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Cost Estimation of Thyroid Disorders in Germany

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To assess the economic effects of thyroid disorder-related morbidity in Germany, a systematic review of national and international literature from 1981–2001 was performed. Data from insurance companies, the government department of public health, and the federal office of statistics helped characterize the situation in Germany. Being the most important thyroid disease, endemic iodine-deficiency goiter causes economic costs of approximately 2.1 billion DM per year or 1 billion Euros ( ) or 1 billion U.S. dollars. In recent years iodine supplementation of food became better accepted by the German population. This should significantly reduce the prevalence of goiter from 30%–40% to less than 10%. Functional thyroid disorders are observed in 5%–10% of the German population. A more differentiated view of these conditions should lead to specific guidelines for an economic screening and therapy of subpopulations. Lacking valuable data, an actual economic assessment of autoimmune or malignant thyroid diseases cannot be performed. On the other hand, with respect to the costs of specific thyroid therapy, e.g., radioiodine treatment of thyrotoxicosis (mainly toxic nodular goiter), the economic consequences of a new regulation for radiation protection in Germany have been demonstrated recently. Using the actual maximum permissible level of residual activity on discharge from the hospital after radioiodine therapy, length of hospitalization was shortened to 5.1 days in university hospitals and to 5.8 days in nonuniversity institutions. Payment per patient for radioiodine therapy was 1856 and 1530 (median value) in university and nonuniversity hospitals, respectively. In conclusion, better prevention of iodine deficiency and its long-term consequences should effectively reduce direct as well as indirect costs and overall economic impact of endemic goiter as the most important thyroid disease in Germany. Sustainable elimination of iodine deficiency is technically possible, but it needs further commitment and support at all levels.

Introduction

IODINE DEFICIENCY IS THE WORLD'S most common endocrine disorder and the most common preventable cause of mental retardation (1). Most countries, particularly developing ones, have some areas with iodine deficiency. It is remarkable that large segments of Europe (including affluent countries such as Germany, France, Italy, and Belgium) continue to have significant iodine deficiency, even though some of these have been major contributors in the effort to eliminate iodine deficiency disorders in developing countries (2–5). Goiter is the most obvious consequence, but others, including mental retardation, hypothyroidism, reproductive failure, and socioeconomic deprivation are more important. Iodine deficiency damages the local economy in several ways. The pervasive mental retardation and torpor of hypothyroidism make people less productive. Domestic animals, a major component of the economy in most countries, also suffer from the consequences of iodine deficiency, producing less meat, eggs, and wool, and fewer live offspring. In Germany, alimentary iodine supply is insufficient and goiter is still endemic. Iodine deficiency, although moderate to mild, has nevertheless been estimated to cost Germany more than 1 billion U.S. dollars per year solely from its effects on the thyroid, including diagnosis and treatment of hypothyroidism and lost work time (6,7). The best preventive means of iodine deficiency is iodized salt, but iodized oil, iodized water, and iodine drops or tablets are occasionally recommended. In Germany, tablets of potassium iodide are offered as individual supplements. Increased public awareness of this problem is essential and ways to supply people with appropriate iodine should be considered because an iodine supplementation program needs an infrastructure to sustain it, and particular attention must be paid to awareness building and monitoring.

Guidelines for publishing economic evaluation require statements regarding economic importance of the analysis and the viewpoint from which it has been carried out, as well as the specification of alternative programs or interventions, the form of economic evaluation, the outcome measure, the

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method of costing, the time horizon, and adjustment for timing of costs and benefits, and the allowance for uncertainties. Decision analysis can be based on clinical trial data, on retrospective or administrative databases, or on modeling. Choice of outcome measures is the key issue in an economic evaluation (8–11). In cost-effectiveness analysis, benefits are usually measured in natural units. For example, cost utility of periodic screening for mild thyroid failure was analyzed by measurement of baseline serum thyrotropin (TSH) concentration (12). The cost-effectiveness of screening 35-year-old patients with a serum TSH assay every 5 years was $9,223 and $22,595 U.S. dollars per quality-adjusted life years for women and men, respectively. Costs of a TSH assay and symptoms associated with thyroid failure were the most influential factors in sensitivity analyses. Thus, cost-effectiveness favorably compares with other generally accepted preventive medical practices and was most useful in elderly women. In this paper, examples of economic evaluation studies are also presented for the use of radioiodine as first-line therapy for Graves' hyperthyroidism and of toxic nodular goiter.

Cost Estimation of Thyroid Disorder-Related Morbidity

Iodine deficiency in Germany

With the help of Thyromobil, the largest epidemiologic study in united Germany was conducted in the mid-1990s in 32 different locations (13). Goiter prevalence was measured in 5932 Germans. Thyroid enlargement was 40%; it was 21% in children younger than 10 years old while it was 50% and more in subjects older than 10 years of age. Median urinary iodine excretion was 72 μg/g creatinine; range, 58–97 μg/g creatinine. Of the investigated persons, 74% and 20% had an excretion less than 100 μg and 50 μg/g creatinine, respectively.

To obtain data regarding alimentary iodine supply and goiter prevalence in the native juvenile population of the city of Mainz (approximately 300,000 inhabitants), capital of the state of Rhenania-Palatinate, southwest Germany, 300 natives (1/1000 inhabitants) and volunteers (median age, 25 years; range, 19–50 years, 164 females) were investigated at our institution. Determination of 24-hour urinary iodine was performed by a modified ceric arsine acid wet ash method (14). Median iodine excretion was 67 μg/L, range, 2–300 μg/L, as well as 54 μg/L, 2–210, and 81 μg/L, 4–300, in the female and male groups, respectively. In 19 subjects (6%), iodine excretion was less than 20 μg/L (severe iodine deficiency), it was 20–49 μg/L in 96 volunteers (32%, moderate), 50–99 μg/L in 126 (42%, mild deficiency), and in 59 subjects (20%) greater than 100 μg/L. Goiter was present in 105 volunteers (35%): 65 females (>18 mL, 40%) and 40 males (>25 mL, 29%). Goiter prevalence was 84%, 41%, and 36% in severe, moderate, and mild iodine deficiency, respectively, $p = 0.001$, whereas 6 of 59 subjects (10%) with normal iodine intake had a goiter. Thyroid volume was 26 mL (median), range 6–77 mL, with 22 mL, 6–59 ml, and 29 mL, 8–77, for the female and male groups, respectively. Using thyroid ultrasound (linear transducer 7.5 MHz), 266 subjects had a normal echopattern and 24 (11%) had unifocal or multifocal echo alterations (cysts, calcifications, echosolid nodules). Subclinical hypothyroidism and hyperthyroidism were noted in 7 (2.33%) and 5 (1.66%) subjects, respectively. Two hundred twenty-two (74%) volunteers have been using iodized salt. Thyroid volume and iodine excretion did not differ between subjects ingesting iodized salt and those who were not ($p > 0.05$). Thus, mild to moderate iodine deficiency is still present in the native juvenile population of Mainz.

Cost estimation of iodine deficiency-related disorders

In Germany, every general practitioner can make preliminary diagnoses in patients with thyroid disorders by screening tests of blood samples. Laboratory tests are necessary to distinguish effects of longstanding iodine deficiency from other thyroid diseases producing goiter. Most physicians use a combination of at least two or three *in vitro* tests for each patient. As is true for other diagnostic strategies, costs of thyroid function tests are higher when inexperienced physicians, rather than specialists, investigate patients. In Germany, statistics of health insurance companies clearly show a steady increase in the number of thyroid tests being performed from year to year. Two factors contribute to this increase: a greater awareness of the problems of endemic goiter on the part of patients and physicians, and the availability of more specific diagnostic tests coupled with an increasing knowledge of thyroid disorders in the medical community. However, thyroid function tests are currently overused, and there is no question that a reduction in the frequency of their use would make them more cost effective. In addition to these blood tests, many *in vivo* studies are also done for visible or palpable thyroid enlargement, e.g., ultrasound, radionuclide scanning, and fine-needle aspiration. Once a patient with goiter has been diagnosed, the most frequent treatment is still levothyroxine (LT_4), followed by the combination LT_4 and iodine, and occasionally iodine. LT_4 has become one of the most frequently used medicines in Germany. Furthermore, surgical treatment is often necessary for large nodular goiters, especially those with compressive symptoms. Nearly 100,000 thyroidectomies are performed in Germany each year, requiring 650,000 days of hospitalization. When radioiodine is used to reduce goiter size, patients must be hospitalized in special nuclear medicine wards for approximately 1 week each. In addition to inpatient costs, subsequent outpatient follow-up for endemic goiters and convalescence after discharge from hospitals produces about 300,000 days lost from work. This figure does not include loss of productivity, which is a difficult number to obtain. To summarize, an average of 0.5% of the total costs spent for medical care in Germany is allocated for endemic goiter, about two-thirds for diagnoses and one-third for treatment.

According to the German health insurance companies, the German Federal Office of Statistics, and to data from the pharmaceutical industry (15–25), annual costs for outpatient care average 425 million Euros ( ). Ambulatory care of a patient with thyroid disorders usually encompasses case history, clinical investigation, thyroid ultrasound (seldom an additional scan of the gland), and measurement of thyroid related hormones, e.g., baseline serum TSH, free T_4 and free triiodothyronine (T_3), as well as thyroid peroxidase and TSH-receptor autoantibodies, respectively. The annual costs for medical therapy of thyroid disorders (mainly iodine deficiency goiter and hypothyroidism) average 100 million . As shown in Figure 1, the prescription of LT_4 comprises nearly two thirds of the costs (60 million). It is followed by the

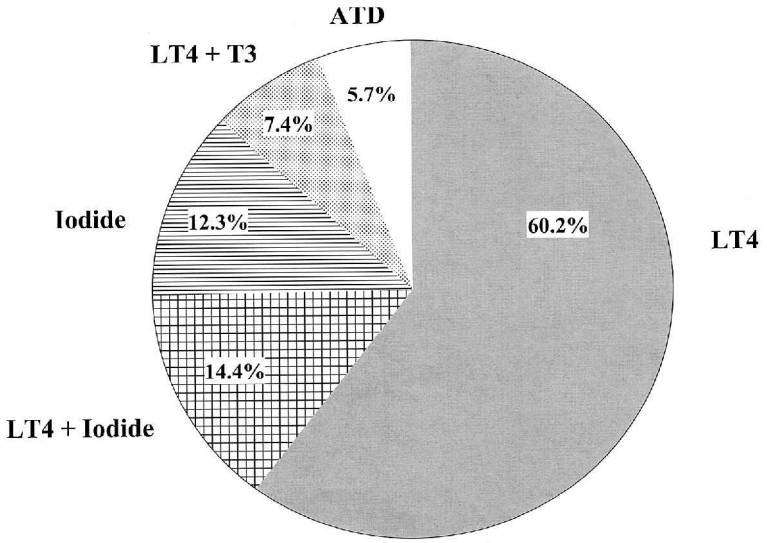

FIG. 1. Distribution of the annual costs for medical therapy of thyroid disorders (mainly endemic, iodine deficiency goiter and hypothyroidism) in united Germany: approximately 100 million Euros ( ). LT_4, levothyroxine; ATD, antithyroid drugs.

combination therapy of LT_4 and iodide (15 million) and iodide monotherapy (12 million) for the treatment of goiter. Furthermore, 7.5 million are spent annually for the T_4/T_3 combination, whereas costs for thyrotoxicosis therapy with antithyroid drugs are 5.5 million , only. With respect to the annual costs of inpatient (hospital) care of thyroid disorder-related morbidity, more than a decade after the unification of Germany, marked differences between the two parts of the country are still observed. As shown in Table 1 A, significantly more inpatient cases and hospital days per case are noted in the eastern part of Germany. Regarding work disablement or lost work time due to thyroid diseases, a similar picture is registered (Table 1B). Compared to West Germany, more cases of work disablement and more days of lost work are noted in East Germany. Taken together and as shown in Figure 2, annual costs for thyroid disorder-related morbidity in Germany (including costs of nearly 25 million for retirement from active professional life) average 2.1 billion DM or 1 billion .

Costs of thyroid surgery

According to the largest health insurance company (AOK), as much as 100,000 thyroid surgeries are being performed per year in Germany. On January 1, 1996, implementation of the new recompense system at the university hospital of Halle, State of Saxony-Anhalt, replaced the former German hospital financing system based on clinic-dependent individual prices. This was the beginning of a new price-performance system of the German hospital market. Since then, for all surgical procedures for benign and malignant thyroid diseases a detailed cost analysis has been performed. The personnel and material input were documented online in the operating theater on a special designed cost-analysis record (26). Cost analysis was based on 14 cases of lobectomy (average operative costs were 968), and 20 each of of unilateral subtotal thyroidectomy (1010), unilateral subtotal thyroidectomy with contralateral lobectomy (1110), and total thyroidectomy (1229) respectively. In 12 cases the costs of total thyroidectomy with cervical and transthoracal lymphadenectomy have also been analyzed (2392).

Cost Estimation of Hyperthyroidism Therapy

Comparison of radioiodine and medical therapy

European countries differ greatly in terms of their financing and organization of health care, and their approaches to pricing and reimbursement. Recently, a cost-effectiveness analysis comparing radioiodine and antithyroid drugs for treatment of Graves' disease was performed (27). As first-line therapy of Graves' hyperthyroidism, antithyroid drugs are favored in Europe, while iodine-131 therapy is favored in the United States. Sensitivity analyses took into account

TABLE 1.

A: Inpatient care in Germany

Annual costs: approximately 250 million

Per 10,000 members	*East*	*West Germany*
Inpatient cases	29	20
Hospital days	251	158
Hospital days/case	9	8

B: Work disablement due to thyroid disorders related morbidity

Annual costs: approximataely 240 million

Per 10,000 members	*East*	*West Germany*
Cases	37	25
Days	1394	720
Days/case	38	28

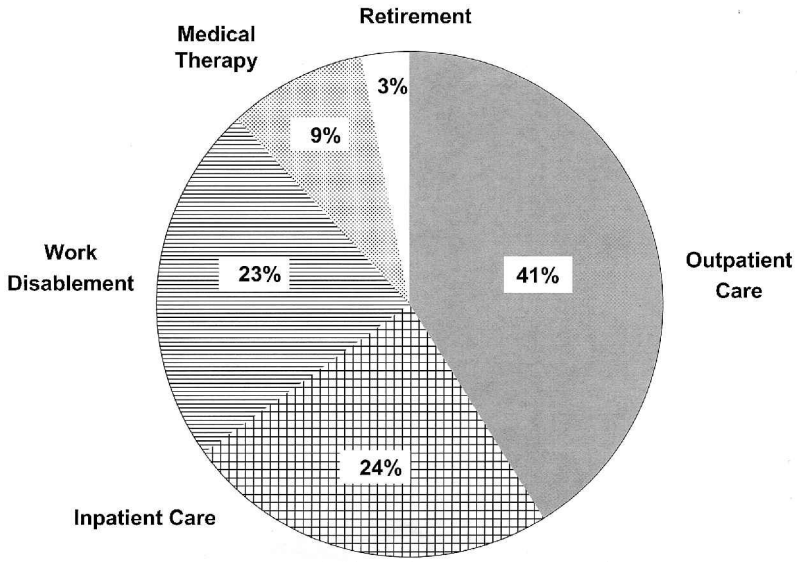

FIG. 2. Distribution of the annual costs for thyroid disorders related morbidity (mainly iodine deficiency and its consequences) in Germany: approximately 2 billion DM or 1 billion Euros ( ).

the long-term relapse rate of conservative or radioiodine therapy, use of diagnostic tests, level of health insurance, decreases in productivity, and a discount factor. Costing models included the costs of follow-up care over 30 years. Costs of hospitalization for radioiodine therapy were calculated for 300 patients, discharged with 250 MBq of iodine-131 residual activity. Antithyroid drugs were considered cost effective when they achieved relapse rate of 50% or less, a decrease in the number of tests needed and reduced working hours. Failure to meet any one of these conditions made primary radioiodine therapy more cost effective in 1593 of 1944 calculated costing models. Repeated conservative therapies clearly increased overall costs. Thus, according to these findings, radioiodine is a cost-effective first-line therapy in patients with a special risk of relapse (e.g. goiter, young age, increased scan uptake of technetium, and/or enhanced titer of TSH-receptor autoantibodies) after primary conservative therapy.

TABLE 2. COST ESTIMATION OF HYPERTHYROIDISM THERAPY IN GERMANY: ROLE OF VARIOUS PARAMETERS AND AVERAGE COSTS IN EUROS

	Thyroid surgery	*Radioiodine therapy*[a]
Graves' disease	2671	3023
Toxic nodular goiter	2415	2505
Age of patients (years)		
< 39	2568	2971
40–59	2318	2322
> 60	2870	2948
Thyroid volume (mL)		
< 39	2172	2222
40–89	2659	2852
> 90	3326	3479
Morbidity		
Without	2690	2971
Mild	2392	2322
Moderate	3161	2948
Average costs	3878 ± 1251	3308 ± 1249
Hospital days (inpatient care)	9.1 ± 2.8	12.5 ± 4.5
Costs/hospital day	436	272

[a]Based on discharge guidelines until 1997

Comparison of thyroid surgery and radioiodine treatment

Cost-analysis of thyroidectomy and radioiodine treatment in patients with thyrotoxicosis was also compared (28,29). Matched by age, gender, comorbidity, volume of goiter, and entity of hyperthyroidism, 18 and 28 patients undergoing thyroid surgery and radioiodine therapy, respectively, were analyzed by the reimbursed costs and by a retrospective calculation of the real costs. Based on the rate for the reimbursed costs, radioiodine treatment was more favorable than thyroidectomy (Table 2). Based on the calculation of the real costs including regional specialties, there was a minimal difference in favor of thyroid surgery because of the selection of large goiters (median, 53 mL), the longer hospitalization after radioiodine treatment because of legal reasons (12.5 days, discharge guidelines until 1997), and the frequent follow-up tests after iodine-131 treatment. Most important cost factors were volume of goiter and age of patient for radioiodine and surgical treatments, respectively. Both surgical as well as nuclear medicine therapy of Graves' disease were more expensive than that of toxic nodular goiter. Based on these data, in order to achieve cost minimization, radioiodine treatment is preferred in cases of small goiters or in older patients with thyrotoxicosis.

Cost accounting has also shown that the volume of thyroid tissue to be treated is the decisive factor in determining the cost of radioiodine therapy. In the case of large goiters, costs of excision and radioiodine therapy are, to a large extent, equivalent. In Germany, remuneration for a goiter resection is calculated from standard charges for total treatment without any consideration of the size and spectrum of medical services offered by different clinics, while remuneration for iodine-131 therapy comes from payments for basic and specific departmental medical services. University departments of nuclear medicine have relatively high basic costs. In the first quarter of 1998, duration of hospitalization after iodine-131 treatment (for all indications combined) was 4.6 days in university hospitals in Germany.

Consequences of new discharge guidelines for radioiodine therapy cost management

Consequences of the new recommendations by the Federal German Radiation Protection Committee for patient discharge guidelines (residual activity of 250 MBq for iodine-131) were calculated for duration of stay and radioiodine therapy cost management (30). For 601 consecutively admitted patients with hyperthyroidism to a German university department of nuclear medicine, both actual duration of stay at the hospital (inpatient care) and duration of stay according to previous guidelines, as well as duration of stay according to recommended values were calculated. Cost analysis considered the cause and volume of goiter, and by using sensitivity analyses included a range of diagnostics, service assessment, and duration of stay. In Germany, inpatient hospital care after iodine-131 therapy is expected to decrease by 35%–50% (average future duration of stay, 4.9 ± 2.8 days) and average costs will decline by 17.4% (from 2283 to 1887). Not including pretreatment diagnostics, cost reduction (service assessment, 17%–24%) is estimated at 21%–25%. Compared to thyroid surgery, iodine-131 therapy costs are expected to be lower for goiters up to at least 60 mL, toxic nodules of at least 25 mL, and toxic multinodular goiters of at least 90 mL. Thus, in the future, iodine-131 treatment will be more cost effective even with large goiters. Because reimbursement is determined by the duration of stay as an inpatient, new reimbursement procedures are now being discussed in Germany.

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