

# Outcomes Following Thyroid and Parathyroid Surgery in Pregnant Women

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**Objectives:** To perform the first population-based measurement of clinical and economic outcomes after thyroid and parathyroid surgery in pregnant women and identify the characteristics of this population and the predictors of outcome.

**Design:** Retrospective cross-sectional study.

**Setting:** Health Care Utilization Project Nationwide Inpatient Sample (HCUP-NIS), a 20% sample of nonfederal US hospitals.

**Patients:** All pregnant women, compared with age-matched nonpregnant women, who underwent thyroid and parathyroid procedures from 1999 to 2005.

**Main Outcome Measures:** Fetal, maternal, and surgical complications, in-hospital mortality, median length of stay, and hospital costs.

**Results:** A total of 201 pregnant women underwent thyroid (n=165) and parathyroid (n=36) procedures and were examined together. The mean age was 29 years, 60% were

white, 25% were emergent or urgent admissions, and 46% had thyroid cancer. Compared with nonpregnant women (n=31 155), pregnant patients had a higher rate of endocrine (15.9 vs 8.1%;  $P < .001$ ) and general complications (11.4 vs 3.6%;  $P < .001$ ), longer unadjusted lengths of stay (2 days vs 1 day;  $P < .001$ ), and higher unadjusted hospital costs (\$6873 vs \$5963;  $P = .007$ ). The fetal and maternal complication rates were 5.5% and 4.5%, respectively. On multivariate regression analysis, pregnancy was an independent predictor of higher combined surgical complications (odds ratio, 2;  $P < .001$ ), longer adjusted length of stay (0.3 days longer;  $P < .001$ ), and higher adjusted hospital costs (\$300;  $P < .001$ ). Other independent predictors of outcome were surgeon volume, patient race or ethnicity, and insurance status.

**Conclusions:** Pregnant women have worse clinical and economic outcomes following thyroid and parathyroid surgery than nonpregnant women, with disparities in outcomes based on race, insurance, and access to high-volume surgeons.

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**E**NDOCRINE DISORDERS ARE common in women of child-bearing age. Thyroid cancer, which has increased in incidence nearly 250% over the past 30 years (from 3.6 to 8.7 cases per 100 000 persons), occurs during pregnancy at nearly double that rate (14.4 per 100 000 persons).<sup>1,2</sup> Hyperthyroidism has been reported in 0.1% to 0.4% of pregnancies.<sup>3</sup> Inadequately treated hyperthyroidism during pregnancy poses significant risks to both mother and fetus.<sup>4</sup> Primary hyperparathyroidism affects 0.15% of the general population, with 25% occurring during the childbearing years.<sup>5</sup> Untreated hyperparathyroidism during pregnancy has been associated with a high rate of fetal complications.<sup>6,7</sup>

The Endocrine Society published guidelines in 2007 regarding the management of hyperthyroidism during pregnancy. The taskforce remarked that, overall, "current evidence is poor," supporting prac-

tice guidelines.<sup>8</sup> There also is a paucity of published literature on surgical outcomes for hyperparathyroidism during pregnancy.

## See Invited Critique at end of article

Outcomes after thyroid and parathyroid procedures during pregnancy have not been well characterized in the surgical literature. We present the first population-based study to examine predictors of clinical and economic outcomes following thyroid and parathyroid procedures in pregnant women.

## METHODS

This was a retrospective cross-sectional analysis of hospital discharge data from 1999 to 2005 from the Health Care Utilization Project Nationwide Inpatient Sample (HCUP-NIS) database, a stratified 20% sample of all inpatient ad-

missions to nonfederal acute-care hospitals maintained by the Agency for Healthcare Research and Quality. It is the largest all-payer inpatient database in the United States, with records from approximately 8 million hospital stays each year. This study received exemption from the institutional review board at Yale School of Medicine, New Haven, Connecticut.

Records were limited to women with benign and malignant thyroid disease and hyperparathyroidism, as identified by *International Classification of Diseases, Ninth Revision (ICD-9)* codes and Clinical Classifications Software. The ICD-9 procedure codes were used to abstract the records of all patients who underwent thyroidectomy (total thyroidectomy, thyroid lobectomy, partial thyroidectomy, substernal thyroidectomy) and parathyroidectomy (total, subtotal, and other parathyroid operations). The HCUP-NIS variable *neomat*, which identifies records with neonatal and maternal diagnoses, was used to identify pregnant women. Nonpregnant women were age-matched to the pregnant women by exact age in years. The matching procedure maximized the number of matches for each case (155 controls per case).

## INDEPENDENT VARIABLES

Pregnancy was the primary independent variable of interest. Other patient-level covariates included age, race (white, black, Hispanic, other, as coded in the NIS), median household income quartile for patient zip code (\$1-\$24 999, \$25 000-\$34 999, \$35 000-\$44 999,  $\geq$ \$45 000), admission urgency (elective vs nonelective), and payer (private, government [Medicaid and Medicare for end-stage renal disease patients], and other [self-pay, no charge]).<sup>9</sup> Thyroid disease was divided into benign and malignant diagnoses, and the year was divided into 2 time periods to account for changes in resource use and technological development. Patient comorbidity was calculated using ICD-9 codes and the Charlson Comorbidity Index.<sup>10-12</sup>

Provider-level covariates included hospital size (small, medium, large), location (urban vs rural), teaching status (teaching vs nonteaching), and region (Northeast, Midwest, South, and West). The HCUP-NIS definitions of hospital size differed by hospital region, location, and teaching status.<sup>13</sup> Hospital and surgeon volume were calculated using the annual number of thyroid and parathyroid procedures associated with each hospital and surgeon identifier. High-volume hospitals or surgeons were defined as those above the 75th percentile, based on the number of thyroid and parathyroid procedures performed per year. There is reportedly an association between hospital volume of very low birth weight admissions and perinatal mortality.<sup>14</sup> We calculated the hospital volume of very low birth weight neonates (less than 1500 g) per year and defined high-volume high-risk obstetric hospitals as those above the 75th percentile.

## OUTCOME VARIABLES

Outcomes of interest were (1) in-hospital complications; (2) in-hospital death; (3) median length of stay (LOS); and (4) median total inpatient hospital costs. Fetal complications included induced, spontaneous, or missed abortion, early or threatened labor, fetal distress, intrauterine death, still birth, neonatal hypocalcemic tetany, and neonatal hypoparathyroidism. Maternal complications included hysterectomy, cesarean section, dilation, and curettage. General surgical complications were categorized as cardiovascular, gastrointestinal, hematologic/vascular, urologic, pulmonary, infectious/wound, and other complications of surgery. Endocrine complications included maternal hypoparathyroidism, hypocalcemia, tetany, and recurrent laryngeal nerve injury. Surgical complications in-

cluded endocrine and general complications combined. Complications were treated as dichotomous variables (0 vs  $\geq$ 1). Total inpatient hospital costs were calculated using the HCUP-NIS adjusted, hospital-specific, cost-to-charge ratios (available for 2002-2005) and adjusted for inflation by converting all costs to 2005 dollars using rates from the Bureau of Labor Statistics.<sup>15</sup>

## STATISTICAL ANALYSIS

Bivariate analysis of the independent variables by outcomes was performed using  $\chi^2$  tests for categorical variables and analysis of variance for continuous variables. Associations between independent and dependent variables were calculated separately for pregnant and nonpregnant women, and an interaction term was used to assess whether the associations differed based on pregnancy status. Multivariate linear regression was used to model continuous outcomes (LOS and total inpatient costs), and multivariate logistic regression was used to model surgical complication rates. The distributions of LOS and costs were highly skewed. A log transformation was used to achieve a more normal distribution for adjusted LOS and cost. Some records did not have surgeon identifiers, race, or insurance data. These records were included in the model as subgroups to assess whether they differed in outcome. Data analysis and management were performed using SAS version 9.1 (SAS Inc, Cary, North Carolina). Statistical significance was set at a probability value of  $P \leq .05$ .

## RESULTS

### DEMOGRAPHICS

In HCUP-NIS, 201 pregnant women and 31 155 age-matched nonpregnant women underwent thyroid or parathyroid procedures between 1999 and 2005. Pregnant women who underwent thyroid and parathyroid procedures significantly differed from their nonpregnant counterparts in race, admission status, insurance type, and time period of treatment (**Table 1**). Pregnant women were more likely to be black, have emergent or urgent admissions, and have government insurance. There were more thyroid and parathyroid procedures performed for pregnant women during the second time period. Pregnant women were more likely to be treated at teaching hospitals. They were more evenly distributed throughout the 4 geographic regions than their nonpregnant counterparts, but a greater proportion of both groups received care in hospitals in the West. Pregnant women were more likely to be treated at hospitals with high thyroid or parathyroid procedure volume and high-risk obstetric volume.

### UNADJUSTED CLINICAL AND ECONOMIC OUTCOMES

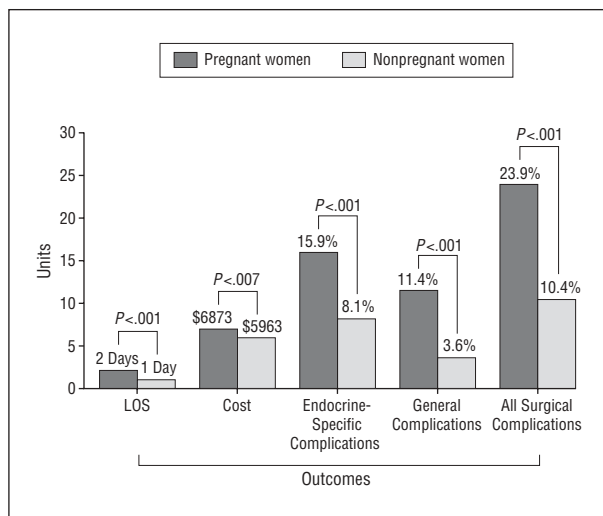
Compared with nonpregnant women, pregnant women who underwent thyroid or parathyroid procedures had significantly longer median hospital stays (2 days vs 1;  $P = .007$ ), higher median inpatient costs (\$6873 vs \$5963;  $P < .001$ ), and higher rates of endocrine (15.9% vs 8.1%), general (11.4% vs 3.6%), and combined surgical complications (23.9% vs 10.4%;  $P < .001$ ) (**Figure**). Pregnant women who underwent thyroid or

**Table 1. Demographics of Pregnant and Nonpregnant Women Who Had Thyroid and/or Parathyroid Surgery**

Characteristics	Women, %		P Value <sup>a</sup>
	Pregnant (n=201)	Nonpregnant (n=31 155)	
<b>Patients</b>			
Mean age, y	28.9	28.9	>.99
<b>Diagnosis</b>			
Thyroid cancer	45.8	41.0	.17
Benign thyroid/parathyroid	54.2	59.0	
<b>Race or ethnicity</b>			
White	60.4	59.2	.18
Black	14.1	7.9	
Hispanic	18.1	21.9	
Other	7.4	11.0	
<b>Admission</b>			
Emergent/urgent	25.4	11.4	<.001
Elective	74.6	88.5	
<b>Insurance</b>			
Private	64.2	75.6	<.001
Government	30.4	15.7	
Other	5.5	8.8	
<b>Charlson comorbidity</b>			
0-1	88.6	89.9	.54
≥2	11.4	10.1	
<b>Income</b>			
Quartile 1, lowest	12.8	10.7	.28
Quartile 2	22.5	18.3	
Quartile 3	26.0	27.1	
Quartile 4, highest	38.8	43.9	
<b>Year</b>			
1999-2001	35.8	46.1	.004
2002-2005	64.2	53.9	
<b>Providers</b>			
<b>Hospital size</b>			
Small	7.5	8.5	.34
Medium	20.4	24.2	
Large	72.1	67.3	
<b>Hospital location</b>			
Rural	5.5	4.2	.38
Urban	94.5	95.8	
<b>Teaching hospital</b>			
Nonteaching	35.8	52.1	<.001
Teaching	64.2	47.9	
<b>Hospital region</b>			
Northeast	15.6	5.4	<.001
Midwest	24.6	8.7	
South	23.5	15.5	
West	36.3	70.4	
Surgeon's mean annual volume, US \$	27	22	.18
Hospital's mean annual volume, No.	83	70	<.03
Hospital's mean annual high-risk OB cases, No.	33	21	<.001

Abbreviation: OB, obstetric.  
<sup>a</sup>Values are significant at  $P \leq .05$ .

parathyroid procedures had fetal and maternal complication rates of 5.5% and 4.5%, respectively. Pregnant women had no in-hospital deaths, compared with 7 deaths among nonpregnant women; there was no significant difference.



**Figure.** Unadjusted outcomes for pregnant and nonpregnant women following thyroid and parathyroid surgery in the United States from 1999 to 2005. LOS indicates length of stay. Values are significant at  $P \leq .05$ .

### PREGNANCY INTERACTION

There were significant differences between pregnant and nonpregnant women in their unadjusted clinical and economic outcomes when stratified by patient and provider characteristics. Differences between pregnant and nonpregnant women in complication rates were most pronounced by diagnosis, race, and hospital size. Pregnant patients undergoing thyroidectomy had higher surgical complications than nonpregnant patients for benign (27% vs 14%) and malignant (21% vs 8%) thyroid diseases ( $P = .007$ ). When stratified by race, white pregnant patients had a 2-fold higher complication rate (21% vs 10%), black pregnant patients had a nearly 5-fold higher rate (48% vs 10%), and Hispanic pregnant patients had a nearly 3-fold higher rate (30% vs 12%) than nonpregnant patients of the same race. However, the pregnancy interaction was not statistically significant ( $P = .14$ ).

Pregnant women had significantly longer LOS than nonpregnant women when stratified by diagnosis, race, admission urgency, insurance, income, time period of treatment, hospital size, and region (**Table 2**). Of note, pregnant and nonpregnant women had significant differences in LOS when surgeon volume and hospital volume were examined. Women who were pregnant had more costly hospital stays than nonpregnant women regarding all patient and provider characteristics except diagnosis, hospital location, and teaching status.

### MATERNAL AND FETAL OUTCOMES

High surgeon volume was associated with lower maternal ( $P = .002$ ) and fetal ( $P = .01$ ) complications on bivariate analyses (**Table 3**). Hospital region (West or Midwest) was associated with a higher rate of maternal complications. None of the other patient and provider characteristics were significantly associated with maternal or fetal complications.

**Table 2. Significant Differences in Unadjusted Economic Outcomes for Pregnant and Nonpregnant Women Following Thyroid and Parathyroid Surgery**

Characteristics	Unadjusted Median LOS, d			Unadjusted Median Cost, Thousands of \$		
	Pregnant	Nonpregnant	<i>P</i> Value <sup>a</sup>	Pregnant	Nonpregnant	<i>P</i> Value <sup>a</sup>
<b>Patient</b>						
<b>Diagnosis</b>						
Thyroid cancer	1	1	]< .001	6.2	6.9	]< .34
Benign thyroid/parathyroid	2	1		8.3	5.5	
<b>Race or ethnicity</b>						
White	2	1	]< .001	6.4	5.9	]< .001
Black	2	2		8.1	5.7	
Hispanic	2	1		12.0	6.8	
<b>Admission</b>						
Emergent/urgent	4	1	]< .001	10.0	5.4	]< .001
Elective	1	1		6.1	5.1	
<b>Insurance</b>						
Private	1	1	]< .001	5.6	5.9	]< .001
Government	3	2		11.6	6.5	
Other	2	2		7.9	6.0	
<b>Charlson comorbidity</b>						
0-1	...	...	]< .001	6.6	5.7	]< .001
≥2	...	...		11.6	8.5	
<b>Income</b>						
Quartile 1, lowest	3	1	]< .001	6.6	5.4	]< .004
Quartile 2	2	1		6.7	5.5	
Quartile 3	1	1		5.7	5.9	
Quartile 4, highest	1	1		6.9	6.6	
<b>Year</b>						
1999-2001	2	1	]< .003	...	...	]< .003
2002-2005	2	1		...	...	
<b>Providers</b>						
<b>Hospital size</b>						
Small	2	1	]< .001	7.2	5.8	]< .001
Medium	1	1		5.4	5.7	
Large	2	1		7.2	6.1	
<b>Hospital region</b>						
Northeast	1	1	]< .001	5.6	5.1	]< .001
Midwest	1	1		6.2	5.3	
South	3	1		8.1	5.2	
West	2	1		7.1	6.5	
<b>Surgeon volume, percentile</b>						
<75th	2	1	]< .001	9.9	5.8	]< .001
≥75th	2	1		7.2	4.9	
<b>Hospital volume, percentile</b>						
<75th	2	1	]< .008	6.4	6.2	]< .02
≥75th	2	1		7.1	5.9	
<b>High-risk OB volume, percentile</b>						
<75th	...	...	]< .47	6.4	6.1	]< .007
≥75th	...	1		7.9	5.8	

Abbreviation: OB, obstetric.

<sup>a</sup>*P* value for pregnancy interaction.

### MULTIVARIATE REGRESSION ANALYSIS

Pregnancy was a significant independent predictor for higher surgical complication rates after adjustment was made for other patient and provider variables associated with this outcome including diagnosis, admission urgency, Charlson comorbidity, race, insurance, and surgeon volume (**Table 4**). In the final model, pregnant women were twice as likely to have surgical complications than similar nonpregnant women ( $P < .001$ ). Patients with more comorbidity were 2½ times more likely to sustain a complication ( $P < .001$ ). Other significant predictors of having a complication after surgery were a thy-

roid cancer diagnosis ( $P = .004$ ), Hispanic ethnicity ( $P = .04$ ), and government insurance ( $P = .02$ ). High-volume surgeons had significantly lower complication rates than low-volume surgeons (odds ratio, 0.6;  $P = .02$ ).

Pregnancy was a significant predictor for increased LOS after adjusting for all other patient and provider variables associated with LOS (**Table 5**). Pregnant women had an adjusted 0.3-day longer hospital stay than nonpregnant women ( $P < .001$ ). The other most powerful independent predictors of longer LOS in the final model were Charlson comorbidity of 2 or more and government insurance (both  $P < .001$ ). Other predictors of LOS were race or ethnicity, type of surgery, and surgeon vol-

**Table 3. Maternal and Fetal Complication Rates for Pregnant Women Following Thyroid and Parathyroid Surgery**

Characteristics	Maternal		Fetal	
	%	P Value <sup>a</sup>	%	P Value <sup>a</sup>
<b>Patient</b>				
Diagnosis				
Thyroid cancer	2.2	.15	2.2	.06
Benign thyroid/parathyroid	6.4		8.3	
Race or ethnicity				
White	5.6	.86	6.7	.49
Black	4.8		0	
Hispanic	3.7		3.7	
Admission				
Emergent/urgent	7.0	.42	9.3	.28
Elective	4.0		4.8	
Insurance				
Private	4.7	.76	6.2	.67
Government	4.9		4.9	
Other	0		0	
Charlson comorbidity				
0-1	5.1	.27	5.6	.80
≥2	0		4.4	
Income				
Quartile 1, lowest	8.0	.09	4.0	.14
Quartile 2	9.1		9.1	
Quartile 3	5.9		9.8	
Quartile 4, highest	0		1.3	
Year				
1999-2001	2.8	.38	0.03	.49
2002-2005	5.4		0.04	
<b>Providers</b>				
Hospital size				
Small	0	.68	6.7	.96
Medium	4.9		4.9	
Large	4.8		5.5	
Hospital location				
Rural	0	.46	9.1	.59
Urban	4.7		5.3	
Teaching hospital				
Nonteaching	4.2	.87	5.6	.97
Teaching	4.7		5.4	
Hospital region				
Northeast	0	.04	7.1	.65
Midwest	2.3		2.3	
South	0		4.8	
West	9.2		7.7	
Surgeon volume, percentile				
<75th	12.0	.002	12.0	.01
≥75th	0		1.2	
Hospital volume, percentile				
<75th	4.2	.90	6.3	.79
≥75th	4.6		5.2	
High-risk OB volume, percentile				
<75th	3.2	.71	3.2	.55
≥75th	4.7		5.9	

Abbreviation: OB, obstetric.  
<sup>a</sup>Values are significant at  $P \leq .05$ .

ume; thyroidectomy was associated with a 0.1-day shorter LOS ( $P < .001$ ), and high surgeon volume was associated with an adjusted 0.1-day shorter LOS ( $P = .01$ ).

Pregnancy also was a highly significant independent predictor of increased hospital cost, with an adjusted \$300 additional cost ( $P < .001$ ). Charlson comorbidity of 2 or more

**Table 4. Multivariate Regression Analysis of Surgical Complications for Pregnant and Nonpregnant Women Following Thyroid and Parathyroid Surgery**

Characteristics	OR	P Value <sup>a</sup>
Pregnancy status		
Pregnant	2.0	<.001
Nonpregnant	1 [Reference]	
Diagnosis		
Thyroid cancer	1.5	.005
Benign thyroid/parathyroid	1 [Reference]	
Charlson comorbidity		
0-1	1 [Reference]	<.001
≥2	2.5	
Race or ethnicity		
White	1 [Reference]	.38
Black	1.2	
Hispanic	1.4	
Insurance		
Private	1 [Reference]	.02
Government	1.5	
Other	1.4	
Surgeon volume, percentile		
<75th	1 [Reference]	.02
≥75th	0.6	

Abbreviation: OR, odds ratio.  
<sup>a</sup>Values are significant at  $P \leq .05$ .

was significantly associated with increased cost ( $P < .001$ ); type of surgery and insurance status also were associated with adjusted cost ( $P = .004$  and  $.007$ , respectively).

#### COMMENT

In this large population-based analysis of clinical and economic outcomes following thyroid and parathyroid surgery during pregnancy, significant differences emerged between pregnant and nonpregnant women regarding all of our outcomes: pregnant women had higher complication rates, longer LOS, and higher hospital costs than similar nonpregnant women. In addition, pregnant women had maternal and fetal complication rates of 4.5% and 5.5%, respectively. Significant predictors of patient outcomes were identified. In particular, higher surgeon volume was an independent predictor of lower complication rates and shorter LOS. Not being white was an independent predictor for higher complication rates and longer LOS. Having government insurance predicted higher complication rates, longer LOS, and higher hospital costs.

These findings are important because most thyroid and parathyroid disease occurs in women, with a significant proportion during the childbearing years. Nearly 75% of parathyroidectomies for primary hyperparathyroidism are performed in women; Graves disease occurs at a female:male ratio of between 5:1 and 10:1, and the incidence of thyroid cancer is 3 times higher in women than in men.<sup>16-18</sup> As a result, attention has focused recently on assembling practice guidelines for the treatment of pregnant patients with endocrinologic disorders.

A literature review of outcomes following thyroid and parathyroid surgery during pregnancy reveals a paucity

**Table 5. Multivariate Regression Analysis of LOS and Cost for Pregnant and Nonpregnant Women Following Thyroid and Parathyroid Surgery**

Characteristics	Adjusted LOS, d	P Value <sup>a</sup>
Type of surgery		
Thyroidectomy	0.9	<.001
Parathyroidectomy	1 [Reference]	
Pregnancy status		
Pregnant	1.3	<.001
Nonpregnant	1 [Reference]	
Admission		
Emergent/urgent	1.2	.002
Elective	1 [Reference]	
Charlson comorbidity		
0-1	1 [Reference]	<.001
≥2	1.3	
Insurance		
Private	1 [Reference]	
Government	1.1	<.001
Other	1.1	<.001
Race or ethnicity		
White	1 [Reference]	
Black	1.1	<.001
Hispanic	1.1	.002
Surgeon volume, percentile		
<75th	1 [Reference]	
≥75th	0.9	.01

Characteristics	Adjusted Cost, Thousands of \$ <sup>b</sup>	P Value <sup>a</sup>
Type of surgery		
Thyroidectomy	0.8	.004
Parathyroidectomy	1 [Reference]	
Pregnancy status		
Pregnant	1.3	<.001
Nonpregnant	1 [Reference]	
Diagnosis		
Thyroid cancer	1.1	.03
Benign thyroid/parathyroid	1 [Reference]	
Charlson comorbidity		
0-1	1 [Reference]	
≥2	1.5	<.001
Insurance		
Private	1 [Reference]	
Government	1.1	.007
Other	1.2	.08

Abbreviation: LOS, length of stay.

<sup>a</sup>Values significant at  $P \leq .05$ .

<sup>b</sup>Cost data are available from 2002 to 2005.

of data. Moosa and Mazzaferri<sup>19</sup> described 14 cases of thyroidectomy for thyroid cancer in pregnant women in the US Air Force Central Tumor Registry from 1962 to 1997 and reported that cancer recurrence among these women was similar to that of women who had thyroidectomy after delivery. Herzon et al<sup>20</sup> described 6 thyroid procedures during pregnancy using the New Mexico Tumor Registry from 1970 to 1991 and reported no difference in survival between pregnant and nonpregnant women. Yasmeeen et al<sup>21</sup> examined thyroid cancer rates during pregnancy or within 1 year after delivery using the California Cancer Registry from 1991 to 1999 and reported no survival difference compared with nonpregnant women

and no difference in maternal or fetal outcomes compared with pregnant women without thyroid cancer.

There are a number of case series and studies of thyroid surgery performed during pregnancy, with outcomes ranging from fetal death to no complications. Cunningham and Slaughter<sup>22</sup> described 5 cases and reported 3 fetal deaths. Nam et al<sup>23</sup> described 6 cases and, compared with patients for whom surgery was delayed until after delivery, there were no differences in fetal or surgical complications or LOS. Doherty et al<sup>24</sup> described 4 cases with no fetal morbidity or mortality. Rosen et al<sup>25</sup> described 2 cases with no recurrent laryngeal nerve injury, hypoparathyroidism, postoperative bleeding, or wound infection. Chong et al<sup>26</sup> described 2 cases with no fetal or maternal complications. Vini et al<sup>27</sup> described 1 case with no thyroid cancer recurrence.

Parathyroidectomy during pregnancy is equally understudied. Delmonico et al<sup>6</sup> reviewed all published cases of hyperparathyroidism during pregnancy from 1962 to 1976 and described 13 patients who had parathyroid surgery after delivery, with an 80% rate of fetal complications (neonatal tetany, hypocalcemia, fetal death, spontaneous abortion, and therapeutic abortion). Kelly<sup>7</sup> reviewed the literature from 1960 to 1991 and found no fetal or maternal morbidity among 8 women who underwent parathyroidectomy during pregnancy. Of the 4 cases of parathyroidectomy after delivery, there was a 100% incidence of neonatal hypocalcemia and tetany.

Outcomes after thyroid and parathyroid procedures during pregnancy have not been well characterized; this study is the first population-based examination of predictors of clinical and economic outcomes. Thyroid and parathyroid procedures generally are considered to be low-risk in the general population, with prior work by Sosa et al<sup>28</sup> describing a complication rate of 7.4% after thyroidectomy in the general population. This study demonstrates increased complication rates, LOS, and cost among pregnant women, along with maternal and fetal morbidity rates of 4.5% and 5.5%, respectively. In comparison, the reported rate of cesarean section and hysterectomy following urgent appendectomy during pregnancy was 7%, and the rate of fetal loss was 4%.<sup>29</sup>

These data suggest that thyroid and parathyroid surgery during pregnancy should be approached with caution and careful deliberation about whether the risks are outweighed by the benefits. Overall, parathyroidectomy during pregnancy is usually indicated for protection of the fetus and prevention of neonatal hypoparathyroidism and tetany. In contrast, thyroidectomy is rarely indicated on an urgent basis unless there is significant concern about the well-being of the mother. For example, airway obstruction from large goiters in symptomatic pregnant women with already-compromised breathing from uterine expansion, advanced differentiated thyroid cancer, and poorly differentiated cancers could justify proceeding to thyroidectomy prior to delivery.

Based on the finding that surgeon volume is significantly associated with patient outcome, it appears to be essential that pregnant patients who require thyroidectomy and parathyroidectomy be directed to high-volume surgeons to optimize their outcomes. This is consistent with prior studies showing that high surgeon volume is associ-

ated with improved clinical and economic outcomes following thyroid surgery among the general population, the elderly, and pediatric subgroups.<sup>30,31</sup> Hospital volume has not been associated with patient outcomes.

Several factors could contribute to the higher endocrine and general complication rates seen in pregnant women. During pregnancy, the thyroid gland can undergo a 20% to 30% increase in volume.<sup>32</sup> This is thought to be due to increase in the production of thyroxine-binding globulin by the liver as a result of elevated estrogen and the thyroid-stimulating activity of  $\beta$ -human chorionic gonadotropin. An increase in thyroid volume could increase the technical difficulty of cervical exploration (ie, identification of the recurrent laryngeal nerve and the parathyroid glands) and increase the likelihood of endocrine complications. In addition, pregnant women could have more severe thyroid and parathyroid disease (ie, more advanced thyroid cancer or larger goiters) at the time of operation, further contributing to operative difficulty.

Vitamin D deficiency could contribute to the higher endocrine complication rate observed in pregnant women; it has been described in up to 73% of pregnant women despite the fact that 70% are taking prenatal vitamins.<sup>33</sup> Vitamin D deficiency is more common among black pregnant women than white.<sup>34,35</sup> This is important in the context of the higher rates of endocrine (ie, hypocalcemia) and surgical complications observed in black and Hispanic pregnant women in the current study.

In this study, not being white was associated with increased LOS and a higher rate of surgical complications. This is consistent with previous work showing racial disparities in outcomes following thyroidectomy in the general population.<sup>36</sup> Pregnant patients with government insurance, compared with private insurance, had higher surgical complication rates, longer LOS, and higher hospital costs. These findings raise the question of whether pregnant patients with government insurance have less prenatal and perinatal care, resulting in more advanced disease or compromised access to high-quality surgical care. Most pregnant patients with government insurance were covered by Medicaid, which appears to be associated with worse outcomes following other kinds of surgery. Medicaid status is associated with lower late survival rates following coronary artery bypass grafting.<sup>37</sup> In bariatric surgery, Medicaid beneficiaries have a prolonged LOS.<sup>38</sup>

There are limitations inherent in using an administrative database. There can be coding errors leading to missed diagnoses and procedures as well as lack of coding leading to missing data. There were missing data for surgeon identifiers, insurance, race, income, and admission status. We performed multivariate regression analyses on the subgroups for whom data were missing and found that, except for subgroups missing admission status, the data were not significantly associated with outcomes. We were unable to adjust for severity of thyroid and parathyroid disease or thyroid cancer stage. We also were unable to look at long-term outcomes, including readmission rates. However, these factors would likely contribute to an underestimation of complication rates, which further underlines the significance of the disparate outcomes between pregnant and nonpregnant women and the findings pertaining to maternal and fetal com-

plications. Owing to the small number of parathyroidectomies during pregnancy, we aggregated thyroid and parathyroid cases. These surgical procedures are comparable in terms of duration, surgical field, and technique; therefore, we believe their outcomes can be analyzed together.

This is the first population-based study examining clinical and economic outcomes following thyroid and parathyroid surgery during pregnancy. Pregnant women are an understudied population at risk for worse outcomes; more studies are needed. Because pregnant patients who have thyroid and parathyroid surgery are relatively uncommon, population-based studies such as this one, or multiinstitutional collaborative research efforts, are essential. Surgeon volume is an important predictor of outcomes, so pregnant women undergoing thyroid and parathyroid procedures should be directed to high-volume surgeons whenever possible. Disparities in outcomes based on race and insurance must be overcome. Optimizing maternal and fetal outcomes requires the collaboration of surgeons, endocrinologists, obstetricians, neonatologists, anesthesiologists, insurers, and policy-makers.

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## INVITED CRITIQUE

This excellent analysis from the innovative group at Yale confirms a personal bias of mine from about 20 years of practice: pregnant patients requiring endocrine surgery of the neck should be treated with caution, perhaps deferring thyroid cancer surgery until after delivery (or performing lobectomy only during the second trimester) under the supervision of a team of experienced clinicians. This caution is being exercised in practice because pregnant patients more commonly receive care at large urban institutions with high-risk obstetrics.

These conclusions reinforce the perhaps mistaken notion that the surgeon or the institution controls the outcome. For instance in Table 3, we see nearly identical rates of maternal and fetal morbidity following surgery, suggesting that maternal complications (largely surgeon-controlled) produce fetal complications. Yet when analyzed by region, we see a 7.1% fetal complication rate in the Northeast with a 0% maternal complication rate. This type of study cannot go beyond observation to tell us what key relationships exist nor how to improve practice. This is a general limitation of using databases that were not designed to answer the question

at hand; this database is claims-based and designed for administrative purposes.

Often one finds data anomalies that challenge the whole database such as the 7 surgical fatalities found in 31 155 women of childbearing age, which seems too high. A related issue with database research is the ease with which parameters can be adjusted and the data reanalyzed. What is the probability of finding a  $P < .05$  after asking 20 questions, or asking the same question 20 different ways such as changing the age until a significant result emerges? There would be great value for database publications to go beyond the confirmatory multivariate regression analysis and give us an understandable indication that the data analysis is robust, such as how minor modifications of groupings affect the results or how many similar inquiries were made that did not produce statistical significance.

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