use vs DPP4i use among eligible patients with COVID-19 in the N3C database. The primary estimand is the odds of mortality following 60 days from diagnosis with COVID-19. The ratio of the odds (OR) between the two drugs will be estimated using targeted maximum likelihood estimation (TMLE).

# Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

# Data sources

**Data sources (types)**

Disease registry

Other

**Data sources (types), other**

Prospective patient-based data collection

# Use of a Common Data Model (CDM)

**CDM mapping**

No

# Data quality specifications

**Check conformance**

Unknown

**Check completeness**

Unknown

**Check stability**

Unknown

### Check logical consistency

Unknown

## Data characterisation

### Data characterisation conducted

No