**Learning Effective Clinical Treatment Pathways for Type-2 Diabetes**

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The authors declare the following disclosures:

Table of contents

2 Abstract 2

3 Amendments and Updates 3

Milestones 3

4 Rationale and Background 3

4.1 Research Questions 4

4.2 Objectives 5

5 Research methods 5

5.1 Study Design 5

5.1.1 Overview 5

5.1.2 Outcome Measures 5

5.1.3 Treatment Pathway 5

5.1.4 Second-Line Treatment Pathway Comparison 6

5.2 DiabetesTxPath Package 9

5.3 Expected Results 9

5.4 Data Sources 11

5.5 Appendix – A 11

# Abstract

Treatment guidelines for the management of type-2 diabetes mellitus (T2DM) are controversial because existing evidence from randomized clinical trials do not address many important clinical questions. An earlier investigation led by Observational Health Data Science (OHDSI) group reveled heterogeneity in the practice of both first and second line treatment choices in T2D with respect to established clinical guidelines. The choice of an optimal second line drug among available options (Sulfonylureas, DPP4-Inhibitors, Thiazolidinediones) remains ambiguous. In this study we seek to compare Sulfonylurea, DPP4-Inhibitors and Thiazolidinediones when prescribed after Metformin for outcomes related to reduction in HbA1c < 7%, events related to Myocardial Infarction, Kidney and Eye related disorders within OHDSI network.

# Amendments and Updates

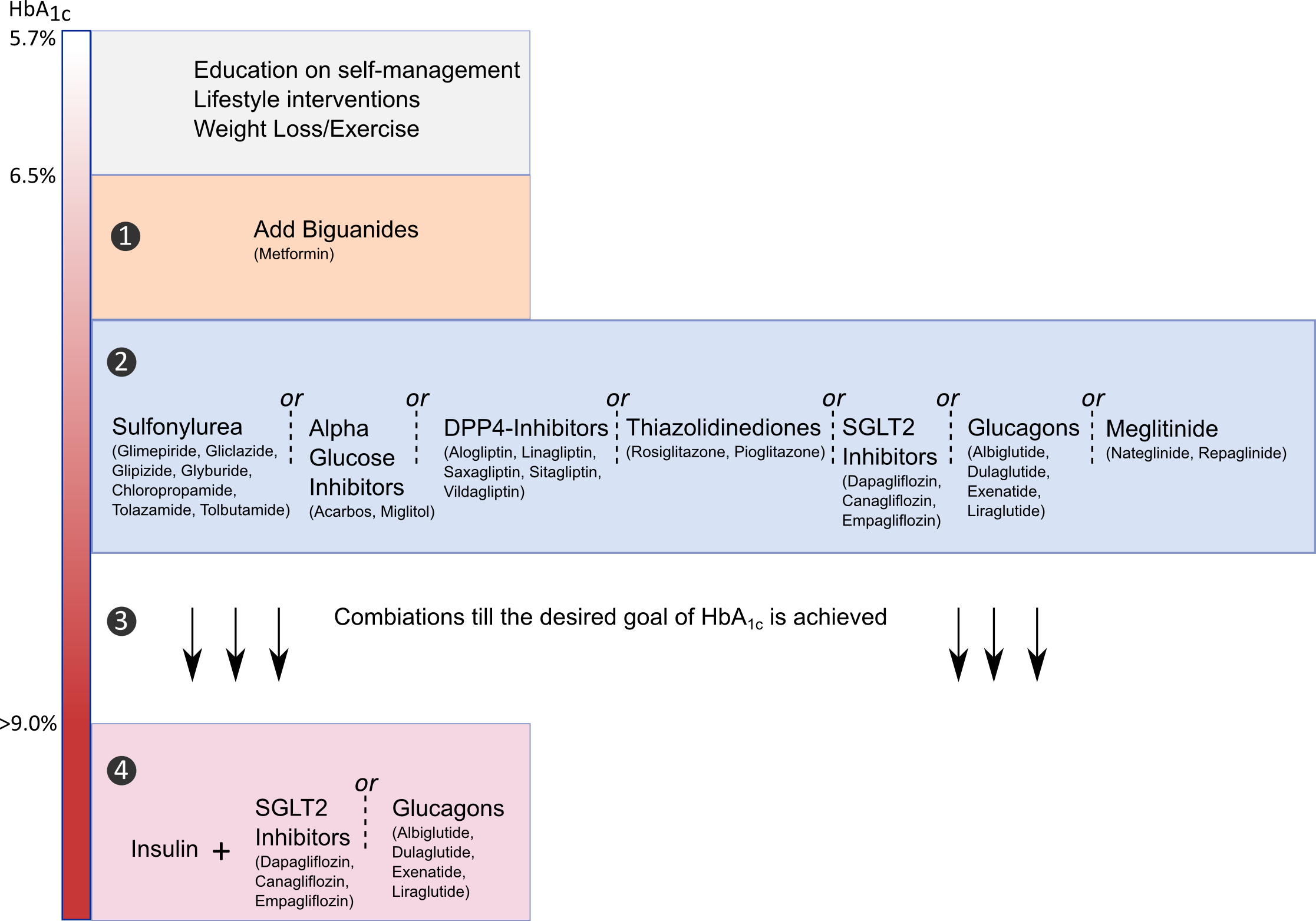
|  |  |  |  |
| --- | --- | --- | --- |
| 0.1 | 13 July 2017 | Rohit Vashisht, and Nigam Shah | Initial draft. |
| 0.2 |  |  |  |
| 0.3 |  |  |  |
| 0.4 |  |  |  |
| 0.5 |  |  |  |

# Milestones

|  |  |
| --- | --- |
| Milestone | Planned / Estimated Date |
| Start of analysis | July-2017 |
| End of analysis | As soon as possible |
| Posting of results | 30 days after analysis |
| Submission of manuscript | 60 days after final results |

# Rationale and Background

Type-2 diabetes (T2DM) affects an estimated 29.1 million people in the United States. Its global prevalence is projected to reach 440 million adults by the end of 2030. Current treatment guidelines **Fig.1**, which are derived from a few randomized controlled trials, recommend the use of metformin as first line mono-therapy. However, when metformin exhibits adverse effects or fails to control diabetes, the second line therapy must be chosen, and there is little consensus on how to choose a second line therapy; with the American Diabetes Association recommending sulfonylureas, meglitinide, pioglitazone or dipeptidyl peptidase 4 inhibitor (DPP4) as second-line agent, and the American Association of Clinical Endocrinologists recommending alpha-glucose inhibitors, DPP4 inhibitors and GLP-1 agonist. Given the availability of myriad treatment options for second-line therapy, the problem of selecting an optimal second-line agent requires urgent attention.



*Figure-1 T2D Treatment Guidelines: The consensus clinical guidelines for the treatment of T2D.*

An earlier investigation by OHDSI group, however, suggested plethora of variations in the practice of medication in T2D as compared to recommended guidelines. Analysis of data across multiple healthcare systems suggested that metformin alone was not the first choice of treatment therapy and other drugs belonging to drug classes such as Sulfonylureas, DPP4-Inhibitors, Meglitinide, Alpha-Glucose Inhibitors, Glucagon, SGLT2-Inhibitors and Thiazolidinediones were also prescribed as initial choice of therapy. Variations in the choices of second-line treatment were also observed. While the objective of the OHDSI’s earlier study was to investigate the patterns in practice of T2D medication, the questions pertaining to the clinical reasons behind variations in the practice of medicine and effectiveness of a given treatment pathways remains to be addressed.

## Research Questions

We aim to investigate the following research objective:

*Which one among Sulfonylurea, DPP4-Inhibitors and Thiazolidinediones when prescribed after Metformin is better in reducing HbA1c < 7% and have fewer incidence related to Myocardial Infarction (MI), Kidney (KD) and Eye (ED) related disorders.*

## Objectives

Primary objective

Utilize observational health care data across multiple healthcare systems to understand the efficacy of Sulfonylurea, DPP4-Inhibitors and Thiazolidinediones when prescribed after Metformin

# Research methods

## Study Design

### Overview

This is a retrospective, observational study. We will use the pre-recorded observational healthcare data across multiple sites to build study cohorts, mainly a treatment cohort, a comparator cohort and an outcome cohort(s) for each combination of drugs as follows:

1. Biguanides (Metformin)
2. Sulfonylureas (Glimepiride, Gliclazide, Glipizide, Glyburide, Chlorpropamide, Tolazamide, Tolbutamide)
3. DPP4-Inhibitors (Alogliptin, Linagliptin, Saxagliptin, Sitagliptin, Vildagliptin)
4. Thiazolidinediones (Rosiglitazone, Pioglitazone)

### Outcome Measures

The outcome measures are defined as a primary outcome and secondary outcome. The levels of HbA1c below or equal to 7% is defined as primary outcome, whereas occurrence of events related to myocardial infraction (MI), kidney related disorders (KD) and eyes related disorders (ED) are defined as secondary outcome measures. For HbA1c the patients will be selected based on their reported HbA1c values (HbA1c concept Id). For myocardial infraction the patients will be select based on occurrence of myocardial infraction related concept IDs as observed in a patients record. Similarly for the kidney related disorders and eyes related disorders the patients were selected based on any occurrence of these events in their record. A detailed list of concept IDs used for HbA1c, MI, KD and ED is provided in the Appendix-A.

### Treatment Pathway

A treatment pathway can be defined as the medication trajectory of a given patient. In principle, a treatment pathway can be of any length, where length is the total number of unique prescriptions that are found in a patients record. For example, in case of a single T2D patient, her/his treatment pathway can be defined as a sequence in which T2D medication was prescribed. If Biguanide was prescribed as initial prescription followed by say Sulfonylurea followed by DPP4-Inhibitors then the treatment pathway for this patient would be Biguanide-to-Sulfonylurea-to-DPP4-Inhibitors. Similarly, if the initial prescription of patient was Sulfonylurea, which was then followed by DPP4-Inhibitors and followed by Biguanides then the treatment pathway of the patient will be defined as Sulfonylurea-to-DPP4-Inhibitors-to-Biguanides. Depending on the total number of unique drugs in a given treatment pathway one can build *first-line*, *second-line*, *third-line* etc. treatment pathways.

In this study we propose to investigate *second-line* treatment pathways. A *second-line treatment pathway* can be defined as sequence representing combination of two drugs in the medication trajectory of a given patient. For example, when Biguanide is the first drug and Sulfonylurea is prescribed later, then the resulting combination would represent a second-line treatment pathway as Biguanide-to-Sulfonylurea. A complete list of resulting second-line treatment pathways is provided in **Table-1**.

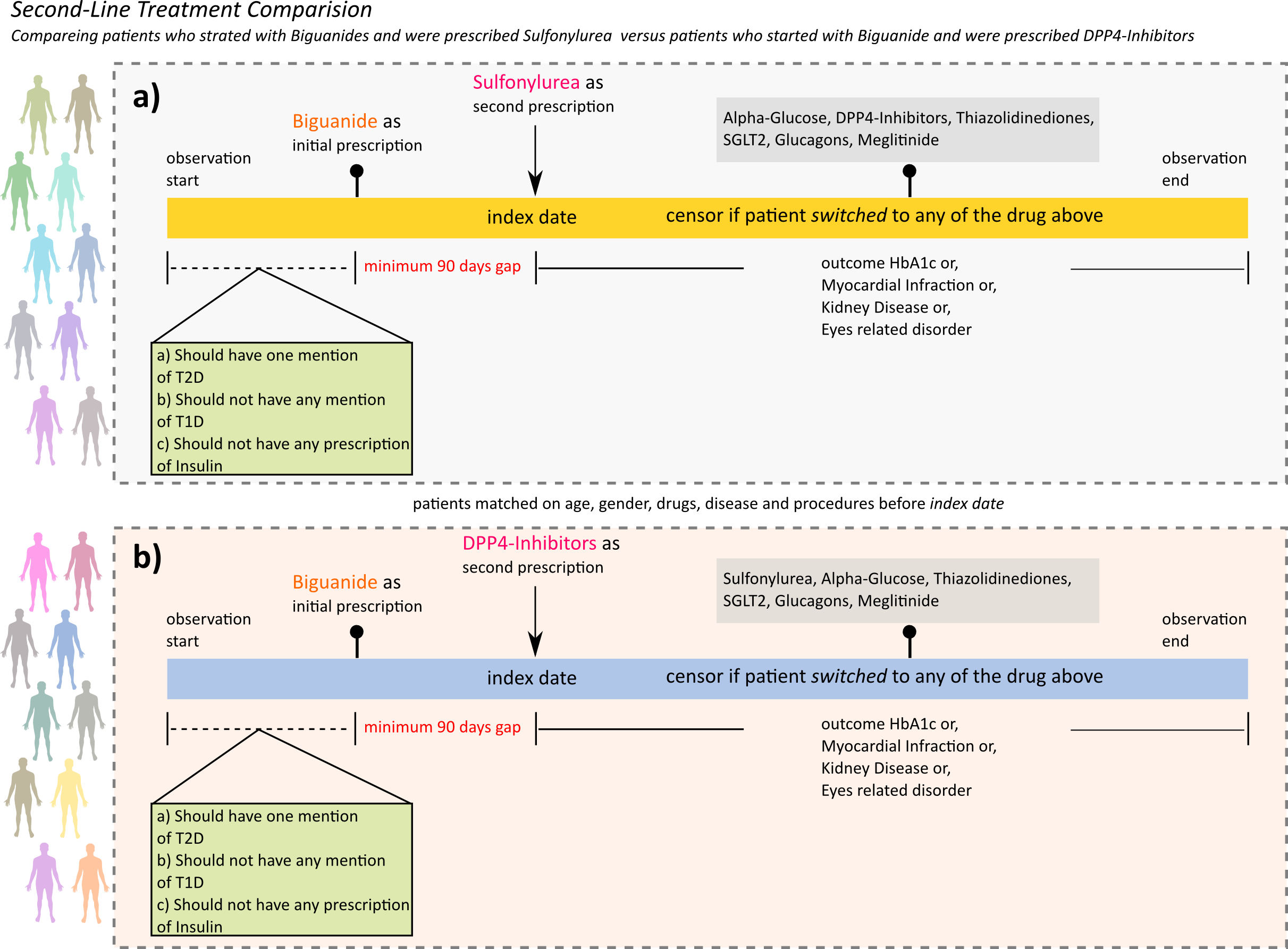
|  |  |
| --- | --- |
| *Second-Line Treatment Pathway* |  |
| Biguanide-to-Sulfonylurea | Patients who started with Biguanide and switched to Sulfonylurea later |
| Biguanide-to-DPP4 Inhibitor | Patients who started with Biguanides and switched to DPP4 Inhibitors later |
| Biguanides-to-Thiazolidinedione | Patients who started with Biguanides and switched to Thiazolidinedione later |
|  |  |

*Table-1 List of second-line treatment pathways considered in this study.*

### Second-Line Treatment Pathway Comparison

We propose to compare the efficacy of a given second-line treatment pathway. The rationale behind doing this is to compare which of the second-line drug among Sulfonylurea, Dpp4-Inhibitors and Thiazolidinedione’s performed better in controlling HbA1c below 7% and have fewer adverse events related to MI, KD and ED when prescribed after Biguanides. An example of comparing Biguanide-to-Sulfonylureas and Biguanide-to-DPP4-Inhibitors as best second-line treatment is illustrated in **Fig. 2(a, b)** respectively. **Fig. 2(a)** represents cohort construction of Biguanide-to-Sulfonylurea. Patients will be selected based on following conditions **(Fig. 2(a))**:

1. All the patients with the first prescription of Sulfonylurea will be selected. The date of prescription will be considered as *index date.*
2. Patients should have at-least one prescription of Biguanides at-least 90 days before the index date.
3. Patients should not have any prescription of other drugs among Alpha-Glucose inhibitors, Dpp4-Inhibitors, Thiazolidinedione’s, SGLT2-Inhibitors, Glucagones and Meglitinide before the index date.
4. Patients should not have any prescription of Insulin before the index date.
5. Patients should have at-least one mention of T2D before the index date.
6. There should not be any mention of T1D before the index date.
7. Patients will be censored if the prescription of any third drug among Alpha-Glucose inhibitors or Dpp4-Inhibitors or Thiazolidinedione’s or SGLT2-Inhibitors or Glucagones or Meglitinide is noted post-index date.
8. The outcome HbA1c <= 7%, MI, KD and ED are defined as first occurrences of these events post-index date.



*Figure-2: Cohort construction for second-line treatment comparison: a) Cohort construction condition for Biguanide-to-Sulfonylurea as second-line treatment pathway b) Cohort construction conditions for Biguanide-to-DPP4-Inhibitors as second-line treatment pathway.*

Similarly **Fig. 2(b)** represents the cohort construction process for the second-line treatment pathway represented by Biguanide-to-DPP4-Inhibitors. Patients will be selected based on following conditions **(Fig. 2(b))**:

1. All the patients with the prescription of DPP4-Inhibitors will be selected. The date at which DPP4-Inhibitors was prescribed will be considered as the *index date*.
2. Patients should have at-least one prescription of Biguanides at-least 90 days prior to the index date.
3. Patients should not have any prescription of other drugs among Sulfonylurea, Alpha-Glucose inhibitors, Thiazolidinedione’s, SGLT2-Inhibitors, Glucagones and Meglitinide before the index date.
4. There should not be any prescription of Insulin before the index date.
5. There should be at-least one mention of T2D before the index date.
6. There should not be any mention of T1D before the index date.
7. Patients will be censored based on the prescription of any third drug among Sulfonylurea, Alpha-Glucose inhibitors, Thiazolidinedione’s, SGLT2-Inhibitors, Glucagones and Meglitinide before end of complete observation.
8. The outcome HbA1c <= 7%, MI, KD and ED are defined as first occurrences of these events post-index date.

The two second-line treatment pathways thus constructed **(Fig. 2(a, b))** can be considered for analysis within CohortMethod pipeline. Towards this, in principle, one can considerer any of the second-line treatment pathway between Biguanide-to-Sulfonylurea and Biguanide-to-DPP4-Inhibitors as a treatment or a comparator cohort and perform the analysis. The Outcome cohorts are defined separately and remain same for all the combinations of second-line treatment pathway comparisons. The complete list of second-line treatment pathway comparison as treatment and comparator cohorts along with their respective censoring conditions and ATLAS cohort Ids is provided in **Table-2**. The corresponding sql and json files are also provided in the accompanying R-Package DiabetesTxPath.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Treatment** | **Comparator** | **Censoring Treatment** | **Censoring Comparator** | **ATLAS Cohort-IDs** |
| Biguanide-to-Sulfonylurea | Biguanide-to-DPP4-Inhibitors | *Alpha-Glucose inhibitors, Dpp4-Inhibitors, Thiazolidinedione’s, SGLT2-Inhibitors, Glucagones and Meglitinide* | *Sulfonylurea, Alpha-Glucose inhibitors, Thiazolidinedione’s, SGLT2-Inhibitors, Glucagones and Meglitinide* | Treatment Cohort Id = 115012  Comparator Cohort Id = 115008  HbA1c Cohort Id = 105683  MI Cohort Id = 105684  KD Cohort Id = 105685  ED Cohort Id = 105686 |
| Biguanide-to-Sulfonylurea | Biguanide-to-Thiazolidinedione | *Alpha-Glucose inhibitors, Dpp4-Inhibitors, Thiazolidinedione’s, SGLT2-Inhibitors, Glucagones and Meglitinide* | *Sulfonylurea, Alpha-Glucose inhibitors, SGLT2 Inhibitors, Meglitinide, DPP4 Inhibitors and Glucagon* | Treatment Cohort Id = 115012  Comparator Cohort Id = 115013  HbA1c Cohort Id = 105683  MI Cohort Id = 105684  KD Cohort Id = 105685  ED Cohort Id = 105686 |

*Table-2 Treatment and comparator cohorts considered as second-line treatment comparisons in this study.*

## DiabetesTxPath Package

The proposed study can be executed with the help of DiabetesTxPath R package. A user needs to define the local database schema and a folder to save the results. Since we seek to compare first-line and second-line treatment options for 4 different outcomes, therefore one can provide the same while executing the study. The function runCompleteStudyTwoPath() can be used to execute the study as follows:

runCompleteStudyTwoPath(connectionDetails = connectionDetails,

cdmDatabaseSchema = cdmDatabaseSchema,

resultsDatabaseSchema = resultsDatabaseSchema,

cdmVersion = cdmVersion,

outComeId = 3,

outComeName = “HbA1c”)

**Important**

The outComeId are fixed are as follows:

1. outComeId = 3 will perform the analysis for HbA1c <= 7%
2. outComeId = 4 will perform the analysis for MI
3. outComeId = 5 will perform the analysis for KD
4. outComeId = 6 will perform the analysis for ED

Similarly, outComeName are fixed as follows:

1. outComeName = “HbA1c” should be used with outComeId = 3
2. outComeName = “MI’ should be used with outComeId = 4
3. outComeName = “KD” should be used with outComeId = 5
4. outComeName = “ED” should be used with outCOmeId = 6

**Very Important**

**This study will be performed if and only if both treatment and comparator cohorts have minimum 150 patients each.**

The package can be accessed at <https://github.com/rohit43/DiabetesTxPath>

## Expected Results

We propose to conduct this study with CohortMethod pipeline, which is integrated within DiabetesTxPath package. We anticipate to obtaine results accorss multiple sites under OHDSI framework. Specifically, we expect results in terms of relative risk and confidence intervals for all the combinations of second-line treatment comparision **(Table-2)** for each of the 4 outcomes (HbA1c <= 7%, MI, KD and ED) as proposed in this study. We also wish to obtain a) propensity score anslysis b) obtain clinical features and c) matching results for each of the first-line and second-line treatment comparision. The package DiabetesTxPath automates the process of results generation. We propose to collate the results across multiple health care systems for each of the outcome as illustrated in **Table-3** for HbA1c only. Please note, the structure of Table-4 remains same for other outcomes such as MI, KD and ED.

|  |  |  |  |
| --- | --- | --- | --- |
| **Treatment Comparison** | **RR(CI)-Stanford** | **RR(CI)-Site 2** | **RR(CI)-Site n** |
| **BiguanideToSulfonylurea-and-BiguanideToDpp4Inhibitor** |  |  |  |
| **BiguanideToSulfonylurea-and-BiguanideToThiazolidinedione** |  |  |  |

**Table – 3** Outcome measure HbA1c < 7%. RR(CI)-Stanford represent the relative risk as obtained by CohortMethod on Stanford data. Red are the First-Line Treatment Comparisions and Black are the Second-line Treatment Comparisions. The R-Package DiabetesTxPath will generate this table as csv files.

## Data Sources

The analyses will be performed across a network of observational healthcare databases. All databases have been transformed into the OMOP Common Data Model, version 5 or OMOP Common Data Model, version 5. The complete specification for OMOP Common Data Model, version 4 is available at: <http://omop.org/cdm>. The complete specification for OMOP Common Data Model, version 5 is available at: <https://github.com/OHDSI/CommonDataModel>. The following databases will be included in this analysis:

* Stanford STRIDE
* Others …

## Appendix – A

Concept ID’s used for outcomes a) HbA1c b) Myocardial infraction c) Kidney related disorder d) Eyes related disorder.

**Concept-IDs for HbA1c**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Name | Concept ID | Concept Code | Concept Name | Domain | Vocabulary | Standard Concept |
| HbA1c\_v2 | 3004410 | 4548-4 | Hemoglobin A1c (Glycated) | Measurement | LOINC | S |
| HbA1c\_v2 | 3007263 | 17855-8 | Hemoglobin A1c/Hemoglobin.total in Blood by calculation | Measurement | LOINC | S |
| HbA1c\_v2 | 3003309 | 4549-2 | Hemoglobin A1c/Hemoglobin.total in Blood by Electrophoresis | Measurement | LOINC | S |
| HbA1c\_v2 | 3005673 | 17856-6 | Hemoglobin A1c/Hemoglobin.total in Blood by HPLC | Measurement | LOINC | S |
| HbA1c\_v2 | 40762352 | 59261-8 | Hemoglobin A1c/Hemoglobin.total in Blood by IFCC protocol | Measurement | LOINC | S |
| HbA1c\_v2 | 40758583 | 55454-3 | Hemoglobin A1c in Blood | Measurement | LOINC | S |
| HbA1c\_v2 | 3034639 | 41995-2 | Hemoglobin A1c [Mass/volume] in Blood | Measurement | LOINC | S |

**Concept ID’s for Myocardial Infraction**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Name | Concept ID | Concept Code | Concept Name | Domain | Vocabulary | Standard Concept |
| MI\_v2 | 45766075 | 703164000 | Acute anterior ST segment elevation myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4178129 | 52035003 | Acute anteroapical myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4267568 | 62695002 | Acute anteroseptal myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 44784623 | 7.8741E+13 | Acute coronary artery occlusion not resulting in myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 312327 | 57054005 | Acute myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 44782769 | 1.7531E+13 | Acute myocardial infarction due to left coronary artery occlusion | Condition | SNOMED | S |
| MI\_v2 | 44782712 | 2.3311E+13 | Acute myocardial infarction due to right coronary artery occlusion | Condition | SNOMED | S |
| MI\_v2 | 45766115 | 703212004 | Acute myocardial infarction during procedure | Condition | SNOMED | S |
| MI\_v2 | 434376 | 54329005 | Acute myocardial infarction of anterior wall | Condition | SNOMED | S |
| MI\_v2 | 45766150 | 703252002 | Acute myocardial infarction of anterior wall involving right ventricle | Condition | SNOMED | S |
| MI\_v2 | 438438 | 70211005 | Acute myocardial infarction of anterolateral wall | Condition | SNOMED | S |
| MI\_v2 | 4243372 | 59063002 | Acute myocardial infarction of apical-lateral wall | Condition | SNOMED | S |
| MI\_v2 | 4108669 | 194809007 | Acute myocardial infarction of atrium | Condition | SNOMED | S |
| MI\_v2 | 4151046 | 282006 | Acute myocardial infarction of basal-lateral wall | Condition | SNOMED | S |
| MI\_v2 | 4275436 | 64627002 | Acute myocardial infarction of high lateral wall | Condition | SNOMED | S |
| MI\_v2 | 438170 | 73795002 | Acute myocardial infarction of inferior wall | Condition | SNOMED | S |
| MI\_v2 | 45771322 | 703251009 | Acute myocardial infarction of inferior wall involving right ventricle | Condition | SNOMED | S |
| MI\_v2 | 438447 | 65547006 | Acute myocardial infarction of inferolateral wall | Condition | SNOMED | S |
| MI\_v2 | 441579 | 76593002 | Acute myocardial infarction of inferoposterior wall | Condition | SNOMED | S |
| MI\_v2 | 436706 | 58612006 | Acute myocardial infarction of lateral wall | Condition | SNOMED | S |
| MI\_v2 | 4324413 | 70998009 | Acute myocardial infarction of posterobasal wall | Condition | SNOMED | S |
| MI\_v2 | 4051874 | 15990001 | Acute myocardial infarction of posterolateral wall | Condition | SNOMED | S |
| MI\_v2 | 4303359 | 79009004 | Acute myocardial infarction of septum | Condition | SNOMED | S |
| MI\_v2 | 4147223 | 30277009 | Acute myocardial infarction with rupture of ventricle | Condition | SNOMED | S |
| MI\_v2 | 4270024 | 401314000 | Acute non-ST segment elevation myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 319039 | 233838001 | Acute posterior myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4126801 | 304914007 | Acute Q wave myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4296653 | 401303003 | Acute ST segment elevation myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 46270162 | 1.57131E+16 | Acute ST segment elevation myocardial infarction due to left coronary artery occlusion | Condition | SNOMED | S |
| MI\_v2 | 46270163 | 1.57131E+16 | Acute ST segment elevation myocardial infarction due to right coronary artery occlusion | Condition | SNOMED | S |
| MI\_v2 | 43020460 | 2.85981E+14 | Acute ST segment elevation myocardial infarction involving left anterior descending coronary artery | Condition | SNOMED | S |
| MI\_v2 | 43020461 | 2.85991E+14 | Acute ST segment elevation myocardial infarction involving left main coronary artery | Condition | SNOMED | S |
| MI\_v2 | 45766076 | 703165004 | Acute ST segment elevation myocardial infarction of anterior wall involving right ventricle | Condition | SNOMED | S |
| MI\_v2 | 46270159 | 1.57129E+16 | Acute ST segment elevation myocardial infarction of anterolateral wall | Condition | SNOMED | S |
| MI\_v2 | 46270160 | 1.5713E+16 | Acute ST segment elevation myocardial infarction of anteroseptal wall | Condition | SNOMED | S |
| MI\_v2 | 45766116 | 703213009 | Acute ST segment elevation myocardial infarction of inferior wall | Condition | SNOMED | S |
| MI\_v2 | 45766151 | 703253007 | Acute ST segment elevation myocardial infarction of inferior wall involving right ventricle | Condition | SNOMED | S |
| MI\_v2 | 46274044 | 1.57129E+16 | Acute ST segment elevation myocardial infarction of lateral wall | Condition | SNOMED | S |
| MI\_v2 | 46270161 | 1.5713E+16 | Acute ST segment elevation myocardial infarction of posterior wall | Condition | SNOMED | S |
| MI\_v2 | 46273495 | 1.57132E+16 | Acute ST segment elevation myocardial infarction of posterobasal wall | Condition | SNOMED | S |
| MI\_v2 | 46270158 | 1.57128E+16 | Acute ST segment elevation myocardial infarction of posterolateral wall | Condition | SNOMED | S |
| MI\_v2 | 46270164 | 1.57132E+16 | Acute ST segment elevation myocardial infarction of septum | Condition | SNOMED | S |
| MI\_v2 | 4119947 | 233835003 | Acute widespread myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4329847 | 22298006 | Myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4170094 | 418044006 | Myocardial infarction in recovery phase | Condition | SNOMED | S |
| MI\_v2 | 4154704 | 371068009 | Myocardial infarction with complication | Condition | SNOMED | S |
| MI\_v2 | 4179525 | 429391004 | New myocardial infarction compared to prior study | Condition | SNOMED | S |
| MI\_v2 | 4200113 | 314207007 | Non-Q wave myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4119949 | 233839009 | Old anterior myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4121467 | 233840006 | Old inferior myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4119950 | 233841005 | Old lateral myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 314666 | 1755008 | Old myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4121468 | 233842003 | Old posterior myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4322145 | 71023004 | Pericarditis secondary to acute myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 319038 | 66189004 | Postmyocardial infarction syndrome | Condition | SNOMED | S |
| MI\_v2 | 4030582 | 129574000 | Postoperative myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4206867 | 311796008 | Postoperative subendocardial myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4207921 | 311792005 | Postoperative transmural myocardial infarction of anterior wall | Condition | SNOMED | S |
| MI\_v2 | 4209541 | 311793000 | Postoperative transmural myocardial infarction of inferior wall | Condition | SNOMED | S |
| MI\_v2 | 4108679 | 194865003 | Rupture of cardiac wall without hemopericardium as current complication following acute myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4108219 | 194866002 | Rupture of chordae tendinae as current complication following acute myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4108220 | 194867006 | Rupture of papillary muscle as current complication following acute myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4124686 | 233843008 | Silent myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4108217 | 194856005 | Subsequent myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 4108677 | 194857001 | Subsequent myocardial infarction of anterior wall | Condition | SNOMED | S |
| MI\_v2 | 4108218 | 194858006 | Subsequent myocardial infarction of inferior wall | Condition | SNOMED | S |
| MI\_v2 | 45766241 | 703360004 | Subsequent non-ST segment elevation myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 45766114 | 703211006 | Subsequent ST segment elevation myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 45766113 | 703210007 | Subsequent ST segment elevation myocardial infarction of anterior wall | Condition | SNOMED | S |
| MI\_v2 | 45773170 | 703209002 | Subsequent ST segment elevation myocardial infarction of inferior wall | Condition | SNOMED | S |
| MI\_v2 | 4108680 | 194868001 | Thrombosis of atrium, auricular appendage, and ventricle as current complications following acute myocardial infarction | Condition | SNOMED | S |
| MI\_v2 | 439693 | 194802003 | True posterior myocardial infarction | Condition | SNOMED | S |

**Concept Id’s for Kidney Related Disorders**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Name | Concept ID | Concept Code | Concept Name | Domain | Vocabulary | Standard Concept |
| KD\_v2 | 4323988 | 71064009 | Acquired polycystic kidney disease | Condition | SNOMED | S |
| KD\_v2 | 4109637 | 253878003 | Adult type polycystic kidney disease type 1 | Condition | SNOMED | S |
| KD\_v2 | 4109809 | 253879006 | Adult type polycystic kidney disease type 2 | Condition | SNOMED | S |
| KD\_v2 | 4109022 | 253880009 | Autosomal dominant polycystic kidney disease in childhood | Condition | SNOMED | S |
| KD\_v2 | 43531578 | 7.71E+11 | Chronic kidney disease due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 443614 | 431855005 | Chronic kidney disease stage 1 | Condition | SNOMED | S |
| KD\_v2 | 43531559 | 7.51E+11 | Chronic kidney disease stage 1 due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 443601 | 431856006 | Chronic kidney disease stage 2 | Condition | SNOMED | S |
| KD\_v2 | 43531566 | 7.41E+11 | Chronic kidney disease stage 2 due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 443597 | 433144002 | Chronic kidney disease stage 3 | Condition | SNOMED | S |
| KD\_v2 | 45763854 | 700378005 | Chronic kidney disease stage 3A | Condition | SNOMED | S |
| KD\_v2 | 45763855 | 700379002 | Chronic kidney disease stage 3B | Condition | SNOMED | S |
| KD\_v2 | 43531653 | 7.31E+11 | Chronic kidney disease stage 3 due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 443612 | 431857002 | Chronic kidney disease stage 4 | Condition | SNOMED | S |
| KD\_v2 | 43531577 | 7.21E+11 | Chronic kidney disease stage 4 due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 443611 | 433146000 | Chronic kidney disease stage 5 | Condition | SNOMED | S |
| KD\_v2 | 43531562 | 7.11E+11 | Chronic kidney disease stage 5 due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 46271022 | 709044004 | CKD - chronic kidney disease | Condition | SNOMED | S |
| KD\_v2 | 46284566 | 9.49401E+14 | CKD G1A1 - chronic kidney disease with glomerular filtration rate category G1 and albuminuria category A1 | Condition | SNOMED | S |
| KD\_v2 | 46284567 | 9.49421E+14 | CKD G1A2 - chronic kidney disease with glomerular filtration rate category G1 and albuminuria category A2 | Condition | SNOMED | S |
| KD\_v2 | 46284570 | 9.49481E+14 | CKD G1A3 - chronic kidney disease with glomerular filtration rate category G1 and albuminuria category A3 | Condition | SNOMED | S |
| KD\_v2 | 46284572 | 9.49521E+14 | CKD G2A1 - chronic kidney disease with glomerular filtration rate category G2 and albuminuria category A1 | Condition | SNOMED | S |
| KD\_v2 | 46287169 | 9.49561E+14 | CKD G2A2 - chronic kidney disease with glomerular filtration rate category G2 and albuminuria category A2 | Condition | SNOMED | S |
| KD\_v2 | 46284575 | 9.49621E+14 | CKD G2A3 - chronic kidney disease with glomerular filtration rate category G2 and albuminuria category A3 | Condition | SNOMED | S |
| KD\_v2 | 46284587 | 9.49881E+14 | CKD G3aA1 - chronic kidney disease with glomerular filtration rate category G3a and albuminuria category A1 | Condition | SNOMED | S |
| KD\_v2 | 46286992 | 9.49901E+14 | CKD G3aA2 - chronic kidney disease with glomerular filtration rate category G3a and albuminuria category A2 | Condition | SNOMED | S |
| KD\_v2 | 46284588 | 9.49921E+14 | CKD G3aA3 - chronic kidney disease with glomerular filtration rate category G3a and albuminuria category A3 | Condition | SNOMED | S |
| KD\_v2 | 46284591 | 9.50061E+14 | CKD G3bA1 - chronic kidney disease with glomerular filtration rate category G3b and albuminuria category A1 | Condition | SNOMED | S |
| KD\_v2 | 46284592 | 9.50081E+14 | CKD G3bA2 - chronic kidney disease with glomerular filtration rate category G3b and albuminuria category A2 | Condition | SNOMED | S |
| KD\_v2 | 46284593 | 9.50101E+14 | CKD G3bA3 - chronic kidney disease with glomerular filtration rate category G3b and albuminuria category A3 | Condition | SNOMED | S |
| KD\_v2 | 46284597 | 9.50181E+14 | CKD G4A1 - chronic kidney disease with glomerular filtration rate category G4 and albuminuria category A1 | Condition | SNOMED | S |
| KD\_v2 | 46284598 | 9.50211E+14 | CKD G4A2 - chronic kidney disease with glomerular filtration rate category G4 and albuminuria category A2 | Condition | SNOMED | S |
| KD\_v2 | 46284599 | 9.50231E+14 | CKD G4A3 - chronic kidney disease with glomerular filtration rate category G4 and albuminuria category A3 | Condition | SNOMED | S |
| KD\_v2 | 46284600 | 9.50251E+14 | CKD G5A1 - chronic kidney disease with glomerular filtration rate category G5 and albuminuria category A1 | Condition | SNOMED | S |
| KD\_v2 | 46284602 | 9.50291E+14 | CKD G5A2 - chronic kidney disease with glomerular filtration rate category G5 and albuminuria category A2 | Condition | SNOMED | S |
| KD\_v2 | 46284603 | 9.50311E+14 | CKD G5A3 - chronic kidney disease with glomerular filtration rate category G5 and albuminuria category A3 | Condition | SNOMED | S |
| KD\_v2 | 198124 | 90708001 | Kidney disease | Condition | SNOMED | S |
| KD\_v2 | 40480635 | 444699000 | Medullary cystic kidney disease type 1 | Condition | SNOMED | S |
| KD\_v2 | 40483823 | 445503007 | Medullary cystic kidney disease type 2 | Condition | SNOMED | S |
| KD\_v2 | 436232 | 28728008 | Polycystic kidney disease, adult type | Condition | SNOMED | S |
| KD\_v2 | 201675 | 28770003 | Polycystic kidney disease, infantile type | Condition | SNOMED | S |
| KD\_v2 | 45771064 | 7.1421E+13 | Hypertension in chronic kidney disease due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 45757447 | 1.40131E+14 | Hypertension in chronic kidney disease stage 2 due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 45757446 | 1.40121E+14 | Hypertension in chronic kidney disease stage 3 due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 45757445 | 1.40111E+14 | Hypertension in chronic kidney disease stage 4 due to type 2 diabetes mellitus | Condition | SNOMED | S |
| KD\_v2 | 45757444 | 1.40101E+14 | Hypertension in chronic kidney disease stage 5 due to type 2 diabetes mellitus | Condition | SNOMED | S |

**Concept Id’s for Eyes Related Disorder**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Name | Concept ID | Concept Code | Concept Name | Domain | Vocabulary | Standard Concept |
| eyes\_v2 | 4196110 | 312947009 | Acute central serous chorioretinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4195495 | 314006008 | Acute central serous retinopathy with subretinal fluid | Condition | SNOMED | S |
| eyes\_v2 | 4210131 | 312929003 | Acute zonal occult outer retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4006784 | 111000003 | Adherent cataract | Condition | SNOMED | S |
| eyes\_v2 | 4338899 | 232017001 | Anterior proliferative vitreoretinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4199963 | 315352000 | Anterior subcapsular cataract | Condition | SNOMED | S |
| eyes\_v2 | 372315 | 1412008 | Anterior subcapsular polar cataract | Condition | SNOMED | S |
| eyes\_v2 | 375256 | 111515007 | Anterior subcapsular polar senile cataract | Condition | SNOMED | S |
| eyes\_v2 | 4318983 | 95691008 | Arteriosclerotic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4105159 | 2951009 | Atopic cataract | Condition | SNOMED | S |
| eyes\_v2 | 4007451 | 110998005 | Axial cataract | Condition | SNOMED | S |
| eyes\_v2 | 4208203 | 312927001 | Bietti's crystalline retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4317977 | 95722004 | Bilateral cataracts | Condition | SNOMED | S |
| eyes\_v2 | 4001501 | 10970008 | Calcified cataract | Condition | SNOMED | S |
| eyes\_v2 | 4070182 | 204124004 | Capsular and/or subcapsular cataract | Condition | SNOMED | S |
| eyes\_v2 | 4070183 | 204125003 | Capsular cataract | Condition | SNOMED | S |
| eyes\_v2 | 375545 | 193570009 | Cataract | Condition | SNOMED | S |
| eyes\_v2 | 4301387 | 77873007 | Cataracta brunescens | Condition | SNOMED | S |
| eyes\_v2 | 381566 | 193602009 | Cataract in eye inflammatory disorder | Condition | SNOMED | S |
| eyes\_v2 | 376973 | 193600001 | Cataract secondary to ocular disease | Condition | SNOMED | S |
| eyes\_v2 | 372894 | 312956001 | Central serous chorioretinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4338904 | 232034009 | Central serous retinopathy with pit of optic disc | Condition | SNOMED | S |
| eyes\_v2 | 4195496 | 314009001 | Central serous retinopathy with small retinal pigment epithelial detachment | Condition | SNOMED | S |
| eyes\_v2 | 4208201 | 312923002 | Chronic central serous chorioretinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4199038 | 314007004 | Chronic central serous retinopathy with diffuse retinal pigment epithelial detachment | Condition | SNOMED | S |
| eyes\_v2 | 4219330 | 39944005 | Combined form of nonsenile cataract | Condition | SNOMED | S |
| eyes\_v2 | 376400 | 11422002 | Combined form of senile cataract | Condition | SNOMED | S |
| eyes\_v2 | 375546 | 193579005 | Combined nonsenile cataract | Condition | SNOMED | S |
| eyes\_v2 | 4008296 | 12195004 | Coronary cataract | Condition | SNOMED | S |
| eyes\_v2 | 378534 | 204127006 | Cortical and zonular cataract | Condition | SNOMED | S |
| eyes\_v2 | 4103579 | 193576003 | Cortical cataract | Condition | SNOMED | S |
| eyes\_v2 | 44783428 | 699521008 | Cortical nonsenile cataract | Condition | SNOMED | S |
| eyes\_v2 | 432895 | 78875003 | Cortical senile cataract | Condition | SNOMED | S |
| eyes\_v2 | 4221495 | 420756003 | Diabetic cataract associated with type 2 diabetes mellitus | Condition | SNOMED | S |
| eyes\_v2 | 4174977 | 4855003 | Diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4226121 | 422034002 | Diabetic retinopathy associated with type 2 diabetes mellitus | Condition | SNOMED | S |
| eyes\_v2 | 4109548 | 193609000 | Drug-induced cataract | Condition | SNOMED | S |
| eyes\_v2 | 4334886 | 232032008 | Drug-induced retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4164176 | 399869005 | High risk proliferative diabetic retinopathy not amenable to photocoagulation | Condition | SNOMED | S |
| eyes\_v2 | 379811 | 267626000 | Hypermature cataract | Condition | SNOMED | S |
| eyes\_v2 | 45757567 | 2.17791E+14 | Hypermature senile cataract | Condition | SNOMED | S |
| eyes\_v2 | 40487893 | 446474007 | Immature cataract | Condition | SNOMED | S |
| eyes\_v2 | 4210432 | 311789006 | Immature cortical cataract | Condition | SNOMED | S |
| eyes\_v2 | 44812346 | 3.73041E+14 | Impaired vision due to diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4195051 | 312924008 | Inactive central serous chorioretinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4210871 | 314008009 | Inactive central serous retinopathy with focal retinal pigment epithelial detachment | Condition | SNOMED | S |
| eyes\_v2 | 376399 | 52421005 | Incipient cataract | Condition | SNOMED | S |
| eyes\_v2 | 40482507 | 445213003 | Incipient senile cataract | Condition | SNOMED | S |
| eyes\_v2 | 45770919 | 3.42291E+14 | Infantile and/or juvenile cataract | Condition | SNOMED | S |
| eyes\_v2 | 4220818 | 399120006 | Infantile cataract | Condition | SNOMED | S |
| eyes\_v2 | 373770 | 193571008 | Infantile, juvenile and presenile cataracts | Condition | SNOMED | S |
| eyes\_v2 | 4319589 | 95724003 | Intumescent cataract | Condition | SNOMED | S |
| eyes\_v2 | 4161420 | 399336001 | Juvenile cataract | Condition | SNOMED | S |
| eyes\_v2 | 4109424 | 193577007 | Lamellar zonular cataract | Condition | SNOMED | S |
| eyes\_v2 | 45770830 | 9.7331E+13 | Macular edema and retinopathy due to type 2 diabetes mellitus | Condition | SNOMED | S |
| eyes\_v2 | 377285 | 849000 | Mature cataract | Condition | SNOMED | S |
| eyes\_v2 | 378743 | 312903003 | Mild non-proliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 45757435 | 1.38911E+14 | Mild nonproliferative retinopathy due to type 2 diabetes mellitus | Condition | SNOMED | S |
| eyes\_v2 | 4152554 | 314766004 | Mixed type cataract | Condition | SNOMED | S |
| eyes\_v2 | 377552 | 312904009 | Moderate nonproliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 45770881 | 1.38921E+14 | Moderate nonproliferative retinopathy due to type 2 diabetes mellitus | Condition | SNOMED | S |
| eyes\_v2 | 4130588 | 264443002 | Morgagnian cataract | Condition | SNOMED | S |
| eyes\_v2 | 4199942 | 315288007 | Necrotizing herpetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 377274 | 399305009 | Nonsenile cataract | Condition | SNOMED | S |
| eyes\_v2 | 373769 | 53889007 | Nuclear cataract | Condition | SNOMED | S |
| eyes\_v2 | 4230391 | 359766000 | Nuclear sclerotic cataract | Condition | SNOMED | S |
| eyes\_v2 | 439297 | 193589009 | Nuclear senile cataract | Condition | SNOMED | S |
| eyes\_v2 | 4235260 | 408410002 | O/E - left eye background diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4255400 | 408412005 | O/E - left eye preproliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4252356 | 408414006 | O/E - left eye proliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4215961 | 414894003 | O/E - left eye stable treated proliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4252215 | 408313004 | O/E - non-referable retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4246964 | 408312009 | O/E - referable retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4255281 | 408311002 | O/E - retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4247107 | 408409007 | O/E - right eye background diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4255399 | 408411003 | O/E - right eye preproliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4255401 | 408413000 | O/E - right eye proliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4212441 | 414910007 | O/E - right eye stable treated proliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4218499 | 417677008 | O/E - sight threatening diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4048060 | 123614006 | Partial cataract | Condition | SNOMED | S |
| eyes\_v2 | 4335999 | 232018006 | Posterior proliferative vitreoretinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4197734 | 315353005 | Posterior subcapsular cataract | Condition | SNOMED | S |
| eyes\_v2 | 436976 | 34533008 | Posterior subcapsular polar cataract | Condition | SNOMED | S |
| eyes\_v2 | 438749 | 5318001 | Posterior subcapsular polar senile cataract | Condition | SNOMED | S |
| eyes\_v2 | 4323127 | 70388009 | Postoperative cataract syndrome | Condition | SNOMED | S |
| eyes\_v2 | 4105172 | 193349004 | Preproliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 40479994 | 441622000 | Presenile cataract | Condition | SNOMED | S |
| eyes\_v2 | 380096 | 59276001 | Proliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 43530685 | 1.501E+12 | Proliferative diabetic retinopathy due to type 2 diabetes mellitus | Condition | SNOMED | S |
| eyes\_v2 | 45757065 | 1.03981E+14 | Proliferative diabetic retinopathy following surgery | Condition | SNOMED | S |
| eyes\_v2 | 4195043 | 312907002 | Proliferative diabetic retinopathy - high risk | Condition | SNOMED | S |
| eyes\_v2 | 4266042 | 399874002 | Proliferative diabetic retinopathy - high risk with clinically significant macular edema | Condition | SNOMED | S |
| eyes\_v2 | 4164174 | 399862001 | Proliferative diabetic retinopathy - high risk with no macular edema | Condition | SNOMED | S |
| eyes\_v2 | 4195044 | 312909004 | Proliferative diabetic retinopathy - iris neovascularization | Condition | SNOMED | S |
| eyes\_v2 | 4210128 | 312906006 | Proliferative diabetic retinopathy - non high risk | Condition | SNOMED | S |
| eyes\_v2 | 4210129 | 312908007 | Proliferative diabetic retinopathy - quiescent | Condition | SNOMED | S |
| eyes\_v2 | 4336000 | 232022001 | Proliferative diabetic retinopathy with new vessels elsewhere than on disc | Condition | SNOMED | S |
| eyes\_v2 | 4338900 | 232021008 | Proliferative diabetic retinopathy with new vessels on disc | Condition | SNOMED | S |
| eyes\_v2 | 45757798 | 4.30801E+14 | Proliferative retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4109401 | 193370005 | Proliferative retinopathy due to sickle cell disease | Condition | SNOMED | S |
| eyes\_v2 | 45763584 | 6.0971E+13 | Proliferative retinopathy due to type 1 diabetes mellitus | Condition | SNOMED | S |
| eyes\_v2 | 45770831 | 9.7341E+13 | Proliferative retinopathy with retinal edema due to type 2 diabetes mellitus | Condition | SNOMED | S |
| eyes\_v2 | 4335998 | 232016005 | Proliferative vitreoretinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4230930 | 40714009 | Punctate cataract | Condition | SNOMED | S |
| eyes\_v2 | 4336003 | 232030000 | Purtscher's retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4208211 | 312960003 | Quinine retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 376103 | 399625000 | Retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 376114 | 312905005 | Severe nonproliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4290822 | 399872003 | Severe nonproliferative diabetic retinopathy with clinically significant macular edema | Condition | SNOMED | S |
| eyes\_v2 | 4266637 | 399873008 | Severe nonproliferative diabetic retinopathy with no macular edema | Condition | SNOMED | S |
| eyes\_v2 | 4088107 | 247064005 | Shrunken cataract | Condition | SNOMED | S |
| eyes\_v2 | 4007944 | 110999002 | Stationary cataract | Condition | SNOMED | S |
| eyes\_v2 | 4269871 | 399876000 | Very severe nonproliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4290823 | 399877009 | Very severe nonproliferative diabetic retinopathy with clinically significant macular edema | Condition | SNOMED | S |
| eyes\_v2 | 4221962 | 399863006 | Very severe nonproliferative diabetic retinopathy with no macular edema | Condition | SNOMED | S |
| eyes\_v2 | 4164632 | 399865004 | Very severe proliferative diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 4266041 | 399871005 | Visually threatening diabetic retinopathy | Condition | SNOMED | S |
| eyes\_v2 | 46272745 | 711162004 | Vitreoretinochoroidopathy with microcornea, glaucoma and cataract | Condition | SNOMED | S |