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Should insulin billing procedure codes be considered for exposure ascertainment in pharmacoepidemiology studies?

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ABSTRACT

Objectives: The purpose of the study was to examine whether Healthcare Common Procedure Coding System (HCPCS) billing codes should be used in conjunction with National Drug Codes (NDCs) to establish insulin exposure episodes.

Materials and Methods: We identified insulin claims billed by NDCs or HCPCS codes in FDA's Sentinel System from 2013 to 2018. We created insulin exposure episodes separately based on NDCs only, HCPCS only, and a combination of both NDC and HCPCS. We considered gaps of <30 days between valid billing codes as continuous exposure. Patients were followed until the earliest of (1) episode end date, (2) death, (3) disenrollment, (4) query end date, and (5) evidence of the opposite exposure defining code type (for cohorts defined by only NDCs or only HCPCS). We examined the median duration of incident episodes, requiring no NDC or HCPCS codes in the 183 days (washout period) before the first billing code and prevalent episodes (no washout period required). For patients with more than 1 treatment episode, we calculated median gap length between episodes.

Results: We identified 107,528,855 insulin claims using NDCs or HCPCS. Of these, 98.5% were billed using NDCs. HCPCS were largely billed during emergency and ambulatory visits (52.5% and 38%, respectively). We identified 6,350,872 incident and 12,922,593 prevalent NDC episodes; and 6,821,075 incident and 13,465,108 prevalent NDC-HCPCS episodes. The median length of the first incident NDC. NDC episodes was 110 days (IQR: 60; 212); 31 (IQR: 19; 31) days for HCPCS only and 90 (IQR: 19-31) for NDC-HCPCS episodes. The median gap between the first and second episodes was shorter for incident NDC episodes than HCPCS episodes (NDC: 49 [IQR: 17; 132]; HCPCS: 249 [IQR: 93; 550]). Prevalent episodes showed similar trends.

Conclusion: HCPCS insulin codes appeared to indicate either 1 time or sporadic occurrences with long gaps between two codes. HCPCS codes in conjunction with NDC codes increased the number but reduced the median length of insulin episodes. Unless studies investigate the effects of insulin administered in specific settings to identify transient adverse reactions treated with insulin, we do not encourage the use of HCPCS to establish insulin exposure episodes.

Keywords: Healthcare Common Procedure Coding System codes, National Drug Codes, Insulin, Exposure ascertainment, Claims

INTRODUCTION

Pharmacoepidemiology studies often rely on National Drug Codes (NDCs) for the identification of insulin products and the creation of insulin exposure episodes in administrative databases. Like non-biologic products, insulin is mostly self-administered and pharmacy dispensing has historically been billed as drug products using NDCs. However, there are some instances where

Healthcare Common Procedure Coding System (HCPCS) codes may be considered for billing for instance, in the reimbursement of insulin administered using a pump or reusable pen or in situations where insulin is administered at the emergency department or physician offices. The use of HCPCS codes for insulin reimbursement has not been quantified and it remains unknown whether incorporating HCPCS codes into the claims-based algorithms for defining insulin exposure, improves the capture of insulin claims and, hence, the accuracy of insulin exposure. Thus, we examined the frequency of different billing codes (NDCs or HCPCS codes) that may be used for insulin product reimbursement. This study was a descriptive analysis to quantify the use of billing codes in a large national administrative database and determine whether HCPCS codes should be used in conjunction with NDC codes to ascertain insulin exposure.

MATERIALS AND METHODS

Data source

We included data from 16 Sentinel Data Partners, between January 1, 2013, and December 31, 2018. The Sentinel Distributed Database is a curated data source composed of data partners, primarily large national and regional insurers and integrated delivery care networks in the United States. Each data partner contributed medical data, including inpatient and outpatient diagnoses, claims for procedures, and pharmacy claims data, including retail and mail order dispensing records.[1] These data are routinely transformed into the Sentinel Common Data Model[2,3] to facilitate queries. Of note for the purposes of this study, the common data model includes care settings for procedures (HCPCS), but not for dispensing (NDC). In general, NDCs are routinely billed out of outpatient pharmacies. This study was conducted as part of the public health surveillance activities under the auspices of the Food and Drug Administration and are, therefore, not under the purview of Institutional Review Boards.[4,5] Adults ages 18 and older were included in our study population; no restrictions on diabetes type or status were applied.

Distribution of billing codes for insulin reimbursement

During the study period, we identified every insulin claim generated by brand NDC (a total of 24 insulin products) or HCPCS insulin code [Online Supplement Table 1]. For each insulin product billed through NDC, we obtained the number of HCPCS codes within 3 days of the dispensed NDC products for the same patient. We also examined the distribution of all insulin NDCs within 3 days of a HCPCS code for the same patient. Finally, we obtained patient characteristics, encounter settings for non-pharmacy insulin claims, and the distribution of type of diabetes diagnosis codes (Type 1 or 2) 6 months before the date of the NDC or HCPCS code.

Insulin exposure episodes

For this analysis, we created insulin episodes using the days' supply on the NDC claim or 1 day for a HCPCS claim. We allowed for 30-day gaps between the calculated end of supply and subsequent claim and added a 30-day extension at the end of each episode's last claim to account for short delays in medication refills. We created insulin episodes separately, based on NDCs, HCPCS, and combination of NDCs and/or HCPCS. With the 30-day extension, all HCPCS exposures had a uniform length of 31 days unless bridged with a subsequent administration during the episode. An incident insulin episode was defined as no NDC (for NDC episodes) or no HCPCS (for HCPCS episodes) or no NDC and no HCPCS (for NDC-HCPCS episode) 6 months before the first claim. We removed this restriction for prevalent insulin episodes. We censored treatment episodes after the 30-day gap allowance expired without a new claim for insulin. We also censored episodes in the event of a new claim for HCPCS during NDC-only, or NDC during HCPCS-only cohorts; death; disenrollment; end of available data; or the study end date, whichever came first. We assessed the median duration (in days) of cumulative and first NDC, HCPCS, and NDC-HCPCS episodes separately. For patients with more than 1 episode of use, we assessed the length of time in days between each episode for both a patient's first observed gap and for all gaps. We also present descriptive statistics to characterize the gaps.

RESULTS

During the evaluation period, we identified 107,528,855 insulin claims using NDCs or HCPCS. Of these, 98.5% were billed using NDCs and 1.6% using HCPCS codes. The most frequent NDCs were for Lantus (37.1%), Novolog (16.2%), and Levemir (16.0%), while the most frequent HCPCS was J1815 (injection, insulin, per 5 units or insulin injection) (97.3%) and J1817 (insulin for administration through DME [i.e., insulin pump] per 50 units) (3.3%) [Table 1]. While almost all NDCs were billed by default as pharmacy claims, the majority of HCPCS codes were billed in the emergency department (52.5%) or during an ambulatory visit (38.0%). In 94.3% of the 1,682,070 HCPCS codes identified, patients had no NDC code on the same date as the HCPCS codes. Thus, the insulin administration could not be associated with any product. The remaining 94,673 (5.6%) HCPCS codes had at a least one branded insulin NDC on the same date as the HCPCS claims date. The most frequent NDCs billed within 3 days of the J1815 code were Lantus (5.6%), Humalog and Novolog (3.3% each), and Levemir (2.5%). The top three NDCs associated with J1817 were Humalog (6.3%), Novolog (5.3%), and Lantus (4.7%). For about 95% of all insulin billed, through NDC or

Table 1: Insulin claims distribution and selected patient characteristics among insulin users.

	All insulin		Insulin by NDCs		Insulin by HCPCS	
Number of claims	107,528,855		105,941,433		1,682,070	
Insulin claims billed by NDC codes						
Lantus and Lantus Solostar	39,326,260	36.6	39,326,260	37.1	N/A	
Novolog	17,167,717	16.0	17,167,717	16.2		
Levemir	16,966,889	15.8	16,966,889	16.0		
Humalog	14,842,175	13.8	14,842,175	14.0		
Insulin claims billed by HCPCS codes						
J1815	1,635,916	1.5	N/A		1,635,916	97.3
J1817	55,272	0.1			55,272	3.3
J1820	11	0.0			11	0.0
K0548	0	0.0			0	0.0
Encounter settings[a]						
Emergency department	887,937	0.8	10,108	0.0	883,308	52.5
Ambulatory visit	666,931	0.6	63,477	0.1	639,676	38.0
Other ambulatory visit†	22,125	0.0	10,160	0.0	18,787	1.1
Non-acute institutional‡	11,695	0.0	83	0.0	11,624	2.1
Inpatient	137,483	0.1	12,737	0.0	130,048	5.6
Pharmacy	105,815,851	98.4	105,851,527	99.9	0	0.0
Demographics						
Number of unique patients	5,944,918		5,617,952		984,969	
Mean age (years)	66.4	12.7	66.4	12.7	64.9	14
Age: 18–44 years	8,269,097	7.7	8,117,463	7.7	166,254	9.9
Age: 45–64 years	33,749,596	31.4	33,216,124	31.4	75,566	34.2
Age: 65+years	65,510,162	60.9	64,607,846	61.0	940,250	55.9
Sex (female)	3,045,963	51.2	2,879,780	51.3	517,254	52.5
Sex (male)	2,898,955	48.8	2,738,172	48.7	467,715	47.5
Presence of diabetes codes –3–180 days from Index:						
Type 1 diabetes code only	4,197,383	3.9	4,187,536	4.0	11,765	0.7
Type 2 diabetes code only	77,375,206	72.0	76,195,803	71.9	1,247,411	74.2
Type 1 or Type 2 diabetes code	102,259,039	95.1	100,722,071	95.1	1,628,421	96.8
Neither Type 1 nor Type 2 diabetes code	5,269,816	4.9	5,219,362	4.9	53,649	3.2

NDC: National Drug Code, HCPCS: Healthcare Common Procedure Coding System, † includes other non-overnight AV encounters such as hospice visits, home health visits, skilled nursing facility (SNF) visits, other non-hospital visits, as well as telemedicine, telephone, and email consultations, ‡ includes hospice, SNF, rehab center, nursing home, residential, overnight non-hospital dialysis, and other non-hospital stays. [a]NDC claims generally do not have an associated encounter setting, however, two data partners do record their NDCs in the procedure table, thus capturing a clinical encounter setting

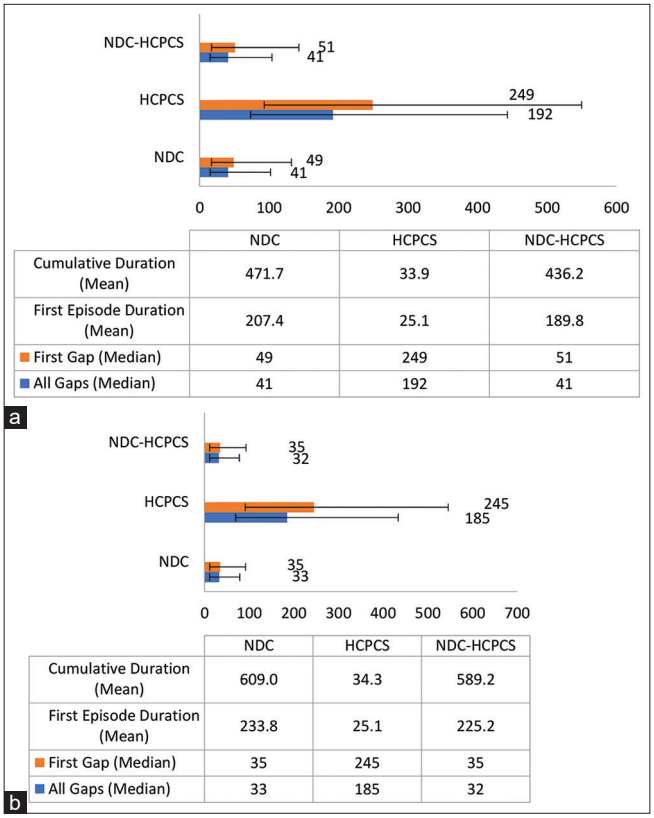
HCPCS, patients had at least one claim with a Type 1 or Type 2 diabetes code in the 3 days before through 180 days after (3.9% Type 1 only; 72.0% Type 2 only; and 95.1% Type 1 or 2).

Insulin exposure episodes

We identified 6,350,872 incident NDC episodes, 1,217,664 incident HCPCS episodes, and 6,821,075 incident NDC-HCPCS episodes. Similarly, we identified 12,922,593 prevalent NDC episodes, 1,240,888 prevalent HCPCS episodes, and 13,465,108 prevalent NDC-HCPS episodes. The median duration (days) of the first NDC episodes was longer than for HCPCS episodes, for both incident (NDC: 110 [IQR: 60; 212]; NDC-HCPCS: 90 [IQR: 58; 191]; and HCPCS: 31 [IQR: 19; 31]) and prevalent (NDC: 120 [IQR: 60; 251]; NDC-HCPCS: 114 [IQR: 60; 237]; and HCPCS: 31 [IQR: 19; 31]) episodes. Similar trends were observed for the cumulative [Figure 1] and subsequent episodes (data not shown). Of all incident NDC episodes, 45% represented single treatment episodes with no gap (no subsequent NDC); of all incident HCPCS episodes, 78% represented single episodes with no gap. The median gap length (in days) between the first and second episodes was much shorter for NDC and NDC-HCPCS episodes than HCPCS episodes, for both incident (NDC: 49 [IQR: 17; 132]; NDC-HCPCS: 51 [IQR: 17; 143]; and HCPCS: 249 [IQR: 93; 550] days) and prevalent episodes (NDC: 35 [IQR: 12; 92]; NDC-HCPCS: 35 [IQR: 12; 93]; and HCPCS: 245 [IQR: 91; 546]) [Figure 1]. We observed similar distributions for all gaps between all observed episodes.

DISCUSSION

In this large observational study of insulin users, we found that only 1.5% of all insulin claims were billed using HCPCS codes. The J1815 code accounted for more than 90% of the



	NDC	HCPCS	NDC-HCPCS
Cumulative Duration (Mean)	471.7	33.9	436.2
First Episode Duration (Mean)	207.4	25.1	189.8
First Gap (Median)	49	249	51
All Gaps (Median)	41	192	41

	NDC	HCPCS	NDC-HCPCS
Cumulative Duration (Mean)	609.0	34.3	589.2
First Episode Duration (Mean)	233.8	25.1	225.2
First Gap (Median)	35	245	35
All Gaps (Median)	33	185	32

Figure 1: Gap between insulin episodes. (a) Duration of the first gap (days [IQR]) for incident Insulin episodes and (b) for prevalent insulin episodes.

HCPCS codes for insulin administration. The majority (~90%) of HCPCS codes were used in emergency departments or in the outpatient office setting. Because of the high proportion of HCPCS as solitary occurrences for the patient, and long gaps between HCPCS when subsequent episodes were observed, HCPCS codes appeared to be either 1 time administrations or sporadic occurrences. In contrast, episodes based on NDC codes are generally consistent with chronic use.

While we were able to capture a greater number of patients and treatment episodes when including HCPCS, relative to assessment through NDCs alone, this might not be a desirable patient identification strategy for insulin use studies. Combining these code types resulted in shorter median episode duration relative to the NDC-only cohorts, illustrating the fact that NDC-HCPCS cohorts represented a mix of two different types of exposure. In studies that examine incident insulin use, the inclusion of HCPCS codes may capture brief emergency department use rather than subsequent chronic use episodes, which are more likely to be of interest in safety assessment.

Our data reveal that emergency administration of insulin products is best captured using HCPCS codes. For studies that examine insulin utilization in these settings or the impact of emergency administration of insulin, one might consider the use of HCPCS codes. However, such studies might be unable to evaluate specific insulin products.

Online Supplement Table 1: List of Healthcare Common Procedure Coding System (HCPCS) procedure codes used to define the exposure.

Code	Description
J1815	Injection, insulin, per 5 units
J1817	Insulin for administration through DME (i.e., insulin pump) per 50 units
S5552	Insulin, intermediate acting (NPH or LENTE); 5 units
S5553	Insulin, long acting; 5 units
S5561	Insulin delivery device, reusable pen; 3 ml size
S5551	Insulin, most rapid onset (Lispro or Aspart); 5 units
S5550	Insulin, rapid onset, 5 units
S5571	Insulin delivery device, disposable pen (including insulin); 3 ml size
S5560	Insulin delivery device, reusable pen; 1.5 ml size
J1820	Injection, insulin, up to 100 units
S5565	Insulin cartridge for use in insulin delivery device other than pump; 150 units
S5570	Insulin delivery device, disposable pen (including insulin); 1.5 ml size
S5566	Insulin cartridge for use in insulin delivery device other than pump; 300 units
K0548	Injection, insulin lispro, up to 50 units

CONCLUSION

Insulin products were billed primarily using NDCs in administrative claims databases. We observed that the frequency of NDC codes alone reflected a pattern of dispensing consistent with chronic insulin use. A small fraction of insulin claims was billed using HCPCS codes, mostly as solitary occurrences for patients in emergency situations and during office visits. NDCs alone best depict chronic insulin exposure for safety assessment studies; however, one might consider the use of HCPCS codes in the assessment of emergency department administration of insulin products, or in situations where there is interest in identifying transient adverse reactions that are treated with insulin, for example, steroid-induced hyperglycemia.

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Take-home message

Unless studies investigate the effects of insulin administered in specific settings or aim to evaluate transient adverse reactions treated with insulin, we do not encourage the use of Healthcare Common Procedure Coding System (HCPCS) to establish insulin exposure episodes.

Disclaimer

The views expressed in this publication are those of the authors and do not necessarily reflect the official policy of the U.S. Food and Drug Administration. Christian Hampp was an employee of the Food and Drug Administration during the time of study conduct. He is now employed by Regeneron Pharmaceuticals, Inc., and owns company stock. Regeneron did not provide study funding, does not hold a marketing license for any of the study drugs, and had no role in manuscript development or decision to publish.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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