

# INCREMENTAL HEALTHCARE RESOURCE UTILIZATION AND COSTS IN U.S. PATIENTS WITH CUSHING'S DISEASE COMPARED WITH DIABETES AND POPULATION CONTROLS

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## BACKGROUND

- Cushing's disease (CD) is a form of Cushing's syndrome (hypercortisolism) caused by overproduction of adrenocorticotropic hormone (ACTH) from a pituitary corticotroph adenoma.
- The estimated U.S. incidence is 8 cases per million population.<sup>1</sup>
- CD is associated with substantial morbidity, ranging from hypertension, osteoporosis, cardiovascular disease, and opportunistic infections.<sup>2</sup>
- Healthcare costs and resource utilization for patients with CD have not been studied extensively.

## OBJECTIVE

- To estimate the healthcare resource use and costs associated with Cushing's disease.

## METHODS

### Study Design and Patient Identification

- Matched cohort study using US insurance claims from the MarketScan® database from 1/1/2008 to 12/31/2012.
- Patients with CD** were defined using CD case-finding algorithm by Burton et al.<sup>3</sup>:
  - At least 1 claim with a diagnosis of Cushing's syndrome (CS) (ICD-9-CM 255.0); AND
  - At least 1 claim with a diagnosis of either pituitary neoplasm; pituitary disorder (e.g., hyperfunction); hypophysectomy; radiosurgery; or bilateral inferior petrosal sinus sampling
- Patients with DM** were selected from a 5% random sample of all enrollees with ≥2 claims of diabetes mellitus (ICD-9-CM: 250.x) and no claim of CS by ICD-9-CM code, thereby no claim of CD.
- Population-based controls** were selected from a 5% random sample of all database enrollees with no claim of CS by ICD-9-CM code, thereby no claim of CD.
- Patients without 1 year of continuous enrollment were excluded.
- CD patients were matched to DM and population-based controls by age, gender, region, and year in a 1:2 ratio.

### Study Measures

- All study measures were based on a 1-year observation period.
- Demographics: age, sex, geographic region
- Charlson Comorbidity Index (CCI) and number of chronic conditions
- Complications related to CD: cardiovascular disease/stroke, depression/anxiety, DM, kidney stones, infections, osteoporosis, vertebral compression fractures
- Healthcare utilization: number of hospitalizations, emergency department (ED) visits, office visits, prescription fills
- Costs: total, pharmacy and non-pharmacy

### Statistical Analysis

- We conducted pairwise comparisons between CD and DM patients and between CD and control patients.
- To analyze differences between cohorts, chi-square tests and t-tests were performed for categorical and continuous variables, respectively.
- Statistical analyses were performed in SAS® 9.4 (SAS Institute, Cary, NC).

## RESULTS

- The study included 1,852 patients with CD: 3,704 matched DM controls and 3,704 matched population controls.
- Mean age was 42.9 years (SD 12.3) and 78.2% were female.
- Patients with CD had statistically significantly higher rates of all comorbidities of interest than both patients with DM (other than DM itself) and controls (**Table 1**).
- Patients with CD were hospitalized more frequently, visited the ED more often, had more office visits, and filled more prescriptions than patients with DM (all p<.001; **Table 2**) or controls (all p<.001; **Table 2**).
- Mean total healthcare costs for patients with CD were \$26,269, versus \$12,282 for those with DM (p<.001) and \$5,869 for controls (p<.001; **Figure 1**).

### TABLE 1. Patient Comorbidities

| Comorbidity, n (%)              | CD (n=1,852) | DM (n=3,704)   | Control (n=3,704) |
|---------------------------------|--------------|----------------|-------------------|
| Cardiovascular disease/stroke   | 203 (11.0)   | 302 (8.2)      | 132 (3.6)         |
| Depression/anxiety              | 457 (24.7)   | 502 (13.6)     | 415 (11.2)        |
| Diabetes mellitus               | 486 (26.2)   | 3,704 (100.0)* | 266 (7.2)         |
| Kidney stones                   | 81 (4.4)     | 76 (2.1)       | 56 (1.5)          |
| Infections                      | 391 (21.1)   | 609 (16.4)     | 424 (11.4)        |
| Osteoporosis                    | 156 (8.4)    | 51 (1.4)       | 49 (1.3)          |
| Vertebral compression fractures | 17 (0.9)     | 5 (0.1)        | 5 (0.1)           |

\* By definition, patients with DM were required to have a claim-based diagnosis of DM.

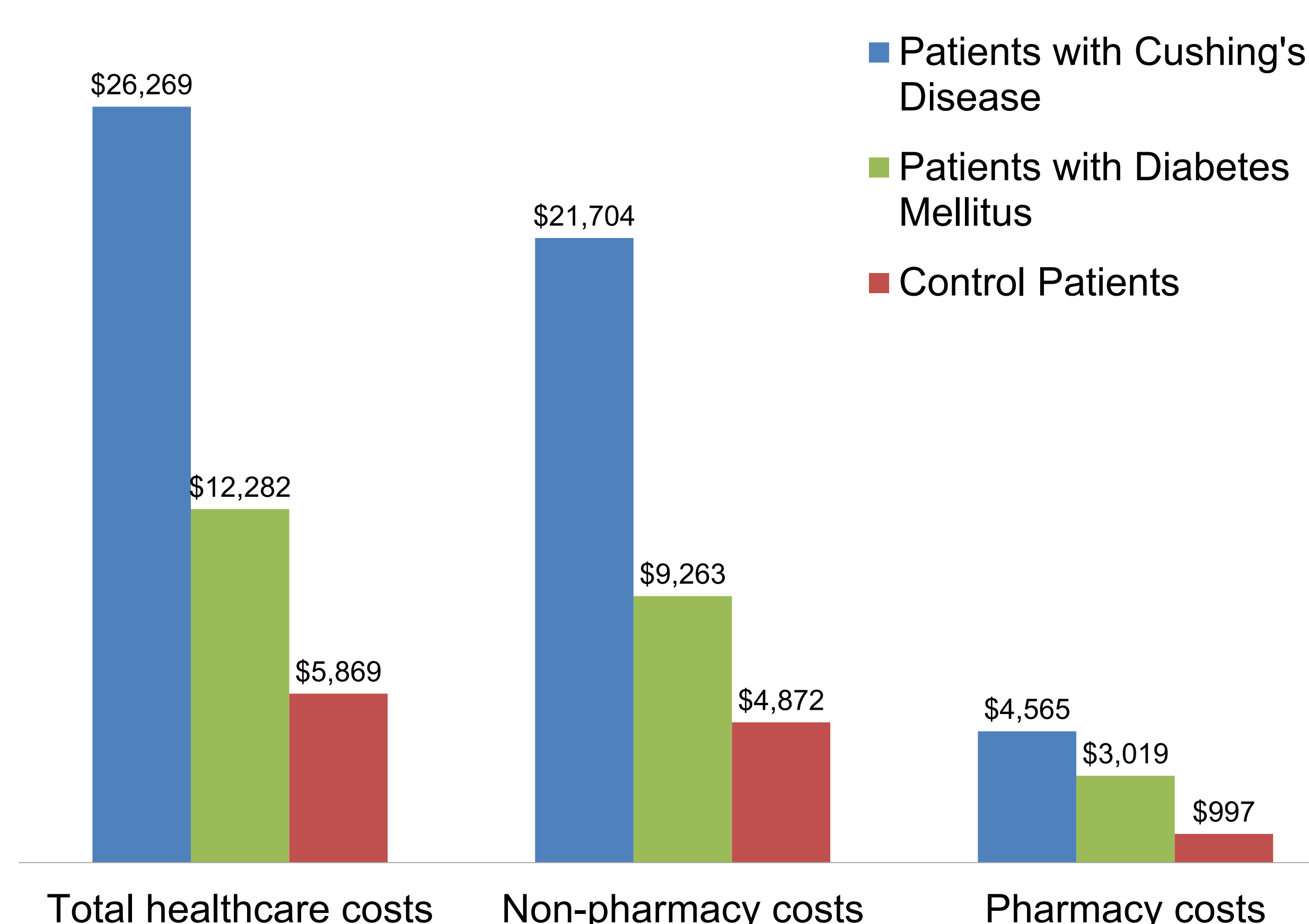
p<.001 for all comparisons (CD vs. DM and CD vs. control).

### TABLE 2. Annual Healthcare Utilization

| No. of inpatient hospitalizations, n (%) | CD (n=1,852) | DM (n=3,704) | Control (n=3,704) |
|------------------------------------------|--------------|--------------|-------------------|
| 0                                        | 1,495 (80.7) | 3,296 (89.0) | 3,497 (94.4)      |
| 1                                        | 226 (12.2)   | 324 (8.7)    | 176 (4.8)         |
| 2                                        | 74 (4.0)     | 55 (1.5)     | 25 (0.7)          |
| 3+                                       | 57 (3.1)     | 29 (0.8)     | 6 (0.2)           |
| No. of ED visits, n (%)                  |              |              |                   |
| 0                                        | 1,381 (74.6) | 2,921 (78.9) | 3,173 (85.7)      |
| 1                                        | 281 (15.2)   | 514 (13.9)   | 395 (10.7)        |
| 2                                        | 107 (5.8)    | 154 (4.2)    | 85 (2.3)          |
| 3+                                       | 83 (4.5)     | 115 (3.1)    | 51 (1.4)          |
| No. of office visits, mean ± SD          | 19.1±17.5    | 10.7±11.3    | 7.1±9.7           |
| No. of prescription fills, mean ± SD     | 51.7±48.6    | 42.7±34.1    | 20.5±23.6         |

p<.001 for all comparisons (CD vs. DM and CD vs. control).

### FIGURE 1. Mean Annual Healthcare Costs



## LIMITATIONS

- Total healthcare costs for controls may be over-estimated, since healthy controls not having claims would not be included in the claims database.
- There are no ICD-9-CM codes specific to CD. The CD algorithm has been published previously, but not validated using medical records.
- Insurance claims are collected for payment, not research.
- Study only included patients with commercial insurance.

## CONCLUSIONS

- The total healthcare cost of CD care was observed to be more than double the cost for diabetic patients and quadruple the cost for population-based controls.
- Our study highlights two potential drivers of this increased cost: higher rates of comorbidities seen in patients with CD, and CD surgical care, a key component of non-pharmacy costs.
- Delay in CD diagnosis, which may prolong symptoms, is another possible cause of increased cost in patients with CD.

## References

- Broder MS, et al. Incidence of Cushing's syndrome and Cushing's disease in commercially-insured patients <65 years old in the United States. *Pituitary*. 2014 May 7. [Epub ahead of print]
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