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The ages and TSH values of patients being prescribed levothyroxine

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Abstract

Background: Levothyroxine is a commonly prescribed medication. Some data suggest that levothyroxine may be initiated for mild degrees of hypothyroidism and used without considering age-specific reference ranges or individual patient factors when prescribing.

Methods: The electronic medical record of a health care system operating in the Washington, DC and Maryland area was interrogated to determine the number of patients who were being prescribed levothyroxine during the time period 2008–2016, the number of prescriptions supplied to these individuals, an associated diagnosis of hypothyroidism, and whether the prescriptions were new or existing prescriptions. Information was also extracted about the age of patients receiving prescriptions and the thyroid stimulating hormone level documented prior to levothyroxine initiation.

Results: Although the number of levothyroxine prescriptions provided annually increased over this time period, when corrected for the number of patients in the database, the percentage of patients receiving levothyroxine prescriptions showed a slight downward trend. Levothyroxine was both most frequently prescribed and frequently initiated in those of ages 50–59 years and 60–69 years. The doses of levothyroxine most commonly prescribed were 50 µg and 100 µg and the pattern of levothyroxine doses being used was unaffected by whether a diagnosis of hypothyroidism was documented or not. Levothyroxine prescription initiation was associated with mean thyroid stimulating hormone values that were modestly elevated and in the range of 7.5–13.8 mIU/L.

Conclusion: This analysis showed that although the percentage of patients being prescribed levothyroxine is stable or slightly declining, with most decrement in those without a diagnosis of hypothyroidism, there is nevertheless continued initiation of levothyroxine in those with mild degrees of thyroid stimulating hormone elevation, and in those of older age, raising concerns about both unnecessary treatment and iatrogenic thyrotoxicosis. Such data suggest the need for great consideration of both the degree of thyroid stimulating hormone elevation and the patient context when considering whether treatment of an elevated thyroid stimulating hormone value, *versus* ongoing monitoring, is indicated.

Keywords: age, hypothyroidism, levothyroxine, prescribing, TSH

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Introduction

Hypothyroidism affects approximately 5% of the United States population, and synthetic thyroxine in the form of levothyroxine (LT4) is the most prescribed therapy for this common condition.[1,2] Autoimmune hypothyroidism is generally progressive, with a decrement in endogenous thyroid function occurring over time, such that overt hypothyroidism would occur if the thyroid hormone deficiency is untreated.[3] However, at the current time hypothyroidism may initially be diagnosed when it is mild or subclinical, at a time that the serum thyroid stimulating hormone (TSH) is minimally elevated below 10 mIU/L and the serum thyroid hormone levels are normal. Symptoms of hypothyroidism are not always specific for this

condition, and each of the symptoms generally associated with hypothyroidism may also have non-thyroid causes.[4] As attribution of the cause of symptoms is not a simple matter,[5,6] many physicians may err on the side of treating mild TSH elevations with the expectation that symptoms may improve. Thus, treatment with LT4 may be initiated for borderline TSH elevations.[7] The authors also hypothesize that LT4 may even be prescribed for unconfirmed serum TSH elevations, or even without TSH elevation, based on the symptoms that the patient is experiencing.

LT4 is being prescribed with increasing frequency, both in the United States[8,9] and in other countries.[10,11] Several studies have shown that the TSH threshold at which LT4 therapy is initiated has fallen over time, such that an increasing number of cases of subclinical hypothyroidism are being treated and the mean or median TSH value at which therapy is initiated has decreased over time.[7,12–14] This trend for increasing treatment and decreasing thresholds has been documented both in the United States[9,14] and in Europe.[7,12,13] Moreover, a recent study showed that if LT4 therapy was discontinued in patients undergoing treatment, while 39% of patients did in fact become hypothyroid as manifest by an elevated TSH, 61% maintained a normal TSH, perhaps suggesting that their treatment was unnecessary.[15] However, the follow-up period in this study was relatively brief at 6–8 weeks, thus hypothyroidism being manifest later during follow-up cannot be excluded.[15] Although national databases show a trend for an increasing number of LT4 prescriptions being provided over time,[16,17] part of this apparent increase may be accounted for by a reduction in the length of prescriptions by prescribers,[10] such that more prescriptions are being generated for the same number of patients each year.

The current analysis examined the prescription of LT4 using the electronic medical record (EMR) of a large health care system (MedStar) operating in the Washington, DC and Maryland area. The MedStar Health System is a non-profit healthcare organization founded in 1998. It operates several physician practice groups and also 10 hospitals in the Baltimore–Washington metropolitan area. Approximately 5000 physicians provide medical care within this system. The MedStar Health System also operates the MedStar Health Research Institute, which employs scientists and investigators engaged in translational and health sciences research. The patient population is likely representative of the general population in terms of age, sex, and socioeconomic status, based on datasets such as the United States Census.[18] The EMR, which is the system in use by all MedStar physicians, was interrogated to determine whether the number of prescriptions being provided for LT4 was changing over time, what the associated diagnosis was, and also to examine prescriptions according to patient age and sex.

Methods

The study was approved by the joint Georgetown University–MedStar Institutional Review Board (study number 2017-0335). Waiver of the need to obtain informed consent from participants was granted. Data extraction was performed by the Biostatistics and Biomedical Informatics component of the Clinical and Translation Science Award program at Georgetown University using Medstar Health Research Institute Databases, including Centricity and Explorys as appropriate. Centricity is an ambulatory care electronic medical record system which can be used for clinical research, including performing retrospective cohort studies. Explorys is a system that interacts with electronic medical records systems and allows for secure storage and analysis of large patient data sets in a manner compliant with ethical regulations. The databases were searched for the years 2008–2016, a period during which significant changes to the database were not occurring. Adult outpatients 18 years and older were included in the search. All LT4 products were searched for, including the following: Levothyroxine, Synthroid, Unithroid, Levoxyl, and Levothroid. The doses of LT4 products that were included were 25, 50, 75, 88, 100, 112, 125, 137, 150, 175, 200, 300 µg. Data regarding other thyroid hormone preparations such as armour thyroid, desiccated thyroid extract, liothyronine (Cytomel) were not collected as these were a small proportion of thyroid hormone prescriptions.

Diagnoses of hypothyroidism, and all diagnoses potentially associated with hypothyroidism, were documented using International Classification of Diseases (ICD) codes. Both ICD -9 and ICD-10 codes were noted. These included, for example, diagnoses of thyroid cancer, Hashimoto's thyroiditis, and thyroidectomy. The design of the EMR

encourages physicians to be as complete and comprehensive as possible in assigning all relevant diagnoses. Such diagnoses were noted if they were present at any time and linked to any visits in the patient's electronic chart. Patients with any of the multiple diagnostic codes for hyperthyroidism were excluded from the analysis, as were hospitalized patients, pediatric patients, and pregnant patients. Prescriptions were classified as pre-existing if any dose of LT4 had been prescribed before, even if there had been a hiatus or a change in dose. Prescriptions were classified as new if no dose of LT4 had been prescribed before. All LT4 prescriptions were normalized to a 90-day period.

The following information was extracted from the electronic medical record:

1. The number of patients in the database annually;
2. The number of patients being prescribed levothyroxine in the database annually;
3. The average age and age distribution of the patients in the database annually;
4. The average age and age distribution of the patients in the database being prescribed levothyroxine annually;
5. The number of levothyroxine prescriptions in the database annually;
6. The number of levothyroxine prescriptions per patient annually;
7. The duration of each levothyroxine prescription in number of days on an annual basis;
8. The sex distribution of patients being prescribed levothyroxine annually;
9. The presence or absence of a diagnosis of hypothyroidism in the patients being prescribed levothyroxine annually;
10. The average levothyroxine dose and distribution of levothyroxine doses annually;
11. The average TSH value and TSH distribution associated with the first levothyroxine prescription in each patient annually.

Statistical analysis

This was a study to determine whether LT4 prescribing was increasing within this population in the same way that has been described nationally, and to determine which factors seemed to be associated with any LT4 prescribing trends observed in this geographic area of the United States. All data extracted from the EMR was summarized using descriptive statistics (mean, standard deviation, median, range for continuous variables, and frequencies and percentages for categorical variables). Factors examined included patient age and sex, and TSH values. Prescriptions were divided according to whether they were written for a diagnosis of hypothyroidism, or written for patients without a diagnosis of hypothyroidism. LT4 prescribing across the age spectrum was examined. Statistical analyses were conducted using the statistical expertise of the Department of Biostatistics and Bioinformatics at MedStar Health Research Institute.

Results

The number of outpatients within the MedStar system increased from 135,150 in 2008 to 547,433 patients in 2016. The number of outpatients being prescribed LT4 increased from 8229 in 2008 to 20,089 in 2016. Using the outpatient population as a denominator, the percent of patients being prescribed LT4 was 6.1% in 2008 and decreased to 3.7% in 2016 (see Figure 1). Outpatients were also divided according to whether or not they had a diagnosis of hypothyroidism documented in their EMR. The percentage of patients being prescribed LT4 with a documented diagnosis of hypothyroidism increased from 2.5% in 2008 to 3.2% in 2012 and then decreased to 2.5% in 2016. The percentage of patients being prescribed LT4 without a diagnosis of hypothyroidism decreased from 3.6% in 2008 to 1.1% in 2016 (see Figure 2).

LT4 doses being prescribed

When the LT4 prescriptions were categorized according to the dose being prescribed, the most commonly prescribed doses were 50, 75, 100, and 125 µg. This pattern was seen regardless of whether or not a diagnosis of hypothyroidism was documented in the patient's chart (see Tables 1 and 2). The 50 µg dose was prescribed for the highest percentage of patients, the percentage being 14.6–16.8% in all patients, 15.1–16.7% in those patients without documentation of hypothyroidism, and 14.1–17.1% in patients with documentation of hypothyroidism.

Patient age at prescription initiation

For patients whose LT4 prescription was initiated during the period of observation, the age of

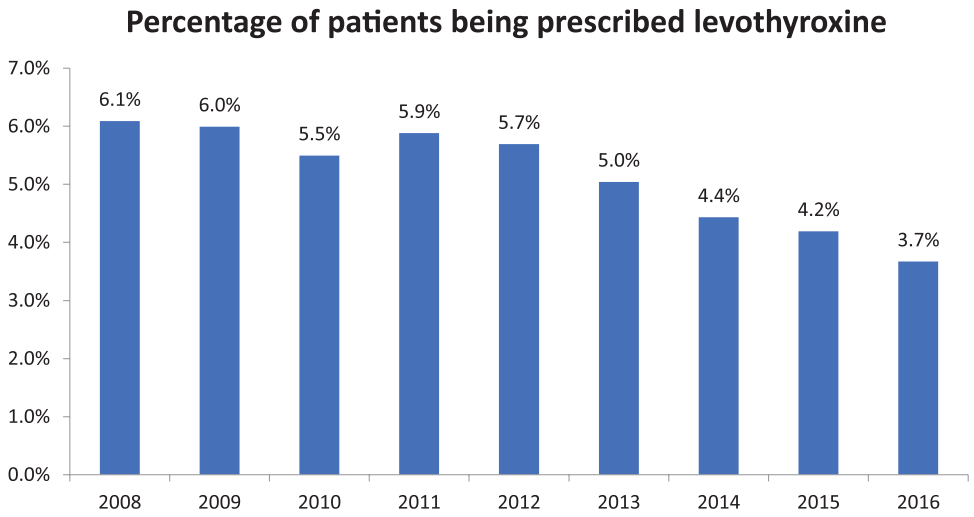

Figure 1. Percentage of patients being prescribed levothyroxine between 2008 and 2016.

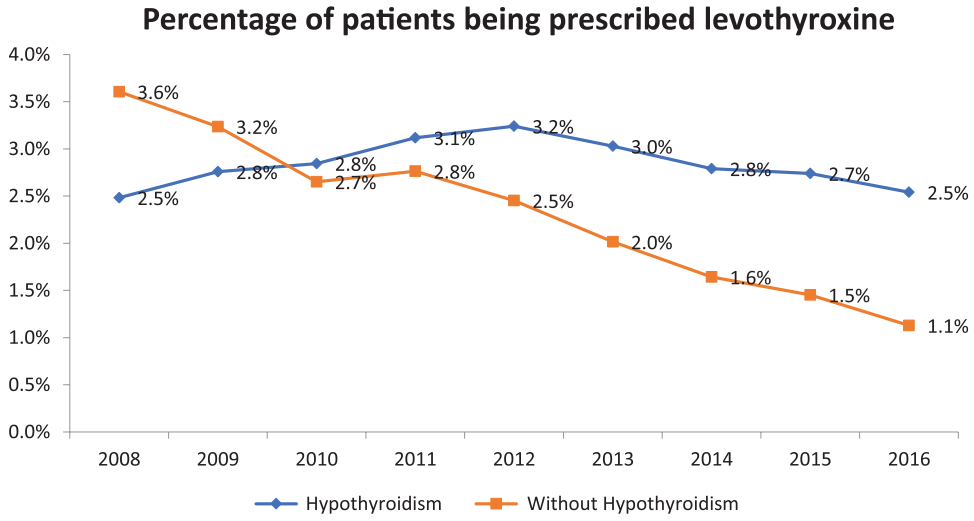

Figure 2. Percentage of patients being prescribed levothyroxine between 2008 and 2016, divided according to whether they carried a diagnosis of hypothyroidism or not.

the patient at prescription initiation was noted. The mean age at initiation for all patients remained constant over the years 2008–2016 at age 54–57 years [see Table 3(a)]. When patients were divided into age deciles, prescription initiation was observed at all deciles, but with the least number of prescriptions being initiated in the 18–29 and 80 years and older age groups [see Table 4(a) and Figure 3]. When patients were divided according to whether or not a diagnosis of hypothyroidism was documented in their EMR, the trend for age at initiation and age decile at initiation were similar for patients with a hypothyroidism diagnosis and those without [see Tables 3(b) and 4(b) and Tables 3(c) and 4(c) respectively].

Age of all patients with LT4 prescriptions

When the age of patients being prescribed LT4, including both existing and new prescriptions, was examined, the mean age of patients ranged from 57 to 62 years of age [Table 5(a)–(c)]. The age of patients being prescribed LT4 with a documented diagnosis of hypothyroidism tended to be a little younger (55–58 years) than those without

Table 1. Levothyroxine prescriptions divided by the percentage of each dose that was prescribed on an annual basis.

Percentage of each dose prescribed per year									
LT4 Dose (μg)	Year								
	2008	2009	2010	2011	2012	2013	2014	2015	2016
25	6.35	6.61	6.70	7.78	8.10	8.64	8.48	8.52	8.35
50	15.00	14.60	14.91	15.56	16.51	16.82	16.40	16.63	16.51
75	14.70	13.74	14.15	14.34	14.60	14.78	15.15	15.19	15.49
88	7.09	7.29	7.63	7.96	8.52	8.59	8.73	8.74	9.23
100	15.96	15.67	14.63	14.76	14.23	14.10	14.37	14.30	14.27
112	8.12	8.53	8.60	8.64	7.99	8.15	8.16	8.08	8.48
125	10.57	10.87	10.68	9.77	9.93	9.45	9.41	9.23	9.02
137	4.20	4.86	4.93	4.76	4.72	4.39	4.54	4.80	4.62
150	8.79	8.53	8.23	7.74	7.31	6.96	6.81	6.77	6.60
175	4.70	4.61	4.99	4.61	4.35	4.53	4.45	4.31	4.17
200	4.16	4.23	4.11	3.67	3.44	3.34	3.29	3.25	3.00
300	0.37	0.47	0.44	0.40	0.30	0.24	0.22	0.19	0.26

Gray shading indicates the most frequently prescribed doses. LT4, levothyroxine.

this diagnosis (58–62 years) [see Table 5(b) and (c)]. When displayed graphically (Figure 4), more patients in the deciles of 50–59 years and 60–69 years had LT4 prescriptions, even though the mean age of the population only increased from 49 years to 51 years over the time period from 2008 to 2016 (see Tables 4 and 6).

Sex of patients with LT4 prescriptions

The percentage of male patients being prescribed LT4 stayed steady over the observation period at approximately 1% of patients. However, the percentage of female patients being prescribed LT4 decreased significantly from 5% in 2008 to 2.9% in 2016 (see Figure 5).

TSH values at time of LT4 prescription initiation

When examining the TSH values available in the patient's EMR prior to initiation of a new LT4 prescription, TSH elevations were noted to be relatively modest with mean TSH values on an annual basis ranging between 7.51 and 13.78 mIU/L (see Table 7), with values being stable at approximately 10 mIU/L between 2014 and 2016.

Discussion

In contrast to other studies or analyses which show increases in LT4 prescribing,[8,16,17,19] our study shows that LT4 being provided for a diagnosis of hypothyroidism remained relatively stable from 2008 to 2016. Moreover, the number of LT4 prescriptions being given to patients without a diagnosis of hypothyroidism declined over the same period. If hypothyroidism is accurately documented in the EMR of these patients, this could suggest that LT4 is being given less frequently for non-specific symptoms. The decline in LT4 prescriptions seemed to occur mostly in women. It is indeed surprising that so many LT4 prescriptions were being written for patients without a documented diagnosis of hypothyroidism. It is suspected that such patients may have been

Table 2. Levothyroxine prescriptions divided by the percentage of each dose that was prescribed on an annual basis, and subdivided by whether a diagnosis of hypothyroidism was documented or not.

LT4 dose (μg)	Percentage of each LT4 dose prescribed per year																	
	2008		2009		2010		2011		2012		2013		2014		2015		2016	
	No hypo	Hypo	No hypo	Hypo	No hypo	Hypo	No hypo	Hypo	No hypo	Hypo	No hypo	Hypo	No hypo	Hypo	No hypo	Hypo	No hypo	Hypo
25	6.8	5.7	7.3	5.8	7.3	6.2	8.1	7.5	8.1	8.1	9.0	8.4	8.5	8.5	8.5	8.5	8.2	8.4
50	15.6	14.2	15.1	14.1	15.0	14.9	15.4	15.7	16.0	16.8	16.7	16.9	15.7	16.8	15.6	17.1	15.5	16.9
75	14.8	14.5	14.0	13.4	14.6	13.8	15.0	13.8	14.7	14.5	15.2	14.5	15.9	14.8	15.4	15.1	15.7	15.4
88	7.7	6.3	7.2	7.3	8.2	7.2	8.2	7.8	9.2	8.0	9.1	8.3	9.1	8.5	9.4	8.4	9.7	9.0
100	16.2	15.6	15.8	15.5	15.3	14.1	16.2	13.6	14.9	13.7	14.7	13.8	14.9	14.1	14.7	14.1	15.1	14.0
112	8.3	7.8	8.7	8.3	8.8	8.4	9.0	8.3	8.1	7.9	8.2	8.1	8.7	7.9	8.8	7.7	9.0	8.3
125	10.1	11.2	11.0	10.8	11.1	10.3	9.1	10.3	10.0	9.9	9.3	9.6	9.4	9.4	9.1	9.3	9.0	9.0
137	3.6	5.0	4.3	5.5	4.4	5.4	4.4	5.1	4.7	4.7	4.2	4.5	4.2	4.7	4.8	4.8	4.7	4.6
150	8.7	9.0	8.1	8.9	7.2	9.1	7.3	8.1	7.0	7.5	6.7	7.1	6.8	6.8	6.4	7.0	6.4	6.7
175	4.1	5.5	4.1	5.1	4.6	5.3	4.1	5.0	4.1	4.5	4.2	4.7	4.0	4.7	4.4	4.3	4.2	4.2
200	3.7	4.8	3.9	4.6	3.2	4.9	2.9	4.3	2.8	3.9	2.6	3.8	2.6	3.6	2.7	3.5	2.5	3.2
300	0.3	0.4	0.3	0.6	0.3	0.5	0.3	0.4	0.3	0.3	0.2	0.3	0.2	0.3	0.2	0.2	0.2	0.3

Gray shading indicates the most frequently prescribed doses.
LT4, levothyroxine

Table 3. Patient age at first initiation of a levothyroxine prescription on an annual basis, with patients divided according to whether they carried a diagnosis of hypothyroidism or not.

Patient group	Year	Patients *n*	Patient age						
			Mean age	SD	Median age	25th pctl	75th pctl	Minimum age	Maximum age
(a) All patients	2008	4376	55	17	55	42	66	18	99
	2009	3639	54	17	54	41	65	18	100
	2010	2905	54	17	54	41	65	18	110
	2011	4911	55	17	55	43	67	18	101
	2012	5099	55	17	56	43	68	18	104
	2013	4967	57	18	57	44	70	18	108
	2014	4634	55	18	56	41	67	18	114
	2015	4078	54	17	55	40	66	18	97
	2016	3237	54	18	55	40	67	18	104
(b) Patients with hypothyroidism	2008	1591	52	17	52	39	64	18	99
	2009	1645	53	17	53	40	64	18	99
	2010	1561	53	17	53	40	63	18	109
	2011	2453	54	17	54	41	65	18	101
	2012	2924	54	17	55	41	66	18	100
	2013	2926	55	18	55	42	67	18	108
	2014	2983	53	18	54	39	65	18	99
	2015	2767	52	17	53	38	64	18	97
	2016	2439	53	18	54	39	66	18	98
(c) Patients without hypothyroidism	2008	2785	56	17	56	44	68	18	98
	2009	1994	54	17	55	41	66	18	100
	2010	1344	55	17	55	43	66	18	110
	2011	2458	56	17	56	45	68	18	99
	2012	2175	57	17	58	45	69	18	104
	2013	2041	60	19	60	47	75	18	104
	2014	1651	58	19	59	45	72	18	114
	2015	1311	57	18	58	44	69	18	97
	2016	798	56	18	57	42	69	18	104

pctl, percentile

Table 4. Number of patients with first initiation of a levothyroxine prescription, divided according to age deciles, with patients divided according to whether they carried a diagnosis of hypothyroidism or not.

Patient group	Age decile	Number of patients with prescription initiation per year								
		Year (mean age of population)								
		2008 (49)	2009 (49)	2010 (49)	2011 (49)	2012 (50)	2013 (50)	2014 (50)	2015 (50)	2016 (51)
(a) All patients	18–29	340	344	248	364	422	383	439	407	325
	30–39	584	512	398	579	627	552	612	589	464
	40–49	746	612	526	865	806	743	686	612	520
	50–59	973	816	680	1130	1134	1083	1010	869	635
	60–69	823	679	524	999	996	896	876	825	633
	70–79	505	367	287	530	646	635	518	446	386
	80+	405	309	242	444	468	675	493	330	274
(b) Patients with hypothyroidism	18–29	164	165	155	204	269	250	311	294	255
	30–39	235	239	233	327	394	363	441	443	358
	40–49	297	301	302	459	481	476	470	436	406
	50–59	364	349	346	549	649	684	667	593	484
	60–69	270	304	257	472	533	524	564	547	464
	70–79	149	158	149	245	371	349	292	275	280
	80+	112	129	119	197	227	280	238	179	192
(c) Patients without hypothyroidism	18–29	176	179	93	160	153	133	128	113	70
	30–39	349	273	165	252	233	189	171	146	106
	40–49	449	311	224	406	325	267	216	176	114
	50–59	609	467	334	581	485	399	343	276	151
	60–69	553	375	267	527	463	372	312	278	169
	70–79	356	209	138	285	275	286	226	171	106
	80+	293	180	123	247	241	395	255	151	82

prescribed LT4 for conditions or symptoms such as obesity, tiredness, and depression.

Our analysis confirms other studies that show that LT4 prescriptions are being written for patients with relatively mild TSH elevations.[7,12,13] This is perhaps illustrated by the pattern of the mean and median TSH values shown in Table 7. Although the mean TSH is mildly elevated, the median TSH is in the high end of the normal range. This could indicate that there are some individuals in the dataset that have high TSH values, possibly meriting treatment, leading to the mean TSH being above the normal range, but that there are a substantial number of patients who only have "high-normal" TSH values, thus

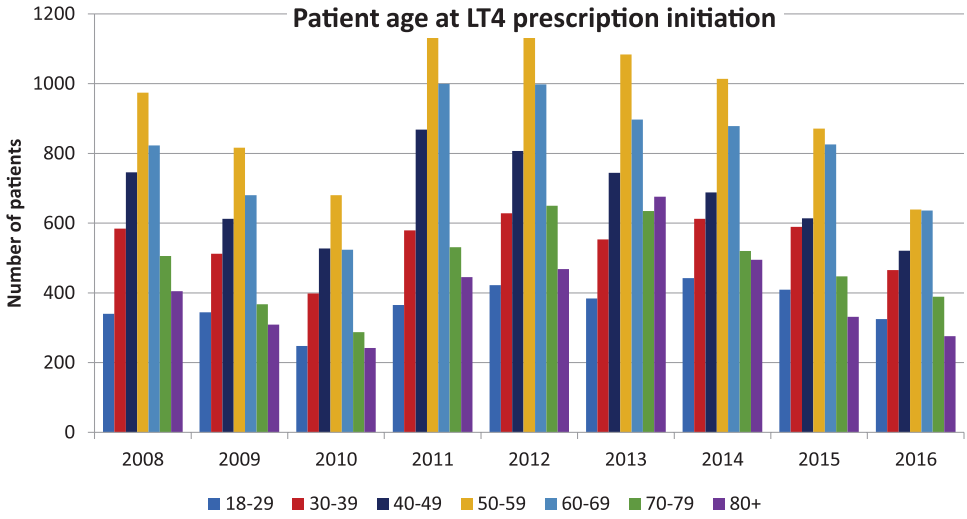

Figure 3. Age at levothyroxine (LT4) initiation divided by age decile and displayed on an annual basis.

accounting for the median TSH actually being in the higher part of the normal range. The mean TSH values prior to prescription initiation during the last 3 years of observation in our study remained steady at 10 mIU/L. It is important to note that often such mild TSH elevations have a tendency to normalize themselves, even without LT4 being initiated, as has been shown in prior studies.[20,21] Our study also confirms other studies that have demonstrated that LT4 initiation is prevalent in older individuals.[14] In the present study LT4 was most frequently initiated in those in the age groups of 50–59 years and 60–69 years but was also initiated in those of 70–79 years and in those over 80 years. Similar patterns were seen for all LT4 prescription (new and existing).

We also present new data about LT4 doses in individuals being prescribed LT4 and the effect of having or not having a diagnosis of hypothyroidism on prescribing patterns. With respect to LT4 doses, the fact that the 50 µg dose was the one most frequently prescribed, irrespective of whether or not a diagnosis of hypothyroidism had been definitely documented, further illustrates that mild degrees of hypothyroidism are being treated, or possibly that hypothyroidism was not present at all. Although the authors do not have data regarding the percentage of patients who had low TSH values following initiation of LT4, it could be hypothesized that in some patients treatment simply lowered their TSH values from the upper to the lower end of the normal range. A full replacement dose of LT4 is approximately 100 µg in someone of about 70 kg with minimal residual endogenous thyroid function. This dose was prescribed in 13.6–15.6% of those with a documented diagnosis of hypothyroidism, and 14.7–16.2% of those with no documentation of hypothyroidism.

Surprisingly, in addition to the pattern of LT4 dosage use not differing on the basis of whether a diagnosis of hypothyroidism was present or not, the ages of patients receiving LT4 did not seem to differ depending on whether a diagnosis of hypothyroidism had been formally documented or not. The mean age of initiation of LT4 prescriptions was similar regardless of whether the patient's EMR contained a diagnosis of hypothyroidism or not. Prescription initiation seemed to be prevalent across all age groups, although the number of prescriptions rose on an annual basis most notably in those of 50–69 years of age. The second most frequent age range in which LT4 was initiated was in those of 60–69 years, with substantial initiation occurring in older age groups also. This is concerning, as there are fewer data about the benefits of LT4 therapy in older age groups,[22] but clear risks of over-replacement.[23] In addition, based on age-specific reference ranges for TSH values,[24] it is possible that many of these older individuals may not actually have hypothyroidism. Although mild TSH elevation may be associated with cardiac dysfunction,[25] there may not be benefits in older individuals,[26] who also have additional considerations because of frailty.[27]

Table 5. Age of all patients with a levothyroxine prescription on an annual basis, with patients divided according to whether they carried a diagnosis of hypothyroidism or not.

Patient group	Year	Patients *n*	Age at prescription						
			Mean	SD	Median	25th pctl	75th pctl	Minimum	Maximum
(a) All patients	2008	8229	57	16	57	45	69	18	99
	2009	10,379	57	17	57	45	68	18	100
	2010	11,289	57	17	57	45	68	18	110
	2011	14,182	57	16	57	46	68	18	111
	2012	16,825	58	17	58	46	69	18	104
	2013	19,234	59	17	59	47	70	18	109
	2014	20,823	59	17	59	47	70	18	114
	2015	21,475	59	17	59	48	70	18	115
	2016	20,088	59	17	60	48	71	18	105
(b) Patients with hypothyroidism	2008	3489	55	16	55	43	66	18	99
	2009	5007	55	17	55	43	66	18	99
	2010	6108	55	16	56	43	66	18	109
	2011	7827	56	16	56	44	67	18	101
	2012	9954	56	16	57	44	68	18	102
	2013	12,001	57	16	57	45	68	18	109
	2014	13,603	57	16	58	46	68	18	110
	2015	14,584	57	16	58	46	69	18	104
	2016	14,426	58	16	59	47	69	18	105
(c) Patients without hypothyroidism	2008	4740	59	16	59	47	71	18	99
	2009	5372	58	17	59	47	70	18	100
	2010	5181	59	17	59	48	71	18	110
	2011	6355	59	16	59	48	71	18	111
	2012	6871	60	16	60	49	71	18	104
	2013	7233	61	17	62	50	73	18	104
	2014	7220	62	17	62	51	73	18	114
	2015	6891	62	17	63	51	73	18	115
	2016	5662	62	17	63	52	74	19	104

pctl, percentile

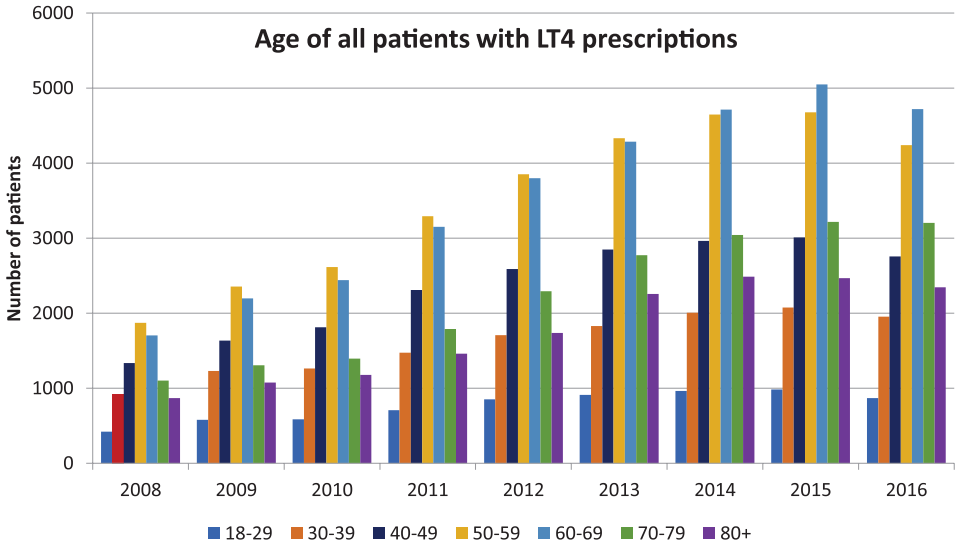

Figure 4. Age of all patients with levothyroxine (LT4) prescriptions divided by decile and displayed on an annual basis.

Table 6. Number of all patients with a levothyroxine prescription, divided according to age deciles, with patients divided according to whether they carried a diagnosis of hypothyroidism or not.

Patient group	Age decile	Number of patients with prescriptions per year								
		Year (mean age of population)								
		2008 (49)	2009 (49)	2010 (49)	2011 (49)	2012 (50)	2013 (50)	2014 (50)	2015 (50)	2016 (51)
(a) All patients	18–29	420	579	584	707	852	910	962	979	867
	30–39	927	1229	1264	1472	1706	1826	2002	2072	1952
	40–49	1337	1636	1812	2305	2583	2843	2960	3000	2750
	50–59	1871	2354	2614	3287	3848	4328	4639	4667	4228
	60–69	1704	2195	2439	3151	3795	4281	4707	5042	4710
	70–79	1100	1306	1394	1788	2286	2767	3036	3209	3194
	80+	867	1076	1176	1458	1734	2254	2481	2462	2337
(b) Patients with hypothyroidism	18–29	225	325	371	436	560	630	691	734	692
	30–39	440	663	779	921	1140	1276	1459	1578	1544
	40–49	617	878	1091	1397	1657	1926	2107	2198	2114
	50–59	817	1147	1424	1840	2329	2811	3152	3284	3149
	60–69	690	1035	1264	1673	2129	2600	3028	3392	3367
	70–79	395	535	651	897	1273	1611	1835	2006	2128
	80+	305	424	526	662	866	1146	1330	1391	1431

Table 6. (Continued)

Patient group	Age decile	Number of patients with prescriptions per year								
		Year (mean age of population)								
		2008 (49)	2009 (49)	2010 (49)	2011 (49)	2012 (50)	2013 (50)	2014 (50)	2015 (50)	2016 (51)
(c) Patients without hypothyroidism	18–29	195	254	213	271	292	280	271	245	175
	30–39	487	566	485	551	566	550	543	494	408
	40–49	720	758	721	908	926	917	853	802	636
	50–59	1054	1207	1190	1447	1519	1517	1487	1383	1079
	60–69	1014	1160	1175	1478	1666	1681	1679	1650	1343
	70–79	705	771	743	891	1013	1156	1201	1203	1066
	80+	562	652	650	796	868	1108	1151	1071	906

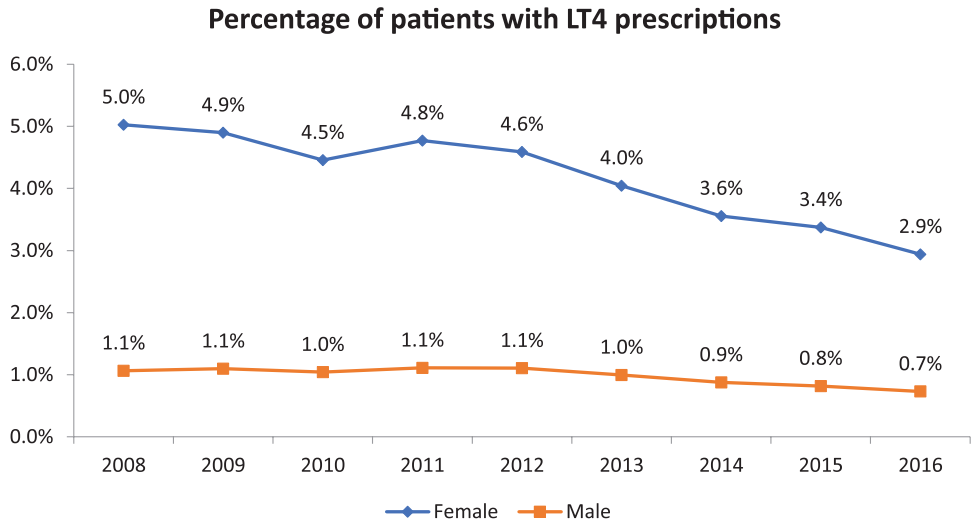

Figure 5. Annual percentage of patients with levothyroxine (LT4) prescriptions divided according to patient sex.

Our study has several limitations. Our data are limited by any inherent inaccuracy of documentation present within the MedStar database. If patients actually did have a diagnosis of hypothyroidism, but this diagnosis was not documented, we would have incorrectly classified them as not having a diagnosis of hypothyroidism. Also, patients moving from a geographic area or physician not covered by the MedStar system might appear to have a new diagnosis of hypothyroidism with a normal serum TSH. Despite the limitations of using a health care database such as this, it is likely that the data generated are relevant and generalizable. However, the strengths of our data include the likelihood that these data are accurate: although prescriptions written by providers outside of the MedStar system would not be captured, "hand-written" prescriptions would be extremely rare due to the lack of availability of prescription pads. Due to the diverse demographics of the MedStar hospitals, we believe there is a high likelihood that these data are representative of the United States in general, with the exception of rural areas.

Table 7. Mean and median TSH value for patients prior to new LT4 prescription initiation.

TSH values prior to new LT4 prescription initiation						
Year	**Values *n***	**Mean**	**SD**	**Median**	**25th pctl**	**75th pctl**
2008	1159	11.04	29.40	3.64	1.62	7.28
2009	1209	10.68	26.78	4.57	1.87	7.35
2010	1156	13.78	41.95	5.08	2.23	8.04
2011	2007	7.51	16.07	4.26	1.99	6.39
2012	2096	8.39	18.42	4.54	1.98	6.77
2013	2163	7.82	16.25	4.69	2.22	6.93
2014	2035	10.09	24.18	4.90	2.17	7.64
2015	1824	10.63	25.57	4.77	1.99	7.81
2016	1510	10.72	25.89	4.78	2.17	7.50

LT4, levothyroxine; pctl, percentile; TSH, thyroid stimulating hormone

In summary, we have shown that although the percentage of patients being prescribed LT4 is stable or slightly declining, with most decrement in those without a diagnosis of hypothyroidism, there is nevertheless continued initiation of LT4 in those with mild degrees of TSH elevation, and in those of older age, raising concerns both about unnecessary treatment and about iatrogenic thyrotoxicosis. Such data suggest the need for great consideration of both the degree of thyroid stimulating hormone elevation and the patient context when considering whether treatment of an elevated thyroid stimulating hormone, *versus* ongoing monitoring, is indicated.

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Author contribution(s)

Jacqueline Jonklaas: Conceptualization; Data curation; Funding acquisition; Methodology; Project administration; Resources; Supervision; Writing-original draft; Writing-review & editing.

Sameer DeSale: Data curation; Formal analysis; Methodology; Resources; Software; Validation; Writing-review & editing.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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