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The Effects of Socioeconomic Status on Children with Well-Differentiated Thyroid Cancer

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Abstract

Background—Well-differentiated thyroid cancer (WDTC) is the most common endocrine malignancy in children. Adult literature has demonstrated socioeconomic disparities in patients undergoing thyroidectomy, but the effects of socioeconomic status on the management of pediatric WDTC remains poorly understood.

Methods—Patients > 21 years of age with WDTC were reviewed from the National Cancer Data Base (NCDB). Three socioeconomic surrogate variables were identified: insurance type, median income, and educational quartile. Tumor characteristics, diagnostic intervals and clinical outcomes were compared within each socioeconomic surrogate variable.

Results—A total of 9585 children with WDTC were reviewed. In multivariate analysis, lower income, lower educational quartile, and insurance status were associated with higher stage at diagnosis. Furthermore, lower income quartile was associated with a longer time from diagnosis to treatment ($p < 0.002$). Similarly, uninsured children had a longer time from diagnosis to treatment

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(28 days) compared to those with government (19 days) or private (18 days) insurance ($p < 0.001$). Despite being diagnosed at a higher stage and having a longer time interval between diagnosis and treatment, there was no significant difference in either overall survival or rates of unplanned readmissions based on any of the socioeconomic surrogate variables.

Conclusion—Children from lower income families and those lacking insurance experienced a longer period from diagnosis to treatment of their WDTC. These patients also presented with higher stage disease. These data suggest a delay in care for children from low-income families. Although these findings did not translate into worse outcomes for WDTC, future efforts should focus on reducing these differences.

Well-differentiated thyroid cancer (WDTC), including both papillary and follicular types, is the most common pediatric endocrine malignancy, accounting for about 1% of pre-pubertal childhood cancers and 7% of adolescent cancers¹ and its incidence in the pediatric population is thought to be increasing.² Papillary thyroid cancer accounts for the majority of pediatric thyroid cancers and is associated with an excellent prognosis.³ Follicular thyroid cancers are less common, comprising approximately 9% of pediatric thyroid cancers, but are a more aggressive form of thyroid malignancy in children.³ Children typically present with higher stage disease and higher complication rates following thyroidectomy than their adult counterparts.^{2, 4}

Lower socioeconomic status has been associated with worse overall and disease-specific mortality in adult patients with WDTC.⁵ In addition, adults with WDTC from lower socioeconomic background and those that are poor/uninsured are more likely to present with higher stage and metastatic disease than those with higher socioeconomic status and those with private insurance.⁶ The effect of disparities in pediatric thyroid cancer is less well understood.⁴ The purpose of this study was to assess whether socioeconomic status affected outcomes for children with WDTC.

METHODS

Data Source

The authors utilized the National Cancer Data Base (NCDB), a data repository that is jointly maintained by the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. Approximately 70% of all newly diagnosed cancers in the United States are captured at the 1,500 CoC-accredited cancer programs and reported to the NCDB.^{7, 8} Data are collected using nationally standardized data coding definitions and data transmission as outlined by the North American Association of Central Cancer Registries.⁷ Data elements include patient characteristics, tumor stage and histology, treatment modality specifics, and basic outcome information. Data definitions are readily available online (<https://www.facs.org/quality-programs/cancer/ncdb/puf>).

Demographic variables examined included age, gender, race/ethnicity, primary payer (uninsured, private/managed care, Medicaid, Medicare, other government), median household income by zip code (less than \$30,000, \$30,000–34,999, \$35,000–45,999, and more than \$46,000), education quartile by zip code (number of adults without high school degree, 21% or more, 13–20.9%, 7–12.9%, less than 7%), rural/urban status, and great circle

distance (miles between the patient's residence and the treating facility). Patient race was classified as White, Black, Asian, American Indian or other. The NCDB uses a second variable for Spanish or Hispanic origins, and this was categorized as either Hispanic or non-Hispanic. Anonymized facility code was used to evaluate facility volume. Outcome variables of interest included tumor stage at diagnosis, days from diagnosis to treatment, overall mortality, and unplanned readmission.

Study cohort

Institutional review board exemption was obtained from the University of Alabama Birmingham Institutional Review Board. Compliance with HIPPA rules was observed at all times. Patients \geq 21 years of age with well-differentiated thyroid cancer from 1998 to 2012 were reviewed from the NCDB. This age range was selected based on previous studies.^{9–11}

Categorization

Well differentiated thyroid was defined as papillary and follicular histology, with all appropriate subtypes included in the analysis: 8002, 8041, 8043, 8044, 8045, 8050, 8052, 8073, 8260, 8290, 8330, 8331, 8332, 8335, 8337, 8340, 8341, 8342, 8343, 8344, 8350, 8450, 8452, 8503, and 8507. Tumor stage was defined by the American Joint Committee on Cancer (AJCC) staging guidelines for thyroid cancer. Three socioeconomic surrogate variables were identified: insurance type, median income in the patient's ZIP code, and percent of people with no high school degree in the patient's ZIP code. The median income and education by ZIP code was classified into quartiles by US Census data from 2012. Hospital volume was based on the number of pediatric thyroidectomies performed at a facility. High-volume centers were defined as the top 10% based on total volume of pediatric thyroidectomies as previously described.⁴

Statistical Analysis

While controlling for age, race/ethnicity and gender, multivariate regression chi-square and pool-variance t-tests were then used to compare tumor characteristics, intervals from diagnosis to staging and diagnosis to treatment, as well as clinical outcome variables within each of the socioeconomic surrogate variables. A multivariate analysis was performed for each clinical outcome variable of interest, with the highest value in each independent variable (such as highest quartile or best insurance) serving as the baseline value. For continuous variables, the mean of the highest value of the categorical independent variable served as the baseline and a multivariate logistic regression was performed, with all values of the continuous dependent variable converted into a binary scheme based on whether they were above ("1") or below ("0") said mean. Kaplan-Meier survival estimates were calculated for each variable of interest using the log-rank test. Statistical analysis was performed using SAS software, version 9.3 (Cary, NC) to evaluate differences between groups. Due to missing data, not all patients could be utilized for every variable. Entries with omission of survival data were completely excluded. Statistical significance was defined as $p < 0.05$.

RESULTS

Demographics and tumor characteristics

A total of 9967 children with well-differentiated thyroid cancer from 1998 to 2012 were identified in the NCDB, of which 9585 (96.2%) met inclusion criteria (Table 1). The mean age at presentation was 17.75 ± 3.14 years. Most patients were female (82.6%) and non-Hispanic White (75.7%) (Table 1). The majority of patients had private insurance (76.3%) followed by government insurance (16.2%) and no insurance (7.6%). The breakdown of the other surrogate socioeconomic variables is in Table 1.

Table 2 summarizes the tumor characteristics, stratified by histology. The histologic distribution of cases in the patient cohort was consistent with previous publications.^{1, 3, 12} Papillary thyroid cancer was the most common histologic type, seen in 90.7% of patients (n=8696) and follicular thyroid cancer made up the remaining 9.3% (n=889). The mean thyroid nodule size was $25.1 \text{ mm} \pm 14.9 \text{ mm}$. Nodes were examined in 67.3% of cases, and of those, 62.4% had nodal disease at presentation. Surgical therapy involved total thyroidectomy in 8204 (85.6%) and partial thyroidectomy or lobectomy in 1181 (12.3%). The remaining 193 patients (1.2%) had no surgical intervention. The reasons for not undergoing surgical intervention in these patients were coded as surgery not part of treatment plan (53.9%), patient lost to follow up (16.6%), surgery refused by patient (13.5%), patient transferred to another facility (11.4%), patient died prior to surgery (3.6%), and surgery considered too risky (1%).

Socioeconomic status and insurance status affects stage at diagnosis of pediatric WDTC

In multivariate analysis, lower income ($p = 0.041$, Hazard Ratio [HR] = 1.98, 1.88 and 1.68 in each successive quartile compared to highest one), lower educational quartile ($p < 0.001$, HR=1.86, 1.50 and 1.12, compared to highest quartile) and insurance status ($p < 0.001$, HR = 2.26 for uninsured and HR = 1.46 for government insurance, as compared to private insurance) were associated with higher stage at diagnosis. Lack of insurance was the most important socioeconomic factor associated with a higher stage at diagnosis. Patients with private and government insurance were more likely to present with stage I disease (91.4% and 89.6%, respectively) compared to patients without insurance (78.6%) (Table 3).

Socioeconomic and insurance status affects time to treatment of pediatric WDTC

Table 4 summarizes the time from diagnosis to treatment by insurance status, income quartile, and education quartile. On multivariate regression, lower median household income and lower education quartiles were associated with a longer time from diagnosis to treatment ($p = 0.002$ and $p = 0.008$, respectively). Similarly, uninsured children had a longer time from diagnosis to treatment (28 days) compared to those with government (19 days) or private insurance (18 days) ($p < 0.001$).

High-volume hospitals

A total of 1366 facilities reported performing pediatric thyroidectomies. The top 10% of facilities (n = 136) contributed to 34.7% of the thyroidectomies performed, and were classified as high-volume centers for the purpose of this study. The high-volume centers

performed on average 38 pediatric thyroidectomies per year (IQR 26–47 procedures) compared to 5 per year at other (low-volume) centers (IQR 2–7 procedures). As demonstrated in Table 5, children from higher median household income and higher educational quartiles were more likely to have their thyroidectomy performed at a high-volume center ($p < 0.001$ and $p = 0.044$, respectively). Insurance status had no statistical correlation with facility volume.

Treatment by socioeconomic and insurance status

Given the difference at stage at presentation, we also evaluated the treatment patients received based on their socioeconomic status. Despite presenting at a higher stage, there was no difference in the surgical procedure performed or in the administration of radioactive iodine (I-131) (Table 6) in those from lower income or educational quartiles. However, patients without insurance were less likely to receive radioactive iodine than those with government or private insurance despite presenting with higher stage disease (Table 6). There was no difference in radioactive iodine administration based on distance from treatment facility or hospital volume.

Overall survival and unplanned readmission rates

Patient median follow-up period was 60.5 months (IQR 32.6–98.6 months). Despite differences in stage at diagnosis and time from diagnosis to treatment, there was no significant difference in either overall survival (Figure 1) or unplanned readmission rates based on any of the socioeconomic surrogate variables. In addition, there were no differences in overall survival or unplanned readmission rates based on timing of surgery, hospital volume, or use of radioactive iodine.

DISCUSSION

This study demonstrated that significant disparities exist in disease stage at diagnosis and time to treatment in children with WDTC. Children from lower income families and those lacking health insurance presented with higher stage disease and experienced a longer period from diagnosis to treatment of their thyroid malignancy. Similar results have been observed in adults with WDTC. Adults with the lowest socioeconomic status and those who are uninsured were more likely to present with metastatic disease compared to those from a highest socioeconomic status and those with private insurance.⁶

In the current study, despite the differences in stage at presentation, there was no difference in the procedures (partial versus total thyroidectomy), but there were fewer uninsured patients receiving radioactive iodine than patients with either government or private insurance. These findings indicate that insurance status may limit access to radioactive iodine therapy. Others have shown that lack of insurance was associated with significantly less likelihood of receiving radioactive iodine in adults with WDTC.^{13, 14} Interestingly, the likelihood of receiving radioactive iodine was not affected by socioeconomic status as we expected. A previous SEER database study demonstrated that in patients with papillary thyroid cancer <45 years of age the use of adjuvant radioactive iodine was significantly impacted by socioeconomic status.¹⁵ Another study in the adult population found that race

and insurance status, but not income, affect the likelihood of receiving radioactive iodine.¹³ Haymart *et al.* found that there was an increased likelihood of radioactive iodine use as hospital volume increases and that hospital characteristics accounted for 29% of the variation of radioactive iodine use.¹³ While lack of insurance may contribute to less access to radioactive iodine, center-level factors also appear to affect access to this therapy. In the current study, however, we did not find a difference in radioactive iodine usage based on distance from treatment facility or hospital volume. Other factors such as refusal of treatment and missed follow-up may also be contributing to this difference in radioactive iodine administration. Future efforts should focus on identifying the specific causes of this difference in radioactive iodine therapy utilization in the pediatric population.

Previous studies in both the pediatric and adult populations have demonstrated that thyroidectomies performed by high-volume endocrine surgeons are associated with less complications, lower costs and shorter patient length of stay.^{4, 16–18} High-volume endocrine surgeons have been defined as those who perform > 30 cervical endocrine procedures per year in adults and children combined.^{4, 16, 17} The NCDB does not provide surgeon specific variables, and therefore, the impact of socioeconomic status on access to a high-volume endocrine surgeon could not be assessed. The use of center volume served as a surrogate for surgeon volume in the current study. High-volume endocrine centers have been defined in the pediatric literature as the top 10% based on their volume of thyroidectomies and parathyroidectomies,⁴ and this definition was applied to the dataset for this study. Children from lower income and education quartiles were more likely to have their thyroidectomy performed at a low-volume center. Low-volume hospitals have been associated with higher complication rates and longer length of stay following thyroidectomy in both the pediatric and adult populations.^{4, 18} Complication rates or length of stay were not available in the NCDB, but we did analyze unplanned readmission rates and overall mortality which were not affected by hospital volume.

The cause for healthcare disparities is complex and multifactorial, involving cultural, racial, language, economic, educational, and geographic barriers. While this study provides an initial insight into the pediatric WDTC population, further studies are needed to identify the reasons for these disparities. One possible cause for these findings may be differences in access to medical care. In addition, improved knowledge of thyroid cancer at both the patient and provider levels may lead to earlier diagnosis. Finally, with the regionalization of surgical care and routing of complex surgical operations to high-volume providers, certain vulnerable populations, such as those from low-income communities, have had limited access to high-volume centers.^{19, 20} This study shows that a similar pattern may be occurring in the pediatric WDTC population. Academic medical centers should consider introducing programs to improve access to high-volume centers in their region.

The limitations of this study are those inherent in working with a large retrospective dataset. The greatest difficulty encountered was related to the lack of clinical variables such as tumor recurrence, disease specific survival, or long-term postoperative complications, thereby limiting the analysis to unplanned readmission rates and overall survival as these are the outcome variables captured in the NCDB. In addition, specific complications associated with thyroidectomy, such as hypoparathyroidism or recurrent laryngeal nerve injury were not

recorded in the NCDB. Many of these complications associated with thyroidectomy may be treated in the outpatient setting, rendering unplanned readmissions a mediocre surrogate for postoperative complications of thyroidectomy. The survival for patients with WDTC is high, so there were no differences in survival based socioeconomic variables. Finally, the NCDB includes data from both adult and pediatric facilities and providers. We were not able to determine at which type of facility or by which type of provider the patient had their thyroidectomy performed. In spite of these limitations, this large multi-institutional dataset allowed for an excellent national perspective on disparities that exist in WDTC in the pediatric population.

CONCLUSION

To our knowledge, this is the largest study evaluating health care disparities in WDTC in the pediatric population. Patients lacking health insurance and those from a lower socioeconomic background were also more likely to present with a higher stage tumor. Children from lower median household income or lower educational background were also more likely to have their procedure at a low-volume center. Although these findings did not translate into worse overall survival outcomes for WDTC, other important outcomes such as recurrence, reoperation, or permanent hoarseness were not measured and should be an area for future research.

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Abbreviations

IQR	Interquartile range
NCDB	National Cancer Data Base
WDTC	well differentiated thyroid cancer

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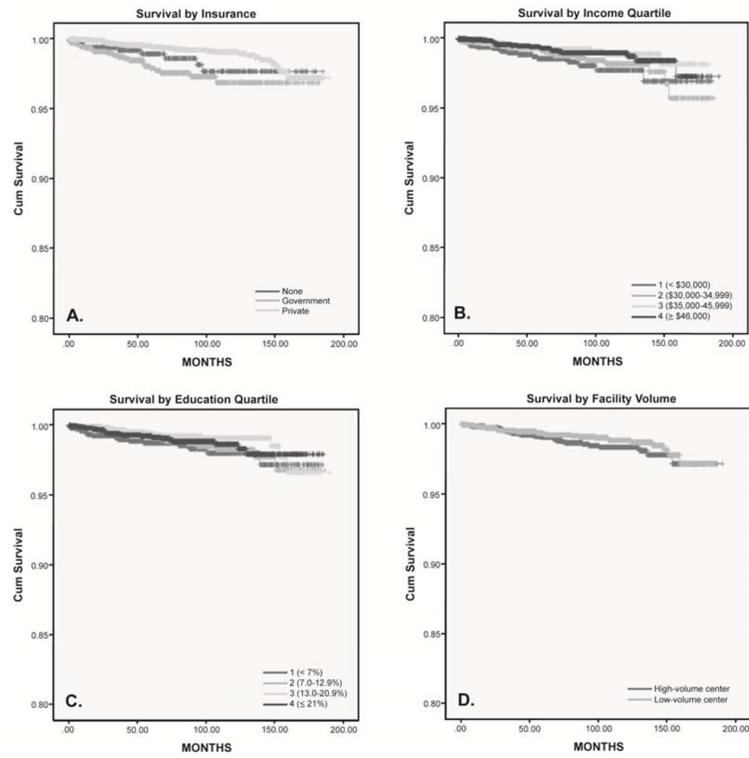


Figure 1. Kaplan-Meier analysis of survival by (a) insurance status, (b) income quartile, (c) education quartile, and (d) facility volume. There was no significant difference in overall survival between the groups based on these variables.

Table 1

Study population

Variable		N	%
Mean Age Years (SD)		17.75 (\pm 3.14)	
Gender	Female	7914	82.6
	Male	1671	17.4
Race/ethnicity	Non-Hispanic White	7258	75.7
	Hispanic White	1020	10.6
	Black	494	5.2
	American Indian	47	0.5
	Asian	391	4.1
	Other	375	3.9
Insurance	None	726	7.6
	Government	1548	16.2
	Private	7311	76.3
Percent without High School Degree	21%	1543	16.1
	13.0–20.9%	2069	21.6
	7.0–12.9%	3000	31.3
	<7.0%	2785	29.1
Income quartile	< \$30,000	1304	13.6
	\$30,000–34,999	2046	21.3
	\$35,000–45,999	2503	26.1
	>\$46,000	3540	36.9

Table 2

Tumor characteristics

Variable	Follicular		Papillary		Total		
	N	%	N	%	N	%	
Stage	I	574	64.6%	5812	66.8%	6386	66.6%
	II	315	35.4%	2884	33.2%	3199	33.4%
Nodes	Negative	589	66.3%	5983	68.8%	6572	68.6%
	Positive	300	33.7%	2713	31.2%	3013	31.4%
Tumor	1 cm	41	5.1%	1644	21.0%	1685	19.5%
Size	> 1 cm	761	94.9%	6183	79.0%	6944	80.5%

Table 3

Tumor stage at presentation by socioeconomic surrogate variables.

Variable	Stage		HR*	p-Value
	I	II		
Insurance	None	416 (57.3%)	310 (42.7%)	2.26
	Government	918 (59.3%)	630 (40.7%)	1.46
	Private	5052 (69.1%)	2259 (30.9%)	ref
	Total	6386 (66.6%)	3199 (33.4%)	<0.001
Income Quartile	1 (< \$30,000)	847 (65.0%)	457 (35.0%)	1.98
	2 (\$30,000–34,999)	1334 (65.2%)	712 (34.8%)	1.88
	3 (\$35,000–45,999)	1675 (66.9%)	828 (33.1%)	1.68
	4 (\$46,000)	2428 (68.6%)	1112 (31.4%)	ref
	Total	6284 (66.9%)	3109 (33.1%)	
Education Quartile	1 (<7.0%)	1015 (65.8%)	528 (34.2%)	1.86
	2 (7.0–12.9%)	1383 (66.8%)	686 (33.2%)	1.50
	3 (13.0–20.9%)	2013 (67.1%)	987 (32.9%)	1.12
	4 (21%)	1878 (67.4%)	907 (32.6%)	ref
	Total	6289 (66.9%)	3108 (33.1%)	0.030

* HR = hazard ratio

Table 4

Time (days) from diagnosis to treatment by insurance status, income quartile and education quartile.

Variable	N	Mean days (SD)*	Mean delay in days	Likelihood of delay (OR) [†]	p-Value
Insurance	None	677	28.14 (61.37)	10.08	2.21
	Government	1441	19.03 (42.09)	0.97	1.33
	Private	6913	18.06 (32.58)	ref	ref
	Total	9031	18.97 (37.20)		
Income Quartile	1 (< \$30,000)	932	19.90 (35.10)	1.78	1.75
	2 (\$30,000–34,999)	1373	19.00 (42.10)	0.88	1.62
	3 (\$35,000–45,999)	2313	18.60 (40.1)	0.48	1.16
	4 (\$46,000)	4069	18.12 (34.7)	ref	ref
	Total	8687	18.73 (36.60)		
Education Quartile	1 (<7.0%)	1430	21.87 (43.48)	4.22	2.04
	2 (7.0–12.9%)	1943	18.69 (37.27)	1.04	1.92
	3 (13.0–20.9%)	2854	18.43 (35.04)	0.78	1.58
	4 (21%)	2626	17.65 (30.80)	ref	ref
	Total	8853	18.89 (35.90)		

* SD = standard deviation

[†]OR = odds ratio

Table 5

Facility volume by insurance status, income quartile and education quartile.

Variable	Facility Volume			p-Value
	Low	High	HR*	
Insurance	None	455 (62.7%)	271 (37.3%)	1.18
	Government	1086 (70.2%)	462 (29.8%)	1.17
	Private	4714 (64.5%)	2597 (35.5%)	ref
	Total	6255 (65.3%)	3330 (34.7%)	0.175
Income Quartile	1 (< \$30,000)	926 (71.0%)	378 (29.0%)	1.52
	2 (\$30,000–34,999)	1443 (70.5%)	603 (29.5%)	1.47
	3 (\$35,000–45,999)	1697 (67.8%)	806 (32.2%)	1.36
	4 (\$46,000)	2071 (58.5%)	1469 (41.5%)	ref
	Total	6137 (65.3%)	3256 (34.7%)	<0.001
Education Quartile	1 (<7.0%)	1068 (69.2%)	475 (30.8%)	1.80
	2 (7.0–12.9%)	1418 (68.5%)	651 (31.5%)	1.65
	3 (13.0–20.9%)	1972 (65.7%)	1028 (34.3%)	1.49
	4 (21%)	1682 (60.4%)	1103 (39.6%)	ref
	Total	6140 (65.3%)	3257 (34.7%)	0.044

* HR = hazard ratio

Table 6

Surgical procedure and radioactive iodine (I-131) therapy by insurance status, income quartile, and education quartile.

Variable	None	Partial Thyroidectomy	Total Thyroidectomy	p-value
Insurance	None	88 (12.1%)	609 (83.9%)	0.09
	Government	37 (2.4%)	1320 (85.3%)	
	Private	127 (1.7%)	6275 (85.9%)	
Income Quartile	1 (< \$30,000)	22 (1.7%)	1093 (83.9%)	0.087
	2 (\$30,000–34,999)	38 (1.9%)	1738 (84.9%)	
	3 (\$35,000–45,999)	53 (2.1%)	2150 (86.0%)	
	4 (\$46,000)	75 (2.1%)	3060 (86.5%)	
Education Quartile	1 (<7.0%)	30 (1.9%)	1319 (85.6%)	0.774
	2 (7.0–12.9%)	44 (2.1%)	1761 (85.1%)	
	3 (13.0–20.9%)	56 (1.9%)	2558 (85.3%)	
	4 (21%)	58 (2.1%)	2405 (86.4%)	
Radioactive Iodine (I-131)				
Insurance	None	338 (46.6%)	388 (53.4%)	<0.001
	Government	571 (36.9%)	977 (63.1%)	
	Private	2651 (36.3%)	4660 (63.7%)	
Income Quartile	1 (< \$30,000)	473 (36.3%)	831 (63.7%)	0.15
	2 (\$30,000–34,999)	765 (37.4%)	1281 (62.6%)	
	3 (\$35,000–45,999)	871 (34.8%)	1632 (65.2%)	
	4 (\$46,000)	1373 (38.8%)	2167 (61.2%)	
Education Quartile	1 (<7.0%)	596 (38.6%)	947 (61.4%)	0.461
	2 (7.0–12.9%)	772 (37.3%)	1297 (61.4%)	
	3 (13.0–20.9%)	1109 (37.0%)	1891 (63.0%)	
	4 (21%)	1008 (36.2%)	1777 (63.8%)	