

## Secular Trends in Thyroid Disease and Self-Perceived Mental Stress Among Swedish Women: A Comparative Cross-Sectional Study of the Two Cohorts 1980-1981 and 2004-2005 from the Population Study of Women in Gothenburg, Sweden

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### Abstract

**Objective:** The aim of this study was to investigate the prevalence of thyroid disease among 38- and 50-year-old Swedish women in 1980-1981 and in 2004-2005. A second aim was to study whether there is any connection between deviant levels of TSH and mental stress or between diagnosed thyroid disease with normalized levels of TSH and mental stress.

**Design:** Prospective study.

**Setting:** Göteborg, Sweden, population about 4,30,000.

**Subjects:** This study is based on material from the Population Study of Women in Gothenburg. The participants are two representative samples of 38- and 50-year-old women who took part in examinations 1980-1981 and 2004-2005.

**Main outcome measures:** Prevalence of thyroid disease as well associations between mental stress and thyroid disease, studied cross-sectionally.

**Results:** The prevalence of thyroid disease has increased in both 38- (with 39%) and 50-year-old (with 56%) women between 1980-1982 and 2004-2005. There was a significant increase in the prevalence, from 0.9% (CI 0.2-2.6) to 3.4% (CI 1.7-6.2) of 50-year-old women with suppressed TSH. No connection was found between high mental stress and deviant levels of TSH. In the 38-year-old women there was a significant connection between high mental stress and diagnosed thyroid disease.

**Conclusion:** The results indicate that the prevalence of suppressed TSH in Swedish women has increased since the early eighties, and that mental symptoms can exist also in successfully treated thyroid disease. However, all of the changes observed consist of relatively few individuals and no certain conclusions can therefore be drawn from the results.

**Keywords:** Women; Population study; Thyroid disease; Mental symptoms

### Introduction

Thyroid disease is a common and possibly underestimated illness in women [1,2]. Both hypo- and hyperthyroidism are five to ten times more common in women than in men. The prevalence of thyroid disease among Swedish women is together about 4 to 10 percent according to previous reports [3]. In Sweden 5 to 7 percent of all women have medication for hypothyroidism and the prevalence of thyrotoxicosis and hyperthyroidism has been reported to be about 1.5 to 3 percent [3].

It is however difficult to compare these different reports since different diagnostic criteria often are being used, for example sometimes solely biochemical findings and sometimes biochemical findings in combination with clinical examination. The results are also dependent on the population studied. Not many Swedish prevalence-studies have been published after 1991, but there is some regarding the incidence. In a study from Malmö, Sweden, the incidence of thyrotoxicosis had increased during the period 1970 to 1990 [4].

Table 1 shows some of the previous Swedish prevalence-studies of hypothyroidism (inclusive subclinical) and hyperthyroidism in female-populations.

### Causes and diagnosis of hypothyroidism and hyperthyroidism

In Sweden and other iodine sufficient countries the most common cause of thyroid disease is autoimmunity [5]. The two diseases Hashimoto's and Graves' which are causing hypo- and

hyperthyroidism respectively, are the two most common organ-specific autoimmune diseases [6]. Besides autoimmunity, hypothyroidism can arise after interventions in the thyroid gland, for example after an operation. Hyperthyroidism includes the forms Graves' disease, toxic multinodular goiter and solitary toxic adenoma.

Psychological stress has been shown to be one risk-factor, especially for the onset of Graves' disease [7,8], although there has also been contradicting results to that theory [9].

It is hard to diagnose early stages of hypothyroidism as well as hyperthyroidism by clinical examination since many of the symptoms associated with the disease are common also in the population in general.

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	Year	Population	Subclinical Hypothyroidism (%)	Hypo-thyroidism (%)	Hyperthyroidism (%)
Kågedahl et al.	1981	Gyn. survey	-	-	1,4
Nyström et al.	1981	Community	1.2	0	1.6*
Falkenberg et al.	1983	Community	0.9	0.6	5.3
Christensen et al.	1984	Community	-	1.3	-
Sundbeck et al.	1991	Community	-	4.0	0.3
Petersen et al.	1991	Community	-	2.5	2.6
E-Mansoury et al. 1984	2005	Health project	-	2.0	-

**Table 1:** Prevalence-studies of hypothyroidism and hyperthyroidism (previously undiagnosed cases and already diagnosed and treated cases are included in respective column) in Sweden.

A recommended laboratory analysis to discover hypothyroidism is TSH, which is the most sensitive test for the disorder and free T4 can give information on the severity of the disorder. The normal range set for TSH for women varies slightly between different caregivers but it has also changed over time. 1980, the normal range for TSH at Sahlgrenska's hospital in Gothenburg stretched up to 8 mU/L, whereas the upper limit for the reference range today is 4,2 mU/L [10]. A level over 10 mU/L together with symptoms verifies the diagnosis of hypothyroidism.

TSH is considered being suppressed in women when it is less than 0.3 mU/L. In 1980 the lower limit for TSH used by Sahlgrenska's hospital was 0.0 mU/L [10].

### Thyroid disease and mental symptoms

Both thyroid disease and subclinical thyroid disease are associated with many symptoms and medical risks [11,12] but at early stages the clinical diagnosis can be difficult and the patient is therefore often diagnosed when the disease is advanced [13]. An often highlighted symptom of thyroid disease is depression [14-16]. For women, but not for men, thyroid disorders are associated with 22% higher risk of depression [17].

Depression is more common in women with hypothyroidism and they have shown to have a seven-fold risk of critical mood deterioration [14,18]. Patients with hypothyroidism have also shown to have dissatisfaction with their health status in relation to controls [19].

Patients with subclinical hypothyroidism have shown to have more psychiatric disorders compared to controls. Depression symptoms and anxiety symptoms are more frequent in patients with subclinical hypothyroidism than it is in euthyroids [20]. In one study over 60% of the patients with subclinical hypothyroidism suffered from depression [16]. Like hypothyroidism, also subclinical hypothyroidism was shown to be associated with worse perception of health status compared to controls, although the latter connection was not statistically significant [19].

Patients with Graves' disease and other forms of thyrotoxicosis are often very affected by the disease. The symptoms are fatigue, palpitations, nervousness, weight-loss, depression, anxiety, sweating and eye-symptoms among others. Mental symptoms are common, also in patients treated for hyperthyroidism. In follow-up studies, patients successfully treated for hyperthyroidism have been shown to have long-term neuropsychiatric symptoms and impaired quality of life [21].

### Risk factors for autoimmune thyroid disease

Smoking, environmental pollution and nutritive substances are reported risk factors [8,22,23] and one of the nutritive factors often highlighted is excessive iodine intake [24,25].

Psychological stress is a component that has been reported as a risk factor for several autoimmune diseases. The potential role of stress in disease development has been particularly noticed for Graves' disease. Evidence from several studies support an association between Graves' and stress [8,26], but there are also contradicting results [9]. There is little information on whether Hashimotos' thyroiditis has a connection with stress or not [26]. Stressful life events do not seem to correlate with non-autoimmune thyrotoxicosis [7].

Both hypo- and hyperthyroidism are treatable though, and screening for thyroid disease has been discussed [13]. More research on potential changes of the prevalence of thyroid disease in women of different ages in Sweden during the last decades is important in order for physicians to be able to effectively find and diagnose affected individuals, and also for the continued discussion whether to introduce screening for the disease.

The aim of this study was to investigate the prevalence of thyroid disease among 38- and 50-year-old Swedish women in 1980-1981 and in 2004-2005. A second aim was to study whether there is any connection between deviant levels of TSH and mental stress or between diagnosed thyroid disease with normalized levels of TSH and mental stress.

### Material and Methods

#### The population study of women in Gothenburg (PSWG)

The participants of this study are two representative samples of 38- and 50-year-old women. These samples are part of a larger longitudinal study of women; the Population study of women in Gothenburg (PSWG) that was initiated in 1968-1969. A representative sample of 1462 women aged 38 to 60, was then invited to a free health examination. The inclusion criteria were based on date of birth (Women born on the 6<sup>th</sup>, 12<sup>th</sup>, 18<sup>th</sup>, 24<sup>th</sup> and 30<sup>th</sup> day of each Month) and information was obtained from the Revenue Office Register. The examinations continued for about 12 months and the participation rate was high, 90.1%. After the initial examination, 5 follow-up examinations have been carried out, where the same examination methods have been used [27].

In 1980-1981 the second follow up was done, when the sample of women born in was supplemented with women born in the same year and had moved to Gothenburg after 1968-1969 and fulfilled the original inclusion criteria [27]. In this examination, 477 women aged 38 and 50 participated; 122 women aged 38 and 355 women aged 50 [28]. The participation rate was 85 and 82% for the 38- and 50-year old women respectively [27].

In 2004-2005 another follow up took place, when most of the women were examined for the first time, but some of them had participated in 1992-1993 [28]. This time 500 women aged 38 and 50 participated; 207 women aged 38 and 293 women aged 50. The participation rate was 60% and 58% for the 38- and 50-year old women respectively. The women who were invited for the first time were all living in Gothenburg, but 50-year old women who had previously participated in the PSWG were invited regardless of where they lived now [28].

Table 2 shows examinations- and participation rates of the cohorts

of 38- and 50 year old women in the study and Figure 1 shows a flow-chart of the invited 38- and 50-year old women in 2004-2005.

### Examination methods in the PSWG

Invitations were sent to the chosen sample, offering a free health examination. The women who accepted were sent a questionnaire with questions regarding medical and social information. When the women came to the examination they had fasted during the night. They underwent several physical examinations and blood-samples were drawn from them. Determination of serum TSH was made from blood specimens that were sampled in the morning prior to intake of L-thyroxine [13]. They also answered additional questionnaires. Information of thyroid disease and medication was obtained through interview and a trough a standardized questionnaire as a part of the total survey of the women. Available medical records regarding previous thyroid disease were also examined [13].

### Definition of thyroid disease

Thyroid disease was considered present in women with either diagnosed thyroid disease or with previously unrecognized thyroid disease. This distinction of the term thyroid disease was made in order to be able to decide whether a potential increase in prevalence could be due to that more women were discovered and diagnosed in 2004-2005 compared to 1980-1981.

Year of birth	1980-1981 examination			2004-2005 examination		
	Age	n	%	Age	n	%
1966				38	207	(60)
1954				50	293	(58)
1942	38	122	(85)			
1930	50	355	(82)			

**Table 2:** Examinations- and participation rates of the cohorts of 38- and 50 year old women in this study (from the Population study of Women in Gothenburg).

Thyroid disease was considered as diagnosed in women who had been medically and/or surgically treated for thyroid dysfunction or in women who had been told by a doctor or a nurse that they had diagnosed thyroid disease. According to these criteria diagnosed thyroid disease was considered present in women with a positive answer to at least one of the questions listed here:

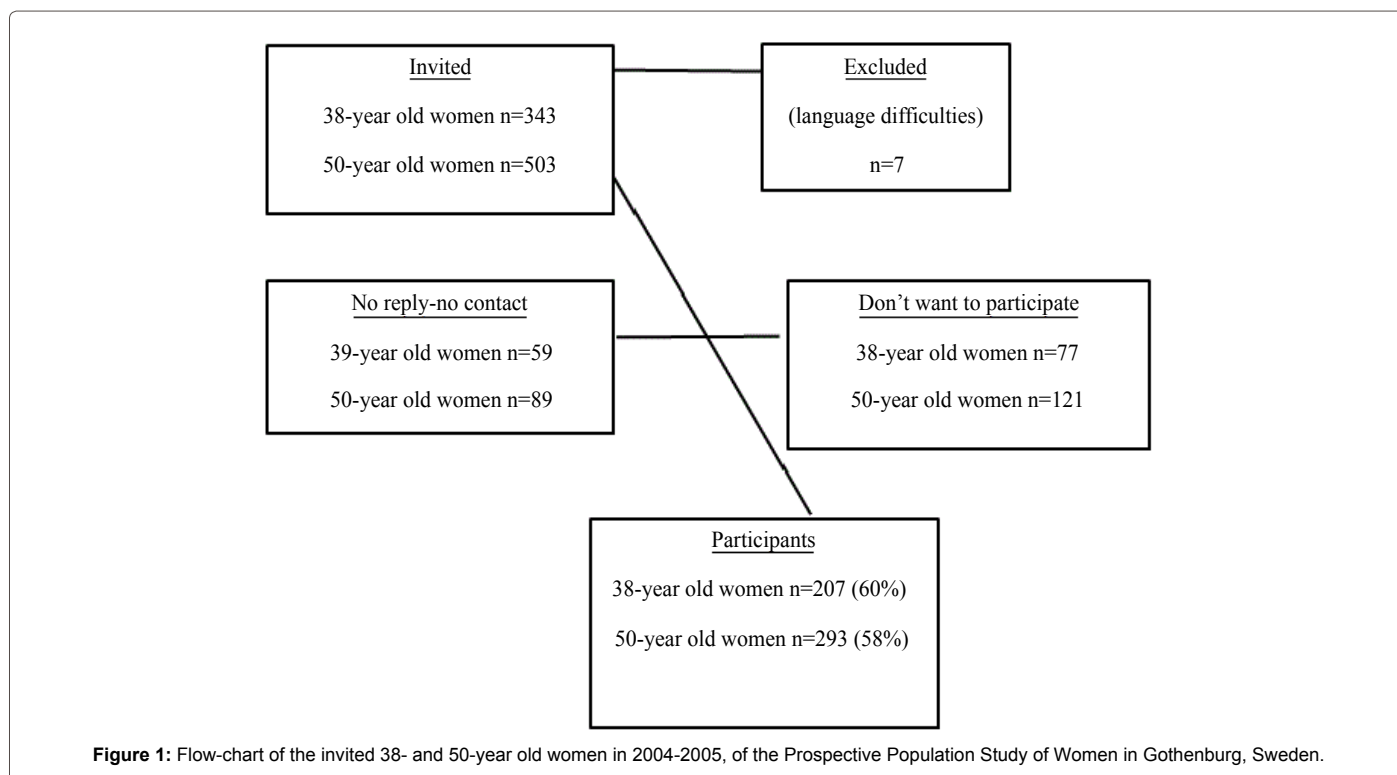
In 1980-1981

1. Do you take thyroid medication?
2. Have you been treated for low metabolism?
3. Have you been treated for high metabolism (or toxic goiter)?
4. Do you take any medication for your metabolism (for example Levaxin or Thyranon)?

In 2004-2005

5. Have you been told by a doctor or a nurse that you have or have had thyroid disease (high-, low metabolism, goiter)?
6. Have you had surgery for thyroid disease?
7. Have you been treated with radioiodine for thyroid disease?
8. Do you medicate with hormone for the metabolism?

These questions were part of the questionnaires used in the examination of the women 1980-1981 and 2004-2005. For each of the two examination-years, the share of women with a positive answer to any of the questions included in the definition that year was defined in percent of the total number of women in the cohort. These calculations were made for both examination-years and for 38- and 50-year-olds respectively and together. The shares of women with diagnosed thyroid disease were then compared between the 1980-1981 and 2004-2005.



## Definition of deviant TSH levels and previously unrecognized thyroid disease

Limits for deviant levels of TSH were defined, both in order to be able to study the share of women with previously unrecognized thyroid disease and to be able to study a potential connection between mental stress and deviant TSH. The same limits to interpret the TSH values were used for both 1980-81 and 2004-05. A TSH level <0.3 mU/L was considered being suppressed and a TSH level >10 mU/L was considered elevated, which is consistent with the recommendations that are used by clinicians today. Today the normal reference range used by the clinical chemistry laboratory at Sahlgrenska's hospital is 0.3-4.2 mU/L for women aged more than 20 years. However, using an upper limit of 10 mU/L exclude potential women with elevated levels of TSH due to non-thyroidal illness. The shares of women with deviant values of TSH according to these limits were calculated for 38- and 50-year-olds separately as well as together and compared between the examination-years.

The share of women with previously unrecognized thyroid disease was compared between the examination-years. Women were considered to have previously unrecognized thyroid disease when they had deviant values of TSH, but no previously diagnosed thyroid disease according to the definition above.

## Definition of mental stress

In both 1980-1981 and 2004-2005 the women were asked about their level of mental stress. After having got the question: "Have you experienced any period of stress (a month or longer), and by stress we mean that you have been irritable, tensed, nervous, anxious, afraid, fearful, sleepless, in conjunction with concern of work, health, family, a conflict or another reason" they were asked estimate their level of mental stress according to a six-degree scale, summarized here:

1. Level 0: Never experienced any period of stress
2. Level 1: Experienced period of stress, but not during the last five years
3. Level 2: Experienced period of stress during the last five years
4. Level 3: Experienced several periods of stress during the last five years
5. Level 4: Living with constant stress the last year
6. Level 5: Living with constant stress the last five years

In this study the women who chose level four (living with constant stress the last year) to describe their mental stress were studied, since this level was considered to best correspond to a high and current

feeling of mental stress. Level five was, although it is also a very high level of stress, deselected, since it was considered to stretch over a too long period of time. The women who defined their mental stress as level four were put together in four groups, in order to be able to study potential connections between mental stress and deviant TSH-levels or presence of diagnosed thyroid disease.

For both examination-years group 1 was compared to group 2 and group 3 was compared to group 4. The 38- and 50-year-old women were compared separately as well as together. The presence of "level 4 in mental stress" among all women in the PSWG was also studied, in order to be able to discover general changes over time.

## TSH and mental stress

Group 1: Share of women with deviant TSH-values and level 4 in mental stress.

Group 2: (control) Share of women with normal TSH-values and level 4 in mental stress.

## Diagnosed thyroid disease and mental stress

Group 3 Share of women with diagnosed thyroid disease and normal TSH-values and level 4 in mental stress.

Group 4 (control) Share of women with no thyroid disease and level 4 in mental stress.

## Statistical Methods

The background data were analyzed using descriptive statistics methods. For statistical analyses SAS version 9.2 was used, SAS Institute Inc. Fisher's exact test was used to test the hypotheses of difference in prevalence. When 38- and 50-year-old women were compared together, the analyses were adjusted for age. P-values<0.05 were considered to be significant.

## Results

### Prevalence of thyroid disease in women

The prevalence of diagnosed and/or treated thyroid disease is higher in 2004 than in 1980. The prevalence has increased in both 38- and 50-year-old women between 1980-1981 and 2004-2005. The change is clearer in the 50-year-olds. In this group diagnosed thyroid disease has increased by 56%. In the 38-year-olds the increase is 39%. However, none of the changes is statistically significant. Table 3 shows prevalence of women with diagnosed thyroid disease and unrecognized thyroid disease in 1980-1981 and 2004-2005 as well as changes in the prevalence of diagnosed and unrecognized thyroid disease in women, between 1980-1981 and 2004-2005.

	Participants n	Diagnosed thyroid disease (n) %	CI	p for the difference 1980- 1981 -2004-2005	Unrecognized thyroid disease (n) %	CI	p for the difference 1980-1981-2004-2005
Age 38							
1980-1981	122	(6) 4.9	1.8-10.4		(2) 1.6	0.2-5.8	
2004-2005	207	(14) 6.8	3.7-11.1	ns	(4) 1.9	0.5-4.9	ns
Age 50							
1980-1981	355	(25) 7.0	4.6-10.2		(4) 1.1	0.3-2.9	
2004-2005	293	(32) 10.9	7.6-15.1	ns	(3) 1.0	0.2-3.0	ns
Total							
1980-1981	477	(31) 6.5	4.5-9.1		(6) 1.3	0.5-2.7	
2004-2005	500	(46) 9.2	6.8-12.1	ns	(7) 1.4	0.6-2.9	ns

**Table 3:** Prevalence of women with diagnosed thyroid disease and unrecognized thyroid disease in 1980-1981 and 2004-2005. Changes in the prevalence of diagnosed, as well as unrecognized thyroid disease between 1980-1981 and 2004-2005.

## Deviant levels of TSH

Table 4 shows prevalence of women with elevated (>10 mU/L) or suppressed TSH (<0.3 mU/L) respectively, and changes in the prevalence of women with elevated or suppressed TSH between 1980-1981 and 2004-2005. There has been a statistically significant increase in the prevalence of 50-year-old women with suppressed TSH between 1980-1981 and 2004-2005, increase from 0.9% (CI 0.2-2.6) to 3.4% (CI 1.7-6.2). The difference among the 38-year-olds in the prevalence was considered as unchanged between 1980-1981 and 2004-2005.

## Mental stress and thyroid disease

Table 5 shows the difference in prevalence of constant mental stress the last year between 38- and 50-year old women with normal TSH-values and women with deviant TSH-values, as well as women with diagnosed thyroid disease (and normal TSH-values) and women with no thyroid disease.

The prevalence of 38- and 50-year-old women stating that they experience constant mental stress the last year has increased. During the study period this level of stress has become about twice as common (from 4.1 to 8.0%) among the 38-year-old women and also among the 50-year-old women there has been an increase (from 4.5 to 5.9%). None of these changes are statistically significant though.

None of the women in the study group with deviant TSH stated that they experienced the studied level of mental stress, but on the other hand the number of women with deviant TSH is small and it is therefore not possible to evaluate if they experience less mental stress than women with normal TSH either.

Among the 38-year-old women with diagnosed thyroid disease and normal TSH the experience of constant mental stress the last year is more common (21% of these women experience constant mental stress) than among women with no thyroid disease (5.6) and the difference is statistically significant. However, the actual number of 38-year-old women with diagnosed thyroid disease and normal TSH who experience constant mental stress is small.

Among the 50-year-old women with diagnosed thyroid disease and normal TSH it is slightly more common to experience constant mental stress than among women with no thyroid disease. (6.7% compared to 5.0%) but this difference is not significant.

In summary, when looking at the 38- and 50-year-old women together, it is about twice as common to experience constant mental stress among women with diagnosed thyroid disease, even when women with diagnosed thyroid disease and deviant TSH are not included.

## Discussion

### Thyroid disease

**Statement of principal findings:** The prevalence of diagnosed and/or treated thyroid disease has increased in both 38- and 50-year-old women between 1980-1981 and 2004-2005. There has been a statistically significant increase from 0.9% to 3.4% in the prevalence of 50-year-old women with suppressed TSH between 1980-1981 and 2004-2005, possibly caused by thyroid disease, but it cannot be excluded that it can have been caused by a high prevalence of non-thyroidal-illness in this specific group. Also, a significant connection

	n	Elevated TSH (n) %	CI*	Suppressed TSH (n) %	CI	p for the difference 1980-1981- 2004-2005
Age 38						
1980-1981	117	(0) 0	0.0-2.5	(2) 1.7	0.2-6.0	
2004-2005	204	(1) 0.5	0.0-2.7	(3) 1.5	0.3-4.2	ns
Age 50						
1980-1981	338	(3) 0.9	0.2-2.6	(3) 0.9	0.2-2.6	
2004-2005	292	(1) 0.3	0.0-1.9	(10) 3.4	1.7-6.2	p < 0.05
Total						
1980-1981	455	(3) 0.7	0.1-1.9	(5) 1.1	0.4-2.5	
2004-2005	496	(2) 0.4	0.0-1.4	(13) 2.6	1.4-4.4	ns

\* p-value for the difference 1980-1981- 2004-2005 is not significant, to small group of women.

**Table 4:** Prevalence of women with elevated (>10mU/L) or suppressed TSH (<0.3 mU/L) respectively. Changes in the prevalence of women with elevated or suppressed TSH between 1980-1981 and 2004-2005.

	n	Constant mental stress the last year (n) %	CI	p for the difference
38 year	Normal TSH	307 (21) 6.8	4.3-10.3	
	Deviant TSH	6 (0) 0	0.0-39.3	ns
50 year	Normal TSH	608 (31) 5.1	3.5-7.2	
	Deviant TSH	17 (0) 0	0.0-16.2	ns
38+50 year olds	Normal TSH	915 (52) 5.7	4.3-7.4	
	Deviant TSH	23 (0) 0	0.0-12.2	ns
38 year	Thyroid disease with normal TSH	19 (4) 21.0	6.1-45.6	
	No thyroid disease	302 (17) 5.6	3.3-8.9	<0.05
50 year	Thyroid disease with normal TSH	45 (3) 6.7	1.4-18.3	
	No thyroid disease	586 (29) 5.0	3.3-7.0	ns
38+50 year olds	Thyroid disease with normal TSH	64 (7) 10.9	4.5-21.2	
	No thyroid disease	888 (46) 5.2	3.8-6.8	ns

**Table 5:** Difference in prevalence of constant mental stress the last year between 38- and 50-year old women with normal TSH-values and women with deviant TSH-values, as well as women with diagnosed thyroid disease (and normal TSH-values) and women with no thyroid disease.

was observed between diagnosed thyroid disease with normalized TSH-levels and high mental stress, indicating that mental symptoms can exist also in successfully treated thyroid disease. On this latter area, previous results have been conflicting [17].

**Strength and weaknesses of the study of thyroid disease:** The Population study of women in Gothenburg is a valuable source of information since it stretches over such a long period. For this study, with the primary aim of studying changes in prevalence over time, it is strength that all of the participating women have been examined in the same longitudinal study – the PSWG. This ensures that the examinations of all of these women have been performed in the same way even though the occasions of the examinations are 24 years apart. However, when discussing the increase seen in diagnosed thyroid disease, it is important to remember that the reference range of TSH has changed over the years. The normal reference range for women in 1980 stretched between 0.0 mU/L and 8.0 mU/L, while, as today the reference range at Sahlgrenska's hospital is 0.3 mU/L to 4.2 mU/L. This fact could have contributed to at least part of the observed increase, since women 2004-2005 with slightly raised levels of TSH might have got a diagnosis, while women in 1980-1981 with the same levels might not have. The questions of both 1980-1981 and 2004-2005 concern the same areas; treatment for high and low metabolism (including surgery) and medication for thyroid disease. Most women with a diagnosed thyroid disease could therefore be expected to be included in 1980-1981 as well as 2004-2005.

One could argue that not only TSH, but also T4 should have been taken in account in this study in order to better distinguish the women with thyroid disease. But on the other hand the levels of T4 also change in non-thyroidal-illness.

However, over the years the participation rates of the PSWG have declined, from 90% in the first examination to about 60% in the examination 2004-2005, and this is of course a weakness of the study. The small number of participants in the different cohorts is also a limitation. If the study-groups had been larger, maybe more of the results in this study would have turned out significant.

**Findings in relation to other studies, discussing particularly any differences in results:** The indication of an increase in the prevalence of thyroid disease seen in this study is consistent with the results in the studies from Benvenega et al. [29] and Berglund et al. [4], where increasing prevalence- and incidence-numbers of diagnosed hypo- and hyperthyroidism respectively were observed. Also, the fact that the prevalence of unrecognized thyroid disease has not increased under the study period, indicates that the observed increase in diagnosed thyroid disease is not only due to that a bigger share of women with thyroid dysfunction are discovered and diagnosed today, but that there has been an actual increase. The total prevalence (both ages) of diagnosed thyroid disease found in this study was 6.5% in 1980-1981 and 9.2% in 2004-2005. This is consistent with the prevalence in the study of women in Gothenburg by Petersen et al. [13], where a similar definition of thyroid disease was used. In that study the total prevalence of thyroid disease was found to be 10% in 1980-1981. In that number however, both diagnosed and previously unrecognized thyroid disease was included and the age-category studied was older. This might have contributed to a higher prevalence-number since the prevalence of thyroid disease increases with age [11]. When looking internationally, the prevalence-number of diagnosed thyroid disease found for 2004-2005 in this study is almost exactly the same as that found in a Canadian study, where the prevalence of self-reported medical diagnosis of thyroid condition was 9.3% in women [17]. However, the comparison-problems described above; that different diagnostic

criteria and different study-populations are being used, exist with most of the previous prevalence studies of thyroid disease carried out and it is therefore difficult to compare results between different studies. This points out the need of more studies of potential prevalence-changes of thyroid disease, since results from studies carried out in different years are often not comparable.

**Meaning of the study: possible mechanisms and implications for clinicians or policy makers:** There has been a statistically significant increase of the prevalence of suppressed TSH for 50-year-old women (from 0.9% to 3.4%). However, as previously mentioned, suppressed TSH can be caused not only by thyroid disease, but also by non-thyroidal-illness such as infections. It is therefore difficult to decide the cause of the increase in suppressed TSH observed here. Suppressed TSH in hospitalized patients is naturally often caused by non-thyroidal-illness and, as pointed out by Petersen et al., this seems to be the case with most of the patients with suppressed TSH in Primary care as well [13]. However, the women participating in the PSWG is not a study-group where infections and other illness is expected to be any higher than in the population in general, and it is therefore not likely that non-thyroidal-illness would be the cause of suppressed TSH as often as in Primary care or hospitals.

Thyroid disease is therefore likely to have caused at least some of the cases of suppressed TSH seen in the 50-year-old women. In the study from Berglund et al. [4], the incidence of Graves' disease had increased between 1970 and 1990. It is of course possible that the prevalence of Graves has increased in Gothenburg as well, and that these cases are responsible for at least some part of the increase seen in suppressed TSH. Since the onset of Graves' most often happens between the age of 40 and 70 this could also explain why the change is only seen in the 50- and not in the 38-year-old women. However, since the share of women with diagnosed thyroid disease in this study has not been subdivided into specific diagnoses, it is not possible to draw any certain conclusions about the causes of the suppressed TSH. Also, the increase of suppressed TSH among 50-year-old women is, although statistically significant, involving relatively few individuals. It would be interesting though to study the changes observed in TSH in future studies to see if there exists an actual trend of declining TSH in middle-aged Swedish women, and if so - what the cause is.

### **Mental stress and thyroid disease**

A significant connection was found between mental stress and thyroid disease among the 38-year-old women (21% of the women with thyroid disease experienced constant mental stress compared to 5.6% among controls). This connection was found even though women with thyroid disease and deviant levels of TSH were excluded from the comparison. This observation was somewhat unexpected, since a study from Petersen et al that was also based on the PSWG [13] has shown that women treated with L-thyroxin do not differ from other women in neither morbidity nor quality of life. And constant mental stress is a factor that must be considered as having an impact on the perceived quality of life. However, other community-based studies have shown conflicting results regarding this area before [17] and one study has shown long-term neuropsychiatric symptoms and impaired quality of life in hyperthyroid patients many years after they had been successfully treated for the disease [21]. In 50-year-old women with thyroid disease the feeling of constant mental stress is slightly more common than in women with no thyroid disease (6.7% vs. 5.0%), but this result is not significant. Nevertheless these results indicate that women with diagnosed thyroid disease might experience more mental stress than controls, even when they have been successfully treated for the thyroid disorder. Clearly there is a need for more research

on the many times conflicting connections between thyroid disease and mental symptoms and for practitioners working in primary care centers it are important to be aware of this group of patients. It is also important that sampling is made on broad indications also in the future, in order to find and diagnose the affected women. The observed significant connection between diagnosed thyroid disease and high mental stress in 38-year-old women indicates that mental symptoms can occur even in successfully treated thyroid disease.

**Material and methods:** However, one must remember that the 38-year-old women in this study were examined for the first time in the PSWG while many of the 50-year-old women had been examined earlier as well. Since follow-ups were offered to all of the women in the PSWG that were found to have a disease, it is possible that some of the 50-year-old women in this study got their diagnosis of thyroid disease through the PSWG at an earlier examination. If that is the case, the prevalence of diagnosed thyroid disease among the 50-year-old women in this study might be higher than in the population in general. However, the changes found in prevalence between the two examination-years are not likely to have been influenced by this fact, since both of the compared 50-year-old cohorts had been examined earlier and none of the 38-year-old cohorts.

Many things have changed during the period of 24 years that this study stretches over. For example smoking has become much less common between both 38- and 50-year-old women [28]. Smoking has been suggested as a risk-factor for Grave's disease. In addition smokers are also found to have lower concentrations of TSH. One could suspect that the increase in diagnosed thyroid disease or in suppressed TSH, in 2004-2005, would be even bigger if smoking had remained on the same level as in 1980-1981.

There is a need for more studies on the complex connections between thyroid disease and mental symptoms and on the potential prevalence-changes in thyroid disease in Sweden.

## Conclusions

In this study, an increase in diagnosed thyroid disease in Swedish women between 1980-1981 and 2004-2005 was observed – a result consistent with the trend of a rising prevalence worldwide. The observed prevalence of diagnosed thyroid disease was high in both 38 and 50-year-old women. It is therefore important that sampling is made on broad indications also in the future, in order to find and diagnose the affected women. The observed significant connection between diagnosed thyroid disease and high mental stress in 38-year-old women indicates that mental symptoms can occur even in successfully treated thyroid disease.

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There were no conflicts of interest.

## Ethical Approval and Participants Consent

The Ethics Committee of the University of Gothenburg approved the study. All subjects gave informed consent to participate, in accordance with the provisions of the Helsinki Declaration.

## References

1. Lichiardopol C, Mota M (2009) The thyroid and autoimmunity. *Romanian journal of internal medicine = Revue roumaine de medecine interne.* 47:207-215.
2. Tome M, Chami R, Petrosians P, Corvilain B, Beckers A (2012) Thyroid

dysfunction: interactions between genetic and environmental conditions. *Revue medicale de Liege.* 67: 314-318.

3. Petersen K, Lindstedt G, Lundberg PA, Bengtsson C, Lapidus L, et al. (1991) Thyroid disease in middle-aged and elderly Swedish women: thyroid-related hormones, thyroid dysfunction and goitre in relation to age and smoking. *J Intern Med* 229: 407-413.
4. Berglund J, Ericsson UB, Hallengren B (1996) Increased incidence of thyrotoxicosis in Malmö during the years 1988-1990 as compared to the years 1970-1974. *J Intern Med* 239: 57-62.
5. Vanderpump MP (2011) The epidemiology of thyroid disease. *Br Med Bull* 99: 39-51.
6. McLachlan SM, Nagayama Y, Pichurin PN, Mizutori Y, Chen CR, et al. (2007) The link between Graves' disease and Hashimoto's thyroiditis: a role for regulatory T cells. *Endocrinology* 148: 5724-5733.
7. Matos-Santos A, Nobre EL, Costa JG, Nogueira PJ, Macedo A, et al. (2001) Relationship between the number and impact of stressful life events and the onset of Graves' disease and toxic nodular goitre. *Clinical endocrinology* 55: 15-19.
8. Yoshiuchi K, Kumano H, Nomura S, Yoshimura H, Ito K, et al. (1998) Stressful life events and smoking were associated with Graves' disease in women, but not in men. *Psychosomatic medicine* 60: 182-185.
9. Effraimidis G, Tijssen JG, Brosschot JF, Wiersinga WM (2012) Involvement of stress in the pathogenesis of autoimmune thyroid disease: a prospective study. *Psychoneuroendocrinology* 37: 1191-1198.
10. Johansson AS (2012) *Klinisk Kemi, Sahlgrenska universitetssjukhuset.*
11. Gaitonde DY, Rowley KD, Sweeney LB (2012) Hypothyroidism: an update. *Am Fam Physician* 86: 244-251.
12. Collet TH, Gussekloo J, Bauer DC, den Elzen WP, Cappola AR, et al. (2012) Subclinical hyperthyroidism and the risk of coronary heart disease and mortality. *Arch Intern Med* 172: 799-809.
13. Petersen K (1991) SftdiSwdUoG. Screening for thyroid disease in Swedish women Gothenburg.
14. Guimarães JM, de Souza Lopes C, Baima J, Sichieri R (2009) Depression symptoms and hypothyroidism in a population-based study of middle-aged Brazilian women. *J Affect Disord* 117: 120-123.
15. Gunnarsson T, Sjöberg S, Eriksson M, Nordin C (2001) Depressive symptoms in hypothyroid disorder with some observations on biochemical correlates. *Neuropsychobiology* 43: 70-74.
16. Demartini B, Masu A, Scarone S, Pontiroli AE, Gambini O (2010) Prevalence of depression in patients affected by subclinical hypothyroidism. *Panminerva Med* 52: 277-282.
17. Fuller-Thomson E, Saini J, Brennenstuhl S (2012) The association between depression and thyroid disorders in a regionally representative Canadian sample. *Psychology, health & medicine* 17: 335-345.
18. Larisch R, Kley K, Nikolaus S, Sitte W, Franz M, et al. (2004) Depression and anxiety in different thyroid function states. *Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et métabolisme* 36: 650-653.
19. Vigario P, Teixeira P, Reuters V, Almeida C, Maia M, et al. (2009) Perceived health status of women with overt and subclinical hypothyroidism. Medical principles and practice: international journal of the Kuwait University, Health Science Centre 18: 317-322.
20. Almeida C, Brasil MA, Costa AJ, Reis FA, Reuters V, et al. (2007) Subclinical hypothyroidism: psychiatric disorders and symptoms. *Revista brasileira de psiquiatria* 29: 157-159.
21. Abraham-Nordling M, Lonn S, Wallin G, Yin L, Nyren O, et al. (2009) Hyperthyroidism and suicide: a retrospective cohort study in Sweden. *European journal of endocrinology / European Federation of Endocrine Societies* 160: 437-441.
22. Duntas LH (2011) Environmental factors and thyroid autoimmunity. *Ann Endocrinol (Paris)* 72: 108-113.
23. Holm IA, Manson JE, Michels KB, Alexander EK, Willett WC, et al. (2005) Smoking and other lifestyle factors and the risk of Graves' hyperthyroidism. *Arch Intern Med* 165: 1606-1611.
24. Teng X, Shan Z, Chen Y, Lai Y, Yu J, et al. (2011) More than adequate iodine

- intake may increase subclinical hypothyroidism and autoimmune thyroiditis: a cross-sectional study based on two Chinese communities with different iodine intake levels. *European journal of endocrinology / European Federation of Endocrine Societies* 164: 943-950.
25. Camargo RY, Tomimori EK, Neves SC, I GSR, Galrao AL, et al. (2008) Thyroid and the environment: exposure to excessive nutritional iodine increases the prevalence of thyroid disorders in Sao Paulo, Brazil. *European journal of endocrinology / European Federation of Endocrine Societies* 159: 293-299.
26. Tsatsoulis A (2006) The role of stress in the clinical expression of thyroid autoimmunity. *Ann N Y Acad Sci* 1088: 382-395.
27. Bengtsson C, Gredmark T, Hallberg L, Hallstrom T, Isaksson B, et al. (1989) The population study of women in Gothenburg 1980-81—the third phase of a longitudinal study. Comparison between participants and non-participants. *Scandinavian journal of social medicine* 17: 141-145.
28. Bjorkelund C, Andersson-Hange D, Andersson K, Bengtsson C, Blomstrand A, et al. (2008) Secular trends in cardiovascular risk factors with a 36-year perspective: observations from 38- and 50-year-olds in the Population Study of Women in Gothenburg. *Scandinavian journal of primary health care* 26: 140-146.
29. Benvenga S, Trimarchi F (2008) Changed presentation of Hashimoto's thyroiditis in North-Eastern Sicily and Calabria (Southern Italy) based on a 31-year experience. *Thyroid : official journal of the American Thyroid Association* 18: 429-441.