

**Comparative Effectiveness of Persistent Use of a Name-Brand Levothyroxine (Synthroid®) vs Persistent Use of Generic Levothyroxine on TSH Goal Achievement: A Retrospective Study Among Patients with Hypothyroidism in a Managed Care Setting**

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## SUPPLEMENTARY MATERIAL

**Table 1: Conditions of Interest**

Condition	ICD-9-CM Diagnosis Code	ICD-10-CM Diagnosis Code
Hypothyroidism	244.0x, 244.1x, 244.8x, 244.9x	E01.8%, E03.8%, E89.0%, E03.9%
Thyroid cancer	193.xx, V10.87	C73.%, D44.0%, Z85.850%
Pregnancy	630.xx to 679.xx, V22.xx to V24.xx	O00.% to O9A.%, Z32.% to Z3A.%
Alopecia	704.0x	L63%, L64%, L65%, L66%,
Anemia	280.xx to 285.xx	D50.0% to D64%,
Celiac disease	579.0x	K90.0%
Constipation	564.0x	K59.0%
Goiter	240.xx to 242.3x	E01.0% to E01.2%, E04%
Hyperlipidemia	272.0, 272.1, 272.2, 272.3, 272.4	E78.0, E78.1, E78.2, E78.3, E78.4, E78.5
Hypertension	401.xx, 402.xx, 403.xx, 404.xx, 405.xx	I10%, I11%, I12%, I13%, I15%
Inflammatory bowel disease	555.xx, 556.xx	K50%, K51%
Obesity	278.0x, V85.3x, V85.4x	E66.0%, E66.1%, E66.2%, E66.8%, E66.9%
Psoriasis	696.1x	L40
Rheumatoid arthritis	714.0x, 714.1x, 714.2x	M05%, M06%
Urticaria	708.x	L50%

**Table 2: Independent baseline variables included in the logistic regression model for propensity scores**

Age in years (continuous)  
 Female vs. Male  
 Health plan type (categorical)  
 Medicare Advantage plan vs. Commercial  
 Region of patient residence (categorical)  
 Index year (categorical)  
 Provider specialty on index prescription claim (categorical)  
 Quan-Charlson Comorbidity Index (continuous)  
 Goiter (yes vs. no)  
 Hypertension (yes vs. no)  
 Hypothyroidism-related outpatient services (yes vs. no)  
 Fill mechanism on index prescription claim (mail vs. retail)  
 Hypothyroidism-related pharmacy dispensing (yes vs. no)

Number of hypothyroidism-related pharmacy claims per patient (continuous)

**Table 3: Independent baseline variables included in the regression model for achievers vs. non-achievers**

TSH goal achievers (yes vs. no)

Synthroid vs. GL cohort

Age in years (40<65 vs. 18<40; 65<75 vs. 18<40; ≥75 vs. 18<40)

Female vs. Male

Health plan type: PPO vs. HMO; CDHP vs. HMO; Other vs. HMO

Region of patient residence: Midwest vs. Northeast; South vs. Northeast; West vs. Northeast; Missing/Unknown vs. Northeast

Index year: 2007 vs. 2006; 2008 vs. 2006; 2009 vs. 2006; 2010 vs. 2006; 2011 vs. 2006; 2012 vs. 2006; 2013 vs. 2006; 2014 vs. 2006; 2015 vs. 2006; 2016 vs. 2006

Provider specialty on index prescription claim: PCP vs. Endocrinologist; Others/unknown vs. Endocrinologist

Quan-Charlson Comorbidity Index: 1 vs. 0; 2 vs. 0; 3+ vs. 0

Goiter (yes vs. no)

Hypertension (yes vs. no)

Alopecia (yes vs. no)

Hyperlipidemia (yes vs. no)

Hypothyroidism-related inpatient hospitalizations (yes vs. no)

Hypothyroidism-related pharmacy dispensing (yes vs. no)

All-cause outpatient services cost (in thousands)

All-cause pharmacy cost (in thousands)

All-cause medical and pharmacy cost (in thousands)

Hypothyroidism-related inpatient cost (in thousands)

Hypothyroidism-related ER cost (in thousands)

Hypothyroidism-related outpatient services cost (in thousands)

Hypothyroidism-related medical and pharmacy cost (in thousands)

*CDHP=consumer-driven health plan; GL=generic levothyroxine; HMO=health maintenance organization; PCP=primary care physician; PPO=preferred provider organization; SD=standard deviation; TSH=thyroid stimulating hormone*

**Table 4. TSH Achievers vs Non-Achievers: Patient Demographics and Clinical Characteristics**

Demographic and clinical characteristics	TSH Goal Achievers	TSH Goal Non-Achievers	Standardized Difference <sup>a</sup>
	(n=49,916)	(n=14,880)	
	n (%) / Mean (SD)	n (%) / Mean (SD)	
Age at index (years), mean (SD), median (IQR)	53.9 (12.69)	54.1 (12.94)	-0.016
Age categories, n (%)			
18 – 39	5,871 (11.8)	1,715 (11.5)	0.007
40 – 64	36,112 (72.3)	10,680 (71.8)	0.013
65 – 74	4,920 (9.9)	1,444 (9.7)	0.005
≥75	3,013 (6.0)	1,041 (7.0)	-0.039
Female, n (%)	38,825 (77.8)	10,525 (70.7)	0.162
Health plan type, n (%)			
PPO	28,515 (57.1)	8,472 (56.9)	0.004
HMO	17,529 (35.1)	5,354 (36.0)	-0.018
CDHP	3,869 (7.8)	1,054 (7.1)	0.025
Medicare Advantage plan, n (%)	6,705 (13.4)	2,161 (14.5)	-0.031
Geographic region of residence, n (%)			
Northeast	12,053 (24.1)	3,690 (24.8)	-0.015
Midwest	9,559 (19.2)	2,845 (19.1)	0.001
South	17,553 (35.2)	5,222 (35.1)	0.001
West	10,744 (21.5)	3,115 (20.9)	0.014
Missing/Unknown	7 (<0.1)	8 (0.1)	-0.022
Prescribing/treating physician specialty <sup>b</sup> , n (%)			
PCP	33,866 (67.8)	10,306 (69.3)	-0.030
Endocrinologist	8,559 (17.1)	2,205 (14.8)	0.064
Others/Unknown	7,491 (15.0)	2,369 (15.9)	-0.025
Comorbidities			
QCI, mean (SD), median (IQR)	0.6 (1.22)	0.7 (1.35)	-0.048
Other comorbidities of interest, n (%)			
Alopecia	883 (1.8)	186 (1.3)	0.043
Anemia	4,522 (9.1)	1,403 (9.4)	-0.013
Celiac disease	124 (0.2)	32 (0.2)	0.007
Constipation	1,177 (2.4)	331 (2.2)	0.009
Goiter	4,888 (9.8)	1,345 (9.0)	0.026
Hyperlipidemia	21,229 (42.5)	6,146 (41.3)	0.025
Hypertension	18,010 (36.1)	5,500 (37.0)	-0.018
Inflammatory bowel disease	292 (0.6)	84 (0.6)	0.003
Obesity	3,281 (6.6)	963 (6.5)	0.004

Psoriasis	412 (0.8)	109 (0.7)	0.011
Rheumatoid arthritis	735 (1.5)	225 (1.5)	-0.003
Urticaria	346 (0.7)	110 (0.7)	-0.005
Laboratory testing <sup>c</sup>			
Patients with TSH result, n (%)	31,967 (64.0)	9,357 (62.9)	0.024
Mean (SD) [median] mIU/L	5.3 (11.41) [3.2]	8.8 (19.47) [4.8]	-0.221
TSH results between 0.3 and 4.12 mIU/L, n (%)	17,158 (34.4)	2,988 (20.1)	0.325

CDHP=consumer-driven health plan; HMO=health maintenance organization; PCP=primary care physician; PPO=preferred provider organization; QCI=Quan-Charlson Index score; SD=standard deviation; TSH=thyroid-stimulating hormone

<sup>a</sup>Standardized difference=difference in means or proportions divided by the pooled standard deviation. An absolute value of the standardized difference <0.1 was used to indicate balance in a variable across the cohorts.

<sup>b</sup>On index prescription claim.

<sup>c</sup>Last serum TSH lab result in the 6-month pre-index period.

**Table 5. TSH Achievers vs Non-Achievers: Costs at baseline and follow-up**

Costs	6-Month Baseline		12-Month Follow Up		p-Value <sup>b</sup> [A vs B]	p-Value <sup>b</sup> [C vs D]
	TSH Goal Achievers <sup>a</sup> [A] (n=49,916)	TSH Goal Non-Achievers [B] (n=14,880)	TSH Goal Achievers [C] (n=49,916)	TSH Goal Non-Achievers [D] (n=14,880)		
	n (%)/ Mean (SD)	n (%)/ Mean (SD)	n (%)/ Mean (SD)	n (%)/ Mean (SD)		
<b>All-cause healthcare costs</b>						
Inpatient hospitalization, mean (SD)	\$1,981 (\$17,377)	\$2,505 (\$21,529)	\$2,046 (\$12,838)	\$2,791 (\$15,228)	.853	.005
ED visits, mean (SD)	\$195 (\$1,073)	\$181 (\$890)	\$326 (\$1,348)	\$334 (\$1,403)	.674	.511
Outpatient services, mean (SD) [median]	\$2,742 (\$7,026) [\$996]	\$2,708 (\$6,641) [\$884]	\$5,412 (\$13,636) [\$2,330]	\$5,671 (\$14,622) [\$2,130]	.002	.071
Pharmacy costs, mean (SD) [median]	\$1,437 (\$3,574) [\$541]	\$1,394 (\$3,856) [\$491]	\$3,396 (\$7,674) [\$1,483]	\$3,423 (\$8,922) [\$1,403]	.001	.234
Total medical costs <sup>d</sup> , mean (SD) [median]	\$4,917 (\$19,548) [\$1,122]	\$5,393 (\$23,552) [\$999]	\$7,784 (\$20,912) [\$2,614]	\$8,797 (\$23,907) [\$2,421]	.168	.822
Total costs <sup>e</sup> , mean (SD) [median]	\$6,355 (\$20,230) [\$2,187]	\$6,787 (\$24,185) [\$2,043]	\$11,180 (\$23,717) [\$5,074]	\$12,220 (\$27,062) [\$4,791]	.122	.795
<b>Hypothyroidism-related healthcare costs<sup>c</sup></b>						
Inpatient hospitalization, mean (SD)	\$897 (\$9,652)	\$1,038 (\$9,411)	\$1,250 (\$8,977)	\$1,683 (\$10,509)	.503	.001
ED visits, mean (SD)	\$50 (\$590)	\$45 (\$484)	\$93 (\$719)	\$98 (\$789)	.039	.849
Outpatient services, mean (SD) [median]	\$265 (\$1,598) [\$90]	\$261 (\$1,182) [\$89]	\$650 (\$2,675) [\$238]	\$691 (\$2,587) [\$251]	.382	.585
Pharmacy fills, mean (SD) [median]	\$37 (\$52) [\$20]	\$38 (\$54) [\$19]	\$174 (\$116) [\$146]	\$180 (\$116) [\$150]	.983	.010

			IQR \$115	IQR \$114		
Total medical costs <sup>d</sup> , mean (SD) [median]	\$1,212 (\$9,815) [\$101]	\$1,343 (\$9,505) [\$101]	\$1,994 (\$9,553) [\$261]	\$2,472 (\$11,035) [\$280]	.341	.023
Total costs <sup>e</sup> , mean (SD) [median]	\$1,249 (\$9,815) [\$143]	\$1,382 (\$9,505) [\$144]	\$2,168 (\$9,552) [\$442]	\$2,653 (\$11,035) [\$471]	.344	.008

ED=emergency department; HCRU=healthcare resource utilization; SD=standard deviation; TSH=thyroid-stimulating hormone

<sup>a</sup>≥1 Serum TSH lab results between 0.3 and 4.12 mIU/L in 12 months of follow up.

<sup>b</sup>p-Values were based on t-tests for continuous variables and  $\chi^2$  test for categorical variables.

<sup>c</sup>Hypothyroidism-related healthcare utilization was based on medical claims with an ICD-9-CM diagnosis code of [244.0x, 244.1x, 244.8x, or 244.9x] or ICD-10-CM diagnosis code of [E01.8%, E03.8%, E89.0%, or E03.9%] and pharmacy claims for hypothyroidism medications (including levothyroxine, liothyronine, desiccated thyroid, liotrix, and thyroglobulin).

<sup>d</sup>Total medical costs included inpatient, ED, and outpatient costs.

<sup>e</sup>Total costs were the sum of medical and pharmacy costs.