

**Appendix 2: Cohort table and diagnosis codes**

Steps	Selection Criteria	HbA1c value < 7%	HbA1C value <7.5%
		(Base Case)	(Sensitivity Analysis 1)
0	Patients with Type 2 diabetes mellitus diagnosis during the study period (Jan 01, 2012-June 30, 2018)	1,503,408	1,503,408
1	Patients without type 1 diabetes mellitus, polycystic ovary syndrome, gestational diabetes mellitus, or other forms of secondary diabetes during the study period	1,463,418	1,463,418
2	Patients treated with metformin monotherapy (MM) during period Jan 01, 2013 - May 31, 2016, the first date will be metformin date	556,294	556,294
3	No use of metformin, antihyperglycemic agents (AHAs) or insulin in 12 months prior to the first metformin date	289,329	289,329
4	Patients with index HbA1c value (as depicted in columns) in the 1-6 months following metformin date	68,948	83,285
5	Patients with no insulin or AHA between index date and metformin date	62,381	74,558
6	Patients with continuous MM prescription by checking continuous MM prescription (MM prescription within 90 days of preceding prescription) from metformin date to index date	15,611	19,219
7	At least 18 years of age on index date	15,544	19,141
8	Patients with continuous enrollment in the database during baseline period	11,738	14,408
9	Patients with continuous enrollment in the database during follow-up period (24 months)	7,098	8,715
10	Patients with baseline Hba1c value $\geq 6.5\%$ at any point prior to metformin date	<b>4,775</b> <b>(Base Cohort)</b>	<b>6,129</b> <b>(Sensitivity Cohort 1)</b>
11	Patients with 2 or more continuous metformin prescriptions only	<b>1,942</b> <b>(Sensitivity Cohort 2)</b>	NA

**ICD 9 and ICD 10 codes**

	<b>ICD 9</b>	<b>ICD 10</b>
Type 2 diabetes mellitus	250.x0, 250.x2	E11
Type 1 diabetes mellitus	250.x1, 250.x3	E10.9
Complications of pregnancy	630-679	-
Secondary diabetes mellitus.	249.x	E08.x, E09.x
Gestational diabetes mellitus	648.8	024.4
Supervision of normal first pregnancy	V22, v22	-
Polycystic ovarian syndrome	256.4	E28.2



<b>Comorbidities</b>	<b>Source</b>	<b>Code or criteria</b>
Neuropathy	ICD-9 Diagnosis	356.9, 250.6, 358.1, 951.0, 951.1, 951.3, 354.0-355.9, 713.5, 357.2, 596.54, 337.0, 337.1, 564.5, 536.3, 458.0
Nephropathy	ICD-9 Diagnosis	5804, 58081, 58089, 5809, 5810, 5811, 5812, 5813, 58181, 58189, 5819, 5820, 5821, 5822, 5824, 58281, 58289, 5829, 5830, 5831, 5832, 5834, 5836, 5837, 58381, 58389, 5839, 5845, 5846, 5847, 5848, 5849, 585, 5851, 5852, 5853, 5854, 5855, 5856, 5859, 586, 587, 5880, 5881, 5888, 58881, 58889, 5889, 5890, 5891, 5899, 59000, 59001, 59010, 59011, 5902, 5903, 59080, 59081, 5909, 591, 5920, 5921, 5929, 5930, 5931, 5932, 5933, 5934, 5935, 5936, 5937, 59370, 59371, 59372, 59373, 59381, 59382, 59389, 5939, 7880, 7925, V1301, V420, V451, V560, V561, V562, V5631, V5632, V568, 0160, 01600, 01601, 01602, 01603, 01604, 01605, 01606, 2504, 25040, 25041 25042, 25043, 2741, 27410 27411, 27419, 403, 4030, 40300, 40301, 4031, 40310, 40311, 4039, 40390, 40391, 5800
Congestive heart failure	ICD-9 Diagnosis	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4, 425.5, 425.7, 425.8, 425.9, 428
Stroke/ Transient ischemic attacks	ICD-9 Diagnosis	430.x-435.x
Arrhythmia	ICD-9 Diagnosis	427.0 427.1 427.2 427.31 427.32 427.41 427.42 427.5 427.6 427.61 427.69 427.81 427.89 427.9
Peripheral arterial diseases	ICD-9 Diagnosis	093.0x, 437.3x, 440.0x-441.9x,443.1x-443.9x,447.1x,557.1x,557.9x, V43.4X
Diabetic Retinopathy	ICD-9 Diagnosis	250.5x
Acute Coronary Syndrome	ICD-9 Diagnosis	411.1
Acute Myocardial Infarction	ICD-9 Diagnosis	411.x, 410.x, 412.x
Angina	ICD-9 Diagnosis	413.9
Revascularization	CPT CODE	3722, 33520, 33515
Peripheral Vascular Disease	ICD-9 Diagnosis	0930, 4373, 440, 441, 4431, 4432, 4438, 4439, 4471, 5571, 5579, V434



### List of AHA drugs

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- Sulfonylureas
  - Antidiabetic - Amino Acid Derivatives
  - Biguanides
  - Meglitinide analogues
  - Alpha-Glucosidase Inhibitors
  - Dipeptidyl Peptidase-4 (DPP-4) Inhibitors
  - Dopamine Receptor Agonists – Antidiabetic
  - Insulin sensitizing agents
  - Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors
  - Glucagon-like peptide-1 (GLP-1) receptor agonists
  - Amylin analogues
  - Antidiabetic combinations
  - Bile acid sequestrants (colesevelam HCl)
  - Insulin
    - Rapid Acting:
      - o Insulin lispro (Humalog)
      - o Insulin aspart (NovoRapid)
      - o Insulin glulisin (Apidra)
    - Intermediate-acting:
      - o Insulin isophane/NPH (Humulin I, Insulatard, Insuman Basal)
    - Long-acting:
      - o Insulin glargine (Lantus)
      - o Insulin detemir (Levemir)
      - o Insulin degludec (Tresiba) Pre-mix:
        - o Insulin aspart and protamine aspart (Novomix 30)
        - o Insulin lispro and protamine lispro (Humalog Mix25, Humalog Mix50)
        - o Insulin neutral and isophane (Humulin M3, Insuman Comb, Mixtard)
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