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ORIGINAL RESEARCH

Economic Burden of Postsurgical Chronic Hypoparathyroidism: A US Medicare Claims Retrospective Analysis

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ABSTRACT

Introduction: Approximately 75% of hypoparathyroidism (HypoPT) cases result from removal of or injury to parathyroid glands during anterior neck surgery. HypoPT persisting 6 months following surgery carries a significant economic burden. This study aims to describe the economic burden of postsurgical chronic HypoPT in the Medicare population.

Methods: Data from the Medicare 100% Limited Data Set between July 1, 2017, and March 31, 2020, were utilized to identify newly diagnosed adults with a confirmed HypoPT diagnosis (n = 1,166) after surgery (index) and their healthcare resource utilization (HCRU) and costs compared with those of control patients who were non-HypoPT (n = 11,258). Continuous enrollment for ≥ 6 months pre- and ≥ 12 months post-index was required. Individuals with postsurgical chronic HypoPT were matched 1:2 to controls on age, gender, race, region, Charlson Comorbidity Index score, and index year. Three economic burden definitions for HCRU and costs were evaluated in unmatched and matched groups: all-cause, direct HypoPT, and HypoPT plus related long-term complications.

Results: Compared with matched controls (n = 1,107), individuals with postsurgical chronic HypoPT (n = 607) had significant differences in baseline number of hospitalizations (0.53 vs. 0.14), outpatient visits (11.40 vs. 1.51), and total medical costs (US$160,899 vs. $21,288). Over a median of 31 months of follow-up, mean all-cause total medical costs per patient per year (PPPY) were significantly higher

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among individuals with postsurgical chronic HypoPT ($227,036 vs. $109,306; $P < 0.001$), largely attributable to higher all-cause medical utilization among the postsurgical chronic HypoPT group (0.72 vs. 0.37 hospitalizations PPPY; 14.4 vs. 7.44 outpatient visits PPPY). Multivariable regression analysis showed that all-cause cost burden among patients with postsurgical chronic HypoPT was 1.57–3.00 times higher, depending on adjustment for baseline renal comorbidities, compared with controls.

Conclusion: The economic burden of postsurgical chronic HypoPT in patients who use Medicare is substantial, highlighting the need for innovative treatments to improve outcomes and quality of life.

Keywords: Economic burden; Healthcare resource utilization; Postsurgical chronic hypoparathyroidism

Key Summary Points

Why carry out this study?

We conducted the study to delineate economic implications, healthcare resource utilization, and costs of patients with postsurgical chronic hypoparathyroidism versus patients without hypoparathyroidism in the Medicare population in the US.

What was learned from the study?

Greater healthcare resource utilization and significantly higher costs were observed at baseline among patients with postsurgical chronic hypoparathyroidism compared with controls in both matched and unmatched cohorts.

The higher levels of healthcare resource utilization and greater costs persisted into the follow-up period as an increased incremental burden (whether measured as all-cause, hypoparathyroidism only, or hypoparathyroidism plus related complications).

INTRODUCTION

Hypoparathyroidism (HypoPT) is an endocrine disease caused by insufficient levels of circulating parathyroid hormone (PTH) with multiorgan involvement. Insufficient levels of PTH lead to hypocalcemia, hyperphosphatemia, and elevated fractional excretion of calcium [1]. HypoPT is primarily due to injury or removal of the parathyroid gland during anterior neck surgery, and is considered chronic if it persists for more than 6 months after surgery, per the 2016 Endocrine Society Guidelines [2], 2019 Canadian and International Consensus Statement [3], and 2022 European Society of Endocrinology Consensus Statement [4]. The 2022 Guidelines from the Second International Workshop consider HypoPT to be permanent if it persists > 12 months following surgery and highlight that the most common definition of permanent HypoPT is a continued requirement for conventional therapy (consisting of active vitamin D and calcium) [5].

Individuals suffering from HypoPT may encounter a spectrum of severe and potentially life-threatening short-term and long-term complications, including neuromuscular irritability, renal issues, extraskeletal calcifications, and cognitive impairment [1, 2, 6–14]. Conventional therapy for HypoPT aims to alleviate hypocalcemia but does not address insufficient PTH [15]. Individuals with chronic HypoPT who receive long-term conventional therapy may have an increased risk of renal complications compared with the general population [16]. Reduced calcium reabsorption in the kidneys due to HypoPT and high doses of oral calcium and active vitamin D lead to increased urinary excretion of calcium. This hypercalciuria can increase the risk of calcium deposits in the kidneys and lead to chronic kidney disease (CKD) [1, 2, 12, 15, 17].

Individuals with postsurgical chronic HypoPT may experience a range of physical and cognitive symptoms and impacts on functioning and well-being, coupled with postsurgical chronic HypoPT-related comorbidities [8, 18]. These conditions are known to substantially disrupt a patient's daily life and often require outpatient treatments, emergency department (ED) visits,

and, in some cases, hospitalizations [8, 19, 20]. Consequently, postsurgical chronic HypoPT carries a significant economic burden, including increased healthcare resource utilization (HCRU), diminished work productivity, and increased patient costs [21–23]. While existing literature underscores the high burden of postsurgical chronic HypoPT from both patient and healthcare perspectives, there is a notable gap in knowledge about HCRU and costs. Evidence is especially limited among adults enrolled in the Medicare program in the United States (US), and it is crucial to address this gap, considering this demographic constitutes over one-third of HypoPT cases in the US [24].

Therefore, this study aimed to address this evidence gap by comparing HCRU and costs in patients with postsurgical chronic HypoPT versus control patients without HypoPT among the Medicare Fee-For-Service population in the US. Additionally, to achieve a more detailed understanding of the economic implications of postsurgical chronic HypoPT, the determinants of increased HCRU and costs were explored.

METHODS

Data Source

This retrospective study utilized Medicare 100% Limited Data Set (LDS) administrative claims from January 1, 2017, to March 31, 2021. The LDS standard analytical files include beneficiary-level information such as demographics, diagnosis, procedure, claim dates, cost, and payment information. The LDS contains data for both institutional and non-institutional providers (i.e., inpatient hospital, outpatient hospital, skilled nursing facility, home health, and hospice).

Patient Selection and Study Design

The patient identification period was July 1, 2017, to March 31, 2021. Medicare beneficiaries aged 18 years or older were categorized into 2 groups: patients with postsurgical chronic HypoPT (n = 1,166) and those without HypoPT (n = 11,258). For individuals with chronic postsurgical HypoPT, the first claim for HypoPT (ICD-10 codes E200, E208, E209, or E892) after a related surgical procedure acted as the index diagnosis (i.e., index date). A patient needed at least 1 claim of a HypoPT-related surgical procedure in the 6-month baseline period prior to index diagnosis, and an additional confirmatory second HypoPT diagnosis in the ≥ 6–12 months from index diagnosis to be considered a patient with postsurgical chronic HypoPT.

The control group included those without a HypoPT diagnosis in the patient identification period but with at least 1 medical claim of any type during the study period. For enrollees without HypoPT, a synthetic index date was assigned based on the distribution of time between the first medical claim of any kind and the index date as observed among individuals with postsurgical chronic HypoPT. Both patient groups had to have had continuous enrollment in Medicare for at least 6 months before and 12 months after the index date. Patients were followed from the index date until the time of death, end of data coverage, or Medicare enrollment, whichever occurred first. Figure 1 illustrates the study design.

Ethical Approval

Due to the de-identified nature of the retrospective dataset, the study did not require ethics committee review. Permission for reuse of the Medicare 100% Limited Data Set was granted by its owner.

Patient and Baseline Characteristics

Baseline sociodemographic characteristics (age, gender, race, ethnicity, census region), clinical characteristics (Charlson Comorbidity Index [CCI] score, cardiovascular complications, infections, renal complications, mental ill-health, fracture, cataract, hypocalcemia, neurological complications), and HCRU and costs (number of hospitalizations, number of outpatient visits, total medical costs) were considered for inclusion in this analysis.

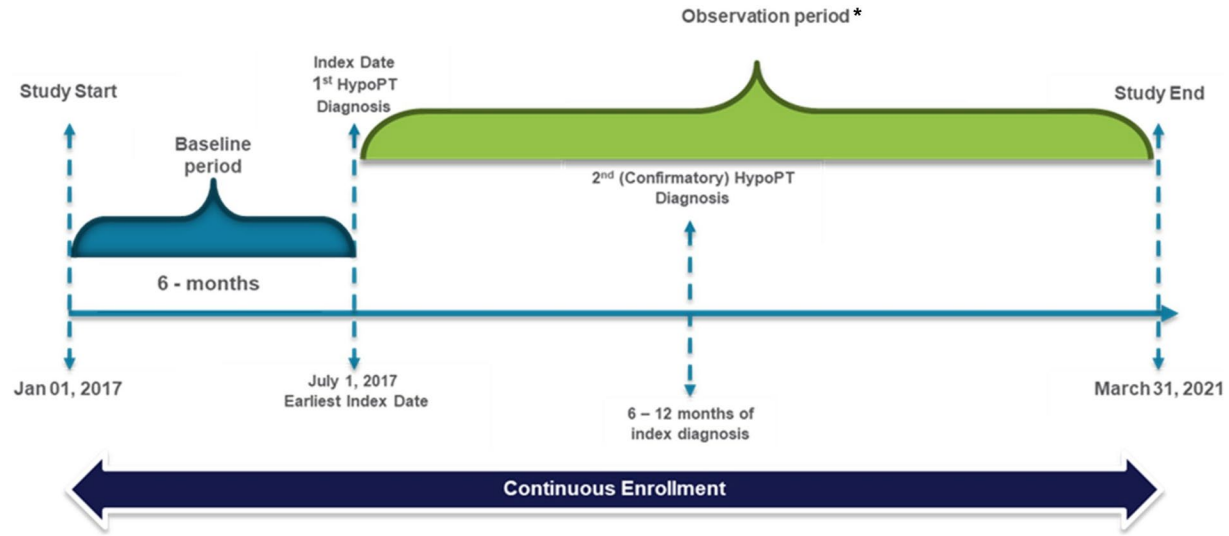


Fig. 1 Study design. *Patients were followed from the index date until the time of death, end of data coverage, or end of Medicare enrollment, whichever occurred first. *HypoPT* hypoparathyroidism

Healthcare Resource Utilization and Costs

To quantify the economic burden, three definitions of HCRU and costs were determined for each patient: all-cause, HypoPT-only, and HypoPT plus related long-term complications. The all-cause burden definition included HCRU and costs from any type of claim. The HypoPT-only definition comprised HCRU and costs from claims with a HypoPT diagnosis code only, which, by definition, would result in 0 values for that particular burden definition for control patients without HypoPT. The HypoPT plus related long-term complication definition included HCRU and costs from claims with either a HypoPT diagnosis code and/or a relevant HypoPT-related long-term complication diagnosis code. The use of the third burden definition allows for a more thorough assessment of HCRU and costs associated with both HypoPT and its related complications. A list of these complications is provided in Table S1 in the Supplementary Material.

HCRU was measured in terms of the number of hospitalizations, ED visits, home health visits, hospice visits, skilled nursing facility visits, and outpatient visits. Costs were assessed both as total medical costs and individually for each category mentioned.

Study Outcomes

Study outcomes included the number and proportion of patients receiving each type of HCRU among the two study cohorts. Also calculated was the average use per patient per year (PPPY) for each resource type and its cost, comparing the two groups. Costs were adjusted for inflation to 2021 US dollars based on the medical care component of the Consumer Price Index.

Statistical Analysis

Analyses for all study objectives were conducted among both unmatched and matched cohorts and then compared with their respective control groups. Via a matching algorithm, a 1:2 matching ratio was employed where individuals with postsurgical chronic HypoPT were matched to potential controls based on age, gender, race, region, CCI score, and index year. The algorithm allowed for a variable ratio between the number of matched cases and control patients, as guided by Faries et al. (2020) and Stuart et al. (2010) [25, 26]. The decision to use a 1:2 matching ratio

aimed to optimize sample size retention while ensuring a balance in baseline characteristics.

Within both the unmatched and matched samples, descriptive statistics were reported for baseline characteristics, HCRU, and costs, stratified by patients with postsurgical chronic HypoPT versus those without HypoPT. Baseline sociodemographic and clinical characteristics are described; frequencies and percentages are reported for categorical variables, and mean, median, and range are reported for continuous ones.

Adjusted multivariable regression analysis was performed to compare all-cause total medical costs and specific HCRU (i.e., all-cause hospitalizations and outpatient visits) between the unmatched study groups. Generalized linear models with a gamma distribution and log-link function were used for modeling costs, while Poisson distribution with a log-link function was used for modeling resource utilization. The main model (i.e., Model 1) was fully adjusted for age, gender, race, region, and comorbidities and complications at baseline. Additional models aimed to investigate the specific factors influencing all-cause total medical costs and specific HCRU. Model 2 did not adjust for baseline nephrocalcinosis, nephrolithiasis, or stage 3–5 CKD to explore the effect of renal complications on the burden coefficient for postsurgical chronic HypoPT. Model 3 explored the determinants of all-cause total medical costs and specific HCRU, irrespective of whether or not patients were flagged as having postsurgical chronic HypoPT. A cost ratio > 1.0 with a *P* value below 0.05 indicated a significant influence on all-cause total medical costs. All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Patient and Baseline Characteristics

Following the study criteria, a total of 1166 patients with postsurgical chronic HypoPT and 11,258 patients without HypoPT were included (Fig. 2). After matching, there were 607 patients with postsurgical chronic HypoPT and 1107 control patients without HypoPT. Unmatched patients with postsurgical chronic HypoPT were slightly older (median age of 69 vs. 64 years) and a greater proportion were female (76% vs. 57%) than those without HypoPT. Compared with controls at baseline, patients with post-surgical chronic HypoPT had a higher CCI score (3.24 vs. 0.73) and a much higher prevalence of long-term complications, including stage 3–4 (14.1% vs. 1.8%) and stage 5 (12.4% vs. 1.8%) CKD, nephrocalcinosis (59.9% vs. 0.6%), nephrolithiasis (8.3% vs. 1.0%), urinary tract infections (9.9% vs. 2.2%), and congestive heart failure (13.1% vs. 3.0%). Moreover, during the baseline period, patients with post-surgical chronic HypoPT experienced a significantly higher number of hospitalizations (0.62 vs. 0.07), outpatient visits (11.51 vs. 1.39), and increased medical costs ($152,021 vs. $11,117) than the unmatched controls (Table S2 in the Supplementary Material).

After matching, the following baseline differences remained: there was a higher prevalence of stage 3–4 (8.6% vs. 5.5%) and stage 5 (15.8% vs. 4.5%) CKD, nephrocalcinosis (59.6% vs. 1.0%), nephrolithiasis (9.9% vs. 1.2%), urinary tract infections (7.9% vs. 2.9%), and congestive heart failure (10.4% vs. 7.0%) for the patients with postsurgical chronic HypoPT compared with the control group (Table 1). Although less pronounced than in the unmatched cohort, significant differences in baseline number of hospitalizations (0.53 vs. 0.14), outpatient visits (11.40 vs. 1.51), and total medical costs ($160,899 vs. $21,288) were still observed.

Healthcare Costs and Healthcare Resource Utilization

In the follow-up period, comparison of the matched cohorts' all-cause healthcare costs revealed that patients with post-surgical chronic HypoPT had approximately $117,730 higher average total medical costs PPPY than control patients without HypoPT ($227,036 vs. $109,306, $P < 0.001$) (Fig. 3a). Notably, specific categories like hospitalizations ($50,301 vs. $30,207; $P = 0.002$), ED visits ($3,354 vs. $1,450;

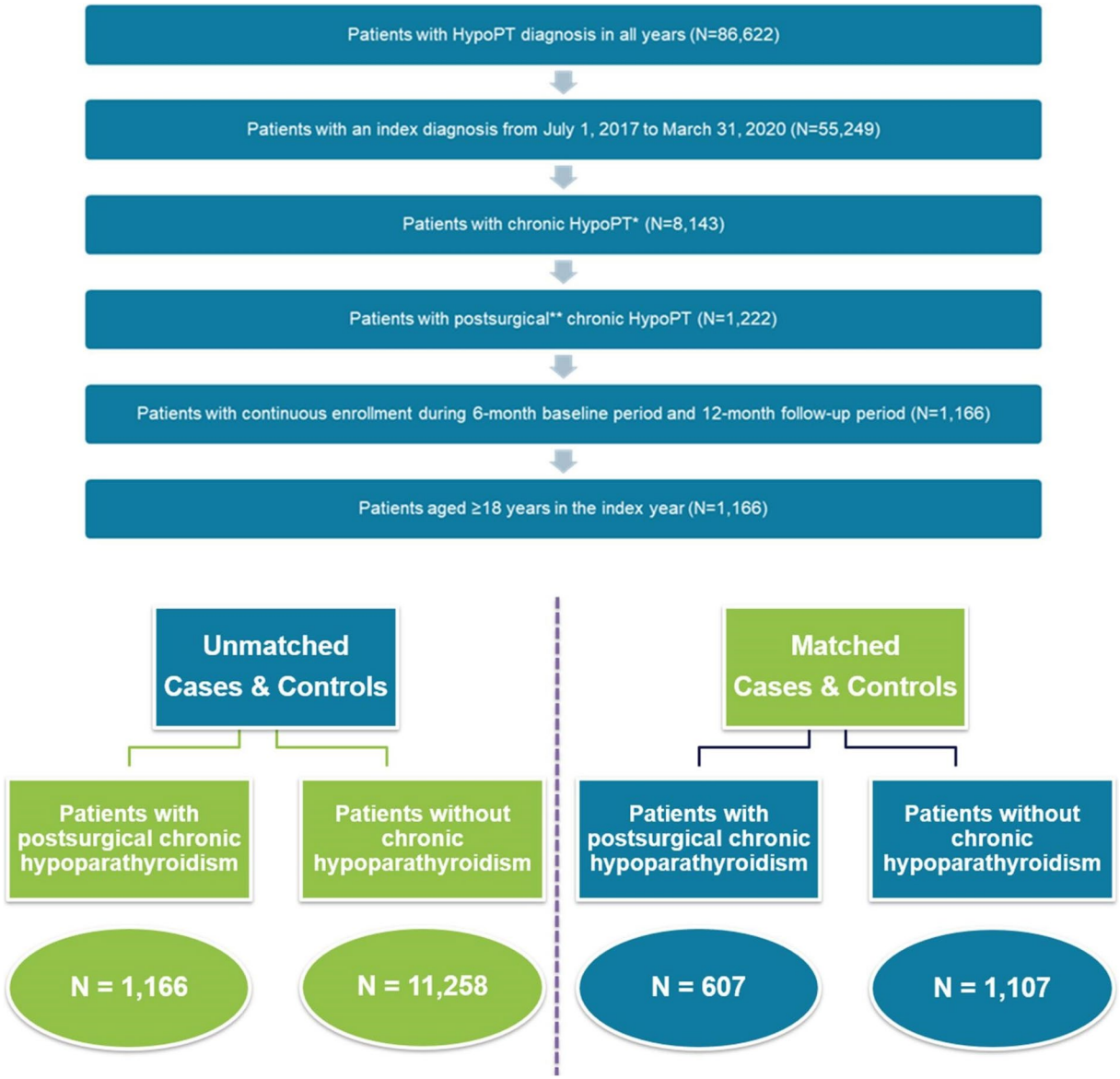


Fig. 2 Patient attrition and overall study population before and after matching. *Confirmatory diagnosis within 6–12 months of index diagnosis was required. **Hypoparathyroidism-related surgeries (including thyroidectomy, parathyroidectomy, goiter removal, excision procedures on the parathyroid, and resection of the thyroid gland) in the 6-month baseline period. *HypoPT* hypoparathyroidism

$P < 0.001$), and outpatient visits ($174,915 vs. $77,462; $P < 0.001$) exhibited significantly higher average healthcare costs PPPY for patients with post-surgical chronic HypoPT as compared with matched controls without HypoPT (Fig. 3a). On average, the HypoPT-only specific total medical costs were $60,669 PPPY while HypoPT plus complication-related economic burden was significantly higher by $107,356 for patients with post-surgical chronic HypoPT compared with matched controls without HypoPT (Fig. 3b).

The all-cause HCRU comparison among the matched cohort indicates that patients with post-surgical chronic HypoPT had, on average, a significantly higher number of

Table 1 Sociodemographic and clinical characteristics of patients with postsurgical chronic hypoparathyroidism and matched control patients without hypoparathyroidism

		Medicare enrollees			
Variable	**Statistic or category**	**All**	**Patients with postsurgical chronic hypoparathyroidism**	**Matched Medicare control patients without hypoparathyroidism**	***P* value**
		(*n* = 1,714)	**(*n* = 607)**	**(*n* = 1,107)**	
Follow-up period after index diagnosis (months)	*n*	1,714	607	1,107	0.865[W]
	Mean (SD)	29.75 (8.92)	29.68 (8.87)	29.79 (8.95)	
	Median (Q1–Q3)	31.0 (23.0 to 37.0)	31.0 (22.0 to 37.0)	31.0 (23.0 to 37.0)	
	Range	12.0 to 45.0	12.0 to 44.0	12.0 to 45.0	
Age at index diagnosis	*n*	1714	607	1,107	0.686[W]
	Mean (SD)	63.69 (9.59)	62.72 (11.17)	64.22 (8.55)	
	Median (Q1 to Q3)	65.0 (63.0–69.0)	66.0 (58.0–70.0)	65.0 (64.0–68.0)	
	Range	20.0–92.0	22.0–92.0	20.0–92.0	
Age categorical, *n* (%)	18–65 years	861 (50.2%)	301 (49.6%)	560 (50.6%)	0.648[C]
	66–75 years	776 (45.3%)	275 (45.3%)	501 (45.3%)	
	76 + years	77 (4.5%)	31 (5.1%)	46 (4.2%)	
Gender, *n* (%)	Male	437 (25.5%)	158 (26.0%)	279 (25.2%)	0.707[C]
	Female	1,277 (74.5%)	449 (74.0%)	828 (74.8%)	
Race, *n* (%)	White	1354 (79.0%)	472 (77.8%)	882 (79.7%)	0.967[C]
	Black	265 (15.5%)	97 (16.0%)	168 (15.2%)	
	Asian	12 (0.7%)	< 11[b]	< 11[b]	
	Hispanic	44 (2.6%)	17 (2.8%)	27 (2.4%)	
	North American Native	< 11[b]	< 11[b]	< 11[b]	
	Other[c]	< 11[b]	< 11[b]	< 11[b]	
	Unknown	29 (1.7%)	12 (2.0%)	17 (1.5%)	
Geographic region, *n* (%)	North Central	560 (32.7%)	195 (32.1%)	365 (33.0%)	0.986[C]
	Northeast	234 (13.7%)	84 (13.8%)	150 (13.6%)	
	South	653 (38.1%)	232 (38.2%)	421 (38.0%)	
	West	267 (15.6%)	96 (15.8%)	171 (15.4%)	

Table 1 continued

Variable	Statistic or category	Medicare enrollees			
		All	Patients with post-surgical chronic hypoparathyroidism	Matched Medicare control patients without hypoparathyroidism	*P* value
		(*n* = 1,714)	(*n* = 607)	(*n* = 1,107)	
Year of index date, *n* (%)	2017	379 (22.1%)	137 (22.6%)	242 (21.9%)	0.926[C]
	2018	758 (44.2%)	265 (43.7%)	493 (44.5%)	
	2019	515 (30.0%)	181 (29.8%)	334 (30.2%)	
	2020	62 (3.6%)	24 (4.0%)	38 (3.4%)	
Charlson Comorbidity Index Score (continuous)	*n*	1,714	607	1,107	0.120[W]
	Mean (SD)	1.96 (2.28)	2.11 (2.41)	1.87 (2.20)	
	Median (Q1–Q3)	1.0 (0.0–3.0)	2.0 (0.0–3.0)	1.0 (0.0–3.0)	
	Range	0.0–14.0	0.0–14.0	0.0–13.0	
Charlson Comorbidity Index Score (categorical), *n* (%)	0	607 (35.4%)	206 (33.9%)	401 (36.2%)	0.726[C]
	1	277 (16.2%)	97 (16.0%)	180 (16.3%)	
	2	330 (19.3%)	118 (19.4%)	212 (19.2%)	
	3 +	500 (29.2%)	186 (30.6%)	314 (28.4%)	
Charlson Comorbidity Index Score (categorical expanded), *n* (%)	0	607 (35.4%)	206 (33.9%)	401 (36.2%)	0.692[C]
	1	277 (16.2%)	97 (16.0%)	180 (16.3%)	
	2	330 (19.3%)	118 (19.4%)	212 (19.2%)	
	3–5	360 (21.0%)	129 (21.3%)	231 (20.9%)	
	6–8	108 (6.3%)	42 (6.9%)	66 (6.0%)	
	9 +	32 (1.9%)	15 (2.5%)	17 (1.5%)	
Hypoparathyroidism-related complications	Acute myocardial infarction, *n* (%)	16 (0.9%)	< 11[b]	[b]	0.444[E]
	Congestive heart failure, *n* (%)	140 (8.2%)	63 (10.4%)	77(7.0%)	0.013[C]
	Stroke, *n* (%)	29 (1.7%)	< 11[b]	[b]	0.619[C]
	Arrhythmia, *n* (%)	36 (2.1%)	22 (3.6%)	14 (1.3%)	0.001[C]
	Ischemic heart disease, *n* (%)	205 (12.0%)	88 (14.5%)	117 (10.6%)	0.017[C]
	All infections, *n* (%)	379 (22.1%)	192 (31.6%)	187 (16.9%)	< 0.001[C]

Table 1 continued

Variable	Statistic or category	Medicare enrollees			
		All	Patients with post-surgical chronic hypoparathyroidism	Matched Medicare control patients without hypoparathyroidism	*P* value
		(*n* = 1,714)	(*n* = 607)	(*n* = 1,107)	
	Hospitalization for all infections, *n* (%)	110 (6.4%)	53 (8.7%)	57 (5.1%)	0.004[C]
	Upper respiratory tract infections, *n* (%)	115 (6.7%)	63 (10.4%)	52 (4.7%)	< 0.001[C]
	Urinary tract infections, *n* (%)	80 (4.7%)	48 (7.9%)	32 (2.9%)	< 0.001[C]
	Nephrocalcinosis, *n* (%)	373 (21.8%)	362 (59.6%)	11 (1.0%)	< 0.001[C]
	Nephrolithiasis, *n* (%)	73 (4.3%)	60 (9.9%)	13 (1.2%)	< 0.001[C]
	Cataracts, *n* (%)	33 (1.9%)	17 (2.8%)	16 (1.4%)	0.051[C]
	Chronic kidney disease stage 3 or 4, *n* (%)	113 (6.6%)	52 (8.6%)	61 (5.5%)	0.015[C]
	Chronic kidney disease stage 5, *n* (%)	146 (8.5%)	96 (15.8%)	50 (4.5%)	< 0.001[C]
	Delirium, *n* (%)	< 11[b]	< 11[b]	< 11[b]	> 0.999[E]
	Depression, *n* (%)	187 (10.9%)	117 (19.3%)	70 (6.3%)	< 0.001[C]
	Fracture, *n* (%)	37 (2.2%)	17 (2.8%)	20 (1.8%)	0.176[C]
	Hallucination/Agitation, *n* (%)	< 11[b]	< 11[b]	< 11[b]	0.194[E]
	Hypocalcemia, *n* (%)	[b]	30 (4.9%)	< 11[b]	< 0.001[C]
Number of hospitalizations	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	0.28 (0.75)	0.53 (1.09)	0.14 (0.42)	
	Median (Q1–Q3)	0.0 (0.0–0.0)	0.0 (0.0–1.0)	0.0 (0.0–0.0)	
	Range	0.0–12.0	0.0–12.0	0.0–3.0	

Table 1 continued

Variable	Statistic or category	Medicare enrollees			*P* value
		All	Patients with post-surgical chronic hypoparathyroidism	Matched Medicare control patients without hypoparathyroidism	
		(*n* = 1,714)	(*n* = 607)	(*n* = 1,107)	
Number of outpatient visits	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	5.01 (6.09)	11.40 (6.31)	1.51 (1.03)	
	Median (Q1–Q3)	2.0 (1.0–8.0)	10.0 (7.0–14.0)	1.0 (1.0–2.0)	
	Range	0.0–44.0	1.0–44.0	0.0–14.0	
Number of SNF visits	*n*	1,714	607	1,107	0.002[W]
	Mean (SD)	0.02 (0.28)	0.05 (0.40)	0.01 (0.19)	
	Median (Q1–Q3)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
	Range	0.0–6.0	0.0–5.0	0.0–6.0	
Number of home health visits	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	0.04 (0.26)	0.09 (0.39)	0.02 (0.14)	
	Median (Q1–Q3)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
	Range	0.0–3.0	0.0–3.0	0.0–2.0	
Number of hospice visits	*n*	1,714	607	1,107	> 0.999[W]
	Mean (SD)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	
	Median (Q1–Q3)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
	Range	0.0–0.0	0.0–0.0	0.0–0.0	
Number of ED visits	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	0.49 (1.28)	0.90 (1.95)	0.27 (0.56)	
	Median (Q1–Q3)	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.0 (0.0–0.0)	
	Range	0.0–24.0	0.0–24.0	0.0–4.0	
Total hospitalization costs ($)	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	20,026.34 (79,659.46)	35,501.51 (105,932.1)	11,540.86 (58,959.45)	
	Median (Q1–Q3)	0.0 (0.0–0.0)	0.0 (0.0–30,703.4)	0.0 (0.0–0.0)	
	Range	0.0–1,438,851	0.0–1,438,851	0.0–1,193,645	

Table 1 continued

Variable	Statistic or category	Medicare enrollees			*P* value
		All	Patients with post-surgical chronic hypoparathyroidism	Matched Medicare control patients without hypoparathyroidism	
		(*n* = 1,714)	(*n* = 607)	(*n* = 1,107)	
Total outpatient costs ($)	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	50,316.33 (141,678.2)	124,545.9 (216,756.7)	9614.12 (25,762.73)	
	Median (Q1–Q3)	6,375.9 (731.5–39,297.5)	45,666.7 (31,449.1–76,447.9)	1,248.4 (372.6–6073.4)	
	Range	0.0–1,374,087	880.3–1,374,087	0.0–295,085.8	
Total SNF costs ($)	*n*	1,714	607	1,107	0.002[W]
	Mean (SD)	277.07 (3,594.57)	627.88 (5,562.39)	84.71 (1,718.99)	
	Median (Q1–Q3)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
	Range	0.0–83,451.6	0.0–83,451.6	0.0–54,194.3	
Total home health costs ($)	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	110.44 (794.14)	224.11 (1,184.12)	48.12 (444.45)	
	Median (Q1–Q3)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
	Range	0.0–14,040.5	0.0–14,040.5	0.0–7983.3	
Total hospice costs ($)	*n*	1,714	607	1,107	> 0.999[W]
	Mean (SD)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	
	Median (Q1–Q3)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
	Range	0.0–0.0	0.0–0.0	0.0–0.0	
Total ED costs ($)[a]	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	977.93 (2861.50)	1691.68 (4203.38)	586.57 (1602.59)	
	Median (Q1–Q3)	0.0 (0.0–393.4)	0.0 (0.0–1648.3)	0.0 (0.0–0.0)	
	Range	0.0–41,746.2	0.0–41,746.2	0.0–15,520.0	
Total medical costs ($)	*n*	1,714	607	1,107	< 0.001[W]
	Mean (SD)	70,730.19 (176,057.3)	160,899.4 (259,689.1)	21,287.80 (64,403.01)	
	Median (Q1–Q3)	15,159.2 (1024.5–56,779.8)	58,091.0 (37,408.9–118,889.3)	2003.9 (521.7–12,910.1)	
	Range	19.5–1,814,984	10,914.4–1,814,984	19.5–1,193,645	

Table 1 continued

Variable	Statistic or category	Medicare enrollees			
		All	Patients with post-surgical chronic hypoparathyroidism	Matched Medicare control patients without hypoparathyroidism	*P* value
		(*n* = 1,714)	(*n* = 607)	(*n* = 1,107)	
Components of the Charlson Comorbidity Index	Myocardial infarction, *n* (%)	75 (4.4%)	25 (4.1%)	50 (4.5%)	0.700[C]
	Congestive heart failure, *n* (%)	140 (8.2%)	63 (10.4%)	77 (7.0%)	0.013[C]
	Peripheral vascular disease, *n* (%)	99 (5.8%)	37 (6.1%)	62 (5.6%)	0.675[C]
	Dementia, *n* (%)	13 (0.8%)	< 11[b]	< 11[b]	0.779[E]
	Cerebrovascular disease, *n* (%)	96 (5.6%)	35 (5.8%)	61 (5.5%)	0.826[C]
	Chronic pulmonary disease, *n* (%)	268 (15.6%)	126 (20.8%)	142 (12.8%)	< 0.001[C]
	Rheumatologic disease, *n* (%)	41 (2.4%)	16 (2.6%)	25 (2.3%)	0.625[C]
	Ulcers, *n* (%)	12 (0.7%)	< 11[b]	< 11[b]	0.006[E]
	Mild liver disease, *n* (%)	77 (4.5%)	32 (5.3%)	45 (4.1%)	0.249[C]
	Diabetes without complications, *n* (%)	335 (19.5%)	113 (18.6%)	222 (20.1%)	0.473[C]
	Diabetes with chronic complications, *n* (%)	216 (12.6%)	72 (11.9%)	144 (13.0%)	0.494[C]
	Hemiplagia, *n* (%)	[b]	< 11[b]	15 (1.4%)	0.949[C]
	Moderate or severe renal disease, *n* (%)	316 (18.4%)	158 (26.0%)	158 (14.3%)	< 0.001[C]
	Any tumor/leukemia/lymphoma, *n* (%)	295 (17.2%)	105 (17.3%)	190 (17.2%)	0.944[C]

Table 1 continued

Variable	Statistic or category	Medicare enrollees			
		All	Patients with post-surgical chronic hypoparathyroidism	Matched Medicare control patients without hypoparathyroidism	*P* value
		(*n* = 1,714)	(*n* = 607)	(*n* = 1,107)	
	Moderate or severe liver disease, *n* (%)	< 11[b]	< 11[b]	< 11[b]	0.729[E]
	Metastatic solid tumor, *n* (%)	62 (3.6%)	20 (3.3%)	42 (3.8%)	0.597[C]
	AIDS, *n* (%)	16 (0.9%)	< 11[b]	16 (1.4%)	0.001[E]

Total medical costs were calculated as the sum of inpatient, outpatient, skilled nursing facility, home health agency, and hospice costs

All costs are presented in 2021 US dollars

ED emergency department, *SNF* skilled nursing facility

[a]ED costs are a subcomponent of other categories of costs and thus are not included in Total Medical Costs to avoid double-counting

[b]As per the Centers for Medicare and Medicaid Services' cell suppression policy, no cells with values < 11 can be directly reported or other neighboring cells that allow for the re-identification of cells of values < 11

[c] The demographic terminology reported in this table reflects that reported by the SEER-Medicare race_code variable. No further specification of ethnicities can be provided

[d]*P* value legend: *C* CHISQ, *E* Exact Fisher, *W* Wilcoxon Rank Sum

hospitalizations (0.72 vs. 0.37; $P < 0.001$), home health visits (0.31 vs. 0.20; $P = 0.033$), ED visits (1.57 vs. 0.65; $P < 0.001$), and outpatient visits (14.4 vs. 7.44; $P < 0.001$) compared with matched controls without HypoPT in the follow-up period (Fig. 4a). The average number of hospitalizations and outpatient visits PPPY by different burden definitions among the matched cohort revealed that patients with post-surgical chronic HypoPT experienced 0.19 HypoPT-specific hospitalizations and had 2.48 HypoPT-specific outpatient visits PPPY. Moreover, the HypoPT plus related long-term complication-specific hospitalizations were significantly higher among patients with post-surgical chronic HypoPT (0.66 vs. 0.32; $P < 0.001$), as were the HypoPT plus related long-term complication-specific outpatient visits (6.38 vs. 1.96; $P < 0.001$) in comparison with their matched controls without HypoPT (Fig. 4b). The difference in all-cause healthcare costs and HCRU remained higher for patients with post-surgical chronic HypoPT and compared with unmatched patients without HypoPT (Figure S1 and Figure S2 in the Supplementary Material).

Multivariable Regression Models

Factors influencing all-cause total medical costs between patients with post-surgical chronic HypoPT and unmatched controls are displayed in Table 2. Model 1 showed that post-surgical chronic HypoPT was associated with 57% higher all-cause total medical cost burden (cost ratio: 1.57; $P < 0.001$) than patients without HypoPT. Baseline conditions like stage 3 or 4 (cost ratio: 1.84; $P < 0.001$) and stage 5 (cost ratio: 12.40; $P < 0.001$) CKD displayed a significant effect on all-cause burden. However, there was no association effect observed for

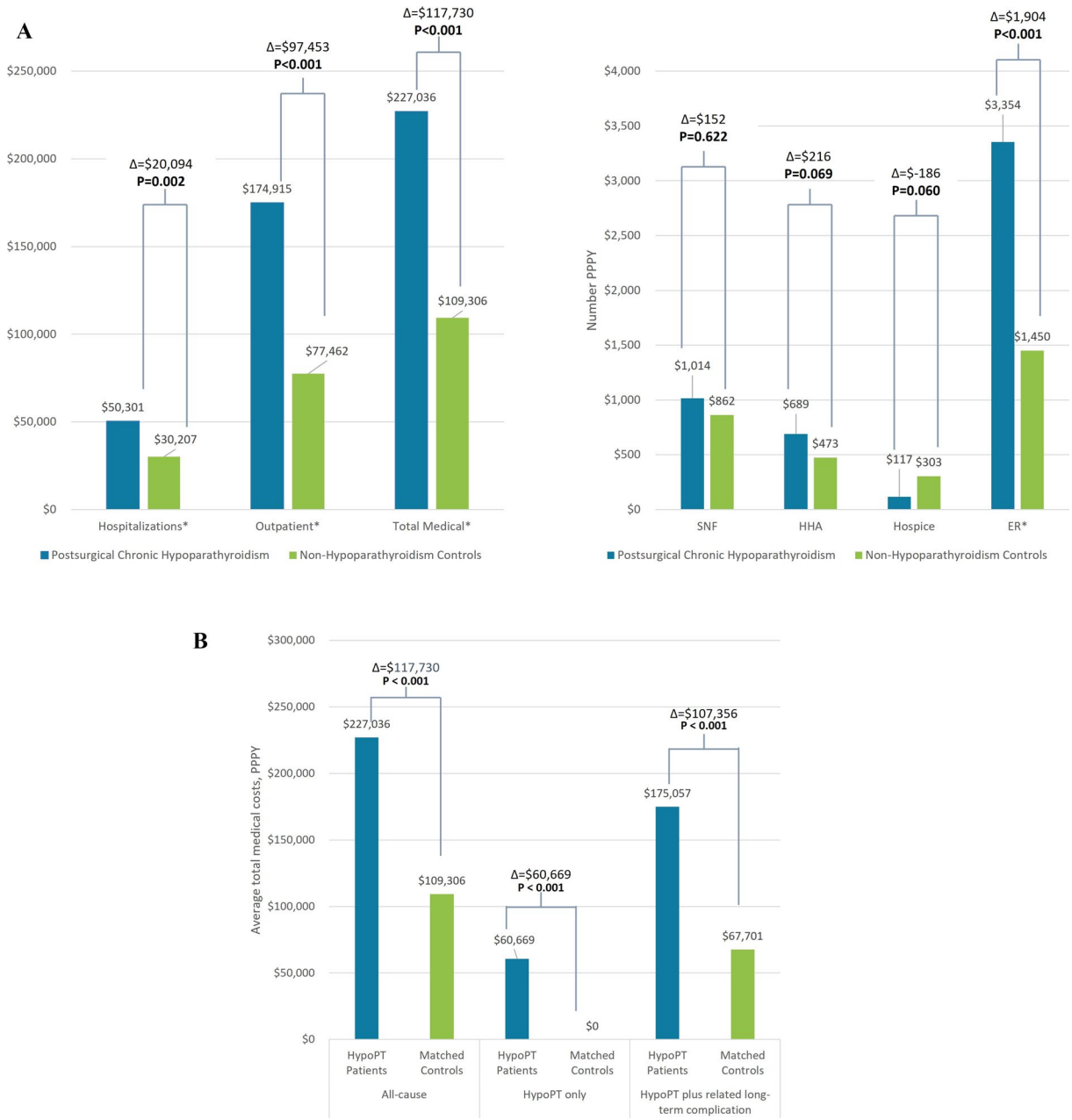


Fig. 3 Healthcare costs per patient per year among patients with post-surgical chronic HypoPT and matched controls during the entire follow-up period: **a** all-cause; *b* total medical costs by burden definitions. Total medical costs were calculated as the sum of inpatient, outpatient, skilled nursing facility, home health agency and hospice costs. ER costs are a cost category of interest that is already captured under inpatient/outpatient costs. All costs are presented in 2021 US dollars. *ER* emergency room, *HHA* home health agency, *HypoPT* hypoparathyroidism, *PPPY* per patient per year, *SNF* skilled nursing facility. **P* value < 0.05

baseline nephrocalcinosis or nephrolithiasis. Model 2 demonstrated that, without adjusting for baseline renal complications, patients with post-surgical chronic HypoPT had 3 times higher all-cause burden (cost ratio: 3.00; $P < 0.001$) than unmatched controls. Model 3 displayed



Fig. 4 Healthcare resource utilization per patient per year among patients with postsurgical chronic HypoPT and matched controls during the entire follow-up period: **a** all-cause; **b** by burden definition. *ER* emergency room, *HHA* home health agency, *HypoPT* post-surgical chronic hypoparathyroidism, *PPPY* per patient per year, *SNF* skilled nursing facility

that, without adjusting for diagnosis of HypoPT, baseline conditions like nephrocalcinosis (cost ratio: 1.35; $P < 0.001$), stage 3 or 4 (cost ratio: 1.93; $P < 0.001$), and stage 5 (cost ratio: 13.13; $P < 0.001$) CKD were associated with a significant increase in all-cause costs, while nephrolithiasis had no significant association effect.

Predictors of all-cause hospitalizations and outpatient visits, respectively, between postsurgical chronic HypoPT and unmatched controls without HypoPT are shown in Tables S3 and S4 in the Supplementary Material.

DISCUSSION

Chronic HypoPT is associated with a substantial burden of disease and high HCRU [8, 19, 21, 27]. To our knowledge, no prior study has

assessed the economic burden of all-cause, disease-specific (i.e., HypoPT), and HypoPT plus related long-term complications in the US Medicare dataset. Examining the Medicare population is especially important, given it represents a significant proportion of all patients with HypoPT. This study demonstrated a significant incremental burden of all-cause, direct HypoPT, and HypoPT plus related long-term complications compared with controls in both matched and unmatched cohorts. The presence of renal disease at baseline emerged as a pivotal determinant influencing the difference in observed economic burden between the study groups. The current study highlighted those clinical distinctions, particularly in that the prevalence of complications and associated costs at baseline persisted into the follow-up period, underscoring the lasting impact of these factors on the economic burden experienced by patients with postsurgical chronic HypoPT.

The all-cause incremental burden associated with postsurgical chronic HypoPT was predominantly attributable to direct HypoPT care and related complications (i.e., $107,356), accounting for over 90% of the overall incremental all-cause burden (i.e., $117,730), while the disease-specific incremental burden of direct HypoPT-only care (i.e., $60,669) constituted approximately 51% of the all-cause burden. This highlights the substantial impact of long-term complications on the economic burden of postsurgical chronic HypoPT extending beyond the disease's direct impact. Further, this study showed a 60% increase in mean inpatient hospitalization costs PPPY in the matched cohort (approximately $50,000 vs. $30,000), while mean ED costs more than doubled PPPY (approximately $3,300 vs. $1,500) between the study cohorts. These findings align with a prior US-based study showing an increase in HypoPT-related inpatient and ED costs from 2010–2018 national data [19]. In that study, mean inpatient costs were $27,500 versus $13,300, while ED costs visits were $5,000 versus $4,300 for patients with HypoPT versus matched controls without HypoPT [19]. The higher average age in this study (63–64 years) compared with the referenced study (40–49 years), as well as differences in study design, may account for the observed differences in cost estimates. A 2017 retrospective cohort study based on US claims data from 2010–2015 also found high levels of healthcare utilization and costs for patients with chronic HypoPT, with mean annual all-cause healthcare expenditures totaling $26,889 [28]. The average age in that study was 54, so the younger cohort could again explain the lower healthcare costs compared with the current study, where mean all-cause medical costs for patients with postsurgical chronic HypoPT were roughly $200,000 PPPY. Nevertheless, the present study adds value to the existing literature by emphasizing the nationally representative economic burden in the Medicare Fee-For-Service population, which has a sizeable prevalence of HypoPT cases [24].

The present study adds to the growing body of evidence on increased HCRU among patients with postsurgical chronic HypoPT. Our study found that patients with postsurgical chronic HypoPT were hospitalized twice as often as controls without HypoPT and that the all-cause HCRU burden was notably higher among these patients. Healthcare resource utilization related to HypoPT and its related complications significantly contributed to the overall all-cause burden compared with controls without HypoPT. While there is a lack of studies assessing HCRU among US-based patients with postsurgical chronic HypoPT, a multicountry cohort study of 614 patients with chronic HypoPT revealed significantly higher outpatient, ED, and hospital visits. It also found that ED visits were generally due to HypoPT-related symptoms, while inpatient hospitalizations were due to HypoPT-related comorbidities, further supporting the findings of the present study [22].

To our knowledge, this study is the first to identify risk factors for HCRU and cost increases among patients with postsurgical chronic HypoPT. This study reveals multidirectional relationships among nephrocalcinosis, nephrolithiasis, CKD, and postsurgical chronic HypoPT influencing the all-cause healthcare burden. A companion study on the clinical burden of postsurgical chronic HypoPT found that, among patients with no renal complications at baseline, patients with postsurgical chronic HypoPT had more than 11 times higher risk of developing nephrocalcinosis and 4 times higher risk of

Table 2 Predictors of all-cause total medical costs during follow-up between unmatched patients with postsurgical chronic hypoparathyroidism and controls without hypoparathyroidism

Gamma model										
		Model 1: Full model			Model 2: Model 1 without nephrocalcinosis, nephrolithiasis, or chronic kidney disease			Model 3: Model 1 without flag for patients with postsurgical chronic HypoPt		
Variable	Level	Cost ratio	Level *P* value	Type 3 *P* value	Cost ratio	Level *P* value	Type 3 *P* value	Cost ratio	Level *P* value	Type 3 *P* value
Pos-surgical chronic HypoPT (Ref: unmatched Medicare controls)	Patients with post-surgical chronic HypoPT	1.57	< 0.001	< 0.001	3.00	< 0.001	< 0.001	–	–	–
Categorical age (Ref: 18–65)	66–75	0.79	< 0.001	< 0.001	0.65	< 0.001	< 0.001	0.85	0.001	< 0.001
	75 +	1.11	0.364		0.72	0.002		1.29	0.023	
Gender (Ref: Male)	Female	0.63	< 0.001	< 0.001	0.59	< 0.001	< 0.001	0.65	< 0.001	< 0.001
Race (Ref: White)	Unknown	1.06	0.520	< 0.001	1.17	0.080	< 0.001	1.05	0.585	< 0.001
	Black	1.53	< 0.001		2.22	< 0.001		1.54	< 0.001	
	Other[a]	1.17	0.251		1.94	< 0.001		1.18	0.239	
	Asian	1.11	0.443		1.79	< 0.001		1.13	0.345	
	Hispanic	1.66	< 0.001		2.69	< 0.001		1.64	< 0.001	
	North American Native	0.73	0.166		1.32	0.207		0.73	0.158	
Region (Ref: South)	Northeast	0.84	< 0.001	< 0.001	0.85	0.001	< 0.001	0.83	< 0.001	< 0.001
	North Central	0.75	< 0.001		0.69	< 0.001		0.75	< 0.001	
	West	0.97	0.548		0.98	0.758		0.97	0.628	
	Other/unknown	4.99	< 0.001		5.28	< 0.001		4.87	< 0.001	
Acute myocardial infarction (Ref: No)	Yes	1.11	0.667	0.662	0.92	0.736	0.739	1.11	0.664	0.659

Table 2 continued

Gamma model										
		Model 1: Full model			Model 2: Model 1 without nephrocalcinosis, nephrolithiasis, or chronic kidney disease			Model 3: Model 1 without flag for patients with postsurgical chronic HypoPt		
Variable	Level	Cost ratio	Level *P* value	Type 3 *P* value	Cost ratio	Level *P* value	Type 3 *P* value	Cost ratio	Level *P* value	Type 3 *P* value
Ischemic heart disease (Ref: No)	Yes	0.99	0.890	0.890	0.97	0.628	0.629	1.03	0.689	0.688
Congestive heart failure (Ref: No)	Yes	1.68	< 0.001	< 0.001	2.47	< 0.001	< 0.001	1.73	< 0.001	< 0.001
Stroke (Ref: No)	Yes	1.61	0.019	0.011	1.72	0.006	0.003	1.60	0.021	0.013
Arrhythmia (Ref: No)	Yes	1.10	0.548	0.542	0.98	0.919	0.919	1.21	0.251	0.238
All infections (Ref: No)	Yes	0.97	0.610	0.612	0.92	0.187	0.192	1.00	0.975	0.975
Hospitalization for all infections (Ref: No)	Yes	2.26	< 0.001	< 0.001	2.60	< 0.001	< 0.001	2.23	< 0.001	< 0.001
Upper respiratory tract infections (Ref: No)	Yes	0.97	0.794	0.794	1.05	0.650	0.649	1.00	0.994	0.994
Urinary tract infections (Ref: No)	Yes	1.16	0.219	0.214	0.90	0.364	0.369	1.16	0.235	0.230
Nephrocalcinosis (Ref: No)	Yes	1.01	0.888	0.887				1.35	< 0.001	< 0.001
Nephrolithiasis (Ref: No)	Yes	0.79	0.102	0.113				0.89	0.429	0.436
Cataracts (Ref: No)	Yes	1.01	0.965	0.965	0.90	0.488	0.495	1.09	0.594	0.589

Table 2 continued

Gamma model										
		Model 1: Full model			Model 2: Model 1 without nephrocalcinosis, nephrolithiasis, or chronic kidney disease			Model 3: Model 1 without flag for patients with postsurgical chronic HypoPt		
Variable	Level	Cost ratio	Level *P* value	Type 3 *P* value	Cost ratio	Level *P* value	Type 3 *P* value	Cost ratio	Level *P* value	Type 3 *P* value
Chronic kidney disease stage 3 or 4 (Ref: No)	Yes	1.84	< 0.001	< 0.001				1.93	< 0.001	< 0.001
Chronic kidney disease stage 5 (Ref: No)	Yes	12.40	< 0.001	< 0.001				13.13	< 0.001	< 0.001
Delirium (Ref: No)	Yes	0.70	0.363	0.389	0.57	0.145	0.181	0.71	0.390	0.415
Depression (Ref: No)	Yes	1.18	0.026	0.023	1.20	0.012	0.010	1.22	0.008	0.007
Fracture (Ref: No)	Yes	0.83	0.201	0.214	0.82	0.140	0.153	0.83	0.199	0.212
Hallucination/agitation (Ref: No)	Yes	1.17	0.663	0.655	1.14	0.713	0.707	1.18	0.651	0.643
Hypocalcemia (Ref: No)	Yes	0.93	0.711	0.714	1.11	0.578	0.572	0.96	0.825	0.826

HypoPT hypoparathyroidism

[a]The demographic terminology reported in this table reflects that reported by the SEER-Medicare race_code variable. No further specification of ethnicities can be provided

any renal complication compared with patients without HypoPT in matched analysis [29]. Without adjusting for baseline renal complications, the HypoPT-adjusted all-cause burden is 3 times higher than controls. This suggests that addressing renal complications could be crucial in reducing overall costs for patients with postsurgical chronic HypoPT. As the burden of medical costs is likely to be greater in patients with severe renal disease, such as those on dialysis or those who are candidates for kidney transplantation, we further examined the economic burden among patients with stage 5 CKD in a subcohort of the overall matched cohort. Among patients who had stage 5 CKD at baseline, average total medical costs PPPY were over $220,000 higher for patients with postsurgical chronic HypoPT than for matched patients without HypoPT ($1,115,991 vs. $895,361), which is about twice what we report for the overall matched cohorts. Additionally, the substantially higher prevalence of nephrocalcinosis among patients with postsurgical chronic HypoPT at baseline versus those without HypoPT (59.9% vs. 0.6%) further supports this notion.

One key strength of this study lies in its use of Medicare claims data, which cover diverse geographic regions across the US and represent a larger portion of the population than conventional clinical trials or chart review studies. This broad scope enhances the generalizability of the study's outcomes to the Medicare population, which has been understudied and underappreciated by healthcare providers in the context of HypoPT. The limitations of this study should be considered. The LDS excludes the capture of prescription drugs, physician claims, and durable equipment claims. Consequently, the study may not fully capture the comprehensive landscape of healthcare utilization and costs. Additionally, the exclusion of other insurance costs, such as those associated with Medicaid for dual-eligible patients, may impact the total cost estimates. Furthermore, the study's findings may not be universally applicable to other postsurgical chronic patients with HypoPT populations, including those with commercial insurance, other public insurance, or no insurance coverage. Finally, the precision of the results may be affected by misclassification errors, a common concern when relying on billing data for diagnoses, as patients could be misclassified due to misdiagnosis or miscoding. For example, it should be noted that this study could not capture disease duration, serum phosphate, or 24-h urinary calcium in regression models, which are known predictors of renal calcifications [30]. Recognizing these strengths and limitations is important for a nuanced understanding of the study's implications.

CONCLUSION

To our knowledge, this is the first study to weigh the economic burden of postsurgical chronic HypoPT against a control group of patients who were non-HypoPT in the Medicare population in the US. The economic burden of individuals with postsurgical chronic HypoPT in the Medicare Fee-For-Service program is substantial, highlighting the need for parathyroid hormone replacement therapy and innovative treatment options that normalize calcium/phosphate balance, reduce symptom burden and long-term complications, and improve health-related quality of life.

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aspects of the work. Viktor V. Chirikov: Made substantial contributions to study conception and design; performed materials preparation, data collection, and data analysis; reviewed the manuscript critically for important intellectual content; approved the final version for publication; agrees to be accountable for all aspects of the work. Kyle Roney: Made substantial contributions to study conception and design; performed materials preparation, data collection, and data analysis; drafted the manuscript; reviewed the manuscript critically for important intellectual content; approved the final version for publication; agrees to be accountable for all aspects of the work. Alden R. Smith: Made substantial contributions to study conception and design; reviewed the manuscript critically for important intellectual content; approved the final version for publication; agrees to be accountable for all aspects of the work. All authors contributed to study conception and design. Materials preparation, data collection, and analysis were performed by Viktor V. Chirikov and Kyle Roney. The first draft of the manuscript was written by Kyle Roney, and all authors commented on versions of the manuscript. All authors read and approved the final manuscript version submitted.

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Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available due to the data use agreement stipulations covering the Medicare Limited Data Set Files, as per the Centers for Medicare and Medicaid Services. The authors thank the individuals who contributed data to the Medicare Limited Data Set used in this study.

Declarations

Conflict of Interest. Wahidullah Noori is an employee of Ascendis Pharma, which funded the study. Christopher T. Sibley is an employee of Ascendis Pharma, which funded the study. Viktor V. Chirikov is an employee of OPEN Health, which received consulting fees from Ascendis Pharma to conduct this study. Kyle Roney is an employee of OPEN Health, which received consulting fees from Ascendis Pharma to conduct this study. Alden R. Smith is an employee of Ascendis Pharma, which funded the study.

Ethical Approval. Due to the de-identified nature of the retrospective dataset, the study did not require ethics committee review. Permission for reuse of the Medicare 100% Limited Data Set was granted by its owner.

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