Short-term effectiveness of mandatory iodization of table salt, at an elevated iodine concentration, on the iodine and goiter status of schoolchildren with endemic goiter[1,2]

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ABSTRACT

Background: Goiter rates and iodine deficiency usually show marked improvement in efficacy studies of mandatory iodization of salt, but little is known about the short-term effectiveness of mandatory iodization.

Objective: The aim of the study was to evaluate, after 1 y, the effectiveness of mandatory iodization of salt at an iodine concentration higher than that occurring under optional iodization on the goiter rates and iodine status of schoolchildren living in an endemically goitrous area.

Design: Goiters, measured by palpation, and urinary iodine concentrations of children in grades 4–7 in 4 schools in a known goitrous area in South Africa were assessed before and 1 y after the introduction of mandatory iodization at a higher iodine concentration than occurred with optional iodization. Estimates of the iodine concentration of iodized salt and the proportion of households using iodized salt were also made.

Results: Iodine concentration in table salt and household use of iodized salt improved within 1 y. Goiter rates, which varied at baseline from 14.3% to 30.2% in the 4 schools, remained unchanged, with an overall mean (±SE) prevalence of $25.6 \pm 2.5\%$ at baseline and of $27.5 \pm 2.7\%$ 1 y later. The distribution of urinary iodine concentrations in the 4 schools improved substantially from the baseline deficient range. The overall median urinary iodine concentration increased from 0.17 to 1.47 μmol/L.

Conclusions: Mandatory iodization of salt virtually eradicated iodine deficiency within 1 y in South African schoolchildren, but the goiter rate in these children did not decline. Measurement of goiters by palpation may not be appropriate in short-term evaluations of mandatory iodization programs.   *Am J Clin Nutr* 2000;71:75–80.

INTRODUCTION

Iodization of salt is generally considered a first-line public health measure for preventing and controlling endemic goiter induced by iodine deficiency (1–3). Although considerable success in eliminating or reducing endemic goiter has been achieved through national salt-iodization programs, eg, in Switzerland (4), endemic goiter persists in some countries with iodization programs and even in some with mandatory iodization programs (5, 6). Mandatory iodization of salt is therefore not an automatic guarantee of the elimination or reduction of iodine deficiency and endemic goiter.

Mandatory iodization of household salt was introduced in South Africa through revised legislation in December 1995. The salt-related regulations of the Foodstuffs, Cosmetics and Disinfectants Act No. 54 of 1972 were revised to make iodization mandatory rather than optional and to increase the concentration of iodine in the form of potassium iodate from 10–20 to 40–60 μg/g. As a result of this new regulation, the availability of iodized salt in food shops was expected to increase from ≈30% (7) to >90% within 6 mo.

The introduction of mandatory iodization has the potential to produce a chain of effects from the production plant to the household, including changes in iodine and goiter status of consumers. The success of such a program can be measured by monitoring key elements in this chain of events and evaluating the effects on consumers (8). We previously showed that introducing mandatory iodization in South Africa at a higher iodine concentration than that occurring with optional iodization resulted in a significant increase in the mean iodine content of retail salt from 14 to 33 μg/g within 1 y (9). Limited information is available on the short-term effect on the iodine and goiter status of schoolchildren of introducing mandatory iodization. The aim of this study was to investigate the effects of mandatory iodization after 1 y in schoolchildren in an endemically goitrous area.

SUBJECTS AND METHODS

Subjects

The study was carried out in the primary schools of 4 communities [Haarlem (school 1), Louterwater (school 2), Krakeel (school 3), and Joubertina (school 4)] in the Langkloof area, a 150-km-long

fruit-producing valley ≈70 km inland from the southeastern coast of South Africa. These 4 communities were chosen because the Langkloof area had been a focal point of studies on endemic goiter in the past (10). In addition, the socioeconomic status of the 4 communities ranged from low to high and there were sufficient numbers of schoolchildren. Children in grades 4–7 (ie, with 4–7 years of schooling) attending primary schools in the 4 communities, situated over a distance of ≈100 km in the Langkloof area, were used as subjects in both the baseline and follow-up studies. In the 2 biggest schools, every second child on the alphabetic class list was selected; in the remaining 2 schools, all the children in these grades were recruited. According to the headmasters of the schools, school attendance rates exceeded 90%. Written consent was obtained from parents or guardians of the children before each phase of the study began. Permission to conduct the study was also obtained from the headmasters and from the ethics committee of the South African Medical Research Council.

Design

Baseline goiter rates, urinary iodine excretion, and related variables were observed in the schoolchildren of the 4 study communities in the month before the introduction of mandatory iodization of household salt in South Africa (10). Measurements were repeated 1 y later in a follow-up study that used the same sampling procedure (children in grades 4–7) to avoid age effects on goiter rates.

Measurements

Identical sampling and data-collection procedures were used in the 2 surveys, which were conducted in the same month of 2 consecutive years. During each of these studies the size of the thyroid gland of each child was visually inspected and palpated and was graded according to the criteria of the World Health Organization, the United Nations Children's Fund, and the International Council for Control of Iodine Deficiency Disorders (11) as not palpable (grade 0), palpable but not visible (grade 1), or palpable and visible (grade 2). Different observers were used in the 2 studies but were standardized against each other. A urine sample (≈20 mL) was obtained from each participating child during usual school hours, corresponding to approximately the second urine void of the day. The urine samples were refrigerated at 4°C until they were analyzed for iodine content by means of manual acid digestion and spectrophotometric detection of iodine by ceric ammonium reduction in the Sandell-Kolthoff reaction (12, 13). Drinking-water samples were collected during baseline and follow-up from the municipal water supply in the 4 communities and were similarly analyzed. The analysis of urinary iodine content was standardized against the Centers for Disease Control in Atlanta in an ongoing quality control program at the time of the study. The CV of this analysis was 4.7% in our laboratory.

At baseline, when iodization was still optional, a short questionnaire completed by the children's parents was used to estimate the proportion of households that used iodized salt. At follow-up, to investigate the proportion of households using iodized salt and the iodine content of iodized salt used, we asked parents to put ≈15 g (3 tsp) of their table salt into iodine-free polyethylene bags provided through the schools. The bags were then tightly sealed until the samples were analyzed. Information on indicators of the socioeconomic status of the head of the household was generated by questionnaire. Several iodized salt samples were purchased from grocers in the area at the time of the baseline and follow-up studies and were subsequently analyzed for iodine content. The retail and household salt samples were analyzed quantitatively for iodine by using an iodometric titration method (14), for which the CVs in our laboratory were 0.68 at 20 μg/g and 1.05 at 60 μg/g.

Data analysis

Follow-up data were not obtained for individual children, but the same sampling procedure was used in the same study population at both sampling times. The overlap between the 2 samples was therefore unknown and could have exceeded 50%. It can be shown that considering the 2 samples as completely independent in the statistical inference represented a conservative approach. This was the result of not using the intrasubject correlation that was present in the portion of the samples that overlapped. The chi-square test was used to compare the prevalence of goiters, and the median 2-sample test was used to compare the age and urine iodine distributions of the baseline and follow-up observations. Year-specific prevalence was estimated, with adjustment for the sampling design and realization.

RESULTS

In 1995, a total of 565 children (71–189 per school) participated in the baseline phase of the study (**Table 1**). In 1996, a total of 536 children (50–184 per school) were recruited into the study. These numbers represented response rates ranging from 74.7% to 97.9% for the different schools in 1995 and from 51.5% to 94.4% in 1996, giving overall response rates of 84.3% and 81.7%, respectively. The low response rate at follow-up in school 4 was due to a lack of motivation to participate. The mean age of the total sample of children of 12.6 y in 1995 and 12.5 y in 1996 did not differ significantly (median 2-sample test, $P = 0.1238$) between the 2 study phases. Data on indicators of socioeconomic status showed a higher level of education, fewer laborers, and more professional people among the heads of households in the school-4 community than in the other 3 communities (Table 1).

Total goiter rates, consisting of the sum of the palpable (grade 1) and visible (grade 2) goiters, in the 4 communities before and 1 y after the introduction of mandatory iodization are shown in **Figure 1**. At baseline, the severity of the prevalence of goiters ranged from mild in school 4 (14.3%) to moderate in schools 1 (26.3%) and 2 (25.0%) to severe in school 3 (30.2%). The prevalence of goiters in these schools remained essentially unchanged 1 y later, and the overall weighted prevalence of $25.6 \pm 2.5\%$ ($\bar{x} \pm$ SE) in 1995, adjusted for the sampling effect and response rate, did not differ significantly (chi-square test for a difference in proportions) from the overall weighted prevalence of $27.5 \pm 2.7\%$ 1 y later.

The distributions of urinary iodine excretion at baseline and 1 y after the introduction of mandatory iodization for each of the 4 schools are shown in **Figure 2**. Before mandatory iodization came into effect, these distributions were skewed toward the low urinary iodine concentrations, particularly in schools 1, 2, and 3, all of which were of low socioeconomic status. In these 3 schools, 39.4%, 55.6%, and 76.6% of children had urinary iodine concentrations in the severely low range (<0.16 μmol/L) and very few (<10%) had urinary iodine concentrations in the adequate range (>0.79 μmol/L). In the fourth school, a low percentage of children (1.5%) had severely low urinary iodine concentrations,

TABLE 1
Characteristics of the study population

	School									
	School 1		School 2		School 3		School 4		Overall	
Characteristic	1995 ($n = 155$)	1996 ($n = 156$)	1995 ($n = 189$)	1996 ($n = 184$)	1995 ($n = 150$)	1996 ($n = 146$)	1995 ($n = 71$)	1996 ($n = 50$)	1995 ($n = 565$)	1996 ($n = 536$)
Response rate (%)	92.8	92.3	97.9	94.4	70.1	74.6	74.7	51.5	84.3	81.7
Age (y)[1]	12.7 ± 1.8	12.4 ± 1.8	12.5 ± 1.8	12.6 ± 1.6	12.9 ± 2.0	12.7 ± 1.9	12.1 ± 1.0	12.0 ± 1.0	12.6 ± 1.9	12.5 ± 1.7
Education[2]										
≤7 y (%)	—	49.0	—	61.4	—	61.5	—	8.0	—	52.2
≥12 y (%)	—	8.7	—	5.5	—	2.1	—	54.0	—	10.5
Occupation[2]										
Laborer (%)	—	49.0	—	64.1	—	43.4	—	6.0	—	49.6
Professional (%)	—	5.3	—	2.2	—	0.7	—	30.0	—	5.6

[1] $\bar{x}$ ± SD.

[2] Refers to heads of households.

about a quarter had adequate urinary iodine concentrations, and the rest were moderately deficient (0.16–0.39 μmol/L) or mildly deficient (0.4–0.78 μmol/L). One year after the introduction of mandatory iodization, these urinary iodine distributions shifted substantially to the right toward higher, or adequate, concentrations (median 2-sample test, $P < 0.0001$ for all 4 schools) (Figure 2). In schools 1, 2, and 4, >80% of the children had urinary iodine concentrations >0.79 μmol/L at follow-up; 78.5% of the samples in school 3 were in this range.

Similarly, the median urinary iodine concentrations in the 4 schools increased markedly from concentrations indicating severe (school 3), moderate (schools 1 and 2), and mild (school 4) iodine deficiency at baseline to concentrations well into the replete range (0.79–1.58 μmol/L) 1 y later (**Table 2**). During this time the overall median urinary iodine concentration increased from 0.17 to 1.47 μmol/L (median 2-sample test, $P < 0.0001$).

The iodine content of 4 samples of retail iodized salt purchased in the study area at the time of the baseline study ranged from 14 to 17 μg/g ($\bar{x}$: 15 μg/g), ie, within the range of 10–20 μg/g that

was legally required before the introduction of mandatory iodization. At follow-up 1 y later, 18 samples were purchased from retailers in the area. The iodine content of these retail samples increased to a mean of 25 μg/g, somewhat below the revised legal requirement of 40–60 μg/g that came into effect with the introduction of mandatory iodization. There was considerable variation in the iodine content of these retail salt samples at follow-up, ranging from 0 to 56 μg/g, resulting in a lower mean value than expected. The higher salt iodine concentration in community 4 than in the other communities was probably related to the higher socioeconomic status of these communities, which would have allowed them to purchase the more expensive brands of salt that had higher iodine concentrations.

To assess the change in the proportion of households using iodized salt as a result of the introduction of mandatory iodization, we established the baseline percentage of households that used iodized salt by questionnaire and used titrimetric analysis to determine the iodine content of salt samples brought to school at follow-up. At baseline, a low percentage of households (6.2% in
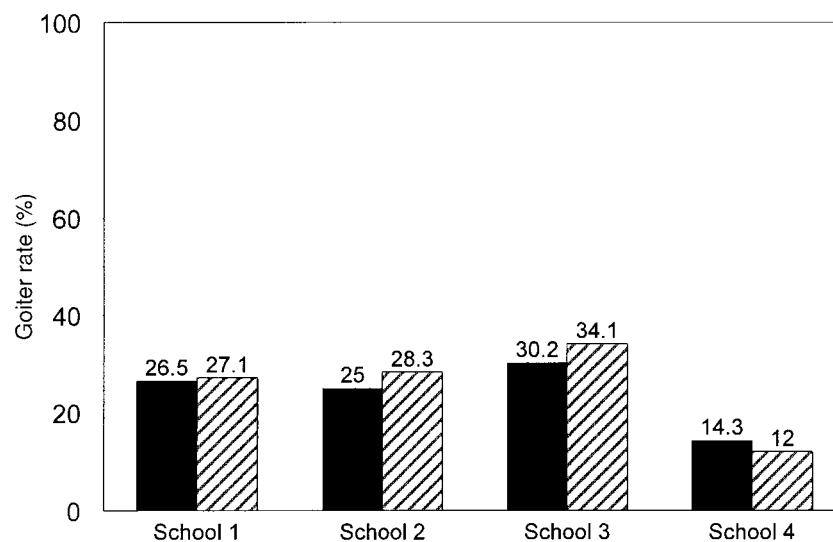

FIGURE 1. Total goiter rates in schoolchildren before (■) and 1 y after (▨) mandatory iodization, at a higher concentration than occurred with optional iodization, began.
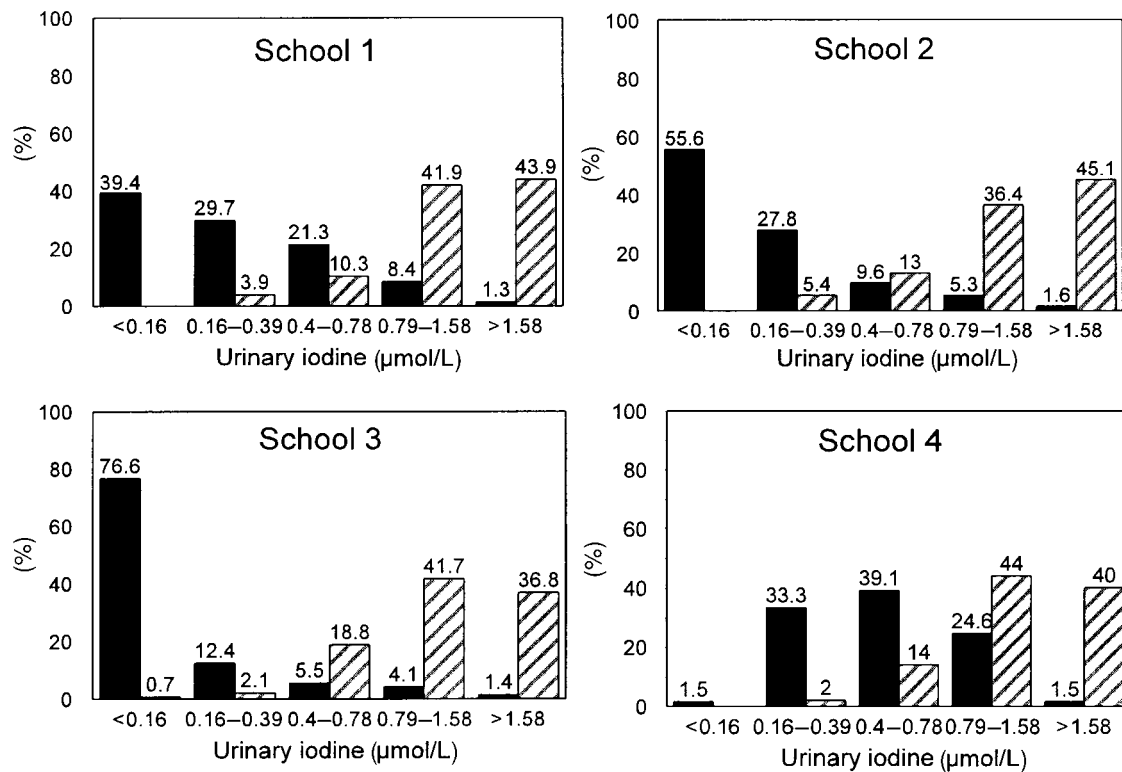
FIGURE 2. Distribution of urinary iodine concentrations in schoolchildren before (■) and 1 y after (▨) mandatory iodization, at a higher concentration than occurred with optional iodization, began. To convert values to μg/L, divide by 0.0079.

school 1, 4.3% in school 2, 25% in school 3, and 45.7% in school 4) reported the use of iodized salt. A year later, >70% of households in each of the communities, for an overall percentage of 82.4% in the whole study area, were using salt iodized at a concentration of >20 μg/g (Table 2). Overall, 15.1% of households had table salt with an iodine concentration within the legally required range of 40–60 μg/g (Table 2), although this required range applies to the production site. In the 3 communities of lowest socioeconomic status, the mean and median iodine concentrations of household salt were very similar, ranging from 24 to 34 μg/g; in the community with the highest socioeconomic status (school 4), mean and median concentrations were higher, exceeding 40 μg/g (Table 2). For the study area overall, the mean (±SD) household iodine concentration was 31 ± 17 μg/g and the median was 29 μg/g.

During both studies, the iodine concentrations of the drinking-water samples taken in the 4 communities remained low, between 0.0 and 0.12 μmol/L.

DISCUSSION

At baseline, rates of iodine deficiency and goiter ranged from mild to severe in the 4 schools, despite the fact that optional iodization had been in operation in South Africa since 1954. The overall baseline prevalence of goiters of 25.6% (range: 14.3–30.2%) was, however, lower than the excessively high rates of between 69% and 93% that prevailed in this area ≈60 y ago (15, 16). Therefore, optional iodization at a concentration between 10 and 20 μg/g and a 30% market share of iodized salt with unequal accessibility (7), as was the case in South Africa for

4 decades before the introduction of mandatory iodization, appeared to have had some beneficial effect but was ineffective in eradicating iodine deficiency and endemic goiter in the study area.

Favorable changes were observed in the process indicators between baseline and follow-up, such as the increase in the proportion of households that used iodized salt and the increase in the iodine concentration of table salt. At baseline, the estimated overall percentage of 15.5% of households using iodized salt appeared to be lower than the national estimate of a 30% iodization rate of table salt before the introduction of mandatory iodization (7). These estimates were in striking contrast with household use of iodized salt in the study area 1 y after mandatory iodization was introduced, when 82.4% of households were using salt with an iodine concentration >20 μg/g (and 90.9% were using salt with an iodine concentration >10 μg/g). Moreover, the mean iodine concentration of retail salt samples collected during this study increased from 15 μg/g (range: 14–17) to 25 μg/g (range: 0–56) 1 y after the introduction of mandatory iodization. The latter mean value was lower than the mean value of 31 μg/g in household salt because of some very low concentrations among the retail salt samples. In another study, conducted in 3 of the 9 provinces in South Africa at the same time as the present study, we showed that the iodine concentration of retail salt increased from a mean of 14 μg/g before mandatory iodization to 33 μg/g 1 y after mandatory iodization was introduced (9). Although the iodine concentration was lower than the legally required concentration of 40–60 μg/g at the production site, it nevertheless validated the observation of an increased iodine concentration in iodized table salt over the study period. On the basis of the improvement in these process indicators, a

TABLE 2
Iodine concentrations in the urine of schoolchildren at baseline and at 1-y follow-up and in salt used in the children's households (collected at 1-y follow-up)

	School									
	School 1		School 2		School 3		School 4		Overall	
Iodine	1995	1996	1995	1996	1995	1996	1995	1996	1995	1996
Urinary iodine										
n	155	155	187	184	145	144	69	50	556	533
Median (μmol/L)	0.21	1.52	0.13	1.52	0.04	1.34	0.51	1.42	0.17	1.47
Iodine in household salt										
n	—	149	—	182	—	144	—	48	—	523
$\bar{x} \pm$ SD (μg/g)	—	24 ± 17	—	33 ± 14	—	30 ± 12	—	43 ± 26	—	31 ± 17
Median (μg/g)	—	24	—	34	—	28	—	47	—	29
Percentage of salt samples with										
>20 μg/g	—	71.8	—	89.0	—	87.5	—	75.0	—	82.4
40–60 μg/g		14.1	—	15.9	—	10.4	—	33.3	—	15.1

similar improvement was also expected in the associated outcome indicators, ie, higher urinary iodine concentrations and a reduction in goiter rates.

Unlike the long-term successful reduction of goiter rates resulting from salt-iodization programs in many countries (1–5), the goiter rates in this study remained unchanged 1 y after iodization became mandatory at a higher iodine concentration than occurred with optional iodization. Although palpation of the thyroid is subject to observer variation (17), the similarity in the varying goiter rates of the children in the 4 schools before and after the introduction of mandatory iodization suggests internal consistency in the data, indicating a strong likelihood of a true lack of change in goiter rates in the short term.

Short-term success in reducing goiter rates was achieved in efficacy studies with iodized oil (18) and low-dose iodine (0.2 mg/d) (19) in adults but not in children receiving biscuits and cold drinks fortified with iodine (20). Todd and Dunn (21) observed reduced thyroid volumes, measured by ultrasound, in their efficacy study in 7–13-y-old children over a 13-mo period after the administration of potassium iodide given at a dosage of 30 mg monthly or 8 mg biweekly. Administration of iodized oil to schoolchildren aged 6–11 y as single iodine doses ≤480 mg did not result in decreased thyroid volumes as measured by ultrasonography over a period of 395 d (22). Only at a higher iodine dose of 960 mg (administered orally) or 480 mg (administered intramuscularly) did the goiter volume decrease significantly after 395 d (22). In our evaluation of the short-term (1 y) effectiveness of mandatory iodization of table salt, the prevalence of goiters in children in the 4 schools remained the same despite the dramatically improved iodine status of these children. Reasons for the lack of change in the goiter rates may be related to insufficient time of exposure to mandatory iodization, the insensitivity of thyroid palpation to small changes in thyroid volume (17), a lesser effectiveness of iodized-salt prophylaxis in reducing the size of goiters in children exposed to iodine deficiency in the first years of life (23), or the possibility that long-standing goiters may become autoimmune (24). This failure of mandatory iodization to induce regression of goiters that are mild-to-borderline severe in children suggests that assessment by palpation of the change in goiter rate may not be an appropriate short-term indicator of the effectiveness of salt-iodization programs.

The dramatic shift toward higher values in the urinary iodine distributions and the similarly impressive increases in the median urinary iodine concentration of children in the 4 schools illustrate the short-term effect of mandatory iodization on an outcome indicator such as urinary iodine excretion in schoolchildren. It is unlikely that factors other than the introduction of mandatory iodization at a higher concentration, which was associated with the favorable changes in process indicators previously alluded to, were responsible for this marked improvement in the iodine status of the children. The iodine concentration of drinking water remained low throughout the study period and sales of seafood, according to the managers of grocery stores in the study area, also remained unchanged.

However, 10–19% of the urine samples from the different communities still had iodine concentrations in the deficient range. Further follow-up studies are required to determine whether these results represent a steady state in urinary iodine concentration or whether further improvement can be achieved over a longer period of exposure to mandatory iodization.

Only table salt—and not salt used for agricultural purposes—is being iodized in South Africa. Strictly speaking, this does not conform to the definition of universal salt iodization, which extends to iodization of salt for animals. However, the introduction of mandatory iodization complied with part of the international mid-decade goal of universal salt iodization, resulting in a remarkable reduction in iodine deficiency in schoolchildren within 1 y.

The generalizibility of these results depends to a large extent on whether a national iodization program can be effectively implemented, whether iodized salt can be distributed efficiently, and whether consumers have unrestricted access to iodized salt. Our data showed that introducing mandatory iodization at a higher concentration than occurred with optional iodization resulted in improved process indicators, ie, a significantly higher mean iodine concentration of table salt and a markedly greater percentage of households using iodized salt, within 1 y. In turn, these changes in process indicators were responsible for the increased dietary intake of iodine, which virtually eradicated the mild-to-severe iodine deficiency in schoolchildren of 4 different communities. However, the goiters in these children did not regress within 1 y, leaving doubt about the appropriateness of assessing goiter by palpation in short-term evaluations of the effectiveness of iodization programs.

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