Time trends in severe hospitalised hypoglycaemia events in persons with type 1 and type 2 diabetes in Scotland during the period 2016-2022

Statistical Analysis Plan

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12 July 2023, v.1

# Introduction

Severe Hospitalised Hypoglycaemia (SHH) represents a significant complication in individuals with diabetes, posing important challenges in the management of diabetes. It is crucial to examine the trends in SHH events over time to understand patterns in their changes and potentially adapt health policies to mitigate their occurrence.

# Study objectives

This study aims at delineating time trends in Severe Hospitalised Hypoglycaemia (SHH) in the National dataset of Scotland over the period 2016-2022 to assess the evolution of this condition in the context of the COVID-19 pandemic, the introduction of flash monitors, and the introduction of new drugs for type 2 diabetes, in particular.

# Study period

The study period will be 1st January 2016 – 30th November 2022.

# Study population

Individuals with type 1 and type 2 diabetes who are present in the SDRN-National Diabetes Dataset (SDRN-NDS) and alive and observable at any point between 1st January 2016 and 30th November 2022 will be included in the study population. Type 2 diabetes will be defined using the SDRN-epi type assignation algorithm. Hospital admission data will derive from Scottish Morbidity Record (SMR) 01 and mortality data will be obtained from National Records of Scotland (NRS).

# Definition of event

Event will be defined as SHH for individuals in the study population with a hospital admission or death involving an ICD-10 diagnosis code of E15, E16.0, E16.1, E16.2 at any level of the reasons for admission or causes of death.

The following ICD-10 condition codes will be used for the selection of individuals with SHH events:

* Nondiabetic hypoglycaemic coma – E15
* Drug-induced hypoglycaemia without coma – E16.0
* Other hypoglycaemia – E16.1
* Hypoglycaemia, unspecified – E16.2

# Definition of outcomes and statistical analysis

For the analysis, we will consider the following outcomes:

* Crude event rates per 100,000 person-days in the study window, calculated as a 56-day rolling mean centered on each day. The rate corresponds to the number of SHH events by the total population at risk for each study day. The analyses will be stratified by sex (female male) and by age (<20, 21-50, and >50). Age bands will be based on the age of each individual at midpoint of their observability period. For Type 2 diabetes, patients age less than 20 will be excluded from the analyses. Further analyses will be stratified by Scottish Index of Multiple Deprivation (SIMD, quantile 1 to 5, Q1 being the most deprived) based on the postcode of residence to observe possible differences according to the socioeconomic status. Other crude rates may also be calculated per year or for the entire study duration to obtain less granular information and summary statistics.
* To provide a better understanding of SHH occurrence and its relationship with calendar time, we will also use the R package *mgcv* to fit generalized additive models (GAM) adjusted for seasonality, day of the week, age band, sex, and SIMD. No imputation of missing data will be performed.

# Observability

The observability status of individuals will be defined using attendance of routine observations and receipt of prescriptions during the study period. If individuals become unobservable during the study period they will be censored on the date at which they first become unobservable. Thus, individuals will be censored for end of study, end of observability, or death.