

Use of T₄, T₄ + T₃, and T₃ in the Dutch Population in the Period 2005–2011

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As chairman of the Dutch Association of Graves' Patients, I was recently invited to speak at a symposium on personalized medicine. The organizers had asked me to present figures on the use of thyroid hormone (especially the combination of T₄ and T₃) in the Netherlands. With the help of the Royal Netherlands Society of Pharmacy (Koninklijke Nederlandse Maatschappij ter bevordering der Farmacie), we approached the Foundation Pharmaceutical Indicators (Stichting Farmaceutische Kengetallen). They were able to provide us with key figures on the use of thyroid hormone in the Netherlands over the period 2005–2011 (courtesy of F. Griens). The Foundation collected prescription data from 843 public pharmacies, which had not changed the unique patient identification numbers in the period 2005–2011. The pharmacies linked to the Foundation constitute a representative sample of all pharmacies in the country. The figures obtained from the 843 pharmacies were extrapolated to all Dutch pharmacies, serving the total population of the Netherlands.

The number of persons using any thyroid hormone medication increased by 53% in the period 2005–2011; the proportion of the total Dutch population using thyroid hormone increased by 49%, whereas the Dutch population size in the same

period increased by 2.1% (table 1). Distinguishing between the various thyroid hormone preparations, the number of persons using only T₄ increased by 53%, those using the combination of T₄ + T₃ increased by 67%, and those using T₃ only increased by 36%. Among the persons using thyroid hormones, the proportion of only T₄ users gradually but consistently decreased from 99.05% in 2005 to 98.98% in 2011. An opposite trend was observed in the T₄ + T₃ users, which slowly but steadily increased from 0.82% in 2005 to 0.90% in 2011. The proportion of only T₃ users did not show a specific trend – it was 0.13% in 2005 and 0.12% in 2011. The assembled data also allowed to analyse whether prescriptions were made by general physicians (GPs) or specialists (table 2). With regard to prescriptions for T₄ there was a clear trend that in the period 2005–2011, T₄ prescriptions by GPs became more frequent (from 79% of all T₄ prescriptions in 2005 to 90% in 2011), whereas T₄ prescriptions by specialists decreased (from 21 to 10%). The annual proportion of persons starting on T₄ fluctuated between 19 and 21% of all thyroid hormone users. Initiation of T₄ treatment by GPs increased (from 62% in 2005 to 71.5% in 2011) at the expense of initiation by specialists (from 38% in 2005 down to 28.5% in 2011). With regard to T₃ prescriptions, a similar picture emerges.

The proportion of T₃ prescriptions by GPs rises from 52% in 2005 to 68% in 2011, under a simultaneous fall in T₃ prescriptions by specialists from 48 to 32%. The annual proportion of persons starting T₃ fluctuated between 0.38 and 0.49% of all thyroid hormone users. Initiation of T₃ treatment was done by GPs in 37% in 2005, but had increased to 45.5% in 2011; the figures for specialists declined from 63 to 54.5%.

Two conclusions can be drawn. The number of persons using thyroid hormone medication increased substantially in the period 2005–2011. And the proportion of thyroid hormone medication prescribed by GPs steadily increased in this period, whereas the proportion prescribed by specialists decreased. How can these remarkable trends be explained? We offer a few causal mechanisms.

First, the growth of the Dutch population size between 2005 and 2011 will have contributed to the increased number of persons taking thyroid hormone. However, this provides only a partial explanation because the relative increase of thyroid hormone users exceeds by far the relative increase of population size.

Second, the composition of the Dutch population is changing with a strong increase of the ageing population. As the incidence of Hashimoto's hypothyroidism increases with advancing age, a greying

Table 1. Thyroid hormone medication in the Dutch population in the period 2005–2011

	2005	2006	2007	2008	2009	2010	2011	Δ, %
Thyroid hormone users, n	304,461	330,059	362,962	391,828	414,524	438,959	464,927	+53
Dutch population, n × 1,000	16,306	16,334	16,358	16,405	16,486	16,575	16,656	+2.1
% of population using thyroid hormone	1.87	2.02	2.22	2.39	2.51	2.65	2.79	+49
T ₄ only, n	301,566	326,833	359,239	387,807	410,218	434,503	460,210	+53
T ₄ + T ₃ , n	2,499	2,819	3,220	3,485	3,818	3,955	4,179	+67
T ₃ only, n	396	407	503	536	488	501	538	+36

Table 2. Prescriptions for T₄ and T₃ in the Dutch population in the period 2005–2011 in %

	2005	2006	2007	2008	2009	2010	2011
Prescriptions for T ₄							
Prescribed by GP	79	81	82	85	88	89	90
Prescribed by specialist	21	19	18	15	12	11	10
Starters on T ₄							
Initiated by GP	62	65	65	67	70	71	72
Initiated by specialist	38	35	35	33	30	29	28
Prescriptions for T ₃							
Prescribed by GP	52	58	58	63	64	66	68
Prescribed by specialist	48	42	42	37	36	34	32
Starters on T ₃							
Initiated by GP	37	41	42	44	45	45	45
Initiated by specialist	63	59	58	56	55	55	55

population will increase the use of thyroid hormones. Nevertheless, this cannot be the whole explanation because the effect of the ageing population is just three times greater than the effect of the general population growth.

Third, the Dutch College of General Practitioners (Nederlands Huisartsen Genootschap) published in 2006 guidelines for the diagnosis and treatment of thyroid function disorders [1, 2]. At the implementation of the guidelines, specific attention was drawn to the condition of subclinical hypothyroidism. It is plausible that the guidelines to a large extent have contributed to the increased use of thyroid hormone, also explaining the shift in prescription behaviour away from the specialists towards the GPs. In further support of this explanation is the introduction of specific software used by laboratories serving GPs. The GP can cross the box 'tiredness', which automatically results in a few labo-

ratory tests including TSH. Many GPs express their amazement when the assay indicates hypothyroidism.

However, we would like to suggest a fourth explanation, which we call the Google hypothesis. Many subjects have vague non-specific complaints, and are inclined to look on the internet what might be wrong. In doing so, it is not unusual to arrive at websites related to thyroid diseases. In the Netherlands, the websites of the thyroid patient associations (Thyroid Foundation Netherlands, Dutch Association of Graves' Patients, Hypo but not Happy) are consulted by more than 10,000 individual visitors per week. It might well be that these visitors subsequently consult their GP with the specific request to determine thyroid function. In this respect it is noteworthy to mention that the relative increase in users of the combination therapy of T₄ + T₃ (as recommended by the Hypo but not Happy group in particular cases) is greater than

the relative increase of only T₄ users. The combination therapy appears to be described increasingly by GPs. Indeed, the GP guidelines in a footnote mention the possibility to use this treatment modality.

We do not know if our explanations account for the whole increase of thyroid hormone use, nor do we know whether this definite trend in increasing use of thyroid hormones will go on or stop within a few years.

References

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- 2 Van Lieshout J, Wessels P, van Rijswijk E, Boer AM, Wiersma TJ, Goudswaard AN: Summary of the practice guideline 'Thyroid Disorders' (first revision) from the Dutch College of General Practitioners. Ned Tijdschr Geneesk 2007;151:2829–2832.