Large Differences in Incidences of Overt Hyper- and Hypothyroidism Associated with a Small Difference in Iodine Intake: A Prospective Comparative Register-Based Population Survey

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Around 3–4 billion people in the world are covered by iodine supplementation programs to prevent developmental brain damage and other iodine deficiency (ID) disorders. Mild ID is associated with more hyperthyroidism and less hypothyroidism in the population than a high iodine intake. Knowledge of the iodine intake levels where the shifts in incidences occur is important for planning of iodine supplementation programs.

A computer-based register linked to thyroid diagnostic laboratories was used to continuously identify all new cases of overt hyper- and hypothyroidism in two population cohorts with moderate and mild ID, respectively (Aalborg, n = 310,124; urinary iodine, 45 μg/liter; and Copenhagen, n = 225,707; urinary iodine, 61 μg/liter). The investigation was initiated before iodization of salt in Denmark and was part of the monitoring program.

In 1997–1998, the incidence rate of overt hyperthyroidism was high in the area with the lowest iodine intake (92.9/100,000 per year) compared with the area with only mild ID (65.4/100,000 per year). Standardized rate ratio was 1.49, and 95% confidence interval was 1.22–1.81. The opposite relationship was present for overt hypothyroidism (moderate ID, 26.5/100,000 per year; mild ID, 40.1/100,000 per year; standardized rate ratio, 0.73; 95% confidence interval, 0.55–0.97). The different incidence rates were confirmed during each of the two following years.

The results of this prospective investigation of the incidence of overt hyper- and hypothyroidism suggest that iodine supplementation of a population may increase the incidence of overt hypothyroidism, even if the population is moderately iodine-deficient. In such a population, the increase in risk of hypothyroidism should be weighed against the risk of ID disorders such as hyperthyroidism due to multinodular toxic goiter. The optimal level of iodine intake to prevent thyroid disease may be a relatively narrow range around the recommended daily iodine intake of 150 μg (J Clin Endocrinol Metab 87: 4462–4469, 2002).

Abbreviations: CI, 95% Confidence interval(s); FT₄, free T₄; GP, general practitioner; ID, iodine deficiency; SRR, standardized rate ratio; TT₄, total T₄.
In this prospective study, we compared the long-term effects of different grades of low iodine intake on the incidence of overt thyroid function abnormalities in two population cohorts with different iodine intake levels (moderate and mild ID) (19) due to differences in water iodine contents in the two localities (20). The results suggest that any increase in iodine intake of a population that is not severely iodine deficient may induce an increase in the incidence of hypothyroidism.

**Subjects and Methods**

**Population cohorts**

The present study is part of the Danish Investigation of Iodine Intake and Thyroid Diseases (DanThyr), which comprises a number of register studies and a cohort study. DanThyr is the official clinical monitoring of the Danish iodine supplementation program, and it is projected to run for 9 yr in its present form. The present register study measured prospectively the incidence rates of hyper- and hypothyroidism in two population cohorts with mild and moderate ID before iodine supplementation.

Two open population cohorts representing the geographical variation in iodine intake in Denmark (19) were selected for monitoring. One population cohort consisted of 310,124 subjects living in the city of Aalborg and the surrounding municipalities in Northern Jutland. This area had moderate ID with a median iodine concentration in urine of 45 μg/liter (estimated iodine excretion, 62 μg/24 h) in subjects taking no supplements. The other population cohort comprised 225,707 subjects living in the geographical area around Bispebjerg and Frederiksberg Hospital in Copenhagen. The area had mild ID with a median urinary iodine concentration of 61 μg/liter (estimated iodine excretion, 93 μg/24 h) when no supplements were taken. Median urinary iodine values were moderately higher if all subjects were included (Aalborg, 55 μg/liter; Copenhagen, 68 μg/liter). The iodine excretion values were obtained in a simultaneous cohort study of 4649 subjects from the two areas (21, 22).

The participants had been randomly selected in certain age and sex groups from the general population (females aged 18–65 yr; and males aged 60–65 yr). In all groups, the urinary iodine excretion was higher in Copenhagen than in Aalborg (21).

As Danish registries of the present population cohorts at January 1, 1998, are given in Tables 1 and 2. Information on the size and composition of population cohorts at January 1, 1998, 1999, and 2000 was obtained from the Danish Bureau of Statistics. The Danish population is relatively homogeneous, and the population iodine intake has remained stable over at least 30–40 yr, with the exception of a subgroup now taking vitamin mineral tablets containing iodine (23, 24).

**Identification of new cases of hyper- and hypothyroidism**

Details of the register and the methodological evaluations performed have been published recently (25). In brief, all blood tests from subjects living in the two study areas were analyzed in one of four clinical chemistry laboratories (one in Aalborg, three in Copenhagen). Results of TSH and thyroid hormone measurements were continuously imported from the laboratory databases into a register database, which automatically identified overt hyperthyroidism (low serum TSH combined with a high serum T3 and/or serum T4), and overt hypothyroidism (high serum TSH combined with a low serum T4). A list of not previously registered cases of biochemical hyper- and hypothyroidism was generated each day and evaluated by: 1) searching in laboratory databases and diagnosis registers of the hospitals in the area, 2) rechecking that the patient lived in one of the two geographical areas, and 3) contacting the patients’ general practitioner (GP) for verification. All new cases were subsequently invited to an interview and physical examination with blood sampling for a final evaluation.

Before the registration was initiated, various details of the methodology were evaluated (25). This included evaluation of the diagnostic performance of the participating laboratories. A reference panel of normal sera (n = 100) was analyzed in the four laboratories. No systematic differences in distribution of values with reference ranges were found. The database identification of new cases was tested by a 60-d run in
Total number and incidence rates of hyper- and hypothyroidism according to age and sex groups in an open population cohort from Copenhagen with mild ID

**TABLE 2.** Incidence rate (new cases from database/100,000 per year)

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Study population Total (F/M %)</th>
<th>Hyper</th>
<th>Hypo</th>
<th>Hyper</th>
<th>Hypo</th>
<th>Hyper</th>
<th>Hypo</th>
<th>Hyper</th>
<th>Hypo</th>
<th>Hyper</th>
<th>Hypo</th>
<th>Hyper</th>
<th>Hypo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–9</td>
<td>23,447 (48.7/51.3)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>7.7</td>
<td>0</td>
<td>0</td>
<td>3.9</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–19</td>
<td>14,397 (49.7/50.3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>95,756 (52.4/47.6)</td>
<td>12</td>
<td>8</td>
<td>1</td>
<td>3</td>
<td>3.9</td>
<td>0</td>
<td>35.4</td>
<td>17.4</td>
<td>20.4</td>
<td>9.3</td>
<td>8.3</td>
<td>5.9</td>
</tr>
<tr>
<td>30–39</td>
<td>39,721 (46.5/53.5)</td>
<td>25</td>
<td>6</td>
<td>7</td>
<td>2</td>
<td>13.0</td>
<td>4.3</td>
<td>74.9</td>
<td>15.0</td>
<td>41.8</td>
<td>9.3</td>
<td>20.7</td>
<td>11.4</td>
</tr>
<tr>
<td>40–49</td>
<td>95,020 (48.5/51.5)</td>
<td>29</td>
<td>8</td>
<td>12</td>
<td>5</td>
<td>20.4</td>
<td>4.3</td>
<td>74.9</td>
<td>15.0</td>
<td>41.8</td>
<td>9.3</td>
<td>20.7</td>
<td>11.4</td>
</tr>
<tr>
<td>50–59</td>
<td>23,605 (50.2/49.8)</td>
<td>19</td>
<td>12</td>
<td>3</td>
<td>1</td>
<td>15.7</td>
<td>0</td>
<td>109.0</td>
<td>85.7</td>
<td>62.6</td>
<td>43.0</td>
<td>31.9</td>
<td>22.5</td>
</tr>
<tr>
<td>60–69</td>
<td>16,674 (55.5/44.5)</td>
<td>28</td>
<td>24</td>
<td>4</td>
<td>5</td>
<td>49.8</td>
<td>24.9</td>
<td>199.4</td>
<td>169.5</td>
<td>132.9</td>
<td>105.2</td>
<td>79.7</td>
<td>60.4</td>
</tr>
<tr>
<td>70–79</td>
<td>18,433 (64.0/36.0)</td>
<td>46</td>
<td>25</td>
<td>11</td>
<td>8</td>
<td>152.9</td>
<td>83.4</td>
<td>187.9</td>
<td>86.1</td>
<td>175.2</td>
<td>85.1</td>
<td>117.1</td>
<td>80.6</td>
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<td>≥80</td>
<td>14,172 (74.1/25.9)</td>
<td>41</td>
<td>39</td>
<td>9</td>
<td>4</td>
<td>50.3</td>
<td>20.1</td>
<td>263.8</td>
<td>237.4</td>
<td>208.4</td>
<td>172.5</td>
<td>117.1</td>
<td>90.6</td>
</tr>
<tr>
<td>All ages</td>
<td>225,707 (52.7/47.3)</td>
<td>201</td>
<td>123</td>
<td>41</td>
<td>25</td>
<td>26.8</td>
<td>17.3</td>
<td>101.7</td>
<td>73.3</td>
<td>65.4</td>
<td>40.1</td>
<td>54.0</td>
<td>40.8</td>
</tr>
</tbody>
</table>

Results from the 13 months of observation in Copenhagen (May 1, 1997, to May 31, 1998). F, Female; M, male.

Evaluation of cases

In two of the laboratories in Copenhagen, serum free T4 (FT4) was analyzed in addition to serum total T4 (TT4). The other laboratories relied on supplementary measurements of serum thyroid binding globulin or a T4 test to evaluate abnormalities of protein binding of T4 and T3 in serum. Because this was a comparative study, cases registered on condition of an abnormal FT4 combined with a normal TT4 were excluded to avoid bias with cases with low TT4 combined with normal FT4 and TT4 but high FT4 (n = 7) or high TSH combined with normal TT4 but low FT4 (n = 16). Cases with abnormal FT4 and missing TT4 (n = 6) were included.

During the final evaluation, another 149 apparently new cases were excluded for the following reasons: normalization of thyroid hormones (serum T4 and T3) within 3 wk without treatment or clinical signs of acute or subacute thyroiditis (n = 105); abnormal protein binding of thyroid hormones (n = 3); amiodarone treatment with low TSH and high FT4 but normal TT4 (n = 16); cases primarily verified by GP to be new, despite earlier treatment for thyroid disease (n = 14); treatment with levo-T4 for a psychiatric disorder (n = 4); substitution with levo-T4 after thyroid surgery (n = 3); overtreatment of subclinical hyperthyroidism with carbimazole (n = 1); and laboratory errors (n = 3). Such detailed evaluation with new blood tests and clinical follow-up was performed in 94.4% of the patients in Aalborg and 88.5% in Copenhagen. Information on cases excluded during evaluation is given in Tables 1 and 2.

From the persons evaluated in this way, we calculated for each population cohort the additional fraction and number of patients with biochemical hyper- and hypothyroidism that hypothetically would have been excluded in each sex and age group, if follow-up had been performed in all patients. Adjustment of incidence values using these data did not alter the values substantially, and no difference in statistical results occurred.

Registration after introduction of iodized salt

The incidence rates of hyper- and hypothyroidism in the study period and during the two subsequent 1-yr periods after introduction of iodine supplementation were compared. The incidence rates were calculated from the number of new cases identified by the register database and verified by contact to GPs, but without follow-up evaluation of patients.

Laboratory activity

The register accumulated information on the number of thyroid laboratory tests in the two population cohorts performed as part of diagnosis and control of thyroid disorders. Overall, the activity was similar in the two areas and moderately increasing during the time period studied. The number of TSH analyses was slightly higher in Copenhagen, whereas more T4 and T3 analyses were performed in Aalborg (Table 3).

**TSH, T3 and T4 analyses used**

Aalborg Hospital Laboratory. TSH, immunoluminometric assay (Limtest, Brahms Diagnostica, Berlin, Germany); reference interval, 0.3–4.5 mU/liter. T3 and T4 competitive RIA (Amerlex-m T3 and T4 RIA Kit, Ortho-Clinical Diagnostics, Raritan, NJ); reference T3, 1.2–2.7 nmol/liter; T4, 60–160 nmol/liter.

Frederikssberg Hospital Laboratory. TSH, time-resolved fluoroimmunometric assay based on direct sandwich technique (AutoDelfia hTSH Ultra kit, Wallac, Inc., Gaithersburg, MD); reference, 0.15–4.5 mU/liter. T3 and T4 time-resolved fluoroimmunoassay based on competitive reaction (AutoDelfia T3 and T4 kit, Wallac, Inc.); reference T3, 0.9–2.7 nmol/liter; T4, 60–160 nmol/liter.
Bispebjerg Hospital Laboratory. TSH, microparticle enzyme immunoassay (Axsym ultrasensitive hTSH II, Abbott Laboratories, Abbott Park, IL); reference, 0.15–5.0 mU/liter. T3, microparticle enzyme immunoassay (Axsym T3, Abbott Laboratories); reference, 1.2–2.3 nmol/liter. T4, fluorescence polarization immunoassay (Axsym, Abbott Laboratories); reference, 60–140 nmol/liter. FT4, microparticle enzyme immunoassay (Axsym FT4, Abbott Laboratories); reference, 9.0–24.0 pmol/liter.

The Laboratory of General Practitioners in Copenhagen. TSH, two-sided chemiluminometric immunoassay (Ciba Corning ACS TSH, Ciba Corning Diagnostic, Medfield, MA); reference, 0.2–5.0 mU/liter. T3, T4, and FT4 competitive immunoassay (Ciba Corning ACS T3, ACS T4, and ACS FT4, all by Ciba Corning Diagnostic); reference T3, 1.1–4.4 pmol/liter; T4, 60–140 nmol/liter; and FT4, 10.0–22.0 pmol/liter.

All involved TSH assays had a functional sensitivity below 0.07 mU/liter.

**Statistical methods**

The 95% confidence intervals (CI) for standardized rate ratios (SRRs) were calculated after log transformation of the respective rates (26). When comparing the total incidence rates, the analyses were performed after age and sex standardization of the Aalborg cohort to the Copenhagen cohort. Female and male incidence rates were compared after age standardization to the Copenhagen females (Fig. 1). Standardization to a female-to-male ratio of 1:1 was performed when comparing incidence rates between different age groups (Fig. 2). The calculations were based on an assumption of Poisson distribution of cases. Level of significance was set to 5%.

The cumulative risk was calculated by a summation of the age-specific incidence rates multiplied by 10, because the risk for each year within the 10-yr age group was assumed to be constant. No correction for prevalent cases was attempted.

### TABLE 3. Thyroid laboratory tests per 100,000 inhabitants per year in the open cohorts from Aalborg (moderate ID) and Copenhagen (mild ID) before and the first 2 yr after iodized salt was introduced

<table>
<thead>
<tr>
<th></th>
<th>Aalborg</th>
<th>Copenhagen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>1st yr after</td>
</tr>
<tr>
<td></td>
<td>Before</td>
<td>1st yr after</td>
</tr>
<tr>
<td>Serum TSH</td>
<td>19,368</td>
<td>21,245</td>
</tr>
<tr>
<td>Serum T3</td>
<td>9,654</td>
<td>11,072</td>
</tr>
<tr>
<td>Serum T4</td>
<td>11,340</td>
<td>11,618</td>
</tr>
<tr>
<td>Serum FT4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Number of tests per 100,000 inhabitants per year performed by the laboratories in the two cohort areas.


\[ b \] Many Danish laboratories are not using measurements of FT4 and FT3 in serum for routine purposes due to the insufficient methodology of most commercial methods. In this study, FT4 was only measured in two of the laboratories in Copenhagen.

**Fig. 1.** The incidence rates of hyper- and hypothyroidism in males and females in two open population cohorts with different levels of iodine intake (Aalborg (\( \square \)) with moderate ID, and Copenhagen (\( \bigotimes \)) with mild ID). The incidence rates were calculated after follow-up evaluation of patients. Both hyper- and hypothyroidism (age standardized) were more common in females than in males in both cohorts [hyperthyroidism, Aalborg, SRR (females/males), 3.24; CI, 2.36–4.44; Copenhagen, SRR, 3.02; CI, 1.99–4.56; and hypothyroidism, Aalborg, SRR (females/males), 3.18; CI, 1.75–5.78; Copenhagen, SRR, 1.97; CI, 1.17–3.30]. The incidence rate of hyperthyroidism was higher in Aalborg than in Copenhagen [SRR (Aalborg/Copenhagen) total, 1.49; CI, 1.22–1.81; females, SRR, 1.65; CI, 1.34–2.04; males, SRR, 1.54; CI, 0.96–2.46]. The incidence rate of hypothyroidism was higher in Copenhagen than in Aalborg [SRR (Aalborg/Copenhagen) total, 0.73; CI, 0.55–0.97; females, SRR, 0.79; CI, 0.57–1.09; males, SRR, 0.49; CI, 0.24–1.0].
The study was approved by the regional Ethics Committees in Northern Jutland and Copenhagen.

**Results**

The primary investigation took place in 1997–98 and lasted 14 months in Aalborg and 13 months in Copenhagen, until iodized salt was introduced in June 1998. Subsequently, data from the first 2 yr after iodization of salt were included. Details on the number of new patients are given in Tables 1 and 2.

The crude incidence rate of overt hyperthyroidism (with no correction for age and sex distribution) was high in Aalborg (92.9/100,000 per year) compared with Copenhagen (65.4/100,000 per year). On the other hand, overt hypothyroidism was more common in Copenhagen (40.1/100,000 per year) than in Aalborg (26.5/100,000 per year). There were small differences in the age composition of the two population cohorts (Tables 1 and 2). Age and sex standardization of the Aalborg cohort to the Copenhagen cohort affected the incidence rates little, and differences between cohorts were statistically significant (hyperthyroidism, SRR (Aalborg/Copenhagen), 1.49; CI, 1.22–1.81; and hypothyroidism, SRR, 0.63; CI, 0.44–0.89). In the other age groups, only nonsignificant tendencies were observed (data not shown).

In both areas, hyper- and hypothyroidism were more common in females than in males (Fig. 1), and the incidence rates of both hyper- and hypothyroidism increased with age (Fig. 2). The pattern of difference between the population cohorts was the same in nearly all subgroups; hyperthyroidism was more frequent in the cohort with moderate ID, whereas hypothyroidism was more frequent in the cohort with mild ID. The cumulative risk of having diagnosed thyroid dysfunction up to the age of 90 yr is shown in Table 4. The highest risk (21.7%) was found in females from Aalborg.

The cumulative risk of having diagnosed thyroid dysfunction before age 90 yr in Aalborg with moderate ID and Copenhagen with mild ID was calculated up to 90 yr of age from the incidence rates given in Tables 1 and 2. F, Female; M, male.

### Table 4. Cumulative risk (%) of having diagnosed thyroid dysfunction before age 90 yr in Aalborg with moderate ID and Copenhagen with mild ID

<table>
<thead>
<tr>
<th></th>
<th>Aalborg (F/M)</th>
<th>Copenhagen (F/M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroidism</td>
<td>11.8 (16.8/5.5)</td>
<td>7.3 (9.9/3.4)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>3.4 (4.8/1.6)</td>
<td>5.1 (6.4/3.4)</td>
</tr>
<tr>
<td>Hyper- or hypothyroidism</td>
<td>15.2 (21.6/7.1)</td>
<td>12.4 (16.3/6.8)</td>
</tr>
</tbody>
</table>

Cumulative risk was calculated up to 90 yr of age from the incidence rates given in Tables 1 and 2. F, Female; M, male.
133.4/100,000 per year in Copenhagen (SRR, 1.35; CI, 1.25–1.47).

In the Aalborg population cohort, an increase in incidence rate of hyperthyroidism was seen in the second year after iodine supplementation (SSR before vs. second year after supplementation, 0.74; CI, 0.68–0.81). No significant alterations were seen in incidence rates of hyperthyroidism in Copenhagen or in hypothyroidism in either population cohort.

Discussion

This prospective comparative epidemiological study showed that the incidence rate of overt hyperthyroidism was much higher in a population cohort with moderate ID than in an otherwise comparable cohort with mild ID. The opposite relationship was present for overt hypothyroidism, where the highest incidence rate was found in the area with mild ID.

Before the recent implementation of widespread iodine supplementation, ID was the most common cause of preventable brain damage in the world (2, 3), and public iodine supplementation programs are thus important parts of global health care. In areas less severely affected, such as Denmark, a low iodine intake predominantly manifests with a high risk of goiter and autonomous thyroid nodules with hyperthyroidism (27). The primary purpose of iodine supplementation in such areas is to prevent goiter and nodular hyperthyroidism. The present study indicates that considerable prevention can be expected already at a relatively low level of iodine supplementation. This is supported by our previous findings in a comparative cohort study (n = 4649) from the same two areas with moderate and mild ID. The prevalence of goiter was considerably higher in the area with moderate ID (22). Moreover, in moderate ID we observed a gradual decrease in median serum TSH with age, as a sign of development of autonomous thyroid nodules. In mild ID, this was much less prominent (28).

The effect of iodine on the thyroid gland is complex, with a U-shaped relation between iodine intake and risk of thyroid disease, because both low and high iodine intake are associated with an increased risk (3, 10, 18). When iodine intake is high, the prevalence of hypothyroidism and diffuse thyroid enlargement is high compared with populations with iodine intake around the recommended level of 150 g/d (11). The mechanism behind this impairment of thyroid function is unknown, but both iodine enhancement of thyroid autoimmunity and reversible iodine inhibition of thyroid function in susceptible subjects are possibly involved (5, 14–17).

There is only limited knowledge of the threshold of iodine intake, above which the increase in hypothyroidism begins. In the present study, we found a high incidence rate of hypothyroidism in Copenhagen with mild ID compared with Aalborg with moderate ID. This suggests that the increase in hypothyroidism, induced by an increase in iodine intake, may start already at low levels of iodine intake. The increase in hypothyroidism may continue over a wide range of iodine intake levels because it was observed in a Chinese study that the most prominent consequence of a change in iodine intake from normal (~150 µg/d) to moderately high (~500 µg/d) was a severalfold increase in the prevalence of thyroid hypofunction (29, 30).

In our study, new cases of hyper- and hypothyroidism were registered as part of the monitoring of a national iodine supplementation program, before and for 2 yr after iodized salt became available. However, the market share was low,
and the average increase in iodine intake was calculated to be around 5 μg/d. The monitoring of two more time periods confirmed the differences between areas observed during the initial study period. In addition, a small but statistically significant increase in the incidence of hyperthyroidism occurred in the area with the lowest iodine intake. Considering the low market share of iodide containing salt, this increase in incidence was unexpected. Further observation will reveal the magnitude and duration of this variation.

The study was observational, based on populations with long-term stable iodine intake. It may take years from the time that an increase in iodine intake takes place until a new steady state in occurrence of hyperthyroidism is reached (31, 32). Initially, there may be a transient increase in the incidence of hyperthyroidism (33, 34), which should then fall to a lower level. Little is known about the dynamics of the epidemiology of hypothyroidism after a sudden change in iodine intake.

The number of patients diagnosed to have hyper- or hypothyroidism in an area may depend on the diagnostic activity. Individuals of the two population cohorts were not actively investigated for thyroid disease, as they were in the classical Whickham survey (35). In general, the health care system and guidelines for investigation of patients were similar in the two areas. The register accumulated information on the number of thyroid function tests performed in the two cohorts. There were small differences with slightly more TSH analyses performed in Copenhagen and more thyroid hormone tests in Aalborg. This difference could not explain the observed differences in incidence rates of thyroid diseases. Many tests are used for control of disease, and a major reason for the small discrepancy in number of tests between areas may be differences in the abnormalities controlled. New cases identified in the present study had to seek medical assistance, and thyroid tests had to be taken. This might theoretically bias results. However, when we actively examined smaller cohorts from the population in the same areas, the pattern observed was the same (28).

In conclusion, small differences in iodine intake of populations with mild and moderate ID are associated with considerable differences in incidence rates of thyroid hyper- and hypofunction. The results suggest that small increases in iodine intake of a population with mild and moderate ID will prevent a considerable proportion of nodular hyperthyroidism and goiter. On the other hand, the increase in incidence of thyroid hypofunction observed with an increase in iodine intake may start already below optimal iodine intake levels. The optimal level of iodine intake to prevent thyroid disease may be a relatively narrow range around the recommended daily intake at 150 μg.

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