Comparison of Type 2 diabetes Pharmacotherapy Regimens Using Targeted Learning

NCT05073692

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Study Protocol

Objectives

This project aims to compare cardiovascular risks (3-point MACE) between four glucose-lowering treatment regiments (SU, DPP4, GLP1, and SGLT2) in patients with type 2 diabetes.

Design

This project is an observational retrospective cohort study using health care data from six health care systems.

Methods

All study aims are addressed by estimating causal effects conceptualized by the comparisons of time-to-event outcomes between exposure regimens in ideal Randomized Clinical Trials (RCTs), i.e., RCTs with perfect compliance and no loss to follow up.

Statistical Analysis Plan

How Data Were Analyzed

Data were analyzed using R.

What Statistical Methods Were Used

We implemented Targeted Learning and Inverse Probability Weighting to estimate three classes of effect measures using longitudinal observational data: hazard ratios (HR), cumulative risk differences (RD), and differences between areas under the survival curves (also termed “restricted mean survival time”). Each of them were evaluated under both the intention-to-treat and per-protocol principles used in the analysis of RCT data.

How Adjustments Were Made for Covariates

All analyses were adjusted for 400 covariates using Super Learning for propensity score estimation, and LASSO for outcome regressions.

Critical Assumption

Analyses relied on the untestable no unmeasured confounding assumption.

For additional details, see:

Neugebauer R, An J, Dombrowski SK, et al. Glucose-Lowering Medication Classes and Cardiovascular Outcomes in Patients With Type 2 Diabetes. JAMA Netw Open. 2025;8(10):e2536100. doi:10.1001/jamanetworkopen.2025.36100

Informed Consent Form

Not Applicable.