Type 1 and Type 2 Diabetes Mellitus Identification Using ICD-9-CM Codes Within a Cohort of New Users of Drugs Labeled for Type 2 Diabetes Mellitus

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BACKGROUND

- Identification of patients with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) using administrative databases alone is challenging given the nature of the use of diagnostic codes. However, accurate identification of these conditions is important for distinguishing off-label and on-label use of anti-diabetic medications.
- T1DM is often coded as ICD-9-CM 250.x1 or 250.x3, and T2DM as ICD-9-CM 250.x0 or 250.x2, with relatively high sensitivity and specificity.[1] There have been algorithms proposed involving use of ratios of diagnostic codes to classify diabetics as T1DM or T2DM; e.g., one may classify an individual as having T2DM if the proportion of T2DM codes out of all diabetes mellitus (DM) codes is greater than 50%, and vice versa.[2]
- Using ICD-9-CM diagnostic codes, we attempted to describe on-label and off label use of drugs that belong to one of the following three antidiabetic drug classes:
  - Sodium-glucose cotransporter-2 (SGLT-2) inhibitors,
  - Dipeptidyl peptidase-4 (DPP-4) inhibitors, and
  - Sulfonylureas.
- Members of these drug classes are only indicated for the use in patients with T2DM. However, use of SGLT-2 inhibitors has been reported to be increasing among T1DM users despite observed adverse events, while favorable results have been found for DPP-4 inhibitor use in T1DM users in conjunction with insulin.[3,4] Sulfonylureas are not used for T1DM treatment.[5]

OBJECTIVE

To evaluate the proportion of T1DM and T2DM diagnostic codes prior to the initiation of medications indicated for T2DM: SGLT-2 inhibitors, sulfonylureas, and DPP-4 inhibitors.

METHODS

- Incident users of SGLT-2 inhibitors, DPP-4 inhibitors, and sulfonylureas were identified via FDA's Sentinel System using claims data from April 1, 2013, to September 30, 2015, among 15 Data Partners. Individuals must have been enrolled for 365 days before drug initiation, and those with gestational diabetes were excluded from the cohort.
- We calculated the total number of prior T1DM codes (250.x1, 250.x3) and T2DM codes (250.x0, 250.x2) prior to drug initiation among the new user cohorts during a 365 day baseline period preceding their incident drug dispensing.
- We examined the proportions of T2DM codes for each drug class separately, and also stratified each by the total number of codes identified for an individual. The strata used were 1, 2 to 5, or ≥6 diabetes codes. We also took various counts, such as the number of new users without either T1DM or T2DM codes or the proportion of each diabetes mellitus code among those diagnosed with T1DM or T2DM codes.

RESULTS
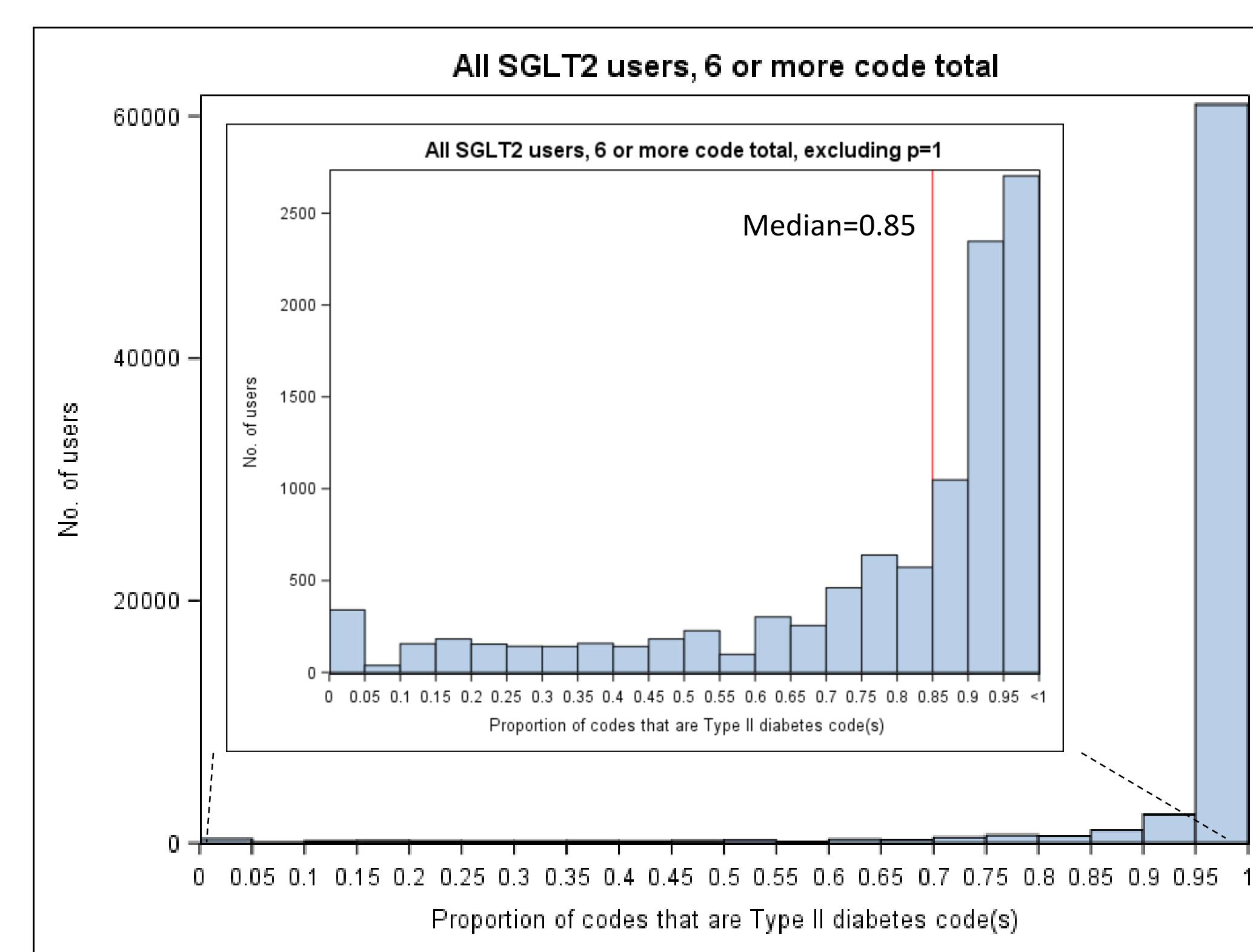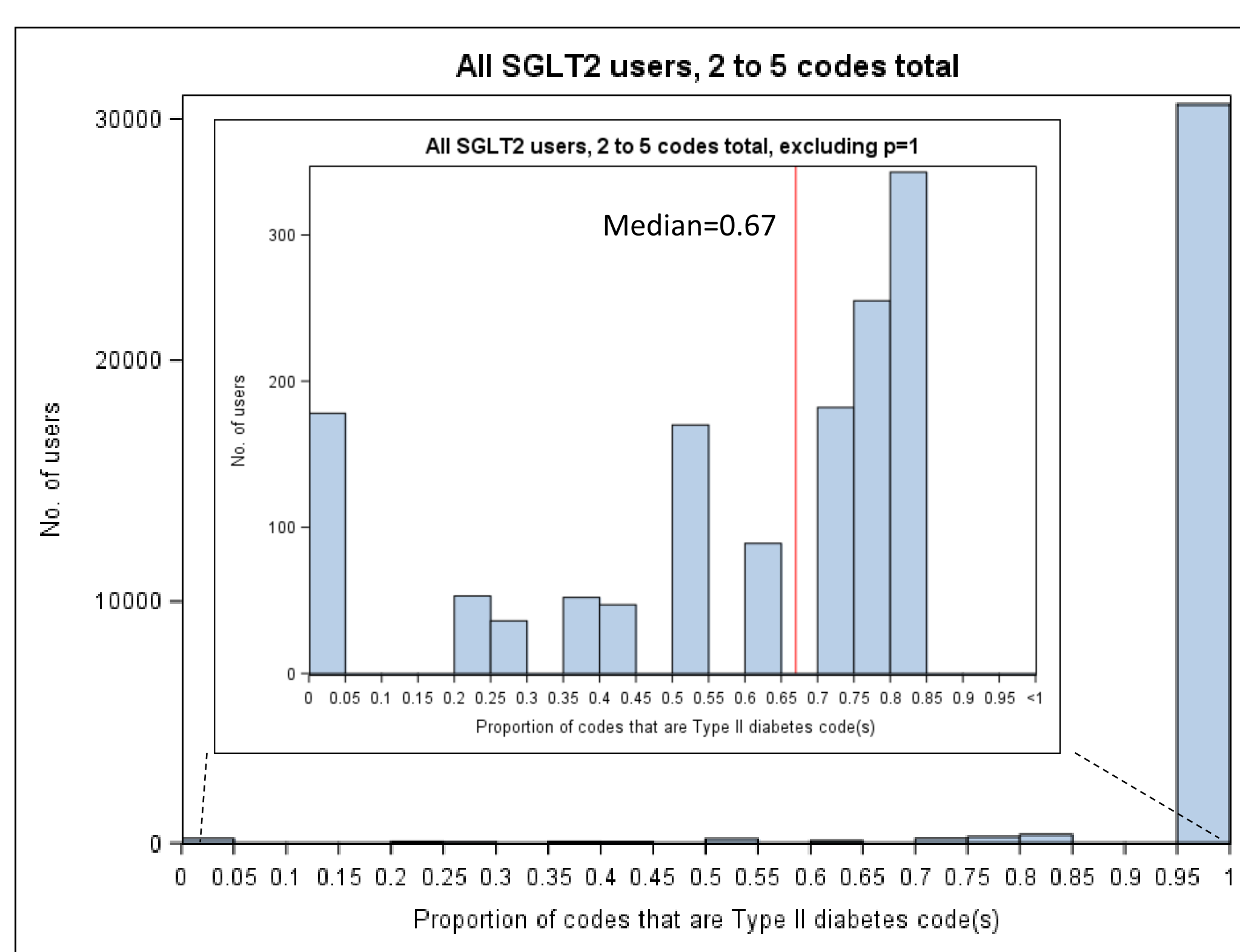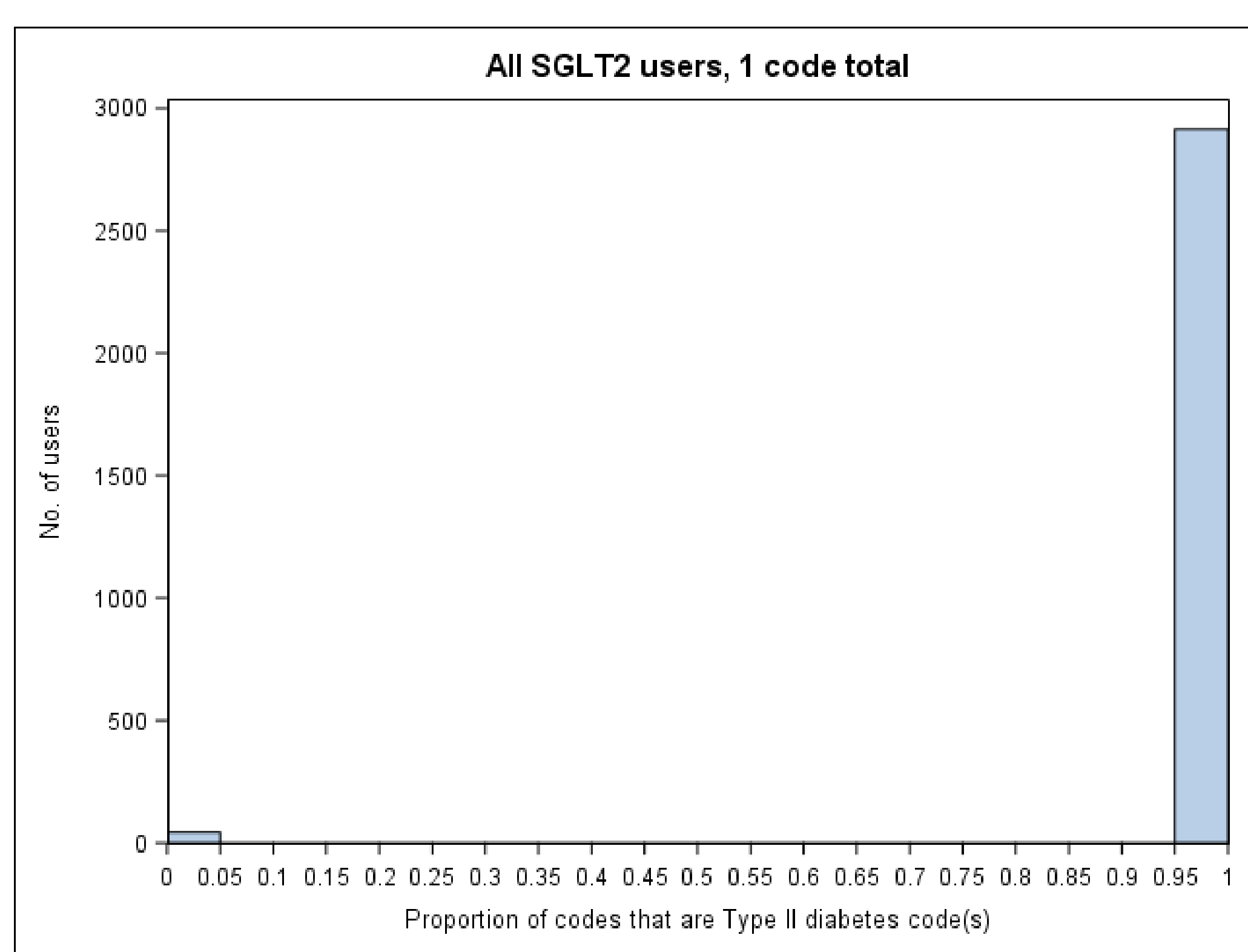
	SGLT-2 inhibitors		Sulfonylureas		DPP-4 inhibitors	
	#	%	#	%	#	%
All new users	106,080	100	256,108	100	167,989	100
No T1DM and T2DM codes co-occurring on any day in the prior 365 days	100,197	94	230,459	90	157,953	94
T1DM and T2DM codes co-occurring on at least one day in the prior 365 days	3,318	3	5,095	2	4,565	3
Neither T1DM nor T2DM codes on any day in the prior 365 days	2,565	3	20,554	8	5,471	3
No T1DM codes (no 250.x1 or 250.x3) in the prior 365 days	94,343	89	240,562	94	154,083	92
No T2DM codes (no 250.x0 or 250.x2) in the prior 365 days	3,126	3	20,954	8	5,725	3
All New Users with any T1DM code (250.x1 or 250.x3) in the prior 365 days	11,740		15,583		13,942	
Presence of T2DM code 250.x0 in the prior 365 days	10,470	89	14,677	94	13,169	94
Presence of T2DM code 250.x2 in the prior 365 days	7,662	65	9,368	60	8,959	64
Presence of both T2DM codes 250.x0 and 250.x2 in the prior 365 days	6,953	59	8,846	57	8,442	61
All New Users with any T2DM code (250.x0 or 250.x2) in the prior 365 days	102,878		234,371		162,155	
Presence of T1DM code 250.x1 in the prior 365 days	8,882	9	12,362	5	11,284	7
Presence of T1DM code 250.x3 in the prior 365 days	3,772	4	3,688	2	3,315	2
Presence of both T1DM codes 250.x1 and 250.x3 in the prior 365 days	1,456	1	956	0	964	1

Note: Cohorts are created independently, so an individual may qualify for multiple cohorts at different index dates. Thus, numbers may not sum to expected values.

- There were 106,080 SGLT-2 inhibitor users, 167,989 DPP-4 inhibitor users, and 256,108 sulfonylurea users. The majority of users for all drugs had prior T2DM codes: 97% of SGLT-2 inhibitors, 97% of DPP-4 inhibitors, 92% of sulfonylurea; conversely, 11%, 8%, and 6% of users, respectively, had a prior T1DM code.
- The proportion of users with only prior T2DM codes (i.e., $p = 1$ in the histograms above) was much higher than those with ≥1 prior T1DM code. For all drugs, a small number had only T1DM codes (i.e., p = 0).
- For users with at least one prior T1DM code (i.e., p < 1), as the total number of diagnostic codes observed during the baseline period increased, the median of the proportion of T2DM codes out of all diabetes codes (red line in graphs) moved towards 1. This implies that users with more codes have relatively fewer T1DM codes assigned.
- Out of all new users of SGLT-2 inhibitor assigned at least one DM code, 2.36% have more T1DM codes than T2DM codes (i.e., p ≤ 0.5). Likewise, for DPP-4 inhibitors, this proportion is 0.95%, and for sulfonylureas, this proportion is 0.83%.
- These proportions were almost identical among patients with a least two DM codes during the baseline period.
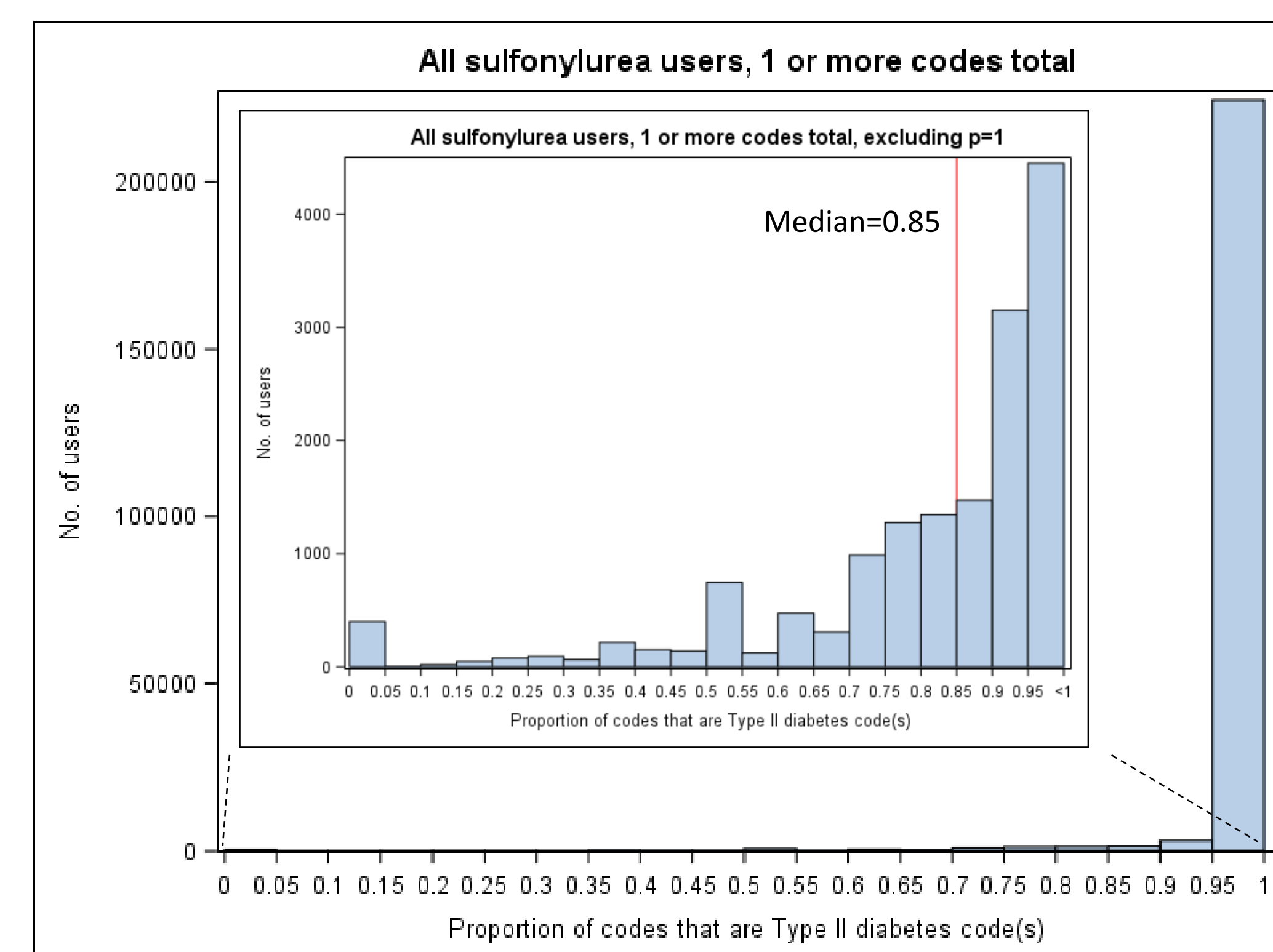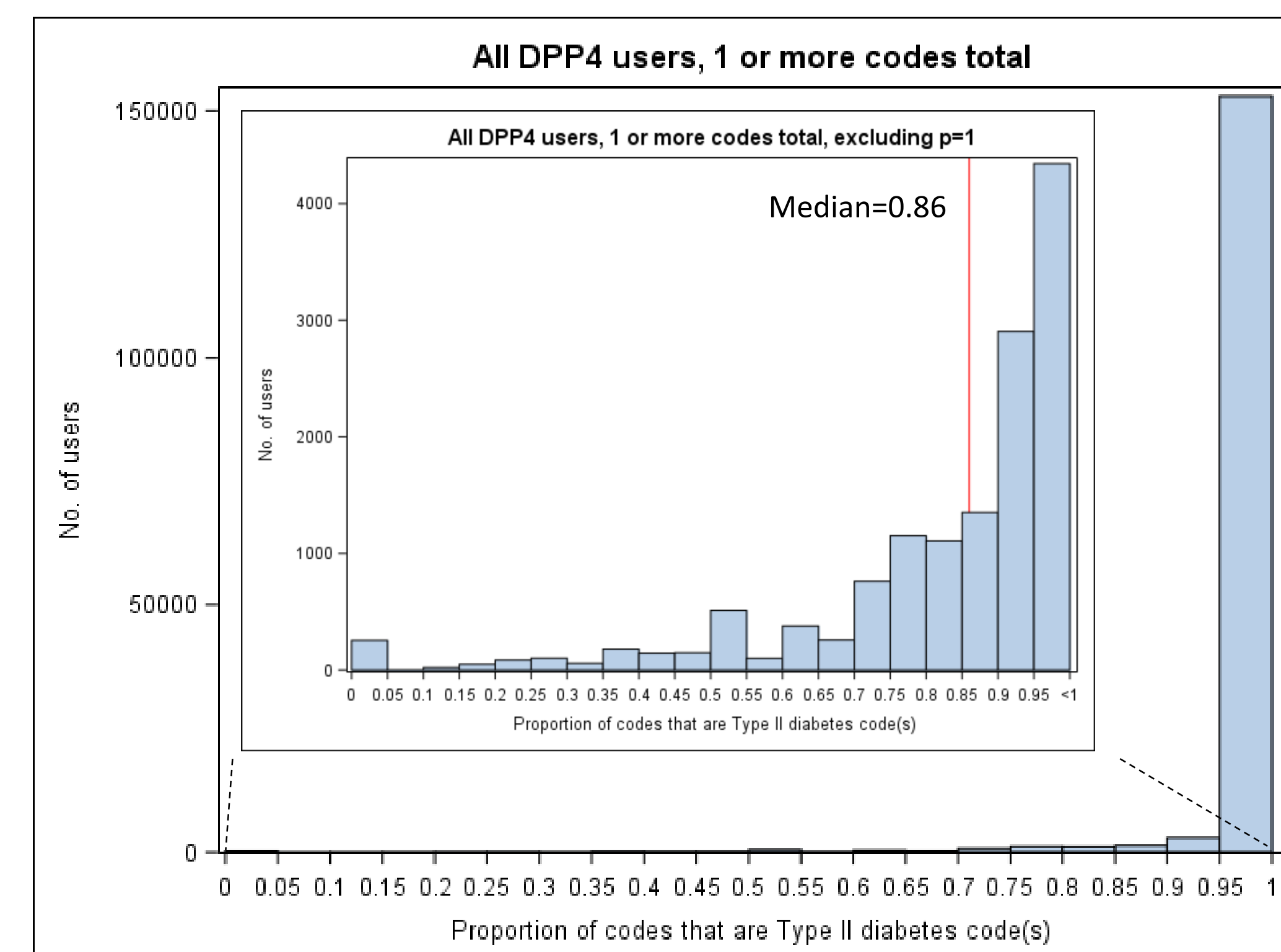
CONCLUSIONS

- Among new users of labeled T2DM anti-diabetic medications, most have documentation of T2DM diagnostic codes in the 365 days prior to the dispensing date.
- Among patients with at least one prior T1DM code, the proportion of T1DM codes out of all DM codes decreased as the total number of codes increased. This suggests that T1DM codes in some patients may be due to miscoding.
- The presence of a small proportion of patients with more T1DM codes than T2DM codes suggests that off-label use occurred among T1DM patients. However, the proportion of potential T1DM patients among all initiators of the study drugs is small.

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DISCLOSURE STATEMENT