The Cost Impact of Non-Infectious Diarrhea in Patients with Carcinoid Syndrome

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BACKGROUND

- Carcinoid syndrome (CS) describes the hormonal effects of carcinoid tumors, including the secretion of serotonin into the systemic circulation causing episodic flushing and diarrhea.[1]
- CS patients with non-infectious diarrhea (NID), one of the most common symptoms of CS, experience profoundly poor sense of well-being.[2]
- Despite the frequent occurrence of this burdensome CS-related symptom, the healthcare costs and utilization associated with NID has not been elucidated.

OBJECTIVE

- To compare adjusted annual overall healthcare utilization and costs among CS patients with non-infectious diarrhea versus CS patients without non-infectious diarrhea.

METHODS

Study Design and Data Source

- Retrospective cross-sectional study using the HIPAA-compliant Truven Health Analytics MarketScan® Database from 1/1/2002 to 12/31/2012.

Patient Population

- Patients newly diagnosed with CS were identified between 1/1/2003 – 12/31/2011 (ID period) based on the following criteria:

Inclusion Criteria:

Patients need to have either 2 claims for CS (ICD-9-CM 259.2) OR 1 claim for CS and 1 claim for carcinoid tumor (CD-9-CM 209.x) during the follow up period to be included in the analysis.

Exclusion Criteria:

Patients had CS in the pre-index period, OR were not continuously-enrolled one year before and one year after the index date.
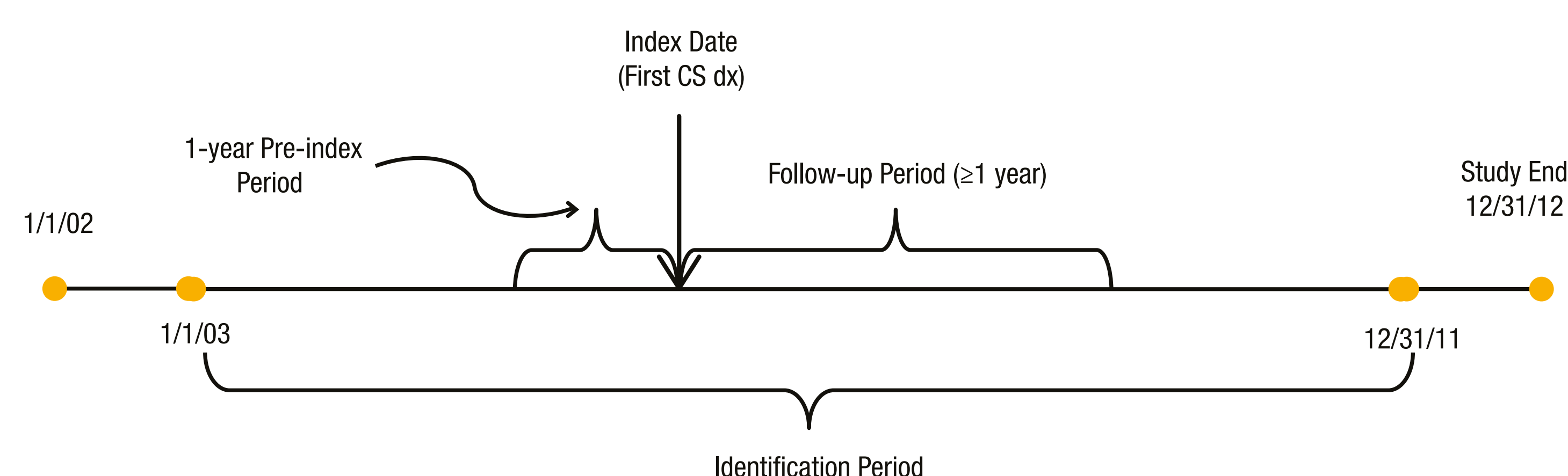
Stratifications:

- CS patients were stratified into those with NID vs. those without NID.
  - NID patients had ICD-9-CM code 564.5 or 787.91 within 1 year after CS diagnosis*.

*Based on our best clinical judgement, these codes should identify patients with non-infectious diarrhea only, and should not overlap with codes for infectious causes of diarrhea including codes for, i.e.salmonella, shigella, yersinia, campylobacter, C. dificile, amebae (including E. histolytica), other bacteria (including E. coli), and viruses (including rotavirus and enterovirus).

Data

- All claims in the 1 year pre-index were used to determine patient demographics, number of chronic conditions,[3] and Charlson comorbidity index (CCI).[4]
- All claims occurring in the 1 year post-index were used to determine the outcome measures of healthcare resource utilization (HRU) and costs.

Statistical Analysis

- Multivariable models, linear regression for number of office visits, negative binomial regression for number of hospitalizations and number of ED visits, and logistic regression for risk of hospitalization and risk of ED visits, were used to adjust outcomes for age, gender, region, number of chronic conditions, and Charlson comorbidity index using SAS® version 9.4.

RESULTS

- Of 2,822 newly-diagnosed CS patients the mean age was 51.5 year, 56.9% were women, and the mean Charlson Comorbidity Index was 3.6.

Table 1. Patient Characteristics

Characteristic	With NID n=534 (18.9%)	Without NID n=2,288 (81.1%)	P Value
Age, mean (SD)	51.3 (9.9)	51.6 (10.1)	0.639
Female, no. (%)	333 (62.4)	1,273 (55.6)	0.005
Charlson comorbidity index, mean (SD)	3.7 (3.9)	3.6 (3.8)	0.643
No. of chronic conditions, mean (SD)	4.0 (2.4)	3.4 (2.0)	<.001

- Unadjusted and adjusted HRU and costs were statistically significantly higher in patients with NID vs. those without NID, except for adjusted ED costs.
- After adjusting for baseline differences between groups, patients with NID had higher mean number of office visits, inpatient hospitalizations, and emergency department (ED) visits (all p<0.001) one year post CS diagnosis.

Table 2. Adjusted[a] HRU Means and Rates with 95% Confidence Intervals (CIs)[b]

Outcome	Adjusted Mean / Rate (95% CI)	
	With NID	Without NID
Number of office visits	24.2 (22.9 - 25.5)	19.0 (18.4 - 19.7)
Number of hospitalizations	0.97 (0.86 - 1.10)	0.61 (0.57 - 0.65)
Number of ED visits	0.67 (0.56 - 0.81)	0.38 (0.34 - 0.42)
Risk of hospitalization	49.4% (45.1% - 53.6%)	39.7% (37.7% - 41.7%)
Risk of ED visit	36.2% (32.2% - 40.5%)	20.7% (19.1% - 22.5%)

[a]Adjusted by age, gender, region, number of chronic conditions, and CCI.
[b]All adjusted HRU mean and rate comparisons had a p<.001.

- Patients with NID had higher adjusted total annual costs: (+$29,890), pharmacy costs (+$2,557), non-pharmacy costs (+$27,334), visit costs (+$16,695), and inpatient hospitalization costs (+$11,431) compared to those without NID (all p≤0.003).
- Adjusted ED costs were similar: $1864 in CS patients with NID vs. $1616 in those without NID (p=0.419).

Figure. Costs (adjusted for demographics, region, no. of chronic conditions, & CCI)
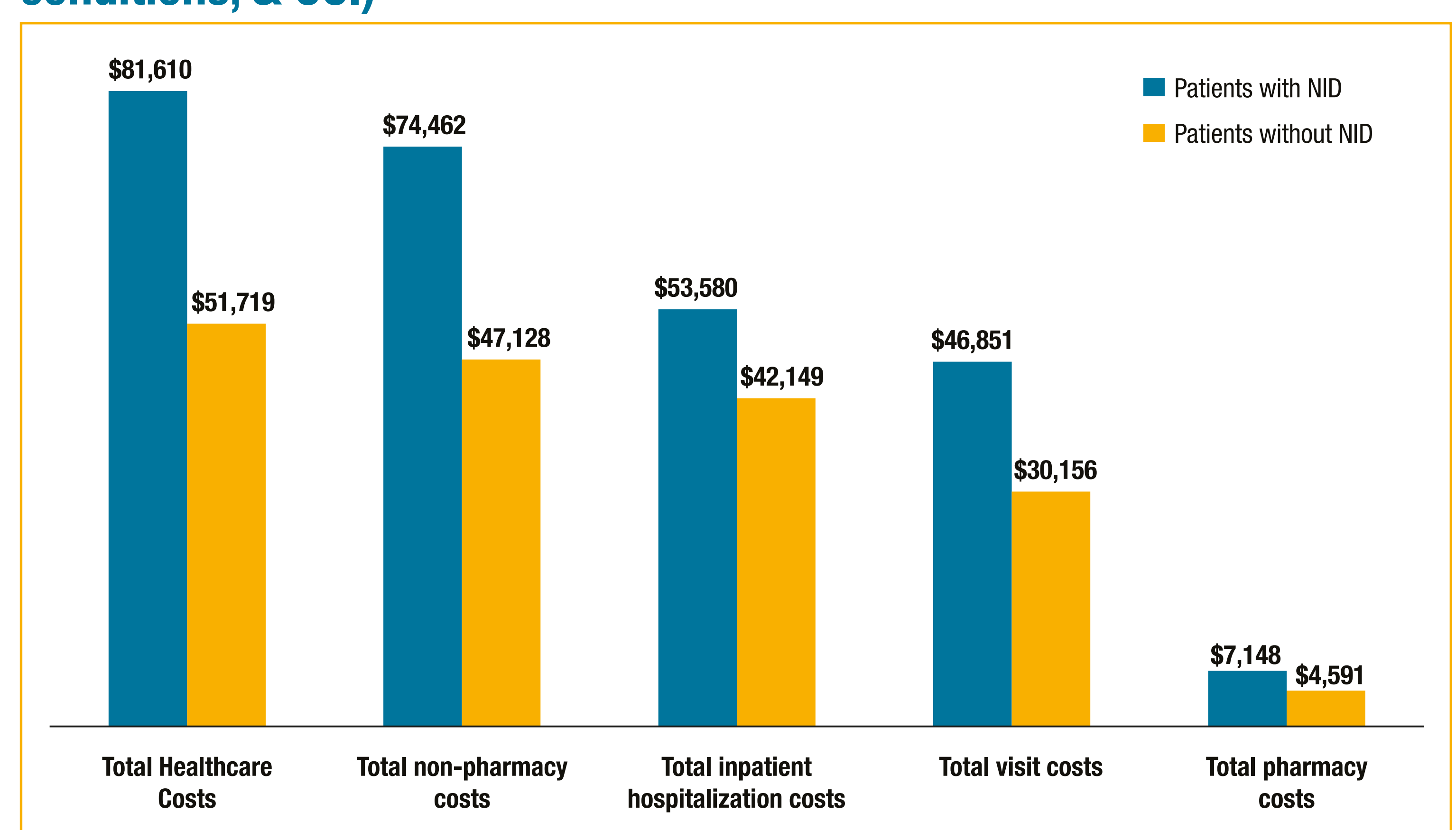
LIMITATIONS

- As in any analysis of insurance claims, miscoding of ICD-9-CM codes may result in errors.
- We selected 2 of the multiple possible codes for diarrhea in order to avoid including infectious diarrhea, but we could not be certain all infectious cases were excluded or all non-infectious cases were included. In addition, our algorithm to identify patients with CS required 2 claims that could have occurred over a > 1 year period. Although the algorithm has not been validated against a gold standard, inaccuracies would have affected both groups equally.
- We adjusted for a variety of potential confounders but not for pre-diagnosis HRU or cost since we only examined newly diagnosed patients in whom controlling for pre-diagnosis resource use would be of limited value.
- Our results are only generalizable to the US commercially-insured population.

CONCLUSIONS

- Our annual prevalence estimate of diarrhea (18.9%) was similar to a published estimate of 17.6% in NET patients in which the majority had CS (72%).
- Overall, our study shows that NID in CS patients is associated with considerable burden, including increases in health care utilization, costs and possibly also associated humanistic burdens, all of which could be the subject of future research.
  - NID in CS patients is associated with a significantly increased annual healthcare utilization and an additional $30,000 in total annual healthcare costs, which predominantly comprise medical costs.
  - The odds of hospitalization among CS patients with NID are about 1.5 times of those without NID.
- It is possible that adequate control of diarrhea in CS patients may reduce healthcare costs, while also bringing about benefit for humanistic outcomes.

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