

Determinants for Use of GLP-1 Receptor Agonists in Canada (EUPAS1000001058)

Table 1: Adaptations to the Darwin EU Protocol (EUPAS1000000828)

Section	Adaptations	Rationale
Objectives	Modified objective 2 based on edits to covariates. Added indication covariate for stratification in objectives 3 and 5.	Modified initial dose to highest strength and removed cumulative dose due to feasibility. Additional covariates for stratification added for Canadian study only.
Study Design	Modified study design diagram.	Adapted based on adaptations from DARWIN EU study.
Study Population and Setting	Added main analyses for public claims only and additional analyses for all claims.	To be consistent with the DARWIN EU study, the main analyses will be limited to publicly reimbursed claims and the study period will begin on September 1, 2019 (date of the first GLP-1 RA listed on the provincial formulary across provinces). To capture a more comprehensive utilization of these drugs in Canada, analyses will also be conducted including all claims in all provinces except in Ontario, where only publicly reimbursed claims are captured.
Exposure	Removed no brand category.	Not applicable to Canadian data as brand available through the DINs.
Other Covariates Including Confounders, Effect Modifiers, and Other Variables	Objective 1: - Modified T2DM and obesity indication definitions. - Added a weight management intent indication cohort.	- Adapted T2DM and obesity definitions due to Canadian data. T2DM will be defined using an algorithm to increase sensitivity. BMI removed from obesity definition as not available. - Given that obesity is not well captured in Canadian data, a weight management intent cohort will be defined based on a hierarchical approach.
Other Covariates Including Confounders, Effect Modifiers, and Other Variables	Objective 2: - Modified list of comorbidities. - Modified initial dose to highest strength and removed cumulative dose.	- Removed selected comorbidities due to feasibility in Canadian data (activity limitation, housebound, mobility and transfer problems, requirement for care, sleep disturbance, social vulnerability, dizziness, dyspnea, and foot problem) and added pulmonary embolism. - Modified due to feasibility in Canadian data.
Other Covariates Including Confounders, Effect Modifiers, and Other Variables	Added indication covariate for stratification in objectives 3 and 5.	Additional covariates for stratification added for Canadian study only.
Data Analysis Plan	Added analysis for all claims for objectives 1 to 3 and 5.	The publicly reimbursed analyses will serve as the primary analyses to maintain alignment with the DARWIN EU protocol. Analyses including all available claims will be conducted as secondary analyses to provide a more comprehensive assessment of GLP-1 RA utilization in Canada and to evaluate the consistency of findings across reimbursement settings.

BMI = body mass index; DARWIN EU = Data Analysis and Real World Interrogation Network Europe; GLP-1 RA = glucagon-like peptide-1 receptor agonist; T2DM = type 2 diabetes mellitus.