Iodised salt for preventing iodine deficiency disorders (Review)

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A B S T R A C T

Background
Iodine deficiency is the main cause for potentially preventable mental retardation in childhood, as well as causing goitre and hypothyroidism in people of all ages. It is still prevalent in large parts of the world.

Objectives
To assess the effects of iodised salt in comparison with other forms of iodine supplementation or placebo in the prevention of iodine deficiency disorders.

Search strategy
We searched the Cochrane Library, Medline, the Register of Chinese trials developed by the Chinese Cochrane Centre, and the Chinese Med Database. We performed handsearching of a number of journals (Chinese Journal of Control of Endemic Diseases, Chinese Journal of Epidemiology, Chinese Journal of Preventive Medicine, and Studies of Trace Elements and Health up to February 2001), and searched reference lists, databases of ongoing trials and the Internet. Date of latest search: November 2001.

Selection criteria
We included prospective controlled studies of iodised salt versus other forms of iodine supplementation or placebo in people living in areas of iodine deficiency. Studies reported mainly goitre rates and urinary iodine excretion as outcome measures.

Data collection and analysis
The initial data selection and quality assessment of trials was done independently by two reviewers. Subsequently, after the scope of the review was slightly widened from including only randomised controlled trials to including non-randomised prospective comparative studies, a third reviewer repeated the trials selection and quality assessment. As the studies identified were not sufficiently similar and not of sufficient quality, we did not do a meta-analysis but summarised the data in a narrative format.

Main results
We found six prospective controlled trials relating to our question. Four of these were described as randomised controlled trials, one was a prospective controlled trial that did not specify allocation to comparison groups, and one was a repeated cross-sectional study comparing different interventions. Comparison interventions included non-iodised salt, iodised water, iodised oil, and salt iodisation with potassium iodide versus potassium iodate. Numbers of participants in the trials ranged from 35 to 334; over 20,000 people were included in the cross-sectional study. Three studies were in children only, two investigated both groups of children and adults and one investigated pregnant women. There was a tendency towards goitre reduction with iodised salt, although this was not significant in all studies. There was also an improved iodine status in most studies (except in small children in one of the studies), although urinary iodine excretion did not always reach the levels recommended by the WHO. None of the studies observed any adverse effects of iodised salt.

Authors’ conclusions
The results suggest that iodised salt is an effective means of improving iodine status. No conclusions can be made about improvements in other, more patient-oriented outcomes, such as physical and mental development in children and mortality. None of the studies specifically investigated development of iodine-induced hyperthyroidism, which can be easily overlooked if just assessed on the basis
of symptoms. High quality controlled studies investigating relevant long term outcome measures are needed to address questions of dosage and best means of iodine supplementation in different population groups and settings.

SYNOPSIS

IODISED SALT SUPPLEMENTATION IMPROVES IODINE STATUS BUT EFFECT ON OTHER OUTCOMES IS UNCLEAR

Iodine deficiency causes mental retardation in children as well as enlarged thyroid glands (goitre) and deficiencies in thyroid hormones in people of all ages. It still exists in large parts of the world. This review looked at studies of iodised salt in the diet that included a comparison group. Six studies, most of them in children but some also in adults, were included. Iodine in the urine increased in all but one study, but there was some concern that small children did not eat enough salt to achieve adequate iodine status. Some studies, but not all, showed a reduction in the enlargement of the thyroid gland (goitre) that can accompany lack of iodine in the diet. Adverse effects were not reported, but these may not have been studied adequately. More high quality long term studies measuring outcomes related to child development, to deaths associated with iodine-deficiency and to adverse effects are needed.

BACKGROUND

IODINE

Iodine is a trace element which is an integral part of the thyroid hormones thyroxine (T4) and triiodothyronine (T3), produced by the thyroid gland, a small butterfly-shaped organ situated in the neck. Thyroid hormones are essential for regulating and stimulating metabolism, temperature control, and normal growth and development (Larsen 1981). Synthesis and release of thyroid hormones are stimulated by thyroid-stimulating hormone (TSH, thyrotropin), which is released from the pituitary gland; this regulation is subject to feedback inhibition.

THE PROBLEM OF IODINE DEFICIENCY

Iodine deficiency (urinary iodine excretion less than 100 µg/day) is the main cause for potentially preventable mental retardation in childhood (WHO 1993). It causes hypothyroidism, resulting in thyroid enlargement, mental retardation, increased neonatal and infant mortality, retardation of growth and development of the central nervous system in children (cretinism), reproductive failure, and an increase of fluid in the tissues (myxoedema) (Delong 1994; Beaufre 2000). There are three main laboratory indicators of iodine deficiency: increased TSH concentration in neonatal blood and cord blood, increased concentration of thyroglobulin, and decreased concentration of iodine in the urine. Development of goitre, i.e. an enlargement of the thyroid gland (due to stimulation of growth by TSH), is common (endemic goitre) and does not need to be accompanied by an abnormality in thyroid hormones (euthyroid goitre).

Iodine deficiency is common, especially in Asia and Africa, but also in large parts of Eastern Europe. Only a small number of countries currently have sustainable iodine sufficiency, and about a third of the world’s population lives in areas with some iodine deficiency. Inland areas, especially mountainous areas like the Alps, Himalayas and the Andes are particularly iodine deficient (Dunn 1998a). Iodine deficiency disorders are a global health problem with nearly two billion people at risk (FAO/WHO/IAEA 1996). In countries such as China, the incidence of iodine deficiency diseases in children and pregnant women in areas of iodine deficiency may be up to 50% (Fong 1981; Chen 1984; Lin 1995; Li 1997). In certain Asian, African and Latin American countries iodine deficiency diseases affect more than 200 million people (WHO 1993).

HISTORY OF PREVENTION OF IODINE DEFICIENCY DISORDERS

Large programmes for the prevention of iodine deficiency - or more specifically endemic goitre - using iodised salt were already initiated in Switzerland and in the USA in the 1920s, where large surveys of goitre incidence before and after the intervention showed the use of iodised salt to be an effective preventative intervention. New Zealand followed in 1941 but only very low iodisation levels were used in the first 20 years. Then in the 1950s and the 1960s a number of European countries followed, with associated reductions in endemic goitre rates. Before 1960, interventions for iodine deficiency disorders were pursued by every country independently. Between 1961 and 1973, the Pan-American Health Organization (PAHO) and the World Health Organisation (WHO) had four international meetings regarding interventions for iodine deficiency. At the fourth meeting in 1973, diagnostic criteria, measures of intervention, and directions of research were suggested. At the fifth meeting in 1983, these diagnostic criteria were revised. In 1986, the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) was established in Kathmandu, Nepal. Based on the proposal of the ICCIDD, the 39th World Health Congress in 1986, declared that iodine deficiency disorders should be controlled within the following ten years. Since its establishment in 1986, the ICCIDD’s work focused on Africa and South-East Asia. The 43rd World Health Congress in 1990 declared that iodine de-
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Deficiency disorders should have disappeared from the earth by 2000. Also in 1990, the 71 heads of States and 80 other officials from 150 governments who attended the World Summit for Children held in New York in 1990 adopted the goal of virtual elimination of iodine deficiency disorders by the year 2000. In response to this recommendation, most of the countries with iodine deficiency problems agreed to try to iodise 90% of all edible salt by 1995. However, iodine deficiency disorders have not yet been eliminated and 36 affected countries have not yet introduced salt iodisation programmes (see Delange 2001).

SALT IODISATION

Iodised salt, iodised bread, iodised water and injecting iodine oil are commonly used for preventing iodine deficiency disorders. Iodised salt is considered the most appropriate means of iodine supplementation for the following reasons: 1. It is consumed by nearly everyone at roughly equal amounts throughout the year, 2. Salt production is limited to a few centres, facilitating quality control, 3. Addition of iodate or iodide does not affect the taste or smell of the salt, and 4. Iodisation is cheap (less than 0.01 US Dollar a day for the estimated amount of salt intake). However, there have been problems with implementing salt iodisation in countries with numerous scattered salt deposits and complex distribution systems, so alternatives are sometimes required (Dunn 1998a).

Salt is commonly iodised using potassium iodate (KIO3) or potassium iodide (KI). Potassium iodate is the more stable and less soluble form, making it the recommended form, especially for use in moist tropical locations. The WHO recommends a daily intake of 90 µg of iodine for infants (0-59 months), 120 µg for schoolchildren (6-12 years), 150 µg for adolescents and adults and 200 µg for pregnant and lactating women. The appropriate level of salt iodisation will depend on the individual consumption of salt, the degree of iodine deficiency in the area and the loss of iodine from the producer to consumer. All these factors will be different in different countries, and levels of salt iodisation have varied substantially between countries and over time. Currently, iodisation levels of 20-40 mg iodine per kg of salt are recommended. In addition, the response to supplemental iodine may be reduced by other factors in the environment, such as consumption of specific goitrogenic foods (for example, cassava (manioc)), and deficiency of other trace elements in the diet, such as selenium (Yang 1997; Köhrle 1999) or iron (Zimmermann 2000).

DIAGNOSIS OF IODINE DEFICIENCY DISORDERS

The following recommendations regarding assessment of iodine deficiency disorders are given by the WHO (in collaboration with the United Nations’ Children’s Fund (UNICEF) and the IC-CIDD) (WHO 2001):

Urinary iodine levels are useful for assessing iodine status as a result of recent iodine intake. Even though intra-individual variation exists, this tends to even out among populations. Twenty-four hour urine samples and relating urinary iodine to creatinine are not recommended.

One variable often measured is thyroid size. However, the determination of thyroid size is not feasible in neonates and it may be of limited use in school children (8-12 years), a group often studied, as the highest prevalence of goitre occurs during puberty and childbearing age. The two most common methods of measuring thyroid size are by palpation or by ultrasonography. While many studies assess goitre by palpation, the WHO suggests that this is not a very useful technique for determining the impact of iodisation programmes, where thyroid volumes may decrease over time, making the assessment difficult. The technique and classification of measurement of goitre by palpation are specified by the WHO. Ultrasonography is the method of choice for assessing the impact of iodisation programmes on thyroid size, an application of the technique is becoming feasible even in remote areas of the world (the ‘thyromobil project’).

Measurement of TSH levels, which are expected to be elevated in iodine deficiency, is not a reliable indicator in school children and adults as differences to normal levels are small and there is a large overlap between values in people who are iodine sufficient and those who are iodine deficient. However, TSH levels are a good indicator of iodine deficiency in neonates. Increased thyroglobulin levels are a good indicator of thyroid hyperplasia resulting from iodine deficiency. Thyroglobulin levels reflect iodine nutrition over months and years, whereas urinary iodine levels measure the more immediate effects of increased iodine intake on iodine status. Measurement of thyroid hormones (T3 and T4) is not recommended, as the tests are difficult and expensive and the measurements are not very reliable indicators of iodine deficiency.

EVIDENCE FROM CONTROLLED STUDIES

Many large surveys on goitre prevalence have been carried out worldwide, but only few controlled trials on the effectiveness of iodised salt for goitre prevention have been done. A Cochrane review (Mahomed 2001) investigates the effect of maternal iodine supplementation in pregnant women. The review suggests that iodine supplementation leads to improved outcomes in the children of the mothers having received the supplements (decreased mortality, decreased prevalence of cretinism and increased scores of psychomotor development). However, as the review only included pregnant women and outcomes in their children, and as none of the included studies used iodised salt, conclusions cannot be drawn regarding the effects of supplementation with iodised salt in the general population. A small number of controlled trials have suggested that iodised salt may be effective at preventing iodine deficiency disorders. There remains some uncertainty whether goitre rates are reduced by the supply of iodised salt (Hintze 1988; Foo 1996; Yang 1997). Furthermore, there is some evidence that correcting for iodine deficiency with excessive supplementation of iodine increases the risk of iodine-induced hyperthyroidism (Delange 1999) and thyroid auto-immunity (Kahaly 1997).
In light of this incomplete evidence and the possibility of adverse effects, a systematic review of controlled trials of iodised salt in comparison to other forms of iodine supplementation in the general population is needed.

OBJECTIVES

To assess the effects of iodised salt in comparison with placebo and other forms of iodine supplementation on the incidence of iodine deficiency disorders.

Additional questions were as follows:
1. If iodised salt is effective, what is the optimum level of salt iodisation under given conditions?
2. Are there any adverse effects associated with salt iodisation (e.g. iodine-induced hyperthyroidism, iodine-induced anaphylaxis)?

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Originally we had intended to include only randomised controlled trials in this review. However, after becoming better acquainted with the literature, we felt that it would be appropriate also to include other types of prospective comparative epidemiological studies. We therefore included in this review any prospective study that had a control group and studied the prevention of iodine deficiency disorders using iodised salt. We were particularly interested in randomised and quasi-randomised trials of a duration of at least one year, but other controlled trials were also considered. Trials using indicators for assessment of iodine deficiency disorders that are approved by the WHO, UNICEF and the ICCIDD were preferred.

Types of participants

The review includes trial participants (adults and children) living in areas with low iodine intake (iodine deficiency). Controlled trials of iodine supplementation before or during pregnancy with outcomes referring only to the neonate were excluded as these have already been included in another Cochrane review (Mahomed 2001).

Types of intervention

We were interested in comparisons of iodised salt (using iodide or iodate) with placebo or with other forms of iodine supplementation (for example, iodised oil, iodised water).

Types of outcome measures

The MAIN OUTCOME MEASURES we considered to be important were:
1. Mortality related to iodine deficiency disorders,
2. Goitre (thyroid size),
3. Physical and mental development in children,
4. Symptoms of hypothyroidism (for example, reproductive failure/infertility, myxoedema, tiredness, lethargy, slowing of mental function, cold intolerance, cardiac complications).

ADDITIONAL OUTCOME MEASURES we considered to be important were:
1. Urinary iodine concentration,
2. Thyroid-stimulating hormone (TSH) concentration in blood and neonatal cord blood,
3. Serum thyroglobulin concentration,
4. Adverse effects (for example, iodine-induced hyperthyroidism),
5. Health-related quality of life (ideally using a validated instrument),
6. Costs,
7. Compliance,
8. Socioeconomic and related effects (for example, school performance, per capita income).

TIMING OF OUTCOME ASSESSMENT

We had planned to assess outcomes in the short (up to six months), medium (seven months to one year) and long (more than one year) term.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

See: Metabolic and Endocrine Disorders Group search strategy

ELECTRONIC SEARCHES


The following Medline search strategy was used and adapted for the different databases:

NOTES: unless stated otherwise, search terms are free text terms; MeSH: Medical subject heading (Medline medical index term); an asterisk (*) stands for ‘any character(s)’

IODINE DEFICIENCY/SUPPLEMENTATION

1. IODINE/ [MeSH term, all subheadings included]
2. iod* [in abstract or title]
3. explode IODIZED-OIL/ [MeSH term, all subtrees and subheadings included]
4. #1 or #2 or #3
5. DIETARY-SUPPLEMENTS/ [MeSH term, all subheadings included]
6. supplement* [in abstract or title]
7. THYROID-GLAND/ [MeSH term, all subheadings included]
METHODS OF THE REVIEW

TRIALS SELECTION

The title, abstract and keywords of every record retrieved were scanned independently by two reviewers (TW, GL) to determine which studies required further assessment. The full article was retrieved when the information given in the titles, abstracts and keywords suggested that: 1. The study used iodised salt as an intervention, 2. The study had a prospective design and a control group. When there was any doubt regarding these criteria from scanning the titles and abstracts, the full article was retrieved for clarification. Disagreements were resolved by discussion. A third reviewer (CC) performed additional searches and trials selection independently.

QUALITY ASSESSMENT OF TRIALS

The quality of reporting of each trial was assessed independently by three reviewers (TW, GL, CC) according to a modification of the quality criteria specified by Schulz (Schulz 1995) and by Jadad (Jadad 1996).

In particular, the following quality criteria were assessed:

1. Minimisation of selection bias - a) was the randomisation procedure adequate? b) was the allocation concealment adequate?
2. Minimisation of performance bias - were the participants and people administering the treatment blind to the intervention?
3. Minimisation of attrition bias - a) were withdrawals and dropouts completely described? b) was analysis by intention-to-treat?
4. Minimisation of detection bias - were outcome assessors blind to the intervention?

Based on these criteria, studies were subdivided into one of the following three categories:

A - all quality criteria met: low risk of bias.
B - one or more of the quality criteria only partly met: moderate risk of bias.
C - one or more criteria not met: high risk of bias.

We had intended to use this classification as the basis of a sensitivity analysis. Additionally, we were going to explore the influence of individual quality criteria in a sensitivity analysis.

After reviewing the literature, we also decided that the following two quality criteria were important:

1. Similarity of the groups at baseline
2. Measurement of the level of salt iodisation and of other potential sources of iodine accessible to the participants

DATA EXTRACTION

Data concerning details of study population, intervention and outcomes were extracted independently by three reviewers (TW, GL, CC) using a standard data extraction form specifically adapted for this review. Data on participants, interventions, and outcomes, as described above, were abstracted. The data extraction form included the following items:

1. General information: published/unpublished, title, authors, reference/source, contact address, country, urban/rural etc., language of publication, year of publication, duplicate publications, sponsor, setting.
2. Trial characteristics: design, duration of follow up, method of randomisation, allocation concealment, blinding (patients, people administering treatment, outcome assessors).
3. Intervention(s): placebo included, interventions(s) (dose, route, timing), comparison intervention(s) (dose, route, timing), co-medication(s) (dose, route, timing), verification of salt iodisation, measurement of other sources of iodine.
4. Participants: sampling (random/convenience), exclusion criteria, total number and number in comparison groups, sex, age, baseline characteristics, diagnostic criteria, duration of iodine deficiency disorders, similarity of groups at baseline (including any co-morbidity), assessment of compliance, withdrawals/losses to follow-up (reasons/description), subgroups.
5. Outcomes: outcomes specified above, any other outcomes assessed, other events, length of follow-up, quality of reporting of outcomes.
6. Results: for outcomes and times of assessment (including a measure of variation), if necessary converted to measures of effect specified below; intention-to-treat analysis.

DATA ANALYSIS

As we did not identify enough high quality randomised controlled trials and as outcome measures were reported in various different ways that could not easily be converted into a standard measure, we decided against doing a meta-analysis. Data were summarised in a narrative format. Different comparisons were analysed separately.

If there are data available for meta-analysis in future, we will proceed as follows: Data will be included in a meta-analysis if they are of sufficient quality and sufficiently similar. We expect both event (dichotomous) data and continuous data. Dichotomous data will be expressed as relative risks. Continuous data will be expressed as weighted mean differences. Overall results will be calculated based on the random effects model. Heterogeneity will be tested for using the Z score and the Chi square statistic with significance being set at p < 0.1. Possible sources of heterogeneity will be assessed by sensitivity and subgroup analyses as described below. Small study bias will be tested for using the funnel plot or other corrective analytical methods depending on the number of clinical trials included in the systematic review.

COMPARISONS

When relevant trials exist, we will consider the following comparisons:
1. Salt iodisation versus non-supplemented control,
2. Salt iodisation versus all other iodine supplementation,
3. Salt iodisation versus each individual type of iodine supplementation (for example, iodised oil, iodised water),
4. Types or doses of salt iodisation compared to each other.

SUBGROUP ANALYSES

We will aim to perform subgroup analyses in order to explore effect size differences as follows, if there is a significant result for one of the main outcome measures:
1. Presence or absence of symptoms of iodine deficiency (for example, goitre),
2. Dose (low, medium, high - based on data),
3. Duration of intervention (short, medium, long - based on data),
4. Gender,
5. Age [children (up to 12 years), adolescents (>12 to 18 years), younger adults (>18 to 40 years), older adults (> 40 years)].

SENSITIVITY ANALYSES

We will perform sensitivity analyses in order to explore the influence of the following factors on effect size:
1. Repeating the analyses excluding any unpublished studies.
2. Repeating the analyses taking account of study quality, as specified above.
3. Repeating the analyses excluding any very long or large studies to establish how much they dominate the results.
4. Repeating the analyses excluding studies using the following filters: diagnostic criteria, language of publication, source of funding (industry versus other), country.

The robustness of the results will also be tested by repeating the analyses using different measures of effects size (risk difference, odds ratio etc.) and different statistical models (fixed and random effects models).

DESCRIPTION OF STUDIES

STUDIES IDENTIFIED

The initial Medline search using the electronic search strategy listed above yielded 1546 studies. After scanning the studies identified and doing the other searches specified, we identified twelve studies which appeared to fulfil the inclusion criteria. Of these, the Medline search identified six, three further references were found scanning reference lists (Marine 1917/20; Kimball 1937; Sooch 1965), another through searching the PAHO database (Scrimshaw 1953), another through handsearching (Yang 1997), and the last one through searching the Internet and consequent personal contact with the department of the author (l’Ons 2000). Most of the studies were published in English, one in Chinese (Yang 1997) and one in Spanish (Scrimshaw 1953).

EXCLUDED STUDIES

Of the twelve studies, six were excluded upon further scrutiny. Reasons for exclusion of studies are given in the Table of Excluded Studies. Reasons for exclusion included studies not being prospective controlled comparisons (Kimball 1937), iodised salt not being the primary intervention (Marine 1917/20; Scrimshaw 1953; van den Briel 2000; Yang 1997), and implausible results (Saowakhontha 1994).

RETRIEVAL OF MISSING DATA
Some missing data were obtained for the study by Zhao et al (Zhao 1999).

DESIGNS OF INCLUDED STUDIES

Details of the characteristics of the included studies are shown in the Table of Included Studies. All studies included were of a parallel design, single centre and had a control group. Four of them (Hintze 1988; Romano 1991; Foo 1996; Zhao 1999) were clearly identified as randomised. Units for allocation of the treatment were either individuals (Hintze 1988; Romano 1991; Zhao 1999) or groups [schools (l’Ons 2000), villages (Foo 1996) or other geographical regions (Sooch 1965)]. The two studies not mentioning randomisation (Sooch 1965; l’Ons 2000) were of this latter category. Trial duration ranged from four months to five years. Trials came both from the developed (Hintze 1988; Romano 1991) and the developing world (Sooch 1965; Foo 1996; Zhao 1999; l’Ons 2000).

PARTICIPANTS OF INCLUDED STUDIES

Numbers of participants of the studies ranged from 35 to over 20,000. Most studies had over hundred participants. Most studies examined children (5 years and younger to 16 years) (Sooch 1965; Hintze 1988; Foo 1996; Zhao 1999) one study examined women of childbearing age (Foo 1996), one studied pregnant women (Romano 1991), and one the general population (Sooch 1965). Studies were all carried out in areas of known iodine deficiency with substantial goitre rates (9.5-83%). Some studies had substantial differences in baseline goitre rates and urinary iodine excretion (Foo 1996; l’Ons 2000).

INTERVENTIONS OF INCLUDED STUDIES

Four of the studies included a control group where no iodine supplementation was used (Sooch 1965; Hintze 1988; Romano 1991; l’Ons 2000). In one study, iodised water was used as a comparison (Foo 1996), one study used iodised oil (Zhao 1999), and two studies compared different forms of iodised salt (specially prepared iodised salt versus commercially available iodised salt in the trial by Zhao et al (Zhao 1999), and salt fortified with potassium iodide versus salt fortified with potassium iodate in the trial by Sooch and Ramalingaswami (Sooch 1965)). Levels of iodisation were 12 to 53 parts per million (ppm). All interventions were given orally. In some studies the salt was supplied to the participants directly (Foo 1996; Zhao 1999; l’Ons 2000) in others the salt that was available for the participants to buy was either iodised or non-iodised (Hintze 1988; Sooch 1965; Zhao 1999). Salt consumption was not prescribed but was that used in normal household consumption.

OUTCOME MEASURES OF INCLUDED STUDIES

None of the studies assessed mortality, physical and mental development in children, symptoms of hypothyroidism, adverse effects, health-related quality of life, or socioeconomic effects. All studies reported goitre rates or a related measure (thyroid volume, neck circumference). Goitre was generally measured by palpation. All studies measured iodine content of the urine. Iodine excretion was measured in a number of different units, which could not always be converted to a unit allowing comparison between studies, due to missing data.

A number of studies (Hintze 1988; Sooch 1965; Zhao 1999) reported on quality checks of their outcome measurements (duplicate measurements, assessment of samples of outcome measurements before the main outcome assessment, etc.).

METHODOLOGICAL QUALITY

Most studies were of poor methodological quality (‘C’). Only one study was of higher quality (Zhao 1999) (‘B’) and described methodological issues in some detail (for example, power calculation, randomisation method, flow of participants, blinding of outcome assessment). An overview of study quality can be found in Table 01.

RANDOMISATION

Four studies were described as randomised (see above). Only one study mentioned the method of randomisation (Zhao 1999), although not in much detail. None of the studies mentioned allocation concealment.

BLINDING

Only one study (l’Ons 2000) mentioned blinding of participants and only one study (Zhao 1999) mentioned blinding of outcome assessment.

DESCRIPTION OF WITHDRAWALS AND LOSSES TO FOLLOW-UP AND INTENTION-TO-TREAT ANALYSIS

Withdrawals and losses to follow-up were described by two studies (Hintze 1988; l’Ons 2000). One study mentioned that there were no losses to follow-up (Zhao 1999). None of the studies mentioned an intention-to-treat analysis.

COMPLIANCE ASSESSMENT

A number of studies used methods to ensure compliance, for example, notices in schools and reminders (Hintze 1988; l’Ons 2000), and to check compliance, for example, checking amounts of iodised salt requested or collecting left-overs of previous deliveries of iodised salt (Zhao 1999; l’Ons 2000).

SIMILARITY OF COMPARISON GROUPS AT BASELINE

In two studies (Foo 1996; l’Ons 2000), there were significant differences between the comparison groups in baseline urinary iodine excretion and goitre rates.

CHECK OF IODISATION LEVELS AND IODINE CON-

TAMINATION
In four studies, the iodine content of the salt and of other iodine supplements (for example, iodised water) was checked (Sooch 1965; Foo 1996; Zhao 1999; l'Ons 2000). In three cases (Sooch 1965; Zhao 1999; l'Ons 2000) some of the salt samples were found to contain different levels (generally lower) of iodine than intended. A number of studies (Sooch 1965; l'Ons 2000) also studied other sources of iodine the participants might be exposed to (for example, iodine in food generally consumed, in the drinking water, in the soil), as well as potential goitrogens in the diet (for example, there were high levels of cassava leaves and tubers (which have a known goitrogenic effect) in the diet of the participants of the study by Foo et al (Foo 1996)).

RESULTS

The effects of the interventions on goitre prevalence and urinary iodine excretion are shown in Table 02.

GOITRE

All studies measuring goitre rates (or thyroid volume) showed a trend towards reduction in goitre rates (or prevention of occurrence of goitre) with the use of iodised salt. These reductions were significant in the studies by Sooch and Ramalingaswami (Sooch 1965), Zhao et al (Zhao 1999) (at least for specially distributed salt and for market salt plus iodised oil), and Foo et al (Foo 1996) (women only). The prevention of increase in thyroid volume in pregnancy with use of iodised salt in the study by Romano et al (Romano 1991) was a significant effect. No significant effects of iodised salt on goitre rates were seen in the study by Hintze et al (Hintze 1988) and the (short term) study by l'Ons et al (l'Ons 2000).

URINARY IODINE EXCRETION

In almost all studies measuring urinary iodine, iodine excretion was significantly increased with use of iodised salt. The only exception was the study by Foo et al (Foo 1996), were iodine excretion was not significantly increased in small children (of less than six years). The WHO target value of iodine excretion of at least 100 µg/L was reached in at least three studies (Foo 1996 (women only); Zhao 1999; l'Ons 2000). It was clearly not reached in the study by Hintze et al (Hintze 1988) and in the children in the study by Foo et al (Foo 1996). From the data, no clear relation can be seen between dose of iodine in the salt and urinary iodine excretion. Similarly, the data do not allow any conclusions regarding differences in iodine excretion rates following salt fortification using KI or KIO3.

DIFFERENT FORMS OF IODINE SUPPLEMENTATION

The study by Sooch showed no differences in the decrease of goitre rates after fortification of salt with either KI or KIO3. In the study by Foo et al (Foo 1996), iodised salt was about as effective as iodised water in women aged 15-40 years, but iodised water was more effective in children below six years. In the study by Zhao et al (Zhao 1999), iodised salt with a carefully controlled iodine content and commercially available iodised salt with a supplementation of iodised oil were more efficient that commercially available iodised salt alone (which had a very variable iodine content).

CHILDREN VERSUS ADULTS

In the study by Sooch and Ramalingaswami (Sooch 1965), children benefited from iodised salt to a similar extent as adults. However, in the study by Foo et al (Foo 1996), small children (below six years) benefited less than adults. The conclusion of that study is similar to the one given by Hintze et al (Hintze 1988), who suggested that salt consumption in children is lower than that of adults and that therefore children might benefit less from salt iodised at a relatively low level.

DISCUSSION

SUMMARY

We only found one randomised controlled trial relating to our question that was of fairly good quality, the other studies examined were of fairly poor quality and some of them were not randomised. The studies did not assess many of the outcome measures we had considered important. The studies identified used differing levels of salt iodisation and different units of measurement, and were therefore not easily comparable. There was a tendency towards goitre reduction with iodised salt, although this was not significant in all studies. There was also an improved iodine status in most studies (except in small children in one of the studies), although this did not always reach the levels recommended by the WHO.

LIMITATIONS OF THE REVIEW

There was only a small number of studies included in this review, none of which abided by the criteria laid down in the CONSORT statement (CONSORT 2001). The only study of slightly higher quality (Zhao 1999) was faced with the problem that the commercially available iodised salt had a very unreliable iodine content. This may demonstrate that in certain parts of the world the quality control of iodisation programmes is a problem, but does not allow any conclusions regarding the effectiveness of salt iodisation per se. Most of the other studies were also faced with major confounders, such as differences in baseline goitre rates (Foo 1996; l’Ons 2000), presence of goitrogens in the diet (Foo 1996), levels of iodisation not reaching the recommended level of iodine intake (Hintze 1988; Foo 1996 (children)), and restriction to pregnant women, in whom iodine requirements are different to those of the general population (Romano 1991). In the study by Sooch and Ramalingaswami (Sooch 1965) the populations studied at the different time points did not consist entirely of the same people, even though the populations studied were fairly well isolated and increases in numbers in the groups at the end of the study may have...
been due to internal effects (for example, children below five years at the beginning of the study growing older). However, all this means that none of the studies were ideally suited to investigate the effectiveness of iodised salt in preventing iodine deficiency disorders and any conclusions must be treated with great caution.

This review focussed on iodised salt as a means of iodine supplementation. While iodised salt is undoubtedly the form of iodine supplementation most widely used and most practical for global use, the results of the review also suggest that it is not suitable for all situations. It may therefore be more useful to compare all the different forms of iodine supplementation, to give a more complete picture. We intend to do this in a future version of this review.

APPLICABILITY

The review included studies from countries of the developing as well as the developed world. It becomes apparent that delivery and quality control of iodised salt is probably more difficult in remote areas in developing countries and this method of iodine supplementation is therefore not without problems. However, the impression also arises that it is the most practicable and well accepted means of providing iodine supplementation.

The studies identified focussed mainly on children and women of childbearing age. While these are probably the most vulnerable to iodine deficiency disorders, future studies should also include other population groups. The question also arises of the most adequate way of iodine supplementation in newborn babies and infants. They will not consume any iodised salt at all. If they are breast fed, it would be interesting to establish if any iodised salt consumed by the mother to achieve an adequate iodine status is also enough to achieve an adequate iodine status in the child.

Studies generally concentrated on measuring iodine status by measuring urinary iodine levels - presumably because these measurements can be easily and quickly obtained. However, these values will not reflect long term iodine status and therefore other indicators should be used, for example, thyroglobulin levels or iodine excretion profiles, to get a more accurate picture of iodine status.

ADVERSE EFFECTS

There have been concerns about adverse effects of iodine supplementation, including iodised salt supplementation. Iodine-induced hyperthyroidism has been observed in a number of iodine supplementation programmes, including programmes using iodised salt (Galofré1994; Todd 1995; Bourdoux 1996). In the cases cited, iodisation levels were much higher than those recommended (Todd 1995; Bourdoux 1996) or iodisation occurred in an area of iodine sufficiency (Galofré1994), however, iodine-induced hyperthyroidism has also been observed when lower levels of iodine were given. An associated increase in cardiovascular mortality has been reported. The data suggest that iodine-induced hyperthyroidism mainly occurs in people over forty years of age with nodular goitres, in whom some thyroid autonomy has developed, i.e. thyroid hormone production is not inhibited by increased levels of iodine (Corvilain 1998). The risk of developing iodine-induced hyperthyroidism seems to be higher when initial iodine deficiency was severe and when the initial rise in iodine intake was great. Increases in cases of iodine-induced hyperthyroidism are often only temporary after the introduction of iodisation programmes, but there are also cases in which the disorder persists. As symptoms of iodine-induced hyperthyroidism are often not very severe and very non-specific, it is easy to overlook the problem unless investigators specifically study hormone levels (Stanbury 1998), which was done in none of the studies included in this review. While surveys suggest that the benefits of iodine supplementation outweigh the risks, the potentially fatal nature of iodine-induced hyperthyroidism places an increased importance on adequate monitoring of the levels of iodine in supplements, on adequate monitoring of the iodine status of populations and on early detection of iodine-induced hyperthyroidism (Dunn 1998b).

AUTHORS’ CONCLUSIONS

Implications for practice

The results suggest that iodised salt is an effective means of improving iodine status and support the current endeavours to achieve universal salt iodisation. Variations in the iodine levels in the salt used by some studies suggest that particular care must be taken to ensure the quality of the production and storage of iodised salt - and that there may be situations in which other forms of iodine supplementation may be more appropriate. There was also a suggestion that forms of iodine supplementation should be reassessed in small children, as their salt intake may not be high enough to guarantee adequate iodine levels through the use of iodised salt. There was no suggestion from the studies that the use of iodised salt with the levels of iodine studied had any unwanted side effects, although this point must be regarded with caution as most studies did not specifically consider adverse effects.

Implications for research

More high quality controlled trials (following the CONSORT criteria) are required for assessing the effects of iodised salt in comparison to other forms of iodine supplementation. These studies should also address the question of the most effective dose to be used (under given conditions). Studies should be large and long term, lasting at least two years, including participants of all ages. The outcomes studied should not be restricted to goitre rates and urinary iodine excretion, but should include the other outcome measures specified above, such as mental and physical development in children, mortality, etc. Special attention should be paid to adverse effects. The effects of iodised salt should be assessed separately for children (including very young children who may have a relatively low salt consumption) and adults.
ACKNOWLEDGEMENTS

We thank Sally Green and Steve McDonald of the Australasian Cochrane Centre for helping develop this review, and the China Medical Board of New York for supporting this review.

POTENTIAL CONFLICT OF INTEREST

None known.

SOURCES OF SUPPORT

External sources of support

- Australia Cochrane Centre AUSTRALIA
- China Medical Board (CMB) USA

Internal sources of support

- Chinese Cochrane Centre CHINA
- West China Hospital of Sichuan University CHINA

REFERENCES

References to studies included in this review

Foo 1996 {published data only}

Hintze 1988 {published data only}

l’Ons 2000 {published data only}

Romano 1991 {published data only}

Sooch 1965 {published data only}

Zhao 1999 {published data only}

References to studies excluded from this review

Kimball 1937

Marine 1917/20


Saowakontha 1994

Scrimshaw 1953
Scrimshaw NS, Cabezas A, Castillo F, Mendez J. Results of the administration of potassium iodate, potassium iodide and placebo on endemic goitre and iodine bound to protein in groups of school children [Resultados de la administracion de yodato de potasio, yoduro de potasio y placebos sobre el bocio endemico y sobre los niveles...
Iodised salt for preventing iodine deficiency disorders (Review)

Copyright ©2005 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd
Stanbury 1998

Todd 1995

WHO 1993

WHO 1994

WHO 1996

WHO 2001

Yang 1997

Zen 1994

Zhao 1995

Zimmermann 2000

* Indicates the major publication for the study

** TABLES **

Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Foo 1996</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Randomised controlled trial, blinding not mentioned</td>
</tr>
<tr>
<td>Units of comparison: Villages</td>
<td></td>
</tr>
<tr>
<td>Duration: One year</td>
<td></td>
</tr>
<tr>
<td>Location: Sarawak</td>
<td></td>
</tr>
<tr>
<td>Participants</td>
<td>101 women (15-50 years) and 65 young children (&lt;= 6 years)</td>
</tr>
<tr>
<td>Goitre prevalence: (women) 83% (but large consumption of goitrogenic food)</td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>1. Iodised salt (47.1±9.7 ppm iodine - unclear if iodate or iodide used) (N=48 women, 33 children)</td>
</tr>
<tr>
<td></td>
<td>2. Iodised water (138.6±43.2 µg/l) (N=53 women, 32 children)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>1. Urinary iodine excretion</td>
</tr>
<tr>
<td></td>
<td>2. Goitre (pulpation, women only)</td>
</tr>
<tr>
<td>Notes</td>
<td>Allocation concealment B</td>
</tr>
</tbody>
</table>

Study | Hintze 1988 |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Randomised controlled trial - not blinded</td>
</tr>
<tr>
<td>Units of comparison: Individuals</td>
<td></td>
</tr>
<tr>
<td>Duration: Four years</td>
<td></td>
</tr>
<tr>
<td>Location: Germany</td>
<td></td>
</tr>
<tr>
<td>Participants</td>
<td>334 children (166 female, 168 male), 10 years at the beginning of the study</td>
</tr>
</tbody>
</table>
### Characteristics of included studies (Continued)

Goitre prevalence: 30.5%

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Iodised salt (iodate, 20 ppm iodine) (N=146)</td>
<td>1. Goitre (palpation)</td>
</tr>
<tr>
<td>2. Plain salt (N=188)</td>
<td>2. Neck circumference</td>
</tr>
<tr>
<td>3. Urinary iodine excretion</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Units of comparison:</th>
<th>Duration:</th>
<th>Location:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Romano 1991</td>
<td>Randomised trial - blinding not mentioned</td>
<td>Individuals</td>
<td>Nine months of pregnancy</td>
<td>Italy</td>
</tr>
<tr>
<td>Participants</td>
<td>35 pregnant women (27.1±3.8 years)</td>
<td>Goitre prevalence: unknown for the given sample, 41% in the 8-15 year olds in the area</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>1. Iodised salt (20 ppm iodide, i.e. 15.27 ppm iodine) (N=17)</td>
<td>2. Control - plain salt, but not specifically distributed (N=18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td>1. Thyroid volume (ultrasonography)</td>
<td>2. Urinary iodine excretion</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Serum TSH levels</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Notes</td>
<td>Allocation concealment: B</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Units of comparison:</th>
<th>Duration:</th>
<th>Location:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sooch 1965</td>
<td>Prospective controlled study, randomisation and blinding unclear</td>
<td>Geographical regions</td>
<td>Five years</td>
<td>Himalayan endemic goitre belt, Punjab</td>
</tr>
<tr>
<td>Participants</td>
<td>Over 20,000 villagers, includes specific investigations of school children 5-16 years, boys versus girls, men versus women</td>
<td>Goitre prevalence: 37.6-47%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>1. Iodised salt (20 ppm KI, i.e. 15.27 ppm iodine) (N over 6000)</td>
<td>2. Plain salt (N over 7000)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Iodised salt (25 ppm KIO3, i.e. 14.83 ppm iodine) (N over 6000)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td>1. Goitre (visual and palpation)</td>
<td>2. [131]I uptake by the thyroid and subsequent excretion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Notes</td>
<td>Allocation concealment: B</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Duration:</th>
<th>Location:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhao 1999</td>
<td>Randomised controlled trial, participants not blinded, outcome assessment blinded</td>
<td>18 months</td>
<td>China</td>
</tr>
<tr>
<td>Participants</td>
<td>205 children 8-10 years (50% male)</td>
<td>Goitre prevalence: 26.1-26.5%</td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>1. Iodised salt (42.25 g/kg KIO3, 25 ppm iodine) (N=69)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Characteristics of included studies (Continued)

2. Market iodised salt (iodine content varied, 13-47 ppm) (N=68)
3. Market iodised salt (iodine content varied, 13-47 ppm) plus oral iodised oil 400 mg (N=68)

Outcomes
1. Goitre (palpation)
2. Thyroid volume (ultrasonography)
3. Urinary iodine concentration

Notes
Allocation concealment  B

Study  l’Ons 2000

Methods
Prospective controlled study, randomisation unclear, participants were blind to the intervention
Units of comparison: Schools
Duration: Four months
Location: South Africa

Participants
112 school children (7-16 years) (102 at follow-up)
Goitre prevalence: 9.5-28.2%

Interventions
1. Iodised salt (first 2 batches 18 and 12 ppm iodine, last batch (last 4-5 weeks) 53 ppm (unclear if iodide or iodate)) (N=39)
2. Plain salt (N=63)

Outcomes
1. Goitre (palpation)
2. Urinary iodine excretion

Notes
Allocation concealment  B

Characteristics of excluded studies

Kimball 1937  Not a prospective controlled study but a case-control study comparing goitre rates in children having used iodised salt and those not having used iodised salt.

Marine 1917/20  Possibly a prospective controlled study, but the intervention was not iodised salt but a syrup of hydriodic acid or ferrous iodide.

Saowakhontha 1994  Prospective controlled study comparing iodised fish sauce, iodised salt, iodised water and placebo. The outcome assessed was urinary iodine excretion only, and the values given seem very implausible, by several orders of magnitude.

Scrimshaw 1953  The intervention was potassium iodide or potassium iodate given as tablets and not in salt.

Yang 1997  The comparison in this controlled trial is iodised salt plus sodium selenite versus iodised salt alone - so this is not assessing the effects of iodised salt.

van den Briel 2000  Although the abstract suggests involvement of iodised salt, the primary intervention of this randomised controlled trial was in fact iodised oil.
### Table 01. Quality of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Randomisation</th>
<th>Alloc. concealment</th>
<th>Blinding</th>
<th>Drop-outs</th>
<th>Simil. at baseline</th>
<th>Iodine measured</th>
<th>Compliance checks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foo 1996</td>
<td>Yes</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>No</td>
<td>Intervention iodine levels checked</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Hintze 1988</td>
<td>Yes</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Described, 14%</td>
<td>Yes</td>
<td></td>
<td>No checks Reminders</td>
</tr>
<tr>
<td>L'Ons 2000</td>
<td>Allocation not described</td>
<td>Not mentioned</td>
<td>Participants</td>
<td>Described, 9%</td>
<td>No</td>
<td>Intervention iodine levels and external iodine contamination checked</td>
<td>Reminders, check of salt used</td>
</tr>
<tr>
<td>Romano 1991</td>
<td>Yes</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Yes</td>
<td>No checks</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Sooch 1965</td>
<td>Allocation not described</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Yes</td>
<td>Intervention iodine levels and external iodine contamination checked</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Zhao 1999</td>
<td>Yes</td>
<td>Not mentioned</td>
<td>Outcome assessors</td>
<td>No drop-outs</td>
<td>Yes</td>
<td>Intervention iodine levels checked</td>
<td>Check of salt used</td>
</tr>
</tbody>
</table>

### Table 02. Effects of the intervention on goitre rates and urinary iodine

<table>
<thead>
<tr>
<th>Study</th>
<th>Goitre</th>
<th>Goitre</th>
<th>Urinary iodine</th>
<th>Urinary iodine</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foo 1996</td>
<td>W o m e n:</td>
<td>W o m e n:</td>
<td>POST-INTERVENTION CHANGE FROM BASELINE</td>
<td>POST-INTERVENTION CHANGE FROM BASELINE</td>
<td></td>
</tr>
<tr>
<td>Iodised salt: 27.1%</td>
<td>-33.3% (p &lt; 0.001 for difference with baseline)</td>
<td>Iodised salt: 168.2 µg/L</td>
<td>+131.4 µg/L (significant compared to baseline, p value not given)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iodised water: 47.2%</td>
<td>-35.8% (p &lt; 0.0002 for difference with baseline)</td>
<td>Iodised water: 114.2 µg/L</td>
<td>+102.9 µg/L (significant compared to baseline, p value not given)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Children:
Table 02. Effects of the intervention on goitre rates and urinary iodine  
(Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Goitre</th>
<th>Goitre</th>
<th>Urinary iodine</th>
<th>Urinary iodine</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Iodised salt: 33.4 µg/L</td>
<td></td>
<td>5.3 µg/L (nonsignificant compared to baseline)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iodised water: 97.6 µg/L</td>
<td></td>
<td>87.0 µg/L (significant compared to baseline, p value not given)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hintze 1988</td>
<td>KIO3 salt: 23.8%</td>
<td>-9.1%</td>
<td>KIO3 salt: 60.1±24.1 µg/g creatinine (-74 µg/L)</td>
<td>13.1 µg/g creatinine (-16 µg/L)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plain salt: 22.5%</td>
<td>-6.2% (difference between groups nonsignificant)</td>
<td>Plain salt: 45.1±18.6 µg/g creatinine (-56 µg/L)</td>
<td>2.3 µg/g creatinine (-3 µg/L) (p &lt; 0.0001 for difference between groups)</td>
<td></td>
</tr>
<tr>
<td>L'Ons 2000</td>
<td>Iodised salt: 12.8%</td>
<td>-15.4%</td>
<td>Iodised salt:</td>
<td>25% (overall p &lt; 0.001 compared +49.4% to baseline)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plain salt: 6.3%</td>
<td>-3.2% (statistical comparison inappropriate due to small numbers)</td>
<td>86.9% &gt;= 100 µg/L 65% &gt;= 200 µg/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Romano 1991</td>
<td>KI salt: thyroid volume ~10.2±2.2 ml</td>
<td>-+4%</td>
<td>KI salt: 100.0±39.0 µg/day</td>
<td>63.0 µg/day (p &lt; 0.01 compared to baseline)</td>
<td>Numbers preceded by ‘~’ were estimates derived from a graph; no p values were reported for difference in iodine excretion between groups</td>
</tr>
<tr>
<td></td>
<td>Plain salt: thyroid volume ~11.7±2.4 ml</td>
<td>+16.25% (p &lt; 0.0001 for difference between groups)</td>
<td>Plain salt: 50.0±37.0 µg/day</td>
<td>19.5 µg/day (no significant difference to baseline)</td>
<td></td>
</tr>
<tr>
<td>Sooch 1965</td>
<td>Children:</td>
<td></td>
<td></td>
<td></td>
<td>As the units of comparison were regions, the numbers of people examined varied between the groups and</td>
</tr>
<tr>
<td>Study</td>
<td>Goitre</td>
<td>Goitre</td>
<td>Urinary iodine</td>
<td>Urinary iodine</td>
<td>Notes</td>
</tr>
<tr>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>---------------</td>
<td>---------------</td>
<td>-------</td>
</tr>
<tr>
<td>KI salt (N=3495):</td>
<td>19.1%</td>
<td>-18.5% (N=2529 pre-intervention)</td>
<td></td>
<td></td>
<td>sometimes increased at follow-up; significance not reported</td>
</tr>
<tr>
<td>KIO3 salt (N=3420):</td>
<td>14.6%</td>
<td>-23.8% (N=2964 pre-intervention)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plain salt (N=4544):</td>
<td>40.3%</td>
<td>+2.5% (N=2027 pre-intervention)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General population:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KI salt (N=3290):</td>
<td>18.1%</td>
<td>-24.3% (N=4400 pre-intervention)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KIO3 salt (N=2821):</td>
<td>16.8%</td>
<td>-23.3% (N=4151 pre-intervention)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plain salt (N=4046):</td>
<td>45.7%</td>
<td>-1.3% (N=5076 pre-intervention)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhao 1999</td>
<td>Distributed KIO3 salt (A): 8.7%</td>
<td>-17.4%</td>
<td>Distributed KIO3 salt: 238 µg/L (95% CI 146-264)</td>
<td>+146 µg/L</td>
<td>Significance levels not clearly reported</td>
</tr>
<tr>
<td>Market KIO3 salt (B): 19.1%</td>
<td>-7.4%</td>
<td>Market KIO3 salt: 302 µg/L (274-347)</td>
<td></td>
<td>+207 µg/L</td>
<td></td>
</tr>
<tr>
<td>Market KIO3 salt plus iodised oil (C): 8.8%</td>
<td>-17.7%</td>
<td>Market KIO3 salt plus iodised oil: 295 µg/L (248-346)</td>
<td></td>
<td>+201 µg/L</td>
<td></td>
</tr>
</tbody>
</table>

This review has no graphs.

**INDEX TERMS**

Medical Subject Headings (MeSH)
Cross-Sectional Studies; Dietary Supplements; Iodine [administration & dosage]; Mental Retardation [prevention & control]; Prospective Studies; Sodium Chloride, Dietary [administration & dosage]

Medical MeSH check words
Humans

**COVER SHEET**

Title: Iodised salt for preventing iodine deficiency disorders

Authors: Wu T, Liu GJ, Li P, Clar C

Contribution of author(s): TAIXIANG WU: Protocol development, searching for trials, quality assessment of trials, data extraction, data analysis, review development.
GUANJIAN LIU: Protocol development, quality assessment of trials, data analysis, statistical advice.
PING LI: Quality assessment of trials, searching for trials, data extraction, data analysis.
CHRISTINE CLAR: Searching for trials, quality assessment of trials, data extraction, review development.

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Review first published 2002/3
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Date of most recent SUBSTANTIVE amendment 14 April 2002
What's New Information not supplied by author
Date new studies sought but none found Information not supplied by author
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Date new studies found and included/excluded Information not supplied by author
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