Effect and safety of salt iodization to prevent iodine deficiency disorders: *a systematic review with meta-analyses*

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WHO Library Cataloguing-in-Publication Data

Effect and safety of salt iodization to prevent iodine deficiency disorders: a systematic review with meta-analyses.

1.Sodium Chloride, Dietary. 2.Iodine. 3.Deficiency Diseases – prevention and control. 4.Food, Fortified. 5.Review. 6.Meta-Analysis. I.Aburto, Nancy J. II.Abudou, Minawaer. III.Candeias, Vanessa. IV.Wu, Tiaxiang. V.World Health Organization.

ISBN 978 92 4 150828 5 (NLM classification: QV 283)

Design and layout: Alberto March

Suggested citation

Aburto N, Abudou M, Candeias V, Wu T. Effect and safety of salt iodization to prevent iodine deficiency disorders: a systematic review with meta-analyses. WHO eLibrary of Evidence for Nutrition Actions (eLENA). Geneva: World Health Organization; 2014.

Contents

Abstract

Background: Iodine deficiency, one of the most prevalent micronutrient deficiencies globally, is the main cause of potentially preventable mental retardation in childhood, as well as a spectrum of morbidities referred to as iodine deficiency disorders. Iodization of salt is recommended to prevent and treat many of these disorders.

Objective: To assess the effects and safety of consumption of iodized salt in the prevention of iodine deficiency disorders.

Data sources: The following databases were searched: China National Knowledge Infrastructure, the Cochrane Library, EMBASE, MEDLINE, VIP (the register of Chinese trials developed by the Chinese Cochrane Centre), The Virtual Health Library of the Pan-American Health Organization, WANFANG, the World Health Organization (WHO) International Clinical Trials Platform search portal, and the WHO Global Health Library regional databases. Relevant agencies were contacted, and the reference lists were reviewed.

Study appraisal and synthesis methods: Randomized controlled trials (RCTs), non-RCTs, quasi-experimental, cohort, and multiple cross-sectional studies were included. All studies compared a group of individuals with exposure to iodized salt to a group without exposure to iodized salt. Two or more reviewers independently screened potential studies, extracted study characteristics and outcomes and, when possible, conducted meta-analyses to estimate the effect of iodized salt relative to non-iodized salt. Results are presented as mean differences (MDs), risk ratios (RRs), prevalence ratios (PRs), or odds ratios (ORs), with 95% confidence intervals (CIs).

Results: Two RCTs, 6 non-RCTs, 20 quasi-experimental studies, 16 cohort studies, 42 multiple cross-sectional studies, and 3 studies with mixed designs were included. The numbers of participants ranged from 30 in a cohort study to over 5 000 000 in a multiple cross-sectional registry study. Iodized salt significantly reduced the risk of goitre (non-RCTs RR = 0.59 [95% CI = 0.36 to 0.95]; cohort RR = 0.30 [95% CI = 0.23 to 0.41]; multiple cross-sectional PR = 0.18 [95% CI = 0.14 to 0.22]), cretinism (multiple cross-sectional OR = 0.13 [95% CI = 0.08 to 0.20]), low intelligence (quasi-experimental RR = 0.28 [95% CI = 0.21 to 0.36]; multiple cross-sectional PR = 0.24 [95% CI = 0.07 to 0.82]), and low urinary iodine excretion (multiple cross-sectional PR = 0.45 [95% CI = 0.34 to 0.59]). Iodized salt significantly increased intelligence quotient (quasi-experimental MD = 8·18 [95% CI = 6·71 to 9·65]; multiple cross-sectional MD = 10.45 [95% CI = 4·79 to 16·11]) and urinary iodine excretion (cohort MD = 59.22 [95% CI = 50.40 to 68.04]; multiple cross-sectional MD = 72·35 [95% CI = 44·54 to 100.17]). The results regarding the potential adverse effect of hypothyroidism showed no relationship (cohort OR = 1.14 [95% CI = 0.84 to 1.53]; multiple cross-sectional OR = 1.13 [95% CI = 0.94 to 1.36]), and the results for hyperthyroidism were inconsistent and dependent on study design (cohort OR = 1.36 [95% CI = 1.12 to 1.66]; multiple cross-sectional OR = 0.96 [95% CI = 0.92 to 1.00]). The quality of evidence varied from very low to moderate, depending on outcome and study design.

Conclusions: This review showed that iodized salt has a large effect on reducing the risk of goitre, cretinism, low cognitive function and iodine deficiency. Robust monitoring of salt iodization programmes is important, to ensure safe and effective levels of iodine consumption, especially as countries implement programmes to reduce population salt intake.

Plain language summary

Iodine deficiency causes a spectrum of disorders, from poor growth, retarded development, low urinary iodine excretion and poor cognitive function and goitre, to severe cognitive disability and death. Consistent consumption of small quantities of iodine can prevent these disorders and reverse some, but not all, of the negative effects of iodine deficiency. In 1993, the World Health Organization (WHO), the United Nations Children's Fund (UNICEF) and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) recommended universal iodization of salt to prevent and treat iodine deficiency disorders, and this recommendation remains today. Salt is a good vehicle for iodization because it is consumed almost universally without seasonal variation; there are relatively few production facilities, simplifying quality control; technology for iodization is well established; consumer acceptability of iodized salt is high; and iodization is very inexpensive. However, elevated salt intake results in elevated blood pressure and is associated with cardiovascular disease, and globally most populations consume salt at levels far exceeding needs. Therefore, public health policies based on WHO recommendations seek to reduce population salt intakes.

This systematic review and the corresponding meta-analyses provide the first comprehensive synthesis of available data comparing consumption of, or exposure to, iodized salt on an entire array of iodine deficiency disorders, including goitre, urinary iodine excretion, cretinism, cognitive function and potential adverse effects such as hypothyroidism and hyperthyroidism. Because this review comprised diverse study designs, including randomized controlled trials, non-randomized controlled trials, quasi-experimental, cohort observational, and multiple cross-sectional studies, the study was large enough to explore the effectiveness of iodized salt for preventing iodine deficiency disorders by a number of subgroups, such as age, physiological status, concentration of iodine in the salt, and risk of iodine deficiency disorders at baseline. The additional information on the large number of outcomes and on potential effect modifiers provides important information for assessing and informing an update of the current WHO guidelines on salt iodization, especially in the context of renewed efforts to reduce salt consumption globally.

Background

Iodine deficiency, one of the most prevalent micronutrient deficiencies globally *(1)*, is the main cause of potentially preventable cognitive disability in childhood *(2)*. Iodine is a trace element that is an integral part of the thyroid hormones essential for fetal development, regulation of metabolic activities of cells, and proper growth and development *(3)*. When iodine requirements go unmet, synthesis of thyroid hormones is impaired, resulting in a spectrum of growth, developmental and functional abnormalities referred to as iodine deficiency disorders *(4)*. Goitre, swelling of the thyroid gland, is the most common manifestation of iodine deficiency in both children and adults *(4, 5)*. Severe iodine deficiency during pregnancy results in fetal death or cretinism, marked by severe mental and physical growth retardation. Mild and moderate deficiency during pregnancy hinders fetal development, and offspring are at high risk of speech and hearing defects and impaired motor and physical growth. Iodine deficiency during infancy and early childhood can also cause irreversible deficits in cognitive development.

The World Health Organization (WHO) estimates that approximately 37% of school-age children, 285 million, and nearly 2 billion individuals worldwide, have insufficient iodine intake *(6, 7)*. Mountainous areas are particularly susceptible to iodine deficiency, owing to low levels of iodine in the soil and, thus, the locally grown and raised food *(8)*. However, iodine deficiency is common in many contexts globally and is considered a public health problem in more than 50 countries *(6)*.

WHO, the United Nations Children's Fund (UNICEF) and the International Council for the Control of Iodine Deficiency Disorders Global Network (ICCIDD) promote salt iodization for the control of iodine deficiency disorders because: (i) salt is widely consumed by virtually all population groups in all countries, with little seasonal variation in consumption; (ii) salt production is generally limited to a few centres, facilitating quality control; (iii) technology for salt iodization is well established and relatively easy to transfer to less developed countries; (iv) iodization does not affect the organoleptic properties of salt and, therefore, consumer acceptability is high; and (v) iodization is very inexpensive. To date, more than 120 countries with all levels of deficiency risk are implementing large-scale salt iodization *(9)*. Despite the known benefits of appropriate consumption of iodine, some concern exists that widespread salt iodization could potentially lead to excess iodine intake *(10)*. Furthermore, though policies to support salt iodization and reduce sodium intake are compatible, there is concern that, as populations reduce salt intake to reduce the risk of elevated blood pressure, hypertension and stroke, there may be an increase in iodine deficiency disorders *(11–13)*.

A systematic review of the effectiveness of iodization of salt in preventing iodine deficiency disorders, published in 2002, included data from populations at high risk of iodine deficiency, and controlled trials, and concluded that salt iodization was an effective means of improving iodine status *(14)*. Because it included only six studies, it could not address many outcomes of interest, nor explore potential effect modifiers. The objective of the current systematic review and meta-analyses is to assess the effect and safety of iodized salt compared to non-iodized salt, to prevent the numerous outcomes comprising iodine deficiency disorders. Furthermore, it aims to explore whether results are affected by age, physiological status, concentration of iodine in salt, population salt consumption, or underlying risk of iodine deficiency.

Methods

Study characteristics

Randomized controlled trials (RCTs), non-RCTs, quasi-experimental studies, cohort observational studies and multiple cross-sectional observational studies were included. The participants could be adults (>15 years of age) and children of any age (0–15 years) and of either sex. Populations could be in the general population (free living) or part of specific populations, such as refugees. Studies in apparently healthy populations that may or may not have been at risk or suffered from iodine deficiency were considered. The review also included studies that compared outcomes between groups consuming iodized salt and groups consuming non-iodized salt. Salt could have been fortified with other micronutrients if the only difference between groups was the inclusion of iodine in the fortificant. An attempt was made to collect the following outcomes: all-cause mortality, goitre, mental or physical development, cretinism, cognitive function, urinary iodine concentration, thyroid-stimulating hormone (TSH) concentration, serum thyroglobulin concentration, hypothyroidism, hyperthyroidism, and adverse effects reported by study authors.

Search methods

The following sources were searched: The China National Knowledge Infrastructure (May 2011); the Cochrane Library (Issue 5, 2011), including the Cochrane Controlled Trials Register; EMBASE (1966 to 18 June, 2011); MEDLINE (PubMed 1966 to 31 May, 2011); The Virtual Health Library of the Pan-American Health Organization (May 2011); VIP (the register of Chinese trials developed by the Chinese Cochrane Centre); WANFANG; the WHO International Clinical Trials Registry Platform (18 June 2011); and the WHO Global Health Library regional databases (June 2011). For the detailed search strategy used for the electronic search, see Annex 1. The following websites were also searched: Google, ICCIDD, Thyroid Disease Manager, and the WHO Department of Nutrition for Health and Development. The following organizations were contacted: the Sprinkles Global Health Initiative, the Home Fortification Technical Advisory Group, the nutrition section of UNICEF, the United Nations World Food Programme (WFP), the Micronutrient Initiative (MI), the Global Alliance for Improved Nutrition (GAIN), Helen Keller International (HKI), Sight and Life Foundation, the United States (US) Centers for Disease Control and Prevention (CDC), the Iodine Network, and ICCIDD. The following journals were hand searched: *Chinese Journal of Control of Endemic Diseases*, *Chinese Journal of Epidemiology*, *Chinese Journal of Preventive Medicine* and *Studies of Trace Elements and Health*. The reference lists of identified papers were also scanned.

Data collection and analysis

Selection of studies

Two reviewers independently assessed references for potential relevance. The full manuscript was retrieved when the title, abstract and keywords suggested that the study: (i) compared a group consuming iodized salt to a group consuming non-iodized salt; (ii) reported on an outcome of interest; or (iii) was unclear regarding these criteria. Two reviewers independently assessed all potentially eligible studies, according to the above prespecified inclusion criteria, while two other reviewers assessed the relevance of one third of those selected for full review. An adapted preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart was used to depict the selection of studies for inclusion *(15)*.

Data extraction and management

Two reviewers independently extracted relevant characteristics of the populations and interventions of each study. A third reviewer checked the data, and disagreements were resolved through consensus. In the case of articles originally published in the Chinese language, studies were screened and data extracted in duplicate before translation, and then again after translation to English. Any relevant missing information was requested from the original study authors. In the case of companion papers of a primary study, all available data were simultaneously evaluated, to maximize the yield of information. For RCTs, the risk of bias associated with the method of sequence generation, allocation concealment, blinding, selective reporting, loss to follow-up, and completeness of outcome data was assessed. For observational studies, the risk of bias associated with the method of measuring exposure, collecting outcome data, and selecting participants was also evaluated. The risk of bias was rated as low, unclear or high, according to established criteria *(16, 17)*. A risk of bias graph and a risk of bias summary were generated. The quality of the entire body of evidence was assessed, using the grading of recommendations assessment, development and evaluation (GRADE) methodology *(18)* and GRADEProfiler software (version 3.6, 2011).

Statistical analysis

An overall effect estimate for dichotomous data was calculated as a risk ratio (RR) with 95% confidence interval (CI), or an odds ratio (OR), in the case of rare events *(19)*. For multiple cross-sectional studies, prevalence ratios (PRs) were reported for the overall effect estimate from dichotomous outcomes. For continuous variables, the overall effect estimate was calculated as the difference in means, with 95% CI, between the group consuming iodized salt (intervention) and the group consuming non-iodized salt (control/comparison). To combine data and generate overall effect estimates, RRs, PRs, and mean differences (MDs) were calculated, using the inverse variance method, random effects, and, for ORs, the Peto method, fixed effects meta-analysis in Review Manager software (Copenhagen, 2011) *(17, 19)* was used. When a study reported results for multiple intervention groups with multiple control groups, all comparisons were included in the pooled analysis. When outcomes were assessed at more than one time point, data from the latest time point were used for the pooled analysis, and all relevant time points were used for subgrouping by study duration.

Results were considered to be statistically significant at $\alpha = 0.05$. Evidence was considered conclusive and the estimate precise if the point estimate suggested a benefit or harm and the 95% CI did not overlap a threshold of relevance. If the point estimate was near the null value and the CI did not overlap a threshold of relevance, evidence was considered conclusive of no effect. Conversely, evidence was considered to be inconclusive, and the point estimate imprecise, if the point estimate suggested a benefit or harm but the CI crossed a threshold of relevance. Heterogeneity was assessed through visual inspection of the forest plots and with the I^2 statistic quantifying inconsistency across studies *(20, 21)*. An I^2 statistic of 75% or greater was considered an important level of heterogeneity, and, when found, the data in meta-analyses were combined, while taking note of the heterogeneity and attempting to explain the heterogeneity by examining individual study and subgroup characteristics.

Specific objectives were tested and potential reasons for heterogeneity explored, using the following subgroups: age group (child versus adult versus all ages); concentration of iodine in salt (<20 parts per million [ppm] versus 20–40 ppm versus >40 ppm); mean salt intake (<2 g/day versus 2–4 g/day versus >4 g/day); physiological status (pregnant versus non-pregnant); iodine deficiency in the population at baseline (adequate iodine status versus mild versus moderate versus severe iodine deficiency); and duration of population exposure to iodized salt (<1 year versus 1–5 years versus 5–15 years versus >15 years).

Results

As shown in Fig. 1 (see p.17), the search of electronic databases yielded 9720 publications and other sources identified 90 publications. After scanning the titles, 7113 publications were excluded because of being duplicates or obviously not relevant. Of the 2697 remaining publications, 2416 were excluded after review of the abstract, for not meeting basic inclusion criteria. A total of 281 full-text publications were reviewed and 142 excluded for lack of a comparison between a group consuming iodized salt and a group not consuming iodized salt via intervention, quasi-experiment, cohort or multiple cross-sectional, pre/post study design. Upon review of complete text, another 26 publications were identified as duplicates or companion papers to original studies. Of the 113 potential studies for inclusion, 24 are awaiting classification, as additional information is being sought from the original authors *(22–52)*. Therefore, the current review includes 89 studies. Two studies are RCTs *(53, 54)*. Six are non-RCTs *(55–62)*. Twenty are quasi-experimental studies *(63–92)*. Sixteen are cohort observational studies *(93–111)*. Forty-two are multiple cross-sectional studies *(112–156)*. Three studies with mixed designs were identified: one with cohort, multiple cross-sectional and quasi-experimental components *(157)*; one with cohort and multiple cross-sectional components *(158)*; and one with multiple cross-sectional and quasi-experimental components *(159)*. One study originally reported a non-RCT, and reported subsequent data from a cross-sectional observational follow-up *(60)*. Two ongoing studies were also identified *(160, 161)*.

Studies were published in English, Chinese, French, German and Spanish and were conducted in Argentina, Azerbaijan, Bangladesh, China, Colombia, Cote d'Ivoire, Denmark, Germany, Guatemala, India, the Islamic Republic of Iran, Italy, Kazakhstan, Malaysia, Mongolia, Morocco, Pakistan, Poland, South Africa, Spain, Switzerland, Tajikistan, Thailand, Uganda, the United States of America and Uzbekistan. A summary of the characteristics of included studies is presented in Table 1 (see p. 18) and Annex 2.

Effect estimates

Goitre prevalence

The results for goitre prevalence for all study designs can be found in Table 2 (see pp. 19 and 20). In one RCT study in school-aged children, 4 years of availability of iodized salt in the marketplace, combined with the instruction in the intervention group to consume iodized salt, did not result in a significant change in goitre prevalence relative to control (RR = 1.06 [95% CI = 0.69 to 1.62]). The other RCT qualitatively noted that thyroid volume did not change in a group of pregnant women consuming iodized salt; whereas, in the control group, thyroid volume increased significantly during pregnancy ($P < 0.001$).

Three non-RCTs with four comparisons contributed to a meta-analysis and found iodized salt reduced the risk of goitre relative to control (RR = 0.59 [95% CI = 0.36 to 0.95]). Eleven cohort studies with 13 comparisons contributed to the meta-analysis, which found iodized salt was associated with decreased risk of goitre (RR = 0.30 [95% CI = 0.23 to 0.41]). The meta-analysis of 34 multiple cross-sectional studies with 44 comparisons also associated exposure to iodized salt with decreased prevalence of goitre (PR = 0.18 [95% CI = 0.14 to 0.22]). Additional studies of all designs that could not be included in the meta-analyses supported the findings that iodized salt decreases the risk or prevalence of goitre (see Annex 3).

Subgroup analyses

Subgroup analyses (see Table 2, pp. 19 and 20) of cohort studies and multiple cross-sectional studies suggest that the consumption of iodized salt reduces the risk of goitre regardless of age group, concentration of iodine in salt, or underlying risk of iodine deficiency at baseline, with no significant differences among groups. The risk reduction or prevalence reduction (depending on study design) was significantly larger as the duration of exposure to iodized salt increased. There were insufficient studies to conduct meaningful subgroup meta-analyses by estimated mean salt consumption or physiological status.

Cretinism

There were no RCTs, non-RCTs, or quasi-experimental or cohort studies measuring cretinism that reached the inclusion criteria. The meta-analysis of two multiple cross-sectional studies with two comparisons detected a reduced odds of cretinism with availability of iodized salt (OR = 0.13 [95% CI = 0.08 to 0.20]). One other study reported that, at the survey before iodization of salt of an entire village in China, there were 88 individuals with cretinism and at the follow-up survey of the village 21 years after the introduction of iodized salt, there were only four incident cases of cretinism.

Cognitive function

There were 18 quasi-experimental studies with 31 comparisons that contributed to the meta-analysis of cognitive function and found improved cognitive function, measured by intelligence quotient (IQ), with iodized salt compared to non-iodized salt (see Table 3, p. 21; MD = 8.18 [95% CI = 6.71 to 9.65]). The meta-analysis of 16 studies with 25 comparisons found a reduced risk of low intelligence (IQ < 70) with iodized salt (RR = 0.28 [95% CI = 0.22 to 0.36]). The meta-analysis of two multiple cross-sectional studies with three comparisons found an increase in IQ with iodized salt (MD = 10.45 [95% CI = 4.79 to 16.11]). The results of the one multiple cross-sectional study that measured prevalence of low intelligence were consistent with an improvement in cognitive function with iodized salt (PR = 0.24 [95% CI = 0.07 to 0.82]).

Subgroup analyses

There was a significant increase in IQ when the concentration of iodine in the salt was 20–40 ppm (MD = 7.59 [95% CI = 5.19 to 9.99]); >40 ppm (MD = 14.24 [95% CI = 12.30 to 16.18]); or unknown (MD = 6.51 [95% CI = 4.53 to 8.49]), with a greater improvement at the higher concentration of iodine compared to the other two groups ($P < 0.01$). Iodized salt was also associated with a reduced risk of having low intelligence, regardless of the concentration of iodine in the salt: 20–40 ppm (RR = 0.16 [95% CI = 0.10 to 0.25]); >40 ppm (RR = 0.20 [95% CI = 0.12 to 0.32]); or unknown (RR = 0.40 [95% CI = 0.29 to 0.54]).

There was a significant increase in IQ with iodized salt in those studies in which there was a population risk of mild (MD = 8.31 [95% CI = 5.77 to 10.84]), moderate (MD = 4.01 [95% CI = 1.28 to 6.74]), or severe (MD = 9.05 [95% CI = 6.84 to 11.26]) iodine deficiency, and there was a corresponding significant reduction in risk of low intelligence (mild RR = 0.24 [95% CI = 0.14 to 0.40]; moderate RR = 0.39 [95% CI = 0.16 to 0.95]; severe RR = 0.29 [95% CI = 0.20 to 0.42]). There was no difference in results based on the duration of exposure to iodized salt.

Urinary iodine excretion

The meta-analysis of three cohort studies with nine comparisons that reported urinary iodine excretion as µg/L, and the meta-analysis of two studies with two comparisons that reported µg/g creatinine, detected a significant increase in urinary iodine excretion with iodized salt relative to non-iodized salt (MD = 59.22 [95% CI = 50.40 to 68.04] and MD = 87.35 [95% CI = 49.74 to 124.97]) (see Table 4, p. 22). The meta-analysis of five multiple cross-sectional studies with five comparisons that reported mean urinary iodine excretion as µg/L, and the three studies with four comparisons that reported µg/g creatinine, detected a significant increase in urinary iodine excretion with consumption of iodized salt (MD = 72.35 [95% CI = 44.54 to 100.17] and MD = 104.11 [95% CI = 55.28 to 152.94]).

The meta-analysis of the two non-RCTs with two comparisons reporting risk of iodine deficiency suggested a potential benefit of iodized salt (RR = 0.42 [95% CI = 0.14 to 1.28]). However, there were only 233 participants and 57 events. The meta-analysis of the two cohort studies with six comparisons detected a significant reduction of risk in iodine deficiency with iodized salt (RR = 0.40 [95% CI = 0.26 to 0.60]). The same was found in the meta-analysis of 10 multiple cross-sectional studies with 10 comparisons (PR = 0.45 [95% CI = 0.34 to 0.59]). The RCTs, non-RCTs, cohort studies and multiple cross-sectional studies that could not be incorporated into meta-analyses all reported increased urinary iodine excretion with iodized salt (see Annex 4).

Subgroup analyses

Exposure to iodized salt increased urinary iodine excretion in children, adults and all ages combined. There was no statistical difference in the increase in urinary iodine excretion by concentration of iodine in salt or underlying risk of iodine deficiency. There was no consistent relationship between duration of exposure and urinary iodine excretion. No studies reported salt intake and no studies were conducted in pregnant women (data not shown).

Thyroid hormones

One cohort study reported and detected a significant decrease in TSH (MD = –9.80 [95% CI = –10.85 to –8.75]) in children exposure to iodized salt. The meta-analysis of the two multiple cross-sectional studies with four comparisons reporting TSH detected no change with iodized salt (MD = 0.18 [95% CI = –0.28 to 0.64]). The meta-analysis of one multiple cross-sectional study with three comparisons detected a significant decrease in thyroglobulin with iodized salt (MD = –8.73 [95% CI = –9.31 to –8.14]) *(147)*.

Hypothyroidism and hyperthyroidism

The meta-analyses of four cohort studies with four comparisons and of four multiple cross-sectional studies with four comparisons found no relationship between iodized salt and hypothyroidism (see Table 5, p. 23) (cohort: OR = 1.14 [95% CI = 0.84 to 1.53]; cross-sectional: OR = 1.13 [95% CI = 0.94 to 1.36]). The meta-analysis of two cohort studies with two comparisons showed an increased odds of hyperthyroidism with iodized salt (OR = 1.36 [95% CI = 1.12 to 1.66]). However, the meta-analysis of five multiple cross-sectional studies with five comparisons detected no relationship between iodized salt and hyperthyroidism (OR = 0.96 [95% CI = 0.92 to 1.00]). One study measured the incidence of hyperthyroidism indicated by incident use of anti-thyroid medication in the population of Denmark, and included more than 5 000 000 individuals *(117)*, whereas, all other studies measured low circulating TSH in samples of individuals. Without the study from Denmark, the meta-analysis found that iodized salt reduced the odds of hyperthyroidism (OR = 0.50 [95% CI = 0.40 to 0.63]). There were too few studies to conduct meaningful subgroup analyses of hypothyroidism or hyperthyroidism.

Other adverse outcomes

There was one cohort study that reported consumption of iodized salt significantly increased the odds of elevated positive anti-thyroid microsomal antibody (ATMA) (OR = 2.51 [95% CI = 1.93 to 3.27]). There were two multiple cross-sectional studies with contradictory results. The meta-analysis of those studies detected no increased odds of elevated ATMA with iodized salt (OR = 1.27 [95% CI = 0.94 to 1.71]). The same was true for anti-thyroglobin antibody (anti-Tg) (OR = 1.43 [95% CI = 1.08 to 1.89]). One multiple cross-sectional study of school-aged children reported an increased risk of elevated urinary iodine excretion with 10 years of exposure to iodized salt (RR = 1.35 [95% CI = 1.06 to 1.74]) (see Table 5, p. 23).

Other outcomes

There were no studies reaching inclusion criteria that reported all-cause mortality, mental development or physical development.

Quality of the body of evidence

The risk of bias of included studies is summarized in the risk of bias graph summary table (see Annex 5). The two RCTs were of poor methodological quality and neither followed the consolidated standards of reporting trials (CONSORT) recommendations *(162)*. They did not report details on power calculation, randomization method, flow of participants, or blinding of outcome assessment. The six non-RCTs were at high risk of bias, owing to inadequate allocation concealment, unclear blinding of participants and outcome assessors, unclear risk of attrition bias, and lack of comparability between the intervention and control group in half of all studies*)*. The risk of bias of quasi-experimental, cohort and multiple cross-sectional studies was unclear. Most quasi-experimental and multiple cross-sectional studies had complete outcome data; however, blinding of personnel and outcome assessors was unclear. Four cohort studies did not report outcome data completely and four were unclear. Five cohort studies had unclear sampling methodology or unclear methods in general. All other cohort studies suggested no other form of bias. Of the multiple cross-sectional studies, seven were at high risk of bias because of sampling methods that did not ensure comparability between the participants of surveys, or differences in the methods for measuring outcomes between surveys. Ten had unclear sampling or unclear methods in general.

The quality of evidence (see Annex 6) for goitre ranged from low to moderate. Many studies lacked the detail needed to clearly understand bias; but the large effect sizes detected in quasi-experimental, cohort and multiple cross sectional studies led to the upgrade of that evidence.

For cretinism, the quality of the body of evidence was moderate. All studies were multiple cross-sectional; however, the quality of evidence was upgraded from low to moderate because of the very large effect size.

The quality of evidence for cognitive function was low. All studies were either quasi-experimental or multiple cross-sectional and were conducted in China. It was not possible to assess the risk of bias in most studies because of the limited information in published reports; therefore, the evidence was conservatively downgraded because of the potential of high risk of bias. Nonetheless, because the actual risk of bias was unclear, the evidence was then upgraded, owing to the large effect on both mean difference in IQ and risk of low intelligence. The net effect was therefore that the evidence was graded as low.

The evidence for urinary iodine excretion was low to moderate quality. Data were from cohort and multiple cross-sectional studies; however, all studies reported large effect sizes.

The body of evidence for hypothyroidism was very low quality and that for hyperthyroidism was very low and low quality. The studies reporting hypothyroidism had cohort or multiple cross-sectional designs. The evidence was downgraded, owing to inconsistency. Hyperthyroidism was reported in cohort and multiple cross-sectional studies. The evidence was not downgraded for any reason in the cohort studies; however, the evidence from multiple cross-sectional studies was downgraded because of imprecision.

The evidence for thyroid hormones or other adverse effects was very limited and the quality was either low or very low.

Discussion

This review found that exposure to iodized salt was associated with reduced risk or prevalence of goitre, cretinism, low intelligence or low urinary iodine excretion, as well as increased mean IQ and increased median and mean urinary iodine excretion. There was no clear relationship between iodized salt and any adverse effects, including increased hypothyroidism or hyperthyroidism.

Because of the limited number of RCTs and non-RCTs found in the previous systematic review *(14)*, a broad search strategy was intentionally used for the current review, to include quasi-experimental, cohort observational and multiple cross-sectional studies with pre/post designs. The review also benefited from the ability to search Chinese databases, which included numerous reports from monitoring and evaluation of salt iodization programmes in that country. Though the current review included only two RCTs, the large number of studies, 89, allowed exploration of the many outcomes comprising iodine deficiency disorders; potential adverse effects; and potential effect modification by age, concentration of iodine in salt, underlying risk of iodine deficiency, and duration of exposure.

Data consistently showed a correlation between exposure to iodized salt and reduced risk of goitre. The studies spanned eight decades and multiple countries and continents, including Africa, Asia, Europe, North America and South America. The results were consistent, regardless of age group, concentration of iodine in salt or underlying risk of iodine deficiency. Some results suggested that the longer the population exposure to iodized salt was, the lower the prevalence of goitre would be. The present results are similar to those found in a recent systematic review of the effect of iodine supplementation, mainly in the form of iodized oil, which reported reduced risk of goitre in children receiving iodine *(163)*. Though both interventions appear to be effective in reducing goitre, salt iodization provides an inexpensive platform for unparalleled population reach *(9)*. For this reason, WHO, UNICEF and the ICCIDD Global Network appeal to all countries to iodize salt, regardless of the underlying population risk of iodine deficiency disorder, in order to protect everyone, including the most vulnerable.

The current review found convincing results of the beneficial effect of iodized salt on cretinism. This finding is consistent with a narrative review published in 1989, which concluded that "iodine deficiency correction" during pregnancy reduced cases of cretinism *(164)*. Another review found consumption of iodized oil during pregnancy to be highly effective at reducing incident cretinism *(165)*. A more recent

review reinforced the findings by showing that increased intake of iodine from any source during pregnancy reduced cretinism *(166)*. The latter review also summarized the experimental evidence, which showed that, in animals, iodine deficiency causes fetal brain damage, and adequate iodine consumption during pregnancy is protective. The body of knowledge around the importance of the effect of iodine intake during pregnancy on the brain is undisputed, and the results of the current review support the contention that salt iodization is an effective strategy to increase iodine intake during pregnancy and reduce cretinism and brain damage *(164, 166–169)*.

The current review found that children exposed to iodized salt during gestation, infancy and early childhood had higher IQ and reduced risk of low intelligence compared to unexposed children. A previous meta-analysis of 18 studies of children living in areas with iodine sufficiency versus those living in iodine-deficient areas also concluded that exposure to iodized salt was positively associated with cognition in children *(170)*. Children exposed to iodine had an average IQ score of more than 13 points higher than children not exposed to iodine. The present review has reported a similar increase of approximately 8 to 10 IQ points with exposure to iodized salt. The results were also consistent with a review that found iodine supplementation during pregnancy and infancy improved developmental scores in infants *(166)*, and a separate review that found improved cognitive function with iodine supplementation *(163)*. The evidence suggests that exposure to iodine improves cognitive development in infants and children and iodization of salt is an effective strategy to increase exposure during pregnancy, infancy and early childhood *(171)*. However, the current review did not compare delivery mechanisms for consumption of iodine and cannot determine whether salt iodization is the most effective intervention for reaching pregnant and lactating women and infants, and thus conclusions in this regard cannot be drawn from the current review alone.

Because of the large number of studies in the current review, it was possible to investigate potential adverse effects such as increased hypothyroidism and hyperthyroidism. The meta-analysis of inconsistent individual studies showed no overall effect of iodized salt on hypothyroidism. A previous review without meta-analysis cited four studies that suggested an association between increased population iodine intake and prevalence of hypothyroidism *(172)*. Of these four studies, three were observational reports and the one experimental study was included in the current review. Across all studies, there were few events of hyperthyroidism and the results varied by study design. There have been several studies that correlated iodine-induced hyperthyroidism to the introduction of iodized salt *(173–175)*. In many of these cases, iodization levels were much higher than those recommended *(174, 175)*, or iodization occurred in an area of iodine sufficiency *(173)*. Nonetheless, long-term studies suggest that an increase in the prevalence of iodine-induced hyperthyroidism is temporary and that within a few years of population exposure to iodized salt, the prevalence of hyperthyroidism reverts to baseline levels or even lower *(117, 171)*. The few studies reporting anti-thyroid antibodies had contradictory findings and more data are needed to formulate conclusions regarding these outcomes. Currently, there is little evidence of increasing health risks with population-wide salt iodization programmes. However, potentially serious adverse effects such as hypothyroidism or hyperthyroidism may occur in some individuals with the introduction of iodized salt at the population level. Therefore, salt iodization programmes require robust monitoring and evaluation systems to ensure the population consumes safe levels of iodine *(176)*, and to inform adjustments to iodization programmes, as public health efforts to reduce sodium intake mature.

Many of the analyses suffered from heterogeneity stemming from known (age group, region of world, decade of study implementation, sampling methodology, measurement techniques, iodine status at baseline, iodine concentration in salt, salt consumption patterns, other dietary patterns) and unknown factors. This limitation notwithstanding, the results were very consistent for most outcomes measured. Iodized salt was associated with a lower prevalence of goitre in children, adults and the entire population; in populations consuming iodized salt at <20 ppm, 20–40 ppm, or >40 ppm; and in populations with risk of severe, moderate or mild iodine deficiency at baseline. The other outcomes with sufficient data to make such comparisons (i.e. cognitive function, urinary iodine excretion) showed similar results. Additionally, studies that could not be combined in the meta-analyses for these outcomes were also consistent with a benefit of consuming iodized salt. The heterogeneity of the studies may make the numerical value of the estimated effect sizes less important, but the large effect sizes and consistent results show the value of the meta-analyses *(19)*, despite the heterogeneity, to conclude that iodized salt is effective at reducing the risk of many iodine deficiency disorders.

Limitations of the study

A limitation of the review was an insufficient number of studies reporting the level of salt intake or the level of overall iodine intake to test the potential effect modification of these variables on the ability of iodized salt to reduce iodine deficiency disorders. Additionally, many studies reported the recommended concentration of iodine in fortification programmes as the iodine level in salt, and did not consider the actual level consumed. Though potassium iodate in salt is stable *(10)*, programme monitoring data have shown the presence of suboptimal fortification and some pre-consumption losses during transport, handling and storage. Future studies and monitoring reports should attempt to report the mean salt intake of children, adults and pregnant women, as well as the iodine concentration in salt, in order to test the potential modifying effect of these factors. Furthermore, lack of methodological detail in some studies included in the review led to their exclusion from the meta-analyses and, in some cases, difficulty in assessing the bias of studies or the body of evidence. All studies reporting intelligence outcomes were conducted in China. The body of evidence could be strengthened if these results were reproduced in other countries. Multiple cross-sectional studies without a baseline before iodization were not included in the current review. Including such studies would provide more information on the effectiveness of varying levels of iodine in salt. This information would be particularly important as countries strengthen efforts to decrease overall population salt intake.

Conclusion

The current review is the largest compilation of studies regarding the effect of iodized salt on health outcomes to date. The results suggest that iodized salt is an effective means of improving iodine status and preventing many iodine deficiency disorders. Though the quality of the body of evidence for some outcomes could be strengthened, data were compiled from all over the world; spanning more than eight decades; from rural and urban areas; from low-, middle- and high-income countries; and from countries and regions traditionally plagued by severe iodine deficiency. The results were mostly consistent with a benefit of salt iodization. Moreover, there was little evidence of adverse effects from salt iodization. Continued monitoring of programmes should provide more high-quality evidence on outcomes such as mental and physical development, and on potential adverse effects such as hypothyroidism, hyperthyroidism and elevated urinary iodine excretion. These data are needed to ensure iodization programmes are not inadvertently causing harm.

Additionally, the focus on operational research and monitoring data is particularly important as countries strive to reach global targets for reduced population sodium intake. As sodium intake decreases, iodization levels in salt may need to be adjusted, to ensure that the most vulnerable pregnant women, infants and young children receive the iodine they need.

Contributions

The priority questions to be addressed for the review were discussed and developed by the WHO guideline development group – micronutrients, and the protocol was subsequently developed to address the priority areas of interest for the review of the WHO guideline on salt iodization. Searches were run by NJA and TW. Assessment of inclusion, data extraction and validity assessment were carried out by all authors. Data analyses were completed by NJA, with input from MA, VC and TW. The GRADE evidence profiles were developed by NJA. The first draft of the manuscript submitted for review by the guideline development group – micronutrients was prepared by NJA, with support from MA, VC and TW. Substantial intellectual input on research methods and interpretation of results was provided by all authors. All authors read, provided input to, and agreed the final draft of the manuscript.

Acknowledgements

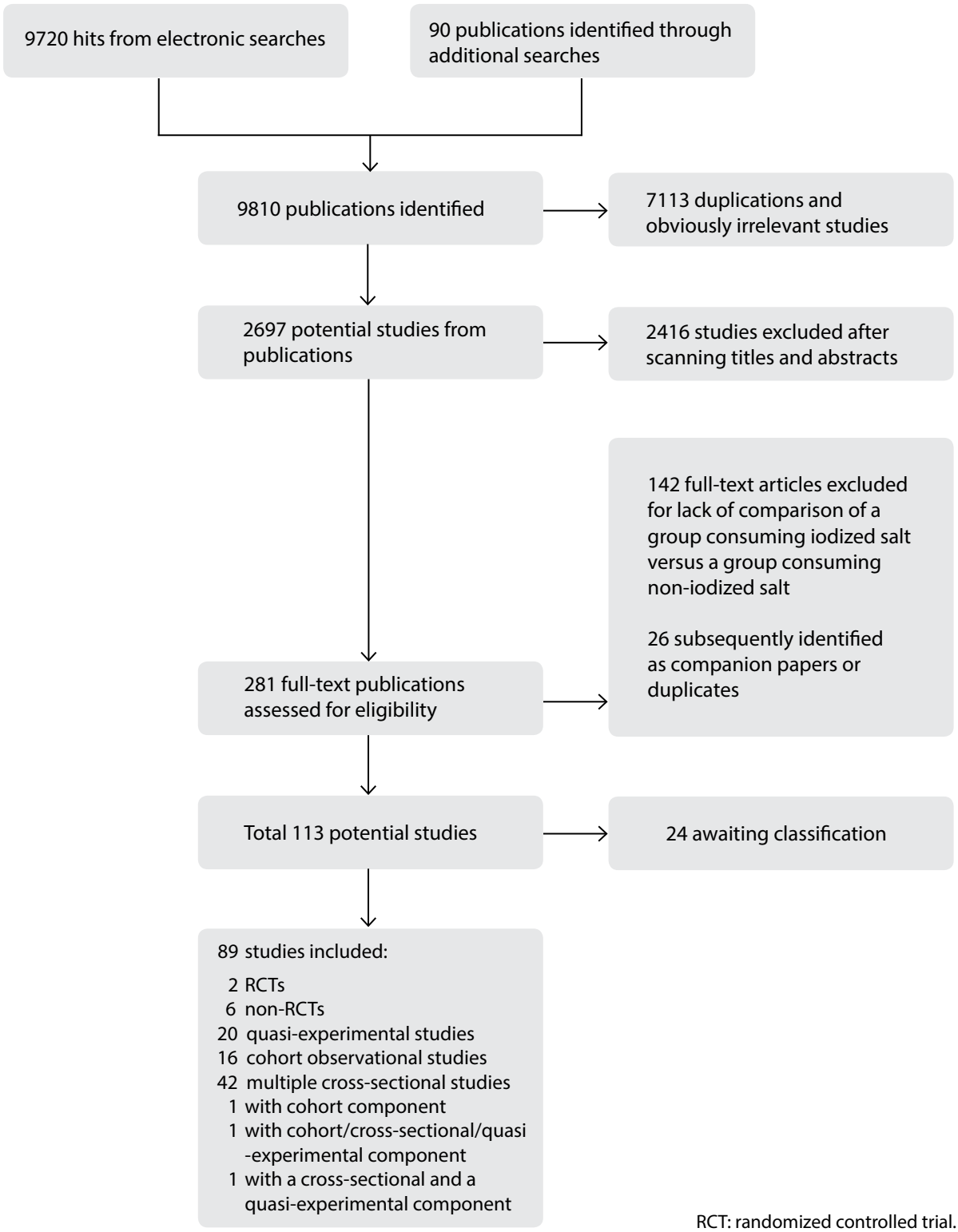
Funding for this review came from various sources, including WHO Department of Nutrition for Health and Development, the Government of Luxembourg, the Bill & Melinda Gates Foundation and the Micronutrient Initiative. Their support is gratefully acknowledged, along with the support provided by members of the WHO guideline development group – micronutrients in providing guidance on document scope.

Declaration of competing interests

MA and TW received funding from the Evidence and Programme Guidance Unit, Department of Nutrition for Health and Development, WHO, to attend technical meetings in Geneva to work in collaboration on the review; there was no further financial support from any organization for the submitted work that might have an interest in the submitted work in the previous 3 years; and there were no other relationships or activities that could appear to have influenced the submitted work.

NJA and VC were staff members of WHO when this work was initiated. NJA is currently a staff member at the United Nations World Food Programme. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the views, decisions or policies of WHO or the United Nations World Food Programme.

Fig. 1 Flowchart of screening, inclusion and exclusion



RCT: randomized controlled trial.

Table 1. Summary of studies reaching inclusion criteria for systematic review on the effect of salt iodization on iodine deficiency disorder

Study design	Number of studies	Sample size	Participants	Duration	Allocation	Intervention[a]	Control/comparison
Randomized controlled trials *(53, 54)*	2	35 to 334 (total = 369)	Children/ pregnant women	6 months to 4 years	Random group assignment	Participants instructed to only purchase and consume iodized salt, or provided iodized salt	Randomly assigned participants instructed to only purchase and consume non-iodized salt
Non-randomized controlled trials *(55–62)*	6	102 to 21 616 (total >32 350)	Children/ women all ages	4 months to 7 years	Clusters (cities) or households non-randomly allocated to receive iodized salt	3 studies: participants were random sample of residents of cities where iodized salt was made available	Random sample of population that did not have iodized salt available
						3 studies: participants received iodized salt directly	Participants received non-iodized salt
Quasi-experimental *(63–92)*	20[b]	91 to 2592 total >14 000)	Children	9 months' gestation plus 1–4 years[c]	Divided population by birth date based on being born before or after USI in village	17 studies: children exposed to iodized salt during gestation, infancy and early childhood through USI	Children from same villages not exposed to iodized salt during gestation, infancy and early childhood
				10–15 years	Compared individuals before and after USI from villages with USI to those without USI	3 studies: children exposed to iodized salt during gestation, infancy and early childhood through USI	Children from similar villages without availability of iodized salt and therefore not exposed to iodized salt
Cohort observational *(93–111)*	16[b]	30–500 000 (total >910 000)	Children/ women/all ages	6 months to 10 years	Entire population of village or random sample of population followed from pre to post availability of iodized salt	4 studies: households provided iodized salt	Same sample of participants measured before iodized salt was available
						8 studies: population exposed to iodized salt through USI implementation	
						4 studies: sample exposed to iodized salt through availability in market	
Multiple cross-sectional *(112–156)*	42[b]	40–5 000 000 (total >7 000 000)[d]	Children/ adults/all ages	1–36 years	Representative cross-sectional surveys	Sample of population measured after iodized salt was available or the implementation of USI	Sample of population measured before iodized salt was available

USI: universal salt iodization.

[a] All studies compared groups that consumed iodized salt to groups that consumed non-iodized salt. There were no studies comparing multiple micronutrient fortified salt with and without iodine.

[b] Three studies had mixed designs. One study measured goitre in both a cohort of individuals and a quasi-experimental sample of individuals, and also measured urinary iodine excretion in multiple cross-sectional studies of children of the same age over time *(157)*. One study measured cretinism in a multiple cross-sectional design and measured a cohort of individuals for all other outcomes *(158)*. One study measured intelligence in two study samples: one was a multiple cross-sectional design and the other was a quasi-experimental design *(159)*.

[c] Most quasi-experimental studies were unclear on the precise period of exposure to iodized salt in the intervention group and merely noted that the intervention group was exposed to iodized salt during the period of gestation and the first years of life.

[d] 41 of 42 studies had a total sample size of 2 000 000. One study was a registry study in Denmark that included >5 000 000 individuals *(117)*.

Table 2. Effect of iodized salt on goitre prevalence, by study design and by subgroup

Study design[a]	Group	Number of studies	Number of comparisons	I^2	RR/PR	95% CI
RCT[b]	All	1	1	—	1.06	0.69 to 1.62
Non-RCT	All	3	4	99	0.59	0.36 to 0.95
Quasi-experimental	All	1	1	—	0.10	0.08 to 0.13
Cohort	All	11	13	99	0.30	0.23 to 0.41
	Age group					
	Children	2	2	100	0.09	0.08 to 0.11
	Adults	1	1	—	0.45	0.27 to 0.75
	All ages	8	10	99	0.32	0.24 to 0.43
	Concentration of iodine in salt, ppm					
	<20	4	6	98	0.39	0.31 to 0.50
	20–40	3	3	99	0.24	0.08 to 0.74
	>40	3	3	96	0.37	0.15 to 0.92
	Underlying risk of iodine deficiency[c]					
	Adequate iodine status	0	—	—	—	—
	Mild iodine deficiency	4	4	100	0.29	0.16 to 0.54
	Moderate iodine deficiency	1	1	—	0.43	0.21 to 0.87
	Severe iodine deficiency	7	8	99	0.30	0.18 to 0.48
	Duration of exposure, years					
	<1	3	3	34	0.64	0.57 to 0.73
	1–5	7	9	99	0.28	0.20 to 0.30
	5–15	1	1	—	0.09	0.08 to 0.10
	>15	0	—	—	—	—

Study design[a]	Group	Number of studies	Number of comparisons	I^2	RR/PR	95% CI
Multiple cross-sectional	All	34	44	100	0.18	0.14 to 0.22
	Age group					
	Children	23	32	100	0.22	0.17 to 0.29
	Adults	2	2	99	0.17	0.04 to 0.85
	All ages	11	11	100	0.10	0.06 to 0.16
	Concentration of iodine in salt, ppm					
	<20	2	2	54	0.11	0.07 to 0.17
	20–40	17	24	99	0.21	0.15 to 0.28
	>40	8	9	100	0.13	0.06 to 0.25
	Underlying risk of iodine deficiency[c]					
	Adequate iodine status	3	4	92	0.20	0.12 to 0.34
	Mild iodine deficiency	9	11	99	0.11	0.07 to 0.18
	Moderate iodine deficiency	7	11	99	0.35	0.25 to 0.49
	Severe iodine deficiency	15	16	100	0.15	0.10 to 0.22
	Duration of exposure, years					
	<1	1	1	—	1.07	0.88 to 1.30
	1–5	9	10	100	0.29	0.18 to 0.46
	5–15	16	25	100	0.17	0.12 to 0.24
	>15	6	6	100	0.08	0.04 to 0.17

95% CI: 95% confidence interval; ppm: parts per million; PR: prevalence ratio; RCT: randomized controlled trial; RR: risk ratio.

[a] Studies that could not be combined in the appropriate meta-analysis by study design all showed reduced prevalence of goitre with iodized salt (1 non-RCT, 1 quasi-experimental, 1 cohort and 5 multiple cross-sectional studies).

[b] One RCT in pregnant women reported no increase in thyroid volume during pregnancy with iodized salt versus increase in thyroid volume in control.

[c] Risk estimated by prevalence of goitre or median urinary iodine excretion in the population.

Table 3. Effect of iodized salt on change in intelligence quotient, by study design and by subgroup

Study design[a]	Group	Number of studies	Number of comparisons	I^2	MD	95% CI
Quasi-experimental	All	18	31	89	8.18	6.71 to 9.65
	Concentration of iodine in salt, ppm					
	<20	0	—	—	—	—
	20–40	5	11	86	7.59	5.19 to 5.19
	>40	3	3	0	14.24	12.30 to 16.18
	Underlying risk of iodine deficiency[b]					
	Adequate iodine status	3	3	93	5.35	-4.06 to 14.76
	Mild iodine deficiency	6	8	91	8.31	5.77 to 10.84
	Moderate iodine deficiency	4	4	52	4.01	1.28 to 6.74
	Severe iodine deficiency	12	13	88	9.05	6.84 to 11.26
	Duration of exposure, years					
	<1	0	—	—	—	—
	1–5	10	19	87	8.17	6.17 to 10.18
	5–15	5	5	87	9.44	5.95 to 12.94
	>15	0	—	—	—	—
Multiple cross-sectional	All	2	3	92	10.45	4.79 to 16.11

95% CI: 95% confidence interval; MD: mean difference; ppm: parts per million.
[a] No randomized controlled trials (RCTs), non-RCTs or cohort observational studies reaching inclusion criteria reported on the effect of iodized salt on change in intelligence.
[b] Risk estimated by prevalence of goitre or median urinary iodine excretion in the population.

Table 4. Effect of iodized salt on change in urinary iodine excretion

Study design[a]	Group	Units	Number of studies	Number of comparisons	I^2	MD[b]	95% CI
Cohort	All	µg/L	3	9	100	59.22	50.40 to 68.04
	All	µg/g creatinine	2	2	92	87.35	49.74 to 124.97
Multiple cross-sectional	All	µg/L	5	5	99	72.35	44.54 to 100.17
	All	µg/g creatinine	3	4	99	104.11	55.28 to 152.84

95% CI: 95% confidence interval; MD: mean difference; ppm: parts per million.

[a] No randomized controlled trials (RCTs), non-RCTs or quasi-experimental studies reaching inclusion criteria reported on the effect of iodized salt on change in urinary iodine excretion in such a way as could be combined in meta-analyses.

[b] Studies that reported median urinary iodine excretion and could not be combined in the meta-analyses reported increased urinary iodine excretion with iodized salt (1 RCT, 3 non-RCTs, 6 cohort and 16 multiple cross-sectional studies).

Table 5. Effect of iodized salt on hyperthyroidism, hypothyroidism and other adverse effects

Outcomes	Study design	Group	Number of studies	Number of comparisons	I^2	Peto OR	95% CI
Hypothyroidism							
	Cohort	All	4	4	91	1.14	0.84 to 1.53
	Multiple cross-sectional	All	4	4	90	1.13	0.94 to 1.36
Hyperthyroidism							
	Cohort	All	2	2	0	1.36	1.12 to 1.66
	Multiple cross-sectional[a,b]	All	5	5	89	0.96	0.92 to 1.00
Elevated anti-thyroid microsomal antibody							
	Cohort	Adults	1	1	—	2.51	1.93 to 3.27
	Multiple cross-sectional	All	2	2	96	1.27	0.94 to 1.71
Elevated anti-thyroglobin antibody							
	Multiple cross-sectional	All	2	2	97	1.43	1.08 to 1.89
Elevated urinary iodine excretion							
	Multiple cross-sectional	Children	1	1	—	1.35	1.06 to 1.74

95% CI: 95% confidence interval; OR: odds ratio.

[a] Removing the one study from Denmark that included more than 5 000 000 individuals from medical registries, the meta-analysis of three studies with three comparisons reported Peto OR = 0.50 (95% CI = 0.40 to 0.63) *(117)*.

[b] There was one multiple cross-sectional study that reported qualitatively no difference in the prevalence of hypothyroidism or hyperthyroidism before and after 12 years of exposure to iodized salt.

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Annex 1. Electronic search strategy

Unless otherwise stated, search terms are free text terms; MeSH = Medical Subject Heading (Medline medical index term); exp = exploded MeSH; the dollar sign ($) stands for any character(s); the question mark (?) = to substitute for one or no characters; tw = text word; pt = publication type; sh = MeSH; adj = adjacent.

The Cochrane Library (Issue 5 2011) and EMBASE (1966 to 18 June, 2011), MEDLINE (PubMed 1966 to 31 May 2011); The Virtual Health Library of the Pan-American Health Organization (May 2011); WHO International Clinical Trials Registry Platform (18 June 2011); and the WHO Global Health Library regional databases (June 2011) used a similar search strategy:

#1 iodine deficiency disorders/[MeSH term, all subheadings included]
#2 goitre
#3 endemic goitre
#4 cretinism
#5 hyperthyroidism
#6 hypothyroidism
#7 #1~#6/OR
#8 iodized salt [in all fields]
#9 salt
#10 salt iodization
#11 iodine fortification
#12 #8~#11/OR
#13 #7 AND #12

A similar search strategy was used for The China National Knowledge Infrastructure (May 2011); VIP (the register of Chinese trials developed by the Chinese Cochrane Centre); and WANFANG, using the following translated terms:

#1 碘缺乏病
#2 克汀病
#3 甲状腺肿
#4 地方性甲肿
#5 甲状腺机能亢进
#6 甲亢
#7 甲状腺机能低下
#8 甲低
#9 #1~#8/OR
#10 碘
#11 碘盐
#12 #10 OR #11
#13 #9 AND #12

Annex 2. Characteristics of included studies

Aghini-Lombardi et al., 1993 *(112)*

Methods	**Multiple cross-sectional observational study** conducted in Toscana, Italy
Participants	All schoolchildren (6–14 years) from two villages
Interventions	Iodized salt at 15 parts per million (ppm) became available in the two villages. Before the intervention, no iodized salt was available for purchase.
Outcomes	1. Goitre rate measured by palpation 2. Thyroid volume determined by ultrasound examination (only in the follow-up survey and therefore not included in this review) 3. Urinary iodine concentration
Publication details	Published in a peer-reviewed journal
Stated aim of study	To evaluate the efficacy of local legislative measures of iodized salt 10 years after introducing the iodized salt
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 15 ppm 6. Duration: 10 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre prevalence)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding of participants or personnel
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with similar number of inhabitants and school-aged children at both time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Same villages surveyed

Azizi et al., 2002 *(113)*

Methods	**Multiple cross-sectional observational study** conducted in Shahriar, Islamic Republic of Iran The sampling technique was stratified random sampling, resulting in 48 urban and rural centres as primary sampling units. The same 48 primary sampling units selected for the first survey were sampled during the follow-up surveys. The first survey was conducted before iodized salt was available and the second survey was conducted 12 years after the introduction of iodized salt in the country.
Participants	All adults and children in the randomly selected households
Interventions	Iodized salt at a concentration of 40 ppm (parts per million) in the form of potassium iodide was made available in the area.
Outcomes	1. Goitre 2. Urinary iodine excretion (UIE; µg/L) 3. Thyroid hormones – levels of tri-iodothyronine (T_3), thyroxine (T_4) and thyroid-stimulating hormone (TSH) 4. Anti-thyroid antibodies (anti-M and anti-Tg) 5. Hypothyroidism (reported qualitatively) 6. Hyperthyroidism (reported qualitatively)
Publication details	Published in a peer-reviewed journal
Stated aim of study	To compare the prevalence of goitre, UIE, thyroid hormone levels, and thyroid antibodies between 1983 and 1995
Notes	1. Design: multiple cross-sectional 2. Age: all 3. Group: non-pregnant 4. Salt consumption: unknown 5. Iodine concentration: 40 ppm 6. Duration: 12 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre prevalence) The data on prevalence of goitre data were given by percentage only, it was not possible to extract exact the number of goitres. The rate of consuming iodized salt was investigated and found to be approximately 50% of households consuming iodized salt from 1991 to 1994, and 90% in 1995 at the time of the follow-up survey. Authors reported qualitatively that there was no difference in the prevalence of hypo- or hyperthyroidism between the two surveys.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding of participants or personnel
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Multiple cross-sectional samples drawn in similar fashion with more participants at follow-up than baseline
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Multiple cross-sectional samples drawn in similar fashion and same villages surveyed

Baczyk et al., 2007 *(114)*

Methods	**Multiple cross-sectional observational study** conducted in Wielkopolska Region, Poland Cross-sectional surveys of goitre, urinary iodine excretion (UIE), and adverse effects were conducted before and 9 years after obligatory salt iodization in Poland.
Participants	Children aged 8–12 years, living in urban and rural areas and of both sexes
Interventions	Iodized salt at a concentration of 30 mg/kg (potassium iodide) was made available.
Outcomes	1. Goitre as measured by ultrasound 2. Hyperthyroidism 3. Hypothyroidism 4. UIE 5. Anti-thyroglobulin antibodies (TgAb) (data not used because only measured at baseline) 6. Anti-thyroid microsomal antibodies (data not used because only measured at follow-up)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To provisionally determine all changes of children's thyroid pathology occurring after the introduction of salt iodization
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 30 ppm (parts per million) 6. Duration: 9 years 7. Baseline iodine deficiency disorder (IDD) status: moderate IDD based on median UIE • All data were presented as percentages without confidence intervals; the number of events was calculated by the percentages and the total number of participants. • 1992 and 2005 data were compared as the endpoint but not 2000. • For UIE only, the population median was reported without a range and therefore the data could not be used in the quantitative analysis (baseline: 49 µg/L and follow-up: 107 µg/L).

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear for laboratory outcomes; not blinded for goitre
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional surveys with similar sample sizes
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Sampling methodology in two surveys not described in sufficient detail to discern potential bias

Bauch et al., 1990 *(115)*

Methods	**Multiple cross-sectional observational study** conducted in the former East Germany Adults were selected from four geographic regions of East Germany to measure urinary iodine concentration before the introduction of the blanket prophylaxis programme of salt iodization at the national level in East Germany. Salt iodization was introduced in salt for human consumption in 1985 and for animal consumption in 1986. The first cross-sectional survey was conducted in 1985. In 1986/1987, a second survey was conducted to measure urinary iodine concentration from persons living in the same areas of East Germany after the introduction of iodized salt.
Participants	Sample of adult population of East Germany
Interventions	Iodized salt was provided at a concentration of 25 ppm (parts per million) in a national programme.
Outcomes	Urinary iodine excretion (UIE)
Publication details	Published in a peer-reviewed journal in German
Stated aim of study	To evaluate the effect of the blanket prophylaxis programme of salt iodization at the national level in East Germany
Notes	1. Design: multiple cross-sectional 2. Age: adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 25 ppm 6. Duration: 1–2 years 7. Baseline iodine deficiency disorder (IDD) status: not reported

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Participants not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional surveys with larger sample size at follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Similar sampling methodology in two surveys

Bimenya et al., 2002 *(116)*

Methods	**Multiple cross-sectional observational study** conducted in Uganda. A sample of 2880 schoolchildren aged 6–12 years from 72 primary schools in six districts of Uganda were selected for evaluation of goitre in 1999, 5 years after the provision of iodized salt in the form of universal salt iodization in the country of Uganda. The results of goitre were compared to the results of a similar study conducted in 1991, 3 years before universal salt iodization in Uganda. Study districts were randomly selected but geographic representation was ensured through stratification of country. Probability proportionate to size (PPS) sampling was used to select the sample of schools and random sampling was used to select the students from each school; 40 students attending selected schools were included.
Participants	Schoolchildren aged 6–12 years
Interventions	Iodized salt was provided at a concentration of 50 ppm (parts per million) through universal salt iodization in the country.
Outcomes	1. Goitre 2. Urinary iodine excretion (UIE; lack of baseline data precluded use of this outcome in this review)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To monitor the universal salt iodization programme by determining the prevalence of goitre in the country, establishing the proportion of household populations consuming adequately iodized salt, and determining the levels of iodine intake using UIE
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm 6. Duration: 5 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre prevalence)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Participants not blinded
Blinding of outcome assessment (detection bias)	High risk	Assessors not blinded
Incomplete outcome data (attrition bias)	Unclear risk	Multiple cross-sectional surveys with unclear number of participants at baseline
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Sampling methodology for baseline survey not described

Cerqueira et al., 2009 *(117)*

Methods	**Multiple cross-sectional observational study** conducted in Denmark This study was a nationwide registry study covering all inhabitants in Denmark during the period 1 January 1995 to 31 December 2007. Every person in Denmark is assigned a unique, permanent, 10-digit identification number at birth or immigration. The identification number facilitates the use of registers and makes individual longitudinal follow-up possible. Pharmacies are required by law to register all prescriptions dispensed at an individual level, which makes the registry highly valid. The register includes information on the identification number of the patient, date of dispensing, ATC (Anatomical, Therapeutic, Chemical) code, strength, and quantity dispensed (in defined daily doses). Both anti-thyroid medication and thyroid hormone are sold solely as prescription drugs in Denmark and were registered. The incidences of thyroid conditions were indicated through monitoring the incident use of anti-thyroid medication.
Participants	All inhabitants in Denmark
Interventions	Iodized salt was provided at a concentration of 13 ppm (parts per million; potassium iodide) through the national programme. It was estimated at 50 µg/day.
Outcomes	The number of incident users of anti-thyroid medication
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To analyse the nationwide effect of the Danish iodine fortification programme on the incidence of hyperthyroidism, by monitoring the incident use of anti-thyroid medication
Notes	1. Design: multiple cross-sectional 2. Age: children and adults 3. Group: not specifically pregnant women 4. Salt consumption: 4.5 g/day 5. Iodine concentration: 13 ppm 6. Duration: 12 years 7. Baseline iodine deficiency disorder (IDD) status: combination of a moderate IDD region and a mild IDD region (based on median µg/L) • Iodine intake was estimated at 50 µg/day. • Data in this paper allow the estimate of salt consumption of 4.5 g/day; however, the study of Pedersen et al., 2002 *(100)* also has data regarding salt iodization in Denmark, which suggests a salt consumption of 5.5–6 g/day. • Iodine fortification was at a concentration of 8 ppm potassium iodide to all salt from June 1998 on a voluntary basis. Iodization of salt became mandatory in July 2000, at a concentration of 13 ppm potassium iodide. All salt for household use and for commercial production of bread was fortified.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional surveys with large numbers of participants at all time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Methodology for selecting samples same at all time points

Charania et al., 1988 *(118, 119)*

Methods	**Multiple cross-sectional observational study** conducted in Pakistan. Villages in the Gilgit and Hunza regions of Pakistan were stratified by accessibility to a main road and then randomly selected. Households within villages were then randomly selected. Villagers in randomly selected households had goitre and urinary iodine concentration measured. The first survey was conducted in 1978 and is described as baseline (pre-iodization) though the manuscript says salt fortified with iron became available in Pakistan in 1977. Iodized salt then became available in this region of Pakistan. A second survey was completed in 1987 (9 years later). Samples of participants were selected in the same way and came from the same villages. Goitre was measured by palpation, using World Health Organization (WHO) classification.
Participants	Children (less than 5 years of age) and ALL (children 5 years of age and older, adolescents and adults reported together)
Interventions	Iodized salt was provided through a national programme, at a concentration of 30 ppm (parts per million).
Outcomes	1. Goitre 2. Urinary iodine excretion (UIE; only measured at follow-up so not included in this review)
Publication details	Two articles published in peer-reviewed journals in English, reporting the same results of this study
Stated aim of study	1.To ascertain the magnitude, extent and pattern of iodized salt consumption 2. To ascertain the impact of the supply of iodized salt to the target area 3. To ascertain the effect of health education on the community and the extent of their knowledge of the benefits of iodized salt 4. To establish the difference in impact of iodized salt on areas with easy access as compared with remote areas, and on the roadside villages as compared with remote villages
Notes	1. Design: multiple cross-sectional 2. Age: children (and ALL ages but adults not reported separately) 3. Group: not specifically pregnant women 4. Salt consumption: 8 g/day (estimated) 5. Iodine concentration: 70 ppm (however, the results show that the amount of salt in households that was actually iodized varied by accessibility of village) 6. Duration: 9 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD based on goitre (not reported using WHO criterion of school-aged children) • Iodine consumption 300 µg/person/day Iodine concentration in salt was found to differ by household. Accessibility to the road was associated with the presence of iodized salt in the household.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional surveys with more participants at follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Methodology for selecting samples said to be the same but sample size was twice as large at follow-up, putting the methodology into question

Chen et al., 1976 *(120)*

Methods	**Multiple cross-sectional observational study** conducted during 1964–1965 and June 1971 in Taiwan, China
Participants	Total of 155 primary schools, including 89 926 children at baseline and 77 605 children at follow-up
Interventions	Universal salt iodization was implemented in the Taiwan in 1969. There were five areas of investigation, mainly categorized by baseline iodine status: 1. hyperendemic (goitre >40% in boys: >50% girls) – iodized salt measured at 28 ppm (parts per million); 2. mesoendemic (goitre 20–40% in boys: 25–50% girls) – iodized salt measured at 29 ppm; 3. hypoendemic (goitre 2–20% in boys: 5–25% girls) – iodized salt measured at 29 ppm; 4. nonendemic (goitre <5% in boys and girls) – iodized salt measured at 33 ppm; 5. aboriginal (not defined) – iodized salt measured at 28 ppm.
Outcomes	Goitre prevalence
Publication details	Published in English language in a peer-reviewed journal
Stated aim of study	To examine the effectiveness of salt iodization on goitre prevalence in schoolchildren in Taiwan
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 28–33 ppm 6. Duration: 6 years 7. Baseline iodine deficiency disorder (IDD) status: moderate IDD (based on goitre prevalence)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported but unknown whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Low attrition rate (high participant numbers at both time points)
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Samples selected in a similar way at both time points

Chen et al., 1984 *(93, 94)*

Methods	**Cohort observational study** conducted in China
Participants	5329 villagers were investigated
Interventions	Iodized salt was provided. The iodine concentration reduced across the time: • 18.948 mg/kg in the first month; • 16.543 mg/kg in the third month; • 9.77 mg/kg in the sixth month. No control intervention was used.
Outcomes	1. Goitre prevalence 2. Urinary iodine concentration (only reported qualitatively) 3. Test for tri-iodothyronine (T_3), thyroxine (T_4), thyroid-stimulating hormone (TSH) concentration (only reported qualitatively)
Publication details	Published in a Chinese language journal
Stated aim of study	To estimate the effect of iodized salt on goitre prevalence
Notes	1. Design: cohort observational 2. Age: children and adults 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: • 18.948 mg/kg in the first month; 20 ppm (parts per million) • 16.543 mg/kg in the third month; 16 ppm • 9.77 mg/kg in the sixth month; 10 ppm 6. Duration: 6 months 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre prevalence; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported/unknown
Incomplete outcome data (attrition bias)	Low risk	Low attrition
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Methods not described in detail

Chen et al., 1991 *(63)*

Methods	**Quasi-experimental study** conducted in Liaoyang, Fuxin, Fushun, Xinchengzi of Liaoning province, China Children of villages who were born before iodization of salt were compared to children in the villages born after iodization of salt.
Participants	Children aged 5–15 years at the time that intelligence was measured (1988) Cretinism cases were excluded from the study.
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children who were not exposed to iodized salt until an undetermined age. There were three cohorts (not clear if this categorization was by village or by group of children at baseline based on urinary iodine excretion [UIE]): • mild iodine deficient; • moderate iodine deficient; • severe iodine deficient.
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese language journal
Stated aim of study	Not stated
Notes	Intelligence measured with Combined Raven's Test for Rural China Comparisons made within iodine deficiency category (not clear if the categories were analogous to the village), to control for potential biases 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown (not reported) 6. Duration: unknown length of intervention group exposure to iodized salt other than gestation (9 months) compared to comparison group 7. Baseline iodine deficiency disorder (IDD) status: three cohorts (not clear if this categorization was by village or by group of children at baseline based on UIE): • mild iodine deficient • moderate iodine deficient • severe iodine deficient

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No mention of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias)	Unclear risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Groups comparable at baseline – same villages/ same IDD status

Chen et al., 1999 *(121)*

Methods	**Multiple cross-sectional study**, before–after design carried out in the Hui-an county, Fujian province, China
Participants	Randomly sampled 8–10-year-old children from 30 primary schools, each school sampled 40 children Total: • 1343 children in 1995 • 1247 children in 1997
Interventions	A survey was conducted in 1995 before the availability of iodized salt. Salt then became iodized throughout the province at a concentration of 33 ppm (parts per million). There was then another survey conducted with the same methods in 1997.
Outcomes	1. Goitre prevalence 2. Urinary iodine concentration µg/L (only median reported so included in summary table but not meta-analysed)
Publication details	Published in a Chinese language journal
Stated aim of study	Report of monitoring of universal salt iodization programme
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 33 ppm (parts per million) 6. Duration: 2 years 7. Baseline iodine deficiency disorder (IDD) status: moderate IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	Two cross-sectional surveys of similar sample size
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Same schools sampled at both time points to decrease bias

Chen et al., 2001 *(122)*

Methods	**Multiple cross-sectional study**, before–after design, conducted in Nonghai city, Fuanjian province, China
Participants	30 primary schools selected; 40 children randomly sampled from each school; a total of 1200 children examined in both before and after supplementation of the iodized salt
Interventions	A survey in the schoolchildren was conducted in 1995 before the availability of iodized salt. In 1996, the government started providing families iodized salt on a monthly basis. A second survey was conducted in the same schools in 1997. The concentration of Iodine in the salt was 33 ppm (parts per million; 1/30 000).
Outcomes	1. Goitre prevalence 2. Urinary iodine concentration (median reported; results found in summary table) 3. % of students with urinary iodine <100 µg/L
Publication details	Published in a Chinese language journal
Stated aim of study	To observe the effectiveness of using iodized salt for iodine deficiency disorder (IDD)
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. concentration: 33 ppm 6. Duration: 2 years 7. Baseline IDD status: moderate IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported/unknown
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional design with same sample size at both time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Same methodology to choose participants from same population groups at each time point

Chen et al., 2002 *(123)*

Methods	**Multiple cross-sectional observational study** conducted in Hui-an, Fujian, China Primary schoolchildren aged 8–10 years were randomly selected for inclusion in the baseline survey of goitre before the introduction of iodized salt. A follow-up survey was conducted 3 years after the introduction of iodized salt and goitre was again measured in randomly sampled schoolchildren.
Participants	Schoolchildren aged 8–10 years
Interventions	Two methods were used to introduce iodized salt in two separate provinces. In Hui An County (HAC), the government distributed iodized salt on the basis of 6 kg/person/year and non-iodized salt was taken completely off the market. In Quan Gang Region (QGR), iodized salt was introduced in the market and non-iodized salt was also still allowed to be in the market. There were two cohorts: • HAC (only iodized salt available); • QGR (iodized and non-iodized salt on the market).
Outcomes	1. Goitre prevalence 2. UIE (reported as median in manuscript and data found in summary table without meta-analysis) 3. % of children with urinary iodine excretion (UIE) <100 µg/L (no baseline numbers provided and therefore this outcome could not be included in the analyses or tables)
Publication details	Published in a Chinese language journal
Stated aim of study	To compare the effect of the two methods of availability of iodized salt on the prevention of iodine deficiency disorder (IDD) (For the purpose of the systematic review, the data from the post-distribution surveys at both localities were compared to the pre-distribution survey in the same location.)
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 3 years 7. Baseline IDD status: moderate IDD (based on goitre)/mild IDD (based on UIE)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional survey with similar number of participants at each time point
Selective reporting (reporting bias)	Unclear risk	No baseline data provided for % of children with UIE <100 µg/L
Other bias	Unclear risk	Methodology for follow-up survey was not described though it was assumed to be the same as baseline as the sample size was similar.

Chen et al., 2005 *(64)*

Methods	**Quasi-experimental study** conducted in Jiangshan township, Longyan city, Fujian province, China Children of the severe iodine deficiency disorder (IDD) area that were born before iodization of salt (comparison group) were compared to children in the villages born after iodization of salt (experimental group). Iodized salt was supplied to the village, beginning in 1982. Children were sampled (sampling methodology not reported) in 1990 and intelligence tests administered.
Participants	All children aged 7–14 years living in the villages at time that intelligence was measured were eligible and sampling was undertaken but methods not described (1985)
Interventions	Universal salt iodization was carried out at unknown concentration.
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Combined Raven's Test in China (CRT-C2) 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown (not reported) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) and duration of exposure during infancy and early childhood varied from 1 to 6 years 7. Baseline IDD status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition was not reported but sample sizes were fairly similar and samples relatively large
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Children sampled from the same villages, to reduce bias

Dai et al., 2008 *(124, 125)*

Methods	**Multiple cross-sectional study** conducted in Xiamen city, Fujian province, China Schoolchildren aged 8–10 years were randomly sampled from 90 schools before supplementation of iodized salt in 1995. Goitre and urinary iodine excretion (UIE) were measured in these children. Another similar cross-sectional survey was conducted 12 years after introduction of iodized salt.
Participants	Schoolchildren aged 8–10 years
Interventions	Comprehensive intervention was used in local salt mines and manufacturing facilities, to all salt on the market. Coverage was reported at 90% at follow-up survey. There were three cohorts; though the intervention was the same, the results were divided into: • urban; • suburban; • rural.
Outcomes	1. Goitre prevalence 2. UIE (reported as median in manuscript and results found in summary table but not used in meta-analysis)
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To assess the effect of iodized salt on goitre and UIE in school-aged children
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 12 years 7. Baseline iodine deficiency disorder (IDD) status: based on UIE/(based on goitre): • urban: adequate iodine status/(mild IDD) • suburban: adequate iodine status/(moderate IDD) • rural: mild IDD/(moderate IDD)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Multiple cross-sectional survey with fewer participants at follow-up than baseline
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Survey methodology similar at all time points and probability proportionate to size (PPS) sampling used

Dong et al., 1988 *(65)*

Methods	**Quasi-experimental study** conducted in Jiuling and Daxi villages in China Children of each village who were born before iodization of salt were compared to children in the village born after iodization of salt.
Participants	Children aged 7–13 years at the time that intelligence was measured
Interventions	Experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1–3 years of age. There were two cohorts: • iodine-deficient village (before and after salt iodization); • iodine-sufficient village (before and after salt iodization).
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Comparisons made within the village, to control for potential biases 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 33 ppm (parts per million) or 20 ppm (as stated in article) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus 1–3 years of life more than comparison 7. Baseline iodine deficiency disorder (IDD) status: based on goitre: • iodine-deficient village: moderate IDD • iodine sufficient village: adequate iodine nutrition

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No mention of blinding
Blinding of outcome assessment (detection bias)	High risk	No mention of blinding
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Samples comparable at baseline (similar cultural and educational conditions and same villages)

Fei et al., 1996 *(126)*

Methods	**Multiple cross-sectional observational study** conducted in Rizhao city, Shandong province, China A random sample of adults and children was selected for a survey of goitre before iodization of salt. Another survey was conducted 10 years after iodization of salt, to measure goitre in the population.
Participants	Adults and children living in Rizhao city, Shandong province, China
Interventions	Iodized salt was provided at a concentration of 33 ppm (parts per million).
Outcomes	1. Goitre prevalence 2. urinary iodine excretion (UIE) 3. % of children with UIE <100ug/L
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To assess the effect of supplementation of iodized salt on goitre and UIE
Notes	1. Design: multiple cross-sectional 2. Age: children and adults 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 33 ppm 6. Duration: 10 years 7. Baseline IDD status: severe IDD (based on goitre prevalence)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No mention of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias)	Unclear risk	Multiple cross-sectional survey with >40 000 participants at baseline and only approximately 4000 at follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Methods were unclear but the very large difference in sample size makes the potential for bias due to sampling differences high

Foo et al., 1996 *(95)*

Methods	**Cohort observational study** in Malaysia The original study design was a randomized controlled trial (RCT) conducted in Malaysia. The groups were randomly allocated to receive iodized salt or iodized water. The randomization was not described. The data used in this analysis from this study were the baseline and follow-up data from the group that received the iodized salt. The randomization to groups did not include a control group and therefore the comparison between group data could not be used. A baseline survey was conducted. The group received iodized salt for 1 year, at which time a follow-up survey in the same participants was conducted.
Participants	Women aged 15–40 years and children 6 years and younger
Interventions	Iodized salt was provided at 50 ppm (parts per million). A second village received iodized water but the results from that village were not included in the review. There were two cohorts: • women; • children.
Outcomes	1. Goitre prevalence (data were only reported for women) 2. Urinary iodine excretion (UIE; median population urinary iodine concentration is reported for before and after intervention; however, the range is not reported. The data from the median could not be used in the quantitative summary analysis)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To compare the effect of iodized salt and iodized water on goitre and UIE in women and children in rural villages in Malaysia
Notes	1. Design: cohort observational 2. Age: children and adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm 6. Duration: 1 year 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not RCT
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	No loss to follow-up reported
Selective reporting (reporting bias)	Unclear risk	All outcomes reported for women but goitre not reported for children
Other bias	Low risk	Groups chosen to be similar in living conditions, access to road and city, etc.

Fu et al., 1987 *(66)*

Methods	**Quasi-experimental study** conducted in Qiaotou and Dunzhi of Dayuan township, China Children of each village who were born before iodization of salt were compared to children in the village born after iodization of salt.
Participants	Children aged 4–15 years at the time that intelligence was measured (1987) Cluster sampling method used for selection of participants
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1–2 years of age. • One cohort • Children born before iodization of salt versus children born after iodization of salt
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Comparisons made within village, to control for potential biases 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm (parts per million) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus 1 to 2 years of life more than comparison 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No mention of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Children in both groups were from the same village but comparison was between 10–11 year olds and 4–5 year olds

Fu et al., 2001 *(127)*

Methods	**Multiple cross-sectional observational study** conducted in Shangping township and Fuchen township, China The study involved sampling of children in each township before and after salt iodization and intelligence was measured. Iodization began in 1984 after 9-year-old children were measured. In 1999, 9-year-old children were tested, all of whom were born after salt iodization. The sampling method was not reported.
Participants	Children aged 9 years at the time that intelligence was measured
Interventions	There were two cohorts (both populations sampled before and after salt iodization): • Shangping (iodine-deficient village); • Fuchen (iodine-sufficient village).
Outcomes	Intelligence of children: • mean intelligence quotient (IQ)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Good-enough Test (draw-a-person test) at baseline and Chinese Binet Scale at follow-up Comparisons made within village, to control for potential biases 1. Design: multiple cross-sectional 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm (parts per million) 6. Duration: 9 years 7. Baseline iodine deficiency disorder (IDD) status: as noted by authors but indicator used not specified: • Shangping: severe IDD • Fuchen: adequate iodine status

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No mention of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias)	High risk	As multiple cross-sectional, attrition not reported; however, sampling methods were also not reported and the *n* values for after salt iodization were much lower than those before iodization
Selective reporting (reporting bias)	Unclear risk	% of participants with intelligence quotient (IQ) <70 not reported as expected
Other bias	High risk	Different measures of IQ used at baseline and follow-up

Gatti et al., 1980 *(128)*

Methods	**Multiple cross-sectional observational study** conducted in Argentina Observational study of changes in urinary iodine excretion (UIE) from before to after the provision of iodized salt in a region of Argentina. Data were collected from men and women in the towns of Rosario and Bahia Blanca, Argentina. Only the sample in Rosario had complete data to use in this review. The same sample of men and women had UIE measured at baseline (1966/1967). Salt in the region (Santa Fe province) was iodized by law in the year 1970. A follow-up measurement was made in 1977, 7 years after salt iodization in the region. Change in UIE was measured.
Participants	Adults (men and women) living in Rosario, Argentina, who met the inclusion criteria
Interventions	Iodized salt was provided at the provincial level through mandatory fortification of salt at a concentration of 33 ppm.
Outcomes	UIE (µg iodine/g creatine)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To determine the contribution of iodine from iodized salt to the overall iodine intake in persons living in an area of little naturally occurring iodine in the water
Notes	1. Design: multiple cross-sectional 2. Age: adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 33 ppm urinary iodine excretion (UIE) 6. Duration: 7 years 7. Baseline iodine deficiency disorder (IDD) status: not reported The study had four time points and it is not clear whether at each it was a cross-sectional survey or whether it was repeated measures on the same individuals. The selection process for the included participants was not explained.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Blinding not reported
Incomplete outcome data (attrition bias)	High risk	The study population was very small. It is not clear that the same people were measured at each follow-up. If it were the same people, there was greater than 70% loss to follow-up at time points 2 and 3 relative to baseline and a 35% loss to follow-up at time point 4 relative to baseline.
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Methodology for sampling not reported in detail

Golkowski et al., 2007 *(96)*

Methods	**Cohort observational study** conducted in the southern part of Poland The authors compared thyroid dysfunction in participants prior to (1989–1990) and after implementation of iodine prophylaxis at a national level (1997–1999). A nutritional survey was conducted in randomly selected adults living in southern Poland in 1989–1990. A total of 4176 adults were surveyed. All those participants were contacted again in 1997 to take part in a similar survey in 1997–1999; 1648 participants answered the invitation to participate in 1997. Of those, 1424 were selected, based on exclusion criteria (i.e. had not taken thyroid medicine in their lifetime). Analysis was only of the 1424 who had complete data at baseline and follow-up.
Participants	Adults (age 16 years and older) who had not taken thyroid medicine in their lifetime, living in the southern part of Poland
Interventions	Iodized salt was provided at a concentration of 30 ppm (potassium iodide), through mandatory fortification of household salt.
Outcomes	1.Thyroid-stimulating hormone (TSH) level (median reported in manuscript: results in summary table but not meta-analysed) 2. Thyroid volume (only measured at follow-up) 3. Urinary iodine excretion (UIE) (only measured at follow-up) 4. Hyperthyroidism 5. Hypothyriodism 6. Positive anti-thyroid microsomal antibodies
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To assess the prevalence of hyperthyroidism just after implementation of iodine prophylaxis among adults from an area with iodine deficiency
Notes	1. Design: cohort observational 2. Age: adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 30 ppm 6. Duration: 2 years 7. Baseline iodine deficiency disorder (IDD) status: not reported

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported/unknown
Incomplete outcome data (attrition bias)	High risk	Only 34% of persons measured at baseline were also measured at follow-up (analysis included only those with measures at both times)
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Subjects from same area of Poland and selected randomly for invitation into study

Gongora, 1952 *(55)*

Methods	**Non-randomized controlled trial** (RCT) conducted in Colombia Salt iodization was introduced into one community (Caldas, Colombia) and not into another community (Bogotá, Colombia). The investigators selected participants randomly from schools, to measure goitre before iodized salt was introduced. After 2 years of use of iodized salt in the intervention community, another cross-sectional study, where the sample was said to have been selected in the same fashion as the previous study, was conducted in both communities. The community of Bogotá acted as a control because iodized salt was not used in that community. The methods of selection of participants were not described. Methods of measurement of goitre were not described but it was noted that the same methods were used in both surveys.
Participants	School-aged children in the two communities
Interventions	Iodized salt was introduced to the community at a concentration of 50 ppm (parts per million).
Outcomes	Goitre
Publication details	Published in a peer-reviewed journal in Spanish The complete original report could not be accessed. These results were abstracted from the review article, de León Méndez R. [Eficacia del enriquecimiento de la sal con preparados de yodo, como medio de prevencion del bocio endémico]/Effectiveness of the enrichment of salt with iodine preparations as a means of preventing endemic goiter. Boletín de la Oficina Sanitaria Panamericana 1966;61(1):1–26 (http://hist.library.paho.org/Spanish/BOL/v61n1p1.pdf, accessed 27 October 2014).
Stated aim of study	To evaluate the salt iodization programme in Colombia
Notes	1. Design: non-RCT 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm (parts per million) 6. Duration: 2 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not RCT
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	Unclear risk	No blinding reported
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	High risk	20% in treatment/29% control – no explanation for loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Though both groups were considered severe IDD at baseline, owing to high goitre prevalence, the control group had almost half the prevalence of goitre of that of the experimental group at baseline and the control group was from the capital while the experiment was from less of an urban centre.

Guo, 1984 *(97)*

Methods	**Cohort observational study** conducted in Houchang community, Ziyun county, Guizhou province, China The study report provided data of before–after supplementation of iodized salt.
Participants	All inhabitants of Houchang community Rates of examination for before and after, respectively: 96.19% (4039/4199) and 96.76% (4269/4412)
Interventions	Iodized salt was provided through universal salt iodization at 20 ppm (parts per million).
Outcomes	1. Goitre prevalence 2. Physiologically enlarged thyroid gland (not included in this review) 3. Tri-iodothyronine (T_3; not reported/used to determine prevalence of hypothyroidism) 4. Thyroxine (T_4; added to summary table) 5. Thyroid-stimulating hormone (TSH; median value reported in manuscript: results in summary table but not meta-analysed) 6. Urinary iodine concentration (UIC; median value reported in manuscript: results in summary table but not meta-analysed) 7. Hypothyroidism 8. Rate of absorption of I-131 by thyroid gland (only done in persons described as having iodine deficiency and therefore not included in this review)
Publication details	Published in a Chinese language journal
Stated aim of study	Not stated
Notes	1. Design: cohort observational 2. Age: children and adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20 ppm 6. Duration: 3 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported/unknown
Incomplete outcome data (attrition bias)	Low risk	High response rates
Selective reporting (reporting bias)	Low risk	Most outcomes reported fully
Other bias	Low risk	Entire community measured at each time point and number of deaths/births and emigration/ immigration between surveys accounted for

Han et al., 2006 *(129)*

Methods	**Multiple cross-sectional observational study** conducted in Tianjin, China The participants were sampled by probability proportionate to size sampling (PPS), according to the population. Samples were taken from 30 schools. One hundred and fifty housewives were also sampled, though the selection process was not described.
Participants	Included pupils aged 8–10 years sampled from 30 schools, 600 class five pupils and 994 pupils aged 8–10 years whose drinking water iodine concentration was (median) >150 (300) µg/L 150 housewives sampled, though selection process not described
Interventions	A survey was conducted in 1995, then in 1996 universal salt iodization was implemented. A follow-up study was conducted in 2005. The concentration of iodine in the salt was not reported. There was only one cohort, as results were reported for women and children combined.
Outcomes	1. Urinary iodine excretion (UIE; median reported and results included in a summary table but not meta-analysed) 2. Goitre prevalence
Publication details	Published in a Chinese language journal
Stated aim of study	To evaluate the efficiency over 10 years of iodized salt to prevent and control iodine deficiency disorder (IDD)
Notes	1. Design: multiple cross-sectional 2. Age: children and adults 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 10 years 7. Baseline IDD status: severe based on goitre/mild based on UIE

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported/unknown
Incomplete outcome data (attrition bias)	High risk	Multiple cross-sectional study but sample sizes much smaller at follow-up than at baseline
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Probability proportionate to size sampling (PPS) described and reported that it was same at all time points but no reason given for very different sample sizes

He et al., 1993 *(67, 68)*

Methods	**Quasi-experimental study** conducted in Qiandongnan State of Guizhou Province, China Children of villages who were born before iodization of salt were compared to children in the villages born after iodization of salt.
Participants	Children aged 7–14 years at time that intelligence was measured (1990)
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1–3 years of age. The entire study area was considered an iodine-deficient area at baseline. There were three cohorts: • Miao ethnic group; • Dong ethnic group; • Han ethnic group.
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Comparisons made within ethnic groups, to control for potential biases 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20 ppm (parts per million) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus 1–3 years of life more than comparison 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No mention of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Cluster sampling method used to form representative groups – each of three racial groups compared to same group, to reduce bias

Heydarian et al., 2007 *(130)*

Methods	**Multiple cross-sectional observational study** conducted in Tehran province, Islamic Republic of Iran Cluster random sampling was used to select adults for each survey. The first survey was conducted in 1983–1984 and the second survey was conducted in 1999–2000. National salt iodization became law in 1994. Goitre was assessed by palpation and graded using World Health Organization (WHO) classification. Serum samples were collected and thyroid stimulating hormone (TSH) and anti-thyroid peroxidase (TPOAb) and anti-thyroglobulin (TgAb) antibodies were measured. Free T_4 was also measured in those with abnormal TSH levels. Casual morning urine samples were taken from a subsample of participants, to measure urinary iodine excretion (UIE).
Participants	Adults aged 20 years or older living in Tehran province, Islamic Republic of Iran
Interventions	Iodized salt was provided at 40 ppm (parts per million; potassium iodide).
Outcomes	1. Goitre 2. TSH 3. Positive anti-thyroid peroxidase antibodies (TPOAb+) 4. Positive anti-thyroglobulin antibodies (TgAb+) 5. Hypothyroidism 6. Hyperthyroidism
Publication details	Published in peer-reviewed journal in English
Stated aim of study	To compare goitre rate, serum TSH, thyroperoxidase antibodies, thyroglobulin antibodies, thyroid function, and UIE in the adult population of Tehran before and after national salt iodization
Notes	1. Design: multiple cross-sectional 2. Age: adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 40 ppm 6. Duration: 5 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre; did not use WHO criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Unclear but not likely
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with larger sample size at follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Sampling method described and not the same for the two surveys

Hintze et al., 1988 *(53)*

Methods	**Randomized controlled trial** (RCT) conducted in Göttingen, Germany and a small rural area in the vicinity All schoolchildren were invited to participate. Of the 1160 parents contacted, nearly 50% did not respond, 227 did not wish to participate and the parents of a total of 334 boys and girls agreed to the study and allowed their children to participate. Measurements were taken in the schools of body weight and height, goitre classified by World Health Organization (WHO) standards, and neck circumference. After baseline measurements, students were randomly assigned to group A or group B. The randomization method was not explained. Group A was assigned to buy from the market and consume only iodized salt, while group B was assigned to buy from the market and consume only non-iodized salt. Groups were not blinded to treatment but assessors were blinded. Follow-up measurements of goitre were undertaken at 2 and 4 years and urinary iodine excretion (UIE) was measured yearly. The final 4-year follow-up measure is used in this review.
Participants	Schoolchildren averaging 10 years of age at baseline and with a goitre prevalence of 30.5%
Interventions	1. Iodized salt (iodate, 20 ppm iodine) (*n* = 146) 2. Control (plain salt) (*n* = 188)
Outcomes	1. Goitre 2. Neck circumference 3. UIE (µg iodine/g creatinine; results in summary table because cannot be combined with the other RCT which reports UIE as µg iodine/24 h in pregnant women)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	Quote "The availability of iodinated salt containing 20 mg of iodine as iodate/kg salt consumed on a voluntary basis enabled us to investigate its effect on goitre prevalence and iodine excretion in urine in a longitudinal, prospective, randomised study over 4 years."
Notes	1. Design: RCT 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: 5 g salt/day (estimated) 5. Iodine concentration: 20 ppm (parts per million) 6. Duration: 4 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre) Iodine intake estimated at 100 µg/day If at any time over the course of the study a child presented with grade II goitre, a thyroid nodule, or a UIE of 200 µg/g creatinine, he/she was excluded from the study. There was a total of five participants in each group lost to follow-up for these reasons.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not explained
Allocation concealment (selection bias)	Unclear risk	Allocation methods not explained
Blinding of participants and personnel (performance bias)	High risk	Participants and providers not blinded to treatment
Blinding of outcome assessment (detection bias)	Low risk	Assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Details on attrition were unclear; however, loss to follow-up appeared to be similar between groups and five participants in each group were lost to follow-up because of presenting with grade II goitre, a thyroid nodule or high UIE
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	No other factors to potentially increase bias identified

Hou et al., 2003 *(131)*

Methods	**Multiple cross-sectional observational study** conducted in three districts of Jilin province, China There was only a baseline measure before salt iodization in one village (Helongcheng) and that information is used in this review.
Participants	Probability proportionate to size (PPS) sampling used to get a representative sample of inhabitants in Helongcheng village of Long county The first survey was conducted in 1986, iodized salt was introduced in 1993 and universal salt iodization achieved in 1996. The follow-up survey was conducted in 1999.
Interventions	Monitoring of salt iodization showed concentration levels varied from 21 ppm (parts per million) to 47 ppm, with most measures above 40 ppm.
Outcomes	1. Goitre (only provides prevalence with no denominator value and therefore data cannot be used in meta-analysis) 2. urinary iodine excretion (UIE; measures done differently at baseline and follow-up and therefore cannot be used in meta-analysis) 3. Incidence of hyperthyroidism (measured only in adults)
Publication details	Published in a Chinese language journal
Stated aim of study	To compare hyperthyroidism before and after universal salt iodization
Notes	1. Design: multiple cross-sectional 2. Age: all (adults for hyperthyroidism) 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20–50 ppm 6. Duration: 3 years (of universal salt iodization and 6 years of some exposure to iodized salt) 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Two cross-sectional studies but number of individuals measured was not reported
Selective reporting (reporting bias)	Unclear risk	Prevalence reported but number of individuals not reported
Other bias	Low risk	PPS sampling using same methodology said to have been used in both surveys

Hou and Wang, 2009 *(132)*

Methods	**Multiple cross-sectional observational study** conducted in Lantian county, Shanxi province, China A survey to measure goitre was conducted in 1970, whereby all residents of Lantian county were participants. The same county was surveyed again in 2006 for goitre.
Participants	All residents of Liantian county
Interventions	Iodized salt was provided at an unreported concentration.
Outcomes	Goitre
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To assess the effect of iodized salt on the prevention of goitre
Notes	1. Design: multiple cross-sectional 2. Age: children and adults 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 36 years 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear but not likely
Incomplete outcome data (attrition bias)	Low risk	Two multiple cross-sectional surveys with all inhabitants surveyed
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	All inhabitants surveyed using same census methodology

Hu et al., 1998 *(133)*

Methods	**Multiple cross-sectional observational study** conducted in Taiping village, Hanyin county, Shanxi province All villagers of Taiping village were surveyed for goitre and cretinism in the village before the introduction of iodized salt. Thirty-two years after the introduction of iodized salt, all villagers were again surveyed for goitre and cretinism.
Participants	All villagers
Interventions	Iodized salt was provided at less than 20 ppm (parts per million) for 25 years, then 33 ppm for 5 years and finally 50 ppm for 1 year.
Outcomes	1. Goitre 2. Cretinism
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To assess the effect of supplementation of iodized salt for 32 years
Notes	1. Design: multiple cross-sectional 2. Age: adults and children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm 6. Duration: 32 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear but not likely
Incomplete outcome data (attrition bias)	Low risk	Two multiple cross-sectional surveys with entire village surveyed and high participation rate
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	All inhabitants surveyed using same census methodology

Huang et al., 2004 *(159)*

Methods	**Multiple cross-sectional study** and **quasi-experimental study** conducted in Fujian, China Multiple cross-sectional: in 1994, investigators selected primary schoolchildren in grades 2–5, to test their intelligence quotient (IQ) level. Salt iodization began in 1994, then in 2002 another survey was conducted in children of the same age from the same schools. Quasi-experimental: in 2002, children were divided into those born before 1994 and those born after 1994. Those born before were the comparison group because they did not have exposure to iodized salt during gestation or the first 2 years of life and those born after 1994 did have exposure to iodized salt during first 2 years of life.
Participants	Multiple cross-sectional study: baseline 257 and follow-up 252 children, all grades 2–5 Quasi-experimental study: experiment 52 schoolchildren and comparison 200 schoolchildren
Interventions	Iodized salt was provided to inhabitants through universal salt iodization.
Outcomes	Mental intelligence: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To understand the effect of universal salt iodization on intelligence quotient level of children.
Notes	1. Design: multiple cross-sectional and quasi-experimental 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 8 years 7. Baseline iodine deficiency disorder (IDD) status: severe (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional study had similar numbers at baseline and follow-up and in quasi-experiment attrition was not applicable
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	The groups were comparable at baseline and students from the same school measured in the multiple cross-sectional study, to reduce bias

Ibanez Gonzalez et al., 1956 *(98)*

Methods	**Cohort observational study** conducted in Guejar Sierra, Granada, Spain A random sample of the population living in the town of Guejar Sierra, Granada, Spain was evaluated for goitre before and after the introduction of iodized salt in the community. The sample was described as random but methods of sampling were not described. The methods for measuring goitre were not described; 16 months after the introduction of the iodized salt in the community, the same participants were evaluated again for goitre. The loss to follow-up was not reported.
Participants	Adult and child participants randomly selected from the community; no exclusion criteria described
Interventions	Iodized salt was provided at a concentration of 16.7 ppm (parts per million).
Outcomes	Goitre (only reported prevalence of goitre and thus could not be used in the quantitative analysis)
Publication details	Published in a peer-reviewed journal in Spanish The complete original report could not be accessed. These results were abstracted from the review article, de León Méndez R. [Eficacia del enriquecimiento de la sal con preparados de yodo, como medio de prevencion del bocio endémico]/Effectiveness of the enrichment of salt with iodine preparations as a means of preventing endemic goiter. Boletín de la Oficina Sanitaria Panamericana 1966;61(1):1–26 (http://hist.library.paho.org/Spanish/BOL/v61n1p1.pdf, accessed 27 October 2014).
Stated aim of study	Not stated
Notes	1. Design: cohort observational 2. Age: adults and children 3. Group: not specifically pregnant women 4. Salt consumption: 10 g/day (estimation reported in study) 5. Iodine concentration: 16.7 ppm 6. Duration: 16 months 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre): • intake of 167 µg iodine/day

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear if there was blinding of the outcome assessor
Incomplete outcome data (attrition bias)	Unclear risk	Sample sizes not reported so attrition unknown
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Random selection of individuals in community, taking into account various age groups

I'Ons et al., 2000 *(56)*

Methods	**Non-randomized controlled trial** (RCT) conducted in South Africa Non-randomized controlled trial where two schools were selected for convenience and because there was no iodized salt available in the region where the schools were located. All children in both schools participated. Goitre, measured by palpation and defined using World Health Organization criteria, and urinary iodine excretion (UIE), were measured at baseline and after a 4-month follow-up period. Children in the experiment school were all given iodized salt for use in the household and children in the control school were given non-iodized salt for use in the household.
Participants	All schoolchildren in two communities, aged 7–16 years
Interventions	1. Iodized salt 2. Plain salt
Outcomes	1. Goitre 2. UIE (reported as median; results in summary table) 3. % of population with UIE <100 µg/L
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To evaluate the short-term effect of salt iodized according to the recently revised South African salt legislation on the iodine status of rural primary schoolchildren
Notes	1. Design: non-RCT 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 53 ppm (parts per million)[a] 6. Duration: 4 months 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on UIE) [a] first 2 batches of salt had 18 and 12 ppm iodine, and the last batch (last 4–5 weeks) had 53 ppm unclear if iodide or iodate; *n* = 39) The authors conclusions state "The sample size and duration of intervention were inadequate to estimate the effect of iodized salt on the prevalence of goitre accurately and to detect changes in goitre rates, but is effective in eradicating mild and borderline iodine deficiency within a period of 4 months in primary schoolchildren. We compared the change from baseline of two groups before–after salt iodization."

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of participants and personnel (performance bias)	Low risk	Participants were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	High risk	Control group had more than double the drop-out rate relative to the intervention group
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Schools were chosen because they were very comparable and the students and families very comparable

Jia et al., 2004 *(157)*

Methods	**Cohort observational study**, **quasi-experimental** and **multiple cross-sectional observational study** conducted in Heshui county, Gansu province, China A survey was conducted of all residents of Heshui county in 1990. In that year, universal salt iodization was implemented. Another study of all residents was conducted in 2000. The results of all persons aged over 10 years in 2000 are presented as cohort study results because they were measured at both time points. Individuals aged 0–10 years in 1990 are a comparison group in the quasi-experiment, as they had no exposure to iodized salt and the intervention group is those children aged 0–10 years at follow-up because they did have exposure to iodized salt. The measure of UIE was only reported for 7–14 year olds and is a multiple cross-sectional study.
Participants	All residents of the county were measured for goitre (cohort) and children aged 7–14 years were measured for urinary iodine concentration (multiple cross-sectional).
Interventions	Iodized salt was provided through universal salt iodization at an unknown concentration.
Outcomes	1. Goitre (all) 2. Urinary iodine concentration (children 7–14 years)
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To assess the effect of iodized salt on goitre and urinary iodine concentration
Notes	1. Design: multiple cross-sectional, cohort observational and quasi-experimental 2. Age: all for goitre (cohort), children for goitre (quasi-experimental), children for urinary iodine excretion (UIE; multiple cross-sectional) 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 10 years 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on UIE)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Low attrition reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	All inhabitants measured at both time points and in quasi-experiment it was children from same villages

Jooste et al., 2000 *(134)*

Methods	**Multiple cross-sectional observational study** conducted in South Africa Schools in four communities in South Africa were surveyed for goitre and urinary iodine excretion (UIE). The schools were not representative of any larger population but were selected to have participants of a variety of socioeconomic statuses. In large schools, every other child in grades 4–7 was selected to participate and in smaller schools all children in grades 4–7 were selected to participate. The baseline survey measured goitre and UIE during the month before universal salt iodization was begun in South Africa. The follow-up survey occurred 1 year later, using the same sampling technique.
Participants	Children in grades 4–7 in selected communities in South Africa
Interventions	Iodized salt (potassium iodate) provided at a concentration of 40–60 µg/g through mandatory fortification
Outcomes	1. Goitre 2. UIE (median included in summary table) 3. % population with UIE <100ug/L 4. % of population with UIE >200 µg/L (data not used in the current review as this is not a cut-off for excessive UIE and not an indicator of status
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To evaluate, after 1 year, the effectiveness of mandatory iodization of salt at an iodine concentration higher than that occurring under optional iodization, on the goitre rates and iodine status of schoolchildren living in a goitre-endemic area in South Africa
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 40–60 ppm (parts per million) 6. Duration: 1 year 7. Baseline iodine deficiency disorder (IDD) status: moderate IDD (based on goitre)/moderate IDD (based on UIE) Limited data from quantitative analysis of iodine concentration in salt suggest that the fortification target of 40–60 ppm was not being reached 1 year after universal salt iodization in South Africa. The mean of the 18 samples of salt was only 25 ppm.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple-cross-sectional with similar number of participants
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Participants of similar age and chosen using same methodology

Kimball, 1931 *(57)*

Methods	**Non-randomized controlled trial** (RCT) conducted in the United States of America (USA) Two cross-sectional surveys were conducted in a community that started a salt iodization programme (Detroit, Michigan, USA) and in a community without salt iodization, which acted as a control (Cleveland, Ohio, USA). The first survey was before iodized salt was introduced into the Detroit community and the second survey was 7 years after the introduction of iodized salt in the Detroit community. No iodized salt was introduced into the Cleveland community during this time. The samples were reported to be selected in a similar fashion but details were not reported. The samples were from schoolchildren; however, selection and sample sizes were not reported. Similarity of samples at baseline is unknown; however, the prevalence of goitre at baseline is similar in the two communities and they are in the same region of the country.
Participants	School-aged children attending schools in either Detroit Michigan or Cleveland Ohio, USA, 7–15 years of age
Interventions	Iodized salt was introduced in the community.
Outcomes	1. Goitre (only goitre prevalence is reported and thus the data could not be used in the quantitative analysis in this report; only added to summary table)
Publication details	Published in English in a peer-reviewed journal The complete original report could not be accessed. These results were abstracted from the review article de León Méndez R. [Eficacia del enriquecimiento de la sal con preparados de yodo, como medio de prevención del bocio endémico]/Effectiveness of the enrichment of salt with iodine preparations as a means of preventing endemic goiter. Boletín de la Oficina Sanitaria Panamericana 1966;61(1):1–26 (http://hist.library.paho.org/Spanish/BOL/v61n1p1.pdf, accessed 27 October 2014).
Stated aim of study	To evaluate the salt iodization programme in Detroit Michigan under natural conditions and compare that to a control area without salt iodization.
Notes	1. Design: non-RCT 2. Age: child 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 7 years 7. Baseline iodine deficiency disorder (IDD) status: severe (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No randomization
Allocation concealment (selection bias)	High risk	No allocation
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Only prevalence reported, so number of participants and attrition unknown
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Not clear if groups were comparable at baseline, though goitre prevalence was similar

Kimball, 1946 *(135)*

Methods	**Multiple cross-sectional study** conducted in Michigan, United States of America (USA) All schoolchildren in three counties in Michigan, USA were measured for goitre in 1924 before the introduction of iodized salt to that state. In 1924, iodized salt was introduced to the state of Michigan at a concentration of 20 ppm (parts per million). In 1928 and in 1936, all the schoolchildren in the same schools in the same four counties were again measured for goitre.
Participants	All schoolchildren in the four counties selected for measurement in the state of Michigan, USA
Interventions	Iodized salt was provided at state level at a concentration of 20 ppm.
Outcomes	1. Goitre 2. Adverse effects (qualitatively reported that NO adverse effects were identified or reported)
Publication details	Published in English in a peer-reviewed journal
Stated aim of study	To learn about the efficiency of iodized salt and to determine any harmful effects from its continued use
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20 ppm 6. Duration: 4 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear but not likely
Incomplete outcome data (attrition bias)	Low risk	Two cross-sectional studies with similar sample size
Selective reporting (reporting bias)	Low risk	In terms of adverse effects, the authors note that none were reported
Other bias	Low risk	All children in the same schools measured, to reduce potential bias

Kimiagar et al., 1990 *(99)*

Methods	**Cohort observational study** conducted in the Islamic Republic of Iran
Participants	2034 participants from 368 families were surveyed; of these, a total of 1323 persons were clinically examined.
Interventions	The study randomly selected 60 villages from total of 180 villages in the endemic area, and selected 368 families for inclusion for a total of 1323 participants. A baseline survey was conducted and then all households were provided iodized salt directly for 3 years. A follow-up survey was undertaken at 2 years and at 3 years post introduction of iodized salt.
Outcomes	1. Goitre 2. Tri-iodothyronine (T_3) 3. Thyroxine (T_4) 4. Thyroid-stimulating hormone (TSH) 5. Urinary iodine excretion (UIE; this outcome was the only outcome measured at follow-up and therefore the only data included in meta-analysis)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To collect up-to-date baseline data on all aspects of the problem of iodine deficiency disorder (IDD) in this area of the Islamic Republic of Iran and to arrive at a suitable prophylaxis programme
Notes	1. Design: cohort observational 2. Age: adults and children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 40 ppm (parts per million; 20 µg/kg [1/50 000] for 2 years' duration; 40 µg/kg [1/25 000] for 1 year's duration) 6. Duration: 3 years 7. Baseline IDD status: severe IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	Unclear risk	No blinding reported
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	High risk	Loss to follow-up almost 20%
Selective reporting (reporting bias)	High risk	Only UIE measured/reported at follow-up
Other bias	Low risk	Included individuals randomly selected from villages that had been randomly selected

Li et al., 1991 *(69–72)*

Methods	**Quasi-experimental study** conducted in four villages of Heilongjiang Province in China Children of the village that were born before iodization of salt were compared to children in the village born after iodization of salt.
Participants	Children aged 5–14 years at time that intelligence was measured (1985)
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1–3 years of age. All villages were areas of severe iodine deficiency at baseline. There were two cohorts: • Jixian village (severe iodine-deficiency area); • Taihui village (mild iodine-deficiency area).
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR) Though the study was conducted in five villages, there is only sufficient report of results to include two village in the quasi-experimental study. (The standard deviation of the second village is not included, so only the % of children with IQ <70 points can be included for that village.)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Sampling methodology not reported 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus first years of life more than comparison (exact time of exposure difference between groups not reported) 7. Baseline iodine deficiency disorder (IDD) status: • Jixian: severe IDD (based on goitre) • Taihui: mild IDD (as stated by authors but values and indicators not provided)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding reported
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Sampling methods not reported and, as quasi-experimental, attrition not reported
Selective reporting (reporting bias)	High risk	Only the results of two villages are reported
Other bias	Low risk	Results of experiment and comparison within village, to reduce potential bias

Lv et al., 2009 *(136)*

Methods	**Multiple cross-sectional observational study** conducted in Hebei province, China Probability proportionate to size sampling (PPS) technique was used to select the participants for a survey on urinary iodine excretion (UIE) and goitre. 1200 schoolchildren aged 8–10 years were selected from 30 schools (40 children in each school). At the same time, salt samples were collected from those children's households; 360 urinary specimens were randomly selected from the 1200 children. The same sampling occurred at the baseline survey, conducted before the provision of iodized salt and at the follow-up survey 10 years after the provision of iodized salt through mandatory means in the province. The baseline survey was conducted in 1995 then universal salt iodization was implemented. A follow-up survey was conducted in 2005.
Participants	Schoolchildren aged 8–10 years
Interventions	Iodized salt was provided at a concentration of 35 ppm (parts per million), through mandatory fortification.
Outcomes	1. UIE (median reported and results added to summary table) 2. % population UIE <100 µg/L 3. Adverse effects (% population UIE >300 µg/L) 4. Goitre 5. Iodine concentration in the salt (data not used in this review)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To assess the effect of the mandatory iodized salt programme in Hebei province, China
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 35 ppm (parts per million) 6. Duration: 10 years 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (goitre)/adequate iodine status (based on UIE) Proportion of inadequately iodized salt: • 50.3% in 1995; • 13.6% in 1997; • 2% in 1999; • 3% in 2001; • 9.6% in 2005.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear but not likely
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with similar sample sizes
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Probability proportionate to size (PPS) sampling used for sampling methodology for all surveys

Mostafavi et al., 2005 *(137)*

Methods	**Multiple cross-sectional observational study** conducted in Shiraz, Islamic Republic of Iran Schools in Shiraz, Iran were randomly selected and subsequently students within schools randomly selected for evaluation of goitre. A survey was conducted in 1989 prior to the initiation of universal salt iodization in the Islamic Republic of Iran. Goitre was evaluated in randomly selected students aged 6–18 years, using World Health Organization classification. In 1995, 5 years after the initiation of the universal salt iodization programme in the Islamic Republic of Iran, a second survey using the same methods was conducted to measure the impact of the salt iodization programme on goitre in schoolchildren.
Participants	Children, 6–18 years of age, attending school in Shiraz, Islamic Republic of Iran
Interventions	Iodized salt was provided at an unknown concentration through universal salt iodization in the country.
Outcomes	Goitre
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To evaluate the impact of the salt iodization programme on the prevalence of goitre in schoolchildren in the city of Shiraz
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 5 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with similar sample sizes at both time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Same sampling methodology used, to reduce potential bias

Nicod 1953 *(138)*

Methods	**Multiple cross-sectional observational study** conducted in Switzerland The article provides an overview of the prophylaxis of goitre through the use of iodized salt in various cantons of Switzerland. The study includes data for discharged military adults, national prevalence of goitre, and level of fortification in each canton and when iodization programmes were initiated. The data included in the review come from surveys of school-aged children in two cantons where complete data from pre-iodization and post-iodization of salt is available. No data are available on how students were selected to participate in the evaluations. Numerous indicators of the thyroid size were reported, based on palpation of the neck. The indicators were normal thyroid, large neck and advanced goitre.
Participants	School-aged children in Vaud and Valais cantons, Switzerland
Interventions	Iodized salt was provided at the canton level at 10 ppm (parts per million).
Outcomes	1. Goitre (only prevalence reported, with no sample size, so data included in summary table only) 2. Other indicators of thyroid size (not defined but included in summary table as reported)
Publication details	Published in French in a peer-reviewed journal
Stated aim of study	To evaluate the success of the salt iodization programme in Switzerland
Notes	1. Design: multiple cross-sectional 2. Age: children (two separate cohorts by canton) 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 10 ppm 6. Duration: canton of Valais 6 years/canton of Vaud 30 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre) • Most of the data provided in this manuscript are not specific enough to be extracted. • Each canton decided when to introduce iodized salt and the level of fortification.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Unclear risk	Sample sizes not provided
Selective reporting (reporting bias)	High risk	Only limited information on outcomes available for extraction from article
Other bias	Unclear risk	The limited description of the manuscript leaves the potential for additional bias unclear

Pan et al., 1995 *(73)*

Methods	**Quasi-experimental study** conducted in two townships of Jiling city, China One township was classified as "mild IDD [iodine deficiency disorder]" area and the other as "severe IDD" area, based on historic prevalence of goitre. Children aged 5–14.5 years of the townships were eligible and a sample was drawn for intelligence testing. The sampling method was not described. Universal salt iodization began; however, the date was not stated. Children were divided into two groups: children born before the universal salt iodization (comparison) and children born after universal salt iodization (experiment). The intelligence of children was measured using the Chinese Binet Scale.
Participants	Children aged 5–14.5 years at time that intelligence was measured (date not stated)
Interventions	Universal salt iodization was provided at an unknown concentration.
Outcomes	Intelligence of children: • mean intelligence quotient (IQ; no standard deviation reported and no sample size by group reported; data found in summary table and no meta-analyses)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 9 months' gestation to 4 years (comparison group was born before universal salt iodization and some were born up to 4 years before) 7. Baseline IDD status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Quasi-experimental, so no attrition but sample sizes in each group not reported
Selective reporting (reporting bias)	Unclear risk	% of population with low IQ (mild mental retardation – MMR) not reported as expected
Other bias	Unclear risk	Children selected from same communities, to reduce bias, but sampling method not mentioned and sample sizes not provided

Pedersen et al., 2002 *(100–102)*

Methods	**Cohort observational study** conducted in Copenhagen and Aalberg, Denmark. The entire population of two towns in Denmark with varying degrees of iodine sufficiency/deficiency at baseline were the study populations. Copenhagen was a town with mild iodine deficiency, while Aalberg was a town with moderate iodine deficiency. The overall population in the catchment areas of selected health centres in the towns were the populations studied over time. The same denominator was used at baseline and at each follow-up. The results were normalized to an incident rate of hypothyroidism or hyperthyroidism per 100 000 inhabitants per year. The numbers of incident cases of hypothyroidism or hyperthyroidism were taken from the health laboratory registries and standardized to an incident rate of cases/100 000/year (12 months). The investigation took place from 1997 to 2005 and comprised four periods: 1. 1997–1998, baseline, was before iodization of salt was initiated and lasted 16 months in Aalborg and 14 months in Copenhagen; 2. 1999–2000, with iodization of salt on voluntary basis; 3. 2001–2002, with early mandatory iodization of salt; 4. 2003–2005, with late mandatory iodization of salt. In the period with voluntary iodization of salt, the iodized salt was not used by the food industry and it covered only around 50% of household salt. Accordingly, the average increase in iodine intake was low (on average, 10 µg/day).
Participants	Two open population cohorts representing all inhabitants of Aalborg and Copenhagen, Denmark
Interventions	Iodized salt was provided at a concentration of 8 ppm (parts per million) during a voluntary phase and then at 13 ppm during mandatory salt iodization in Denmark.
Outcomes	1. Incident rate of hypothyroidism 2. Incident rate of hyperthyroidism
Publication details	Three articles from this study published in peer-reviewed journals in English
Stated aim of study	To compare the long-term effects of different grades of low iodine intake on the incidence of hypothyroidism and hyperthyroidism in Denmark
Notes	1. Design: cohort observational 2. Age: all 3. Group: not specifically pregnant women 4. Salt consumption: 5.5–6.0 g/day estimated 5. Iodine concentration: 13 ppm 6. Duration: 7 years (hypothyroidism), 5 years (hyperthyroidism) 7. Baseline iodine deficiency disorder (IDD) status: • Copenhagen: mild iodine deficiency • Aalberg: moderate iodine deficiency Intake of approximately 72 µg iodine/day Data from adults and children collected but results presented as a total number for the entire population

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Low attrition
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Methodology to collect data from all members of population was consistent throughout study

Pongpaew et al., 1998 *(58)*

Methods	**Non-randomized controlled trial** (RCT) conducted in Thailand Concurrent controlled study conducted in four schools in Thailand. Four schools were randomly selected to participate in a baseline study of iodine status and the status of other nutritional indicators. After the baseline study, each of the schools was assigned to one of three interventions (iodinated salt, iodized water, iodized fish sauce) or control (no intervention). In the iodized salt intervention arm, iodized salt was given to the students on a regular basis, for use at all times. The participants were measured again after 1 year of intervention. The data from the iodized salt intervention school and the control school were compared in this review.
Participants	All schoolchildren; 68 intervention/63 control
Interventions	The intervention results used in this analysis were of an intervention of iodized salt. The salt was iodized at 50 g potassium iodate per 1000 kg salt (50 ppm [parts per million]).
Outcomes	1. Urinary iodine concentration 2. % of population with urinary iodine excretion (UIE) <100 µg/L
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To assess the best method of providing iodine to schoolchildren among the interventions of salt, fish sauce and drinking water
Notes	1. Design: non-RCT 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: estimation reported at 5–10 g/day 5. Iodine concentration: 50 ppm 6. Duration: 1 year 7. Baseline iodine deficiency disorder (IDD) status: mild IDD in intervention and adequate iodine status in control (based on UIE) • Intake of 250 µg iodine per day • Ages and numbers of students included in the study not reported

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not RCT
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Reported there was no loss-to-follow up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Baseline characteristics of schools were evaluated before it was decided if school would be intervention or control, and how each was determined was not described

Regalbuto et al., 2010 *(139)*

Methods	**Multiple cross-sectional observational study** conducted in Sicily, Italy This study compared the goitre prevalence in 1977, in 1994 during which the use of iodized salt was less than 1% of the total salt consumed, and in 2007, 10 years after the promotion of iodized salt, which began in 1996. The use of iodized salt reached 44% (28% to 55%). Schoolchildren from different towns were surveyed for goitre, thyroid volume and urinary iodine excretion (UIE). The selection of subjects was not described in detail.
Participants	Schoolchildren areas defined as endemic and not endemic for iodine deficiency, based on baseline UIE Two cohorts each from a different village All results in manuscript reported by village: • Bronte • Maniace
Interventions	30 mg/kg iodized salt (potassium iodate) was used.
Outcomes	1. Goitre 2. Thyroid volume (mL; only assessed at the follow-up and therefore these data are not part of the systematic review) 3. UIE (data in summary table because sample sizes not reported)
Publication details	Published in peer-reviewed journal in English
Stated aim of study	To assess the increase in iodized salt consumption and to re-evaluate goitre prevalence and iodine intake in the population of the endemic area previously studied.
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 30 ppm (parts per million) 6. Duration: 10 years 7. Baseline iodine deficiency disorder (IDD) status: based on goitre: • Bronte: mild IDD • Maniace: moderate IDD

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not clear but not likely
Incomplete outcome data (attrition bias)	High risk	Multiple cross-sectional but much lower sample size at follow-up
Selective reporting (reporting bias)	High risk	Sample sizes for UIE were not reported because of low numbers of participants for this measurement
Other bias	Unclear risk	Methodology for sample selection not described

Romano et al., 1991 *(54)*

Methods	**Randomized controlled trial** (RCT) conducted in Italy Pregnant women were randomly selected from a health-care facility. Women were first stratified by smoking status and then randomly assigned to either group A (iodized salt) or group B (non-iodized salt). Each trimester, measurements were taken at the clinic. Units of comparison: individuals
Participants	Pregnant women with no personal history of thyroid diseases, not having been pregnant before in the previous year, and not taking medications that could have affected thyroid hormone metabolism
Interventions	1. Iodized salt provided at 20 ppm (parts per million; *n* = 17) 2. Control: plain salt, but not specifically distributed (*n* = 18)
Outcomes	1. Thyroid volume (data not used in this review because not reported at follow-up for control group) 2. UIE (µg iodine/24 h; added to summary table because cannot be combined with other RCT because of units of reporting and measurement in children) 3. Serum thyroid-stimulating hormone (TSH) levels (data not used in this review because not reported for follow-up)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To investigate the thyroid size during pregnancy by use of an accurate ultrasonographic technique and to show the role of iodoprophylaxis in the prevention of an increase in thyroid volume in a group of pregnant women who live in an area with moderate iodine deficiency
Notes	1. Design: RCT 2. Age: adult 3. Group: pregnant women 4. Salt consumption: 7–10.6 g/day estimated by authors 5. Iodine concentration: 20 ppm (parts per million) 6. Duration: <1 year (9 months of pregnancy) 7. Baseline iodine deficiency disorder (IDD) status: moderate IDD (based on author's description but no data provided) • Iodine intake 120–180 µg/day

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Detail on randomization not published
Allocation concealment (selection bias)	Unclear risk	Detail on allocation concealment not published
Blinding of participants and personnel (performance bias)	High risk	Subjects not blinded – control group not given salt while experiment group was provided with iodized salt
Blinding of outcome assessment (detection bias)	Low risk	Assessor blinded
Incomplete outcome data (attrition bias)	Low risk	0% attrition
Selective reporting (reporting bias)	High risk	TSH and thyroid volume not reported for follow-up for both groups
Other bias	Low risk	Women had to meet many inclusion criteria, so the groups were comparable at baseline

Rueda Williamson and Pardo Tellez, 1966 *(140)*

Methods	**Multiple cross-sectional observational study** conducted in Colombia A representative sample of school-aged children from one department in Colombia was selected for measurement of goitre status before iodization of salt in Colombia. The first survey was conducted in 1945. Salt was iodized at 50 ppm (parts per million), starting as pilot in 1950, then a law was implemented in 1955 for the country. Large-scale iodization began in 1959 and in 1964 salt in the country varied from 60 to 75 ppm iodine, based on monitoring activities. Another survey sample was measured for goitre 10 years after the implementation of a law requiring iodization of salt. Goitre was defined using World Health Organization standards.
Participants	A representative sample of school-aged children (8700 at baseline and 2166 at follow-up)
Interventions	Iodized salt was provided at a concentration of 60–75 ppm, through a mandatory programme.
Outcomes	Goitre
Publication details	Published in a peer-reviewed journal in Spanish
Stated aim of study	To measure the real effectiveness of salt iodization at the national scale for the prevention of endemic goitre
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 60–75 ppm 6. Duration: 10 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre) The coverage of salt iodization at 60 ppm or higher in the country was found to be 76% in 1964, which was 1 year before the post-iodization survey was conducted. The coverage was found to be 85% in 1966, 1 year after the post survey was conducted. The coverage in 1965, the year of the survey, could be estimated to be between these values.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not clear but not likely
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with similar sample sizes at both time points
Selective reporting (reporting bias)	Low risk	Only outcome measured was goitre and it was fully reported
Other bias	Low risk	Both samples representative of the department of Caldas, Colombia and selected using similar methodology

Salvaneschi et al., 1991 (141)

Methods	**Multiple cross-sectional observational study** conducted in Argentina. Before/after study design with cross-sectional representative surveys of goitre in city of Buenos Aires, Argentina. Goitre was measured using World Health Organization methods and definition. The first survey occurred before the mandatory fortification of salt with iodine and the second survey occurred 18 years after the implementation of mandatory fortification of salt with iodine in the city.
Participants	School-aged children (3882 at baseline and 3365 at follow-up)
Interventions	Iodized salt was provided at a concentration of 33 ppm (parts per million).
Outcomes	Goitre
Publication details	Published in a peer-reviewed journal in Spanish
Stated aim of study	To describe the prevalence of goitre in 1986 after more than 15 years of salt iodization in the city of Buenos Aires and compare that value to those found in 1968 before the iodization of salt in the city
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 33 ppm 6. Duration: 18 years 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with similar samples sizes at both time points
Selective reporting (reporting bias)	High risk	Goitre prevalence reported on fewer participants than measured but reason not given
Other bias	Low risk	Both samples representative of the city of Buenos Aires and selected using similar methodology – probability proportionate to size (PPS) sampling

Saowakhontha et al., 1994 *(59)*

Methods	**Non-randomized controlled trial** (RCT) conducted in four villages of Thailand The four villages sampled in the study were randomly selected from 12 villages. The participants were randomly selected from the inhabitants of the villages. One of three interventions (fish sauce, iodized salt, iodized water) or control were applied to each village. All participants in each village received the intervention assigned to his/her village. The iodized salt group received the salt at the household on a regular basis. The control group received no intervention. The data used in this analysis were from the iodized salt and the control groups.
Participants	Women randomly selected in each of the villages from the age of 1 to 45 years
Interventions	• Group A: fish sauce • Group B: iodized salt provided at 50 ppm (parts per million) to the households of the randomly selected participants • Group C: iodized water • Group D: no intervention (conventional iodine intake, which might have include iodized salt, fish sauce, iodine water, etc.)
Outcomes	Urinary iodine excretion (UIE; the values were reported as µmol iodine/g creatinine; however, the numeric values were 10–1000 times greater than one would expect and therefore were not considered reliable and not included in the summary table or meta-analysis)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To evaluate the best method of providing iodine to this population
Notes	1. Design: non-randomized controlled study 2. Age: adults 3. Group: not specifically pregnant women 4. Salt consumption: 5–10 g/day (estimated) 5. Iodine concentration: 50 ppm 6. Duration: 6 months 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre) • Iodine intake estimated at 250–500 µg/day

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not RCT
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Low attrition
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Though intervention and control were severe IDD areas, goitre prevalence at baseline in intervention group was 68.9% and in control was 36%

Scrimshaw et al., 1966 *(142)*

Methods	**Multiple cross-sectional observational study** conducted in Guatemala Before and after design to monitor the effect of fortification of salt with iodine on goitre rates in schoolchildren in Guatemala. Two cross-sectional studies were conducted, one before and one after the implementation of mandatory salt iodization in the country. The surveys were representative of 19 of the 22 departments of the country. Coverage of salt iodization at sufficient concentration in the country was estimated at 80% at the year of the follow-up survey.
Participants	Schoolchildren aged 6–18 years, representative of 19 of 22 departments in the country (28 787 at baseline and 19 442 at follow-up)
Interventions	Iodized salt was provided at a concentration of 100 ppm (parts per million) via a national programme.
Outcomes	Goitre
Publication details	Published in a peer-reviewed journal in Spanish
Stated aim of study	To evaluate the efficacy of the salt iodization programme
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 100 ppm 6. Duration: 1.5 years 7. Baseline iodine deficiency disorder (IDD) status: severe (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear but not likely
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional design with similar sample sizes at both time points
Selective reporting (reporting bias)	Low risk	Only outcome measured was goitre and it was fully reported
Other bias	Low risk	Both samples representative and selected using similar methodology

Shen, 1991 *(74)*

Methods	**Quasi-experimental study** conducted in villages of Xinzhou county, Hubei province, China Children of three villages in the county were eligible. All three villages began receiving universal salt iodization in 1977. Children were randomly sampled in 1987 (10 years after universal salt iodization) and divided into two groups: children born before (comparison) and children born after universal salt iodization (experiment). The intelligence of children was measured using the Chinese Binet Scale.
Participants	Children aged 6–14 years at the time that intelligence was measured (1987)
Interventions	Universal salt iodization was carried out at a concentration of 20 ppm (parts per million).
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <0 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20 ppm 6. Duration: 9 months' gestation to 4 years (comparison group was born before universal salt iodization and some were born up to 4 years before) 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding reported but not likely
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Comparison from same villages, to reduce bias but sampling methods not reported and *n* value in experiment group was lower (n = 48) than comparison (n = 60)

Shu, 1987 *(75)*

Methods	**Quasi-experimental study** conducted in a suburb of Shenyang, Liaoning province, China Children of three villages in the area were eligible. All three villages received universal salt iodization for 9 years before the measurements were taken. The children born before (comparison) were compared to children born after universal salt iodization (experiment)
Participants	Children aged 5–15 years at time that intelligence was measured (date not reported)
Interventions	Universal salt iodization was provided in unknown concentration.
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 9 months' gestation to 6 years (comparison group was born before universal salt iodization and some were born up to 6 years before) 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (as reported by authors but no data provided)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding reported but not likely
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Comparison from same area for children born before universal salt iodization but sample methodology not reported and sample sizes different and therefore comparability unknown; also, sampling methods not reported and *n* value in intervention group was much lower (n = 61) than in the comparison group (n = 170)

Sooch and Ramalingaswami, 1965 *(60–62)*

Methods	**Non-randomized controlled trial** (RCT) conducted in Punjab, India This study was set up as a prospective controlled study of the effect of iodization of salt on goitre rates. The study was undertaken in the Himalayan endemic goitre belt of northern India. Over 20 000 villagers were surveyed and the analysis of results was divided between children aged 5–16 years attending school, children not attending school and the general population of adults and children combined. The area of the study was divided into three zones. One zone received salt with potassium iodide, one received salt with potassium iodate, and the third was a control zone that did not receive fortified salt. Randomization and blinding were not mentioned in the study reports. All schoolchildren in each of the zones were surveyed at the beginning, in the middle and at the end of the study period. In each zone, two thirds of the villages were sampled and all of the villagers present on the day of survey were included in the surveys. The first, baseline, survey was in 1956, another survey was conducted 5 years later (1962), and a final survey was conducted in 1968. From 1956 to 1962, two zones received the intervention and one zone was the control. In 1956, the control zone was also provided salt fortified with salt and all three villages were followed over time until the final follow-up. Additional data were reported in reference *(62)*, which was of multiple cross-sectional design describing the results after 12 years of salt iodization.
Participants	All villagers in two thirds of the villages in the three zones and all school-aged children Two cohorts reported: • schoolchildren • all other children and adults in the villages (results not presented separated by age)
Interventions	1. Iodized salt was provided to one zone in the concentration of 20 ppm (parts per million) potassium iodide (i.e. 15.27 ppm iodine) and as 25 ppm potassium iodate (i.e. 14.83 ppm iodine) to another zone (the results from the two intervention groups were combined and used as intervention and compared to control). 2. Plain salt was provided.
Outcomes	1. Goitre 2. I-131 absorption rate of thyroid and subsequent excretion (there were no data for this that were measured at baseline and follow-up and these data could not be used in the meta-analysis) 3. Urinary iodine excretion (UIE) measured at follow-up of multiple cross-sections, but no baseline measure for comparison
Publication details	Published in peer-reviewed journals in English
Stated aim of study	To demonstrate the effectiveness of iodine in salt in the prevention of goitre and to test the relative effectiveness of potassium iodide and potassium iodate
Notes	1. Design: non-RCT (and multiple cross-sectional in a subsequent analysis) 2. Age: all and children (non-RCT and children in multiple cross-sectional) 3. Group: not specifically pregnant women 4. Salt consumption: 15 g (estimated) 5. Iodine concentration: 20 ppm potassium iodide, and 25 ppm potassium iodate 6. Duration: 5 years (12 years in a subsequent multiple cross-sectional analysis) 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No randomization mentioned in the published manuscripts
Allocation concealment (selection bias)	High risk	No concealment mentioned in the published manuscripts
Blinding of participants and personnel (performance bias)	High risk	No blinding mentioned in the published manuscripts but unlikely
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding mentioned in the published manuscripts
Incomplete outcome data (attrition bias)	Low risk	All people in villages were measured and attrition not reported but actual numbers were higher at follow-up than at baseline, suggesting low attrition, and measurement of individuals not captured at baseline
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Population in experiment and control similar in habits, customs, dietary practices, socioeconomic status, ethnic origin and severity of goitre at baseline

Szybinski et al., 2001 *(143)*

Methods	**Multiple cross-sectional observational study** conducted in Poland Children attending selected schools were surveyed before and 5 years after the initiation of a national programme for the iodization of salt.
Participants	952 schoolchildren in 1994, and 884 in 1999
Interventions	Iodized salt was provided with potassium iodide concentration of 25 ± 10 mg/kg from 1986, and 30 ± 10 mg/kg from 1997; there was 5 years' follow-up.
Outcomes	1. Prevalence of goitre 2. Urinary iodine excretion (UIE; µg/L) 3. % population with UIE <100 µg/L
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To compare UIE and prevalence of goitre in schoolchildren before and after the initiation of salt iodization in Poland and to analyse regional differences in the effectiveness of iodine prophylaxis
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 30 ppm (parts per million) 6. Duration: 5 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with similar sample sizes at both time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Schools were representative of different areas of country but appears that only some schools from baseline survey were selected for follow-up survey ("randomly")

Tang et al., 1992 *(103)*

Methods	**Cohort observational study** conducted in villages near Kunmin, China
Participants	All inhabitants of four villages
Interventions	A survey of goitre and urinary iodine excretion (UIE) was conducted in four villages. Three villages then provided iodized salt to the villagers and after 3 years the villagers were again surveyed. The fourth village received iodized salt and iodized oil and was not included in this analysis. The three cohorts were: • Houcun; • Guanbo; • Xiaocun. The concentration of iodine varied by village: • Houcun <10 ppm (parts per million); • Guanbo <10 ppm; • Xiaocun <20 ppm.
Outcomes	1. Goitre prevalence 2. Goitre cure rate in patients with goitre at baseline (not included in this review) 3. UIE (μg/L); there was probably a mistake in the UIE figures, in that the standard deviation was too small; the meta-analysis was conducted with and without data from this study 4. Tri-iodothyronine (T_3), thyroxine (T_4), thyroid-stimulating hormone (TSH; not used in this review because not considered practical indicators)
Publication details	Published in a Chinese language journal
Stated aim of study	To find the appropriate level of iodine concentration in salt needed for effective goitre prevention and control
Notes	1. Design: cohort observational 2. Age: all 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: <20 ppm 6. Duration: 3 years 7. Baseline iodine deficiency disorder (IDD) status: based on goitre: • Houcun moderate IDD • Guanbo severe IDD • Xiaocun severe IDD

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Though the methods claim a cohort study of measurement of all villagers, the sample sizes at follow-up were much higher in Guanbo than at baseline (more than twice as high)
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Participants from same villages compared to one another, to reduce bias

Tazhibayev et al., 2008 *(104)*

Methods	**Cohort observational study** in five countries in Eastern Europe and Central Asia Urinary iodine levels were measured in children at sentinel sites in six countries before salt iodization in those countries. The five countries then began salt iodization at the national level at 40 ppm. Four years after the initiation of the salt iodization programmes in Kazakhstan, Mongolia, Tajikistan and Uzbekistan, and 3 years in Azerbaijan, a follow-up survey in the same children measured urinary iodine concentration again. Women were also measured at the follow-up studies but their data are not included. Additionally, baseline data were collected in Kyrgyzstan but, according to the authors, the salt iodization programme in that country was not initiated and therefore there are no follow-up data.
Participants	Children aged 2–15 years in households randomly selected from health clinic registries in the sentinel sites in six countries; review includes the data from five countries with baseline and follow-up data Cohorts: • Azerbaijan • Kazakhstan • Mongolia • Tajikistan • Uzbekistan
Interventions	Iodized salt was provided at 40 ppm (parts per million).
Outcomes	1. Urinary iodine excretion (UIE; µg/L) 2. % of population with UIE <100 µg/L 3. Haemoglobin concentration (not utilized in this review) 4. Ferritin (not utilized in this review) 5. Folic acid (not utilized in this review)
Publication details	Published in peer-reviewed journal in English
Stated aim of study	To determine the potential effectiveness of the food fortification programmes in improving micronutrient status in a sentinel population in each country
Notes	1. Design: cohort observational 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 40 ppm (parts per million) 6. Duration: 4 years in Kazakhstan, Mongolia, Tajikistan and Uzbekistan, 3 years in Azerbaijan 7. Baseline IDD status: based on UIE: • Kazakhstan, adequate iodine status • Mongolia, mild iodine deficiency • Tajikistan, moderate iodine deficiency • Uzbekistan, adequate iodine status • Azerbaijan, adequate iodine status

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Sample size at follow-up not reported so size assumed to be same as baseline
Selective reporting (reporting bias)	Low risk	Only data from Kyrgyzstan not reported but stated it was due to the iodization programme not being initiated
Other bias	Low risk	Participants randomly selected from registries at sentinel site locations in each country

Teng et al., 2009 *(76)*

Methods	**Quasi-experimental study** conducted in Tuanshan township, Huangdi township, Taihe township and Jiangtun township, China Children of each township that were born before iodization of salt were compared to children in the townships born after iodization of salt.
Participants	School-aged children at time that intelligence was measured
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until up to 12 years of age. There was one cohort. Results from all townships were combined; the experiment group was students born after salt iodization and the comparison group was children born before salt iodization.
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Combined Raven's Test in China (CRT-C2) Comparisons were made within village to control for potential biases. 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown (not reported) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus up to 12 years of life more than comparison 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No mention of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	No sampling methodology was reported but it is thought that all children were included and all children from same villages, to reduce potential bias

Vejbjerg et al., 2009 *(144)*

Methods	**Multiple cross-sectional observational study** conducted in Denmark Observational, cross-sectional study conducted in Denmark to evaluate the effect of iodization of salt on thyroid function by comparing thyroid-stimulating hormone (TSH) and hypo- and hyperthyroidism pre/post mandatory salt iodization; 4649 participants were examined in 1997–1998 before salt iodization and 3570 were involved after the introduction of a mandatory iodization programme in 2000. Participants in the first survey were excluded from the second survey and the second survey was age and sex matched to the first survey.
Participants	Adults living in Copenhagen or Aalborg, Denmark who were not taking iodine supplementation and did not have thyroid disease
Interventions	Iodized salt was provided at 13 ppm (parts per million), through mandatory legislation at the national level.
Outcomes	1. Serum TSH (data not used in this review as crude values not sensitive indicator of status). 2. Hypothyroidism (defined using TSH and free thyroxine [fT_4]) 3. Hyperthyroidism (defined using TSH and fT_4) 4. Thyroid volume by ultrasound (values not reported in results of manuscript and only used to help diagnose hypo- and hyperthyroidism) 5. Urinary iodine excretion (UIE; only measured at follow-up and not included in this review)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To evaluate the impact of the introduction of a mandatory iodization programme on thyroid hormone levels, and the prevalence of thyroid dysfunction in the population
Notes	1. Design: multiple cross-sectional 2. Age: adults 3. Group: not specifically pregnant women 4. Salt consumption: 5.5–6.0 g/day estimated (from Pedersen 2002 study *(100)*) 5. Iodine concentration: 13 ppm 6. Duration: 4 years 7. Baseline iodine deficiency disorder (IDD) status: combination of data from a mild and a moderate IDD area based on UIE – iodine intake estimated at 66 µg/person/day

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with similar sample sizes
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Samples were selected to be representative of general population and sampling techniques were the same for both surveys

Wang and Wang, 1981 *(145)*

Methods	**Multiple cross-sectional observational study** conducted in Anqiu county, Shandong province, China
Participants	84% of inhabitants in 1966 and 83.9% in 1980 of nine villages Results from nine groups are reported separately but the selection of those groups is not described and therefore the total values are used in this review.
Interventions	Salt was iodized at 100 ppm (parts per million) for 13 years.
Outcomes	Goitre (as in many Chinese languages articles, "endemic goitre" and "physical enlargement of the thyroid" are both reported – the combined value is used as the definition of goitre for use in this review)
Publication details	Published in Chinese in a peer-reviewed journal
Stated aim of study	To assess the effect of iodized salt in the prevention of iodine deficiency disorder (IDD)
Notes	1. Design: multiple cross-sectional 2. Age: all 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 100 ppm 6. Duration: 13 years 7. Baseline IDD status: severe IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional study with similar sample sizes at both time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Entire population included through census methodology used in both surveys

Wang et al., 1985 *(146)*

Methods	**Multiple cross-sectional observational study**, before–after data, conducted in Chengde city, China A survey was conducted in 1961 and universal salt iodization began in 1962. A follow-up study using the same methods was conducted in 1983.
Participants	All inhabitants of four villages aged from 0 year to 60+ years
Interventions	50 ppm (parts per million) iodized salt was supplied from 1962 to 1982; no control was used.
Outcomes	1. Goitre prevalence (as in many Chinese languages articles, "goitre" and "physical enlargement of the thyroid" or "thyroid enlargement" are both reported – the combined value is used as the definition of goitre for use in this review) 2. Urinary iodine concentration (these data not included in this review because no baseline) 3. I-131 absorption rate of thyroid in a small sample of people with iodine deficiency disorder (IDD; these data not included because no baseline value) 4. Cretinism (reported in summary table)
Publication details	Published in a Chinese language journal
Stated aim of study	To test the effectiveness of salt iodization to prevent goitre and cretinism
Notes	1. Design: multiple cross-sectional 2. Age: children and adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm 6. Duration: 20 years 7. Baseline IDD status: severe IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional study with similar sample sizes at both time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Same survey methods used in both surveys

Wang and Yang, 1985 *(105)*

Methods	**Cohort observational study** conducted in China 120 schoolchildren living in an endemic area of iodine deficiency in China were selected to participate in an evaluation of hearing and markers of iodine status; 30 children were selected from each of four communities, which were selected based on the endemic status of the community for iodine deficiency. Children were excluded if they had mental deficiency as reported by the teacher, had goitre, had a known cause of hearing impairment, or if hearing disorder due to improper vestibular function as assessed by electronystagmography was detected. Three communities were described as endemic for iodine deficiency and one community was described as non-endemic. The only comparisons that had outcomes of interest and thus were included in this review were those from one endemic community measured before the introduction of iodized salt in the community, and the same children measured 3 years after the introduction of iodized salt. No information is given as to how the iodized salt was given to the children or if it was merely provided to the community.
Participants	Children 7–11 years of age at baseline attending school in randomly selected communities in an endemic goitre area of China
Interventions	Iodized salt was provided. There are no details regarding the provision of the salt.
Outcomes	1. Thyroxine (T_4; not used in this review) 2. Thyroid-stimulating hormone (TSH) 3. Urinary iodine excretion (UIE; µg iodine/g creatinine) 4. I-131 uptake (not used in this review) 5. Hearing level (not used in this review)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To search for marginal cases of endemic cretinism and to assess the therapeutic and prophylactic effect of iodized salt administration on the hearing of these inhabitants of endemic areas (Note: no mention was made of inclusion criteria related to cretinism, and children with mental deficiency were excluded from the study.)
Notes	1. Design: cohort observational 2. Age: children 3. Group: not specifically pregnant 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 3 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (as reported by authors but no data provided)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Reported no loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Selection criteria for children pre and post were the same and from same community, to reduce potential bias

Wang et al., 1987 *(78)*

Methods	**Quasi-experimental study** conducted in Huabeitun and Chengguanzhen villages in China Children of the villages that were born before iodization of salt were compared to children in the villages born after iodization of salt.
Participants	All children aged 8, 9, 14 and 15 years living in the villages at time that intelligence was measured (1985)
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1–2 years of age. There were two cohorts: • Huabeitun (severe iodine deficiency area at baseline); • Chengguanzhen (mild iodine deficiency area at baseline).
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) Though the text says % of children with IQ <70 points (mild mental retardation – MMR) is reported, results are only presented for both villages combined.
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Sampling methodology not reported 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown (not reported) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus 1–2 years of life more than comparison 7. Baseline iodine deficiency disorder (IDD) status: • Huabeitun: severe IDD (based on goitre; did not use World Health Organization criterion of school-aged children) • Chengguanzhen: mild IDD (as reported by authors but no data provided)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding reported
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported (stated drop-out was less than 15% though statement is difficult to interpret)
Selective reporting (reporting bias)	Unclear risk	Results for % of children with intelligence quotient (IQ) <70 points (mild mental retardation – MMR) only reported for both villages combined
Other bias	Low risk	Children from same villages compared to one another, to reduce potential bias

Wang et al., 1987 *(79)*

Methods	**Quasi-experimental study** conducted in Xinzhou city, Shanghi province, China Children of Jin village (severe iodine deficiency disorder [IDD] area) where there was no salt iodization were compared to children in Siping village (severe IDD area), which did have salt iodization. Salt iodization was begun in Siping in 1974. The villages were surveyed in 1974 and again in 1985 after 11 years of universal salt iodization in Siping. Measurements were also taken in an area without IDD but those data were not included in this review.
Participants	Children aged 7–13 years at time that intelligence was measured (1985)
Interventions	Universal salt iodization was provided in Siping village at unknown concentration.
Outcomes	Intelligence of children and psychomotor function: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR) • psychomotor function (selective response time, knock test, reversing hand, ratio of grasp power)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 7–11 years (11 years intervention but some participants <11 years of age) 7. Baseline IDD status: moderate IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Villages comparable at baseline

Wang et al., 1992 *(80–82)*

Methods	**Quasi-experimental study** conducted in Ninxia Hui autonomous region, China Children of Shicha village (severe iodine deficiency disorder [IDD] area) where there was no salt iodization were compared to children in Shenzi village (severe IDD area), which did have salt iodization. Salt iodization was begun in Siping in 1968. The villages were surveyed in 1968 and again in 1983 after 15 years of universal salt iodization in Shenzi. Measurements were also taken in an area without iodine deficiency disorder (IDD) but those data were not included in this review. Stratified sampling was used to control for age, with 20 children of each year of age selected randomly for survey and measurements. Children with "brain impairment" were excluded.
Participants	Children aged 7–14 years at time that intelligence was measured (1983)
Interventions	Universal salt iodization was provided in Shenzi village at 50 ppm (parts per million).
Outcomes	Intelligence of children • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Stated that villages were very similar in sociodemographics and environment 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm 6. Duration: 7–14 years (15 years intervention but some participants < 5 years of age) 7. Baseline IDD status: severe IDD (based on goitre; reported for entire population in Shenzi and just for children in Shicha)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported but sampling methodology consistent and sample sizes similar
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Villages comparable at baseline

Wang, 1994 *(83)*

Methods	**Quasi-experimental study** conducted in Hebei province, China Children living in a "severe IDD [iodine deficiency disorder]" area were sampled (methodology not mentioned) and divided into those born before and those born after universal salt iodization. The intelligence of those children was measured.
Participants	Children aged 7–14 years at time that intelligence was measured (date not stated)
Interventions	Universal salt iodization was carried out at unknown concentration.
Outcomes	Intelligence of children • mean intelligence quotient (IQ; standard deviation not provided so data only included in summary table and not meta-analysed) • % of children with IQ <70 points (mild mental retardation – MMR; table does not include the results for this variable though the variable is mentioned)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: exposure duration of experimental group unknown but comparison did not have exposure during pregnancy 7. Baseline IDD status: combined data from an area of severe IDD area and an area of adequate iodine status (as stated by authors but no data provided)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Unclear risk	% of population with intelligence quotient (IQ) <70 not reported as expected
Other bias	Unclear risk	Children within same villages compared, to reduce bias, but sample size of comparison group much larger than experimental group

Wang et al., 2000 *(147)*

Methods	**Multiple cross-sectional observational study**, before–after design, carried out in Hefei and Caohu area, China In two localities, a survey was conducted in 1995 before implementation of universal salt iodization and it was then implemented in 1996, with a follow-up survey in 1997. In one locality, the universal salt iodization began in 1995 and the follow-up survey was in 1996. In all three localities, the follow-up was one year after introduction of universal salt iodization.
Participants	All 7–14-year-old students in selected primary schools, a total of 2644 children, included before supplementation of iodized salt in 1995, and 2395 after supplementation of iodized salt for 1 year in 1996
Interventions	Iodized salt supplementation was carried out for one year, the concentration was not mentioned and no control was used.
Outcomes	1. Urinary iodine concentration (median reported and therefore results presented in summary tables) 2. Goitre prevalence (goitre is reported as prevalence in each locality, whereas the sample size is given as a total for all localities, so the number of affected individuals cannot be calculated – results found in summary table) 3. Perchlorate discharge test, thyroid gland antibody for students with goitre (data not used because only reported for individuals with goitre) 4. Thyroid-stimulating hormone (TSH), tri-iodothyronine (T_3) and thyroxine (T_4; not used in this review) 5. % urinary iodine excretion (UIE) <100 µg/L (only reported for follow-up) 6. % UIE >300 µg/L (only reported for follow-up)
Publication details	Published in a Chinese language journal
Stated aim of study	To understand the effects of universal salt iodization on IDD control and prevention and the iodine nutrition and thyroid function of children
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 1 year 7. Baseline iodine deficiency disorder (IDD) status: based on goitre/(based on UIE): • Chaohu: severe IDD/(moderate IDD) • Dabieshan: moderate IDD/(above requirements) • Hefei: adequate iodine status/(mild IDD)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding reported
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional study with similar sample sizes at both time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Children of same age and from same communities compared to one another, to reduce potential bias

Wang, 2001 *(106)*

Methods	**Multiple cross-sectional observational study**, before–after design, conducted in Qingyuan county, Hebei province The study randomly sampled 10 primary and middle schools and examined all of the students from the 10 sampled schools every year from 1995 to 2000.
Participants	7–14-year-old students from 10 primary and middle schools; 4867 students included before supplementation of iodized salt in 1995, and 2000 in 2000 after supplementation of iodized salt Universal salt iodization began in 1995.
Interventions	Universal salt iodization was carried out at a concentration of 20 ppm (parts per million).
Outcomes	Goitre prevalence
Publication details	Published in a Chinese language journal
Stated aim of study	None stated
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20 ppm 6. Duration: 5 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	High risk	Cohort observational study with much smaller sample sizes at follow-up, with no explanation of attrition rate
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Methodology for sample selection not described

Wang 2005 *(77)*

Methods	**Quasi-experimental study** conducted in Lianoning province, China Children without Down syndrome or other brain impairment were sampled (methodology not mentioned) from Rongxing, Kuanbang, and Pingfangzi townships in June 2002 to December 2003. Rongxing was an iodine-sufficient area and the data were not used in this review. Kuanbang did not have iodized salt from 1985 to 1995 (comparison group). Pingfangzi did have salt iodization. The ages of the children were not mentioned in the manuscript.
Participants	Children of unknown age at time that intelligence was measured (2002–2003
Interventions	Universal salt iodization was provided at unknown concentration (experiment). There was no salt iodization from 1985 to 1995 when tested children were born (comparison group).
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Combined Raven's Test for Rural China 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: exposure duration of experimental group unknown but comparison did not have exposure during pregnancy 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported but sample size of experiment and control similar
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Exact ages of children not reported/comparability between villages not clear

Wang et al., 2009 *(148, 149)*

Methods	**Multiple cross-sectional observational survey** conducted in Gansu province, China Surveys were conducted to assess the effectiveness of salt iodization for the reduction of goitre in school-aged children. A baseline survey was conducted before universal salt iodization was implemented and a follow-up survey conducted 10 years after implementation. Children who were sampled for the measurement of goitre and urinary iodine were randomly selected through multi-stage cluster sampling. In the first stage, schools were randomly selected and in the second stage, students within schools (40 students per school) were randomly selected. The measurement included thyroid examination. In a subsample, urinary iodine was measured (12 students per school). In 1997, 2 years after universal salt iodization was implemented in the province, another survey was conducted to measure the intelligence quotient (IQ) of students. After the baseline survey, universal salt iodization was implemented in the country; 10 years later, a follow-up survey with the same measures was completed in the same schools, using the sample methodology.
Participants	School-age children in Gansu province China (8–10 years of age)
Interventions	Iodized salt was provided at 50 ppm (parts per million) for 5 years and then 35 ppm, through universal salt iodization.
Outcomes	1. Goitre 2. Urinary iodine excretion (UIE; median reported and included in summary table) 3. % of population with UIE <100 µg/L
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To assess the effects of universal salt iodization on the status of iodine deficiency disorder (IDD) in a region of traditionally severe iodine deficiency
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 35 ppm (parts per million)[a] 6. Duration: 10 years 7. Baseline IDD status: severe IDD (based on goitre)/adequate iodine status (based on UIE) [a] Note the concentration was 50 ppm for first 5 years and then 35 ppm for second 5 years of follow-up.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional with similar sample sizes at both time points
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Same methods used to select school-aged children in both surveys, to reduce potential bias

Weber and Manz, 1987 *(107)*

Methods	**Cohort observational study** conducted in Germany 42 families were recruited for the study if the household had adults and children. A baseline measure of urinary iodine excretion (UIE) was taken, then all households were provided with iodized salt for use in the home during a time when use of iodized salt in processed foods was illegal. The families were follow-up after 6 months to measure UIE again.
Participants	78 adults and 73 children from 42 families Four cohorts: • children >6 years • children 6–12 years • adult men • adult women
Interventions	Iodized salt was provided at 20 ppm (parts per million) given to households for use.
Outcomes	UIE (median reported as µg/day and included in summary table)
Publication details	Published as a short communication in English
Stated aim of study	Not specified
Notes	1. Design: cohort observational 2. Age: adults and children 3. Group: not specifically pregnant women 4. Salt consumption: 12.2 g/day adult men; 9.5 g/day adult women; unknown in children 5. Iodine concentration: 20 ppm 6. Duration: 6 months 7. Baseline iodine deficiency disorder (IDD) status: not reported

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	No loss to follow up
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Other bias	Unclear risk	Methods of sample selection were not reported

Wei, 1985 *(150)*

Methods	**Multiple cross-sectional observational study** conducted in Daxin county, Guangxi, China In 1966, 1623 villagers were selected in severe villages of endemic iodine deficiency disorders before supply of iodized salt. Universal salt iodization began in 1967 and in 1981 a follow-up survey was conducted in the same villages.
Participants	Villagers in selected villages in Guangxi, China (1623 at baseline and 543 at follow-up) Six areas were surveyed at baseline; however, only three were surveyed at follow-up. The data from baseline and follow-up from three villages (combined) were used in meta-analysis.
Interventions	Iodized salt was provided at unknown concentration.
Outcomes	Goitre
Publication details	Published in a Chinese provincial journal.
Stated aim of study	To assess the effect of supplementation of iodized salt on goitre
Notes	1. Design: multiple cross-sectional 2. Age: children and adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: 15 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Multiple cross-sectional survey but sample size at follow-up was much less than at baseline
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Other bias	High risk	Methods used for sampling not described but very different sample size numbers suggest high risk of bias

Xu et al., 1984 *(108)*

Methods	**Cohort observational study** conducted in Yushugou village, Dajiagou community, China All villagers were surveyed in 1980 before universal salt iodization began. The entire population of the villages was again surveyed each year until 1984. The data from 1980 and 1984 were used in this meta-analysis as a pre-iodization and post-iodization measure.
Participants	All villagers in Yushuge of Dajiage commune (an area defined as severely iodine deficient at baseline)
Interventions	Universal salt iodization was provided at 50 ppm (parts per million) iodized salt.
Outcomes	1. Goitre incidence 2. Goitre prevalence 3. Goitre cure rate (data not included in this review)
Publication details	Published in a Chinese journal
Stated aim of study	To investigate the effect of 50 ppm concentration of iodized salt on goitre prevention and control
Notes	1. Design: cohort observational 2. Age: children and adults 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 50 ppm 6. Duration: 3 years 7. Baseline iodine deficiency disorder (IDD) status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	All villagers surveyed and the sample size was actually larger at follow-up
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Other bias	Low risk	Same census methodology used to measure all villages with high response rate, so the samples were comparable

Xue and Zhang, 1993 *(151)*

Methods	**Multiple cross-sectional observational study** conducted in Hami, Xinjiang, China Before–after data of supplementation of iodized salt were provided. A survey was conducted in 1975 in areas defined as mild iodine deficiency disorder (IDD), serious IDD, and non-disease (manner of classification of area not explained). Universal salt iodization began in 1975 and a follow-up survey was conducted in the same areas in 1992.
Participants	In 1975, as the baseline, 15 365 people in mild endemic area, 112 074 in the severe endemic area, and 3893 in the non-endemic area In 1992, after supplementation of iodized salt, 2687 in mild endemic area, 48 416 in severe area and 5454 in non-endemic area
Interventions	Iodized salt supplementation was carried out for 18 years (1975 to 1992), the concentration was 35 ppm (parts per million) and there was no control intervention.
Outcomes	1. Prevalence of goitre 2. Concentration of thyroid hormones (tri-iodothyronine [T_3], thyroxine [T_4], thyroid-stimulating hormone [TSH]; only measured at follow-up) 3. Urinary iodine concentration (only measured at follow-up) 4. Prevalence of hyperthyroidism (only measured at follow-up)
Publication details	Published in a Chinese journal
Stated aim of study	To better understand the effects of iodized salt distribution
Notes	Data on thyroid hormones and urinary iodine not included for analysis, owing to lack of data before supplementation of iodized salt 1. Design: multiple cross-sectional 2. Age: children and adults 3. Group: any group other than specifically pregnant women 4. Salt consumption: 10 g/day (not clear how this value was determined) 5. Iodine concentration: 35 ppm 6. Duration: 18 years 7. Baseline IDD status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Multiple cross-sectional survey but sample size at follow-up only half the baseline sample size
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Other bias	High risk	Sampling methodology not described but very different sample sizes suggest high risk of bias

Yang, 1984 *(158)*

Methods	**Multiple cross-sectional observational study (outcome of cretinism)** and **cohort observational study (all other outcomes)** conducted in Pingliang community, Guizhou, China Surveys compared before versus after introduction of iodized salt in Pingliang community, Kaili county, Guizhou province, China, an endemic iodine deficiency disorder (IDD) area. Because all inhabitants were surveyed, goitre, urinary iodine concentration and thyroid function were measured following a cohort design. The measure of cretinism was multiple cross-sectional (incident cretinism).
Participants	The entire population of adults and children of surveyed community – 3117 people in 1979 (95% inhabitants), 3067 people in 1982 (92% inhabitants)
Interventions	Iodized salt was provided at a concentration of <20 ppm (parts per million).
Outcomes	1. Goitre 2. Tri-iodothyronine (T_3), thyroxine (T_4), thyroid-stimulating hormone (TSH; not used in this review) 3. Urinary iodine concentration (µg iodine/g creatinine – only reported in children and no standard deviation; results provided in summary table) 4. Rate of absorption of I-131 of thyroid in individuals with iodine deficiency (because these outcomes were limited to those with iodine deficiencies, the data are not included in this review) 5. Incident cretinism (multi-cross-sectional design)
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To assess the effects of prevention and treatment of IDD through iodized salt
Notes	1. Design: multiple cross-sectional and cohort observational 2. Age: adults and children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: <20 ppm 6. Duration: 3 years 7. Baseline IDD status: severe IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional survey but sample size similar/cohort showed low attrition
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Other bias	Low risk	Census methodology used at both times with high response rate for cohort and multiple cross-sectional survey conducted in same areas, to reduce risk of bias

Yang and Zhang, 1984 *(109)*

Methods	**Cohort observational study** conducted in Qiandongnan autonomous prefecture, China A survey of goitre and cretinism of the entire population of the prefecture was conducted in 1978–1979. Universal salt iodization was then implemented. A follow-up survey was conducted in 1982.
Participants	The entire population of adults and children of surveyed communities in prefecture (227 001 people measured at both time points and those data reported)
Interventions	Iodized salt was provided at a concentration of <20 ppm (parts per million).
Outcomes	1. Goitre 2. Tri-iodothyronine (T_3), thyroxine (T_4), thyroid-stimulating hormone (TSH; not used in this review) 3. Urinary iodine concentration (µg iodine/g creatinine – reported as median and range (only provided for 3 of 40 communes surveyed); results provided in summary table 4. Rate of absorption of I-131 of thyroid in individuals of "target group" – not clear what this group was (data not included in this review) 5. Incident cretinism (only reported for follow-up and therefore could not be included in this review)
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To assess the effects of prevention and treatment of iodine deficiency disorder (IDD) through iodized salt
Notes	1. Design: cohort observational 2. Age: adults and children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: <20 ppm 6. Duration: 3 years 7. Baseline IDD status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Low attrition (entire prefecture)
Selective reporting (reporting bias)	High risk	Some outcomes only reported for specific communes of prefecture
Other bias	Low risk	Same census methodology used at both times, with high participation

Yang and Yang, 2011 *(152)*

Methods	**Multiple cross-sectional observational study** conducted in China The study randomly selected a primary school, with 40–100 schoolchildren aged 8–10 years. The first survey was conducted before the provision of iodized salt in the community and the follow-up surveys, conducted yearly, were conducted up to 15 years after the initiation of iodization of salt in the community. The data include every year from 1995 to 2009, 1995 and 2009 data only were compared in this review.
Participants	8–10-year-old schoolchildren
Interventions	Iodized salt was provided at a concentration of 35 ppm (parts per million), through provision at the population level.
Outcomes	1. Goitre 2. Urinary iodine excretion (UIE; median reported and results in summary table) 3. % population <100 µg/L UIE
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To monitor the effect of preventing iodine deficiency disorder (IDD) by the provision of iodized salt
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 35 ppm 6. Duration: 15 years 7. Baseline IDD status: mild IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Unclear risk	Multiple cross-sectional survey with much lower sample size at follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Sampling methodology was not detailed and very different sample sizes suggest high risk of bias

Yuan et al., 1993 *(153)*

Methods	**Multiple cross-sectional observational study** conducted in Nanhai and Beihe communities of Qianjiang county, Sichuan, China The first survey was conducted in 1978 before provision of iodized salt, and the second survey was conducted in 1992 after provision of iodized salt for 15 years.
Participants	Schoolchildren of primary and middle school
Interventions	Iodized salt was provided at unknown concentration.
Outcomes	Goitre
Publication details	Published as a short report in Chinese
Stated aim of study	To investigate the effect of iodized salt provision on goitre
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: <20 ppm (parts per million) 6. Duration: 15 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Unclear risk	Multiple cross-sectional survey but sample size at follow-up was half of that of baseline
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Other bias	High risk	Sampling methodology was not detailed and very different sample sizes suggest high risk of bias

Yusuf et al., 2008 *(154)*

Methods	**Multiple cross-sectional observational study** conducted in Bangladesh Nationally representative surveys on nutritional status in children and women of reproductive age in Bangladesh were conducted in numerous years and the data provide national estimates of IDD before and after the introduction on iodized salt in that country. Probability proportionate to size (PPS) sampling was used to select households for inclusion, to select a nationally representative sample. The first sample used in this review was from the year 1993. The Salt Byelaw was passed in Bangladesh in 1994 and at that time substantial investments were made in the infrastructure for salt iodization. By 1995, all salt factories were equipped for iodization (the original law was passed in 1989 but no effort was made to enforce it and there was little iodization in the country until 1994). The data from a second nationally representative survey undertaken 10 years later (2005) was used to compare the iodine status of children and women pre and post fortification of salt with iodine.
Participants	Children aged 6–12 years or women aged 15–44 years living in Bangladesh
Interventions	Iodized salt was provided at the national level, at a concentration of 45–50 ppm (parts per million).
Outcomes	1. Goitre (only percentages without sample size reported at baseline; data found in summary table) 2. UIE (values only given for follow-up) 3. % of population with urinary iodine excretion (UIE) <100 µg/L (only percentages without sample size reported at baseline; data found in summary table)
Publication details	Published in English in a peer-reviewed journal
Stated aim of study	To monitor the situation towards the elimination of iodine deficiency disorder (IDD) in Bangladesh
Notes	1. Design: multiple cross-sectional (nationally representative) 2. Age: adults and children 3. Group: not specifically pregnant 4. Salt consumption: unknown 5. Iodine concentration: 45–50 ppm 6. Duration: 10 years 7. Baseline IDD status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Unclear risk	Sample sizes not provided for baseline data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Sampling procedures and weighing reported to have been conducted, to ensure surveys were comparable and nationally representative

Zeng, 1991 *(87–90)*

Methods	**Quasi-experimental study** conducted in the townships of Heba, Shilong and Qianling in Guizhou province China
Participants	Children 7–13 years of age during time of survey of 1989–1990
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1–3 years of age. There were three cohorts: • Heba (iodine-deficient village at baseline) – salt iodized at 20 ppm (parts per million); • Shilong (iodine-deficient village at baseline) – salt iodized at 20 ppm; • Qianling (iodine-sufficient village at baseline) – salt iodized at unknown concentration (not reported).
Outcomes	Intelligence: • Mean intelligence quotient (IQ) • % of children with IQ <70 (mild mental retardation – MMR)
Publication details	Published in a Chinese language journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Comparisons made within village to control for potential biases 1. Design: quasi-experimental 2. Age: children (7–13 years) 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20 ppm (Heba and Shilong) or unknown (Qianling) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus 1 to 3 years of life more than comparison 7. Baseline iodine deficiency disorder (IDD) status (based on goitre; did not use World Health Organization criterion of school-aged children): • Heba: severe IDD • Shilong: moderate IDD • Qianling: adequate iodine status

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Comparable comparison groups that were of similar size and selected in similar manner

Zhang et al., 1988 *(110)*

Methods	**Cohort observational study** conducted in Xiguanying community, Beipiao city, Liaoning province, China 15 villages' residents of an endemic iodine deficiency disorder (IDD) area; established records for each villager – 18 252 villagers in 1974 before supplementation of iodized salt and 13 248 in 1977 after 3 years' supplementation of iodized salt were included
Participants	All villagers in selected villages
Interventions	Iodized salt was provided via universal salt iodization, at a concentration of 100 ppm (parts per million).
Outcomes	1. Goitre
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To investigate the effect of prevention of goitre through provision of iodized salt
Notes	1. Design: cohort observational 2. Age: children and adults 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 100 ppm 6. Duration: 3 years 7. Baseline IDD status: mild IDD (based on goitre; did not use World Health Organization criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	High risk	>20% attrition
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Sampling methodology not explained

Zheng et al., 1995 *(84, 85)*

Methods	**Quasi-experimental study** conducted in Yue village of Lushan county and Lian village of Ye county in Henan Province China
Participants	Children 9–10 years of age during time of survey (date not specified)
Interventions	Children were divided into those born before the implementation of universal salt iodization in 1979. The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt as infants and young children.
Outcomes	• Intelligence quotient (IQ; table is incomplete and no data can be used for this review) • % of children with IQ <70 (mild mental retardation – MMR; table is incomplete and no data can be used for this review)
Publication details	Published in a Chinese language journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Comparisons made within village to control for potential biases 1. Design: quasi-experimental 2. Age: children (9–10 years) 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown 6. Duration: intervention group exposed to iodized salt during gestation (9 months) and the comparison was not (the duration of exposure as infants and young children was not stated) 7. Baseline iodine deficiency disorder (IDD) status: based on goitre: • Yue: severe IDD (did not use World Health Organization (WHO) criterion of school-aged children) • Lian: mild IDD (did use WHO criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Unclear risk	Table in article incomplete
Other bias	Low risk	Children of same village compared to one another and only 1 year apart in age and therefore comparable

Zhou et al., 2004 *(155)*

Methods	**Multiple cross-sectional observational study** conducted in Zhaotong city, Yuannan province, China Randomly sampled students from one primary school A survey of students aged 8–10 years was conducted before iodization of salt and then another sample of students were surveyed 8 years after introduction of iodized salt.
Participants	Schoolchildren, 8–10 years of age
Interventions	Iodized salt was provided at a concentration of 15 ppm (parts per million).
Outcomes	1. Goitre 2. urinary iodine excretion (UIE; median reported; results in summary table)
Publication details	Published in a peer-reviewed journal in Chinese
Stated aim of study	To assess the effect of provision of iodized salt on goitre and UIE
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 15 ppm 6. Duration: 8 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	High risk	Only 40 subjects measured at follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Sampling methodology not detailed

Zhu et al., 1993 *(86)*

Methods	**Quasi-experimental study** conducted in Qingshui, Sizhai and Shilong townships, China Children in each village born before iodization of salt were compared to children of the same village born after iodization of salt.
Participants	Children aged 7–14 years at time that intelligence was measured (1991)
Interventions	Experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1 year of age. There were three cohorts: • Qingshui (severe iodine-deficient area); • Sizhai (mild iodine-deficient area); • Shilong (severe iodine-deficient area).
Outcomes	Intelligence of children: • mean intelligence quotient (IQ)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Comparisons made within villages, to control for potential biases 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20 ppm (parts per million) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus 1 year of life more than comparison 7. Baseline iodine deficiency disorder (IDD) : based on goitre: • Qingshui: severe IDD (did not use World Health Organization (WHO) criterion of school-aged children) • Sizhai: mild IDD (did not use WHO criterion of school-aged children) • Shilong: severe IDD (did not use WHO criterion of school-aged children)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	Blinding not reported
Blinding of outcome assessment (detection bias)	Unclear risk	Blinding not reported
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Unclear risk	% of children with intelligence quotient (IQ) <70 points not reported
Other bias	Low risk	Children within same communities compared to one another, to reduce potential bias

Zhu et al., 1995 *(92)*

Methods	**Quasi-experimental study** conducted in Niuchang, Qingshui and Yiangfeng townships in China Children of each village that were born before iodization of salt were compared to children in the village born after iodization of salt.
Participants	Children aged 7–14 years at time that intelligence was measured (1993); children "with brain impairment from non-iodine factors" were excluded
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1–3 years of age. There were three cohorts: • Niuchang (severe iodine deficiency area at baseline); • Qingshui (severe iodine deficiency area at baseline); • Yiangfeng (severe iodine deficiency area at baseline).
Outcomes	Intelligence of children: • mean intelligence quotient (IQ)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Comparisons made within village, to control for potential biases 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 20 ppm (parts per million) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus 1 year of life more than comparison 7. Baseline iodine deficiency disorder (IDD) status: based on goitre (did not use World Health Organization criterion of school-aged children) • Niuchang: severe IDD • Qingshui: severe IDD • Yiangfeng: severe IDD

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Unclear risk	% of children with intelligence quotient (IQ) <70 not reported as expected
Other bias	Low risk	Children within same communities compared to one another, to reduce potential bias (communities were of different ethnic groups)

Zimmermann et al., 2003 *(156)*

Methods	**Multiple cross-sectional observational study**, conducted in six remote villages in the Danane health district of western Côte d'Ivoire. Surveys of goitre and other indicators of iodine status were conducted in schools of the villages. All children, aged 5–14 years of age, who were present at school on the day of measurement were included in the sample. The first survey was conducted in 1997 before iodized salt was available in the villages, and children from two schools were included. In 1998, universal salt iodization was initiated. Other surveys using similar methods were conducted in schoolchildren in the same villages, yearly until 2001. Students from two schools were surveyed in 1997 and 1998 and six schools were included in the surveys in 1999, 2000 and 2001.
Participants	All children aged 5–14 years, present at school when surveys were conducted
Interventions	Iodized salt was provided at a concentration of 30–50 ppm (parts per million).
Outcomes	1. Goitre 2. Urinary iodine excretion (UIE; median reported and values used in summary table) 3. % of population with UIE <100 µg/L 4. Serum thyroid-stimulating hormone (TSH; not used in this review) 5. Hypothyroidism 6. Serum thyroxine (not measured at follow-up and therefore not included in this review) 7. Thyroid volume (not used in this review)
Publication details	Published in a peer-reviewed journal in English
Stated aim of study	To measure the thyroid size, urinary iodine and thyroid hormones before and after the introduction of universal iodized salt
Notes	1. Design: multiple cross-sectional 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: 30–50 ppm (parts per million) 6. Duration: 3 years 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)/moderate IDD (based on UIE)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	Multiple cross-sectional study with similar sample sizes at each time point
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Sampling methodology similar at all time points and children same age, to reduce risk of bias for secular trends with age

Zimmermann et al., 2004 *(111)*

Methods	**Cohort observational study** conducted in northern Morocco A cohort of children were followed from pre-iodization to 1 year post-iodization and then 14 months after cessation of iodization of salt. Children were recruited and baseline measurement performed. Households were then provided with iodized salt. After 1 year, the same measurements were conducted on the same children. Owing to financial constraints, iodized salt could no longer be provided to the households of the children. Fourteen months after the cessation of provision of iodized salt to the households, the same measurements were again conducted on the selected households.
Participants	Schoolchildren aged 6–16 years
Interventions	Iodized salt was provided at 25 ppm (parts per million), through provision to households.
Outcomes	1. Goitre 2. Urinary iodine excretion (UIE; median reported; results in summary table) 3. % of population with UIE <100 µg/L 3. Whole-blood thyrotropin (not used in this review) 4. Serum total thyroxine (not used in this review) 5. Serum thyroglobulin (not used in this review) 6. Thyroid volume (not used in this review) 7. Hypothyroidism
Publication details	Published in a peer-reviewed journal in English.
Stated aim of study	To describe the evolution of thyroid dysfunction after the discontinuation of salt iodization in a cohort of children in an area of severe endemic goitre
Notes	1. Design: cohort observational 2. Age: children 3. Group: not specifically pregnant women 4. Salt consumption: 7.3–11.6 g/day 5. Iodine concentration: 25 ppm 6. Duration: 1 year 7. Baseline iodine deficiency disorder (IDD) status: severe IDD (based on goitre)/severe IDD (based on UIE) • Estimated intake of iodine 183–290 µg/person/day Data used in this review are those of baseline and follow-up after introduction of iodized salt; however, the authors also followed up children 14 months after the cessation of salt iodization. The authors' conclusions were that there was a rapid regression of iodine status back to that of insufficiency in this sample, within 14 months of cessation of iodization of salt. A number of variables were reported that were not synthesized in the analyses in this review, all of which indicated an improvement in thyroid function with iodization of salt and a return to poorer thyroid function with cessation of iodization of salt. Adverse effects were not detected.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding reported
Incomplete outcome data (attrition bias)	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	All children from two schools included in survey – selection criteria for schools not reported

Zuo et al., 1996 *(91)*

Methods	**Quasi-experimental study** conducted in Wenan county and Shadu county, China Children at two primary schools that were born before iodization of salt were compared to children in the schools born after iodization of salt.
Participants	Children aged 7–13 years at time that intelligence was measured
Interventions	The experiment group was made up of children whose mothers received iodine from iodized salt during pregnancy and children were exposed to iodized salt in infancy; the comparison group comprised children whose mothers did not receive iodine from salt during pregnancy and children were not exposed to iodized salt until 1–3 years of age. There were two cohorts: • students at Qixing primary school; • students at Wagua primary school.
Outcomes	Intelligence of children: • mean intelligence quotient (IQ) • % of children with IQ <70 points (mild mental retardation – MMR)
Publication details	Published in a Chinese journal
Stated aim of study	Not stated
Notes	Intelligence measured with Chinese Binet Scale Students in school were randomly selected for measurement of IQ Comparisons made within schools to control for potential biases 1. Design: quasi-experimental 2. Age: children 3. Group: any group other than specifically pregnant women 4. Salt consumption: unknown 5. Iodine concentration: unknown (not stated in article) 6. Duration: intervention group exposed to iodized salt during gestation (9 months) plus 1–3 years of life more than comparison 7. Baseline iodine deficiency disorder (IDD) status: • Qixing: adequate iodine status (based on goitre; did not use World Health Organization criterion of school-aged children) • Wagua: severe as reported by authors, but data not reported

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomized controlled trial (RCT)
Allocation concealment (selection bias)	High risk	Not RCT
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No mention of blinding
Incomplete outcome data (attrition bias)	Low risk	As quasi-experimental, attrition not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Students from same schools in same villages compared to one another, to reduce potential bias

Annex 3. Summary table: goitre prevalence with and without iodization of salt

Study ID	Country	Study design	Age group	Concentration of iodine in salt, ppm	Goitre prevalence without salt iodization, %	Goitre prevalence with salt iodization, %
Bimenya et al., 2002 *(116)*	Uganda	Multiple cross-sectional	Children	50	74.3	60
Hou et al., 2003 *(131)*	China	Multiple cross-sectional	Children and adults	20–50	18.2	5.5
Ibanez-Gonzalez et al., 1956 *(98)*	Spain	Cohort observational	Children (<10 years)	<20	40.0	8.0
			Children (10–14.9 years)	<20	61.3	27.9
			Adolescents (15–19.9 years)	<20	61.7	33.4
			Adults (≥20 years)	<20	80.0	64.7
Jia et al., 2004 *(157)*	China	Cohort	Children	Unknown	1.9	0.00
Kimball et al., 1931 *(56)*	United States of America	Non-RCT	Children	Unknown (iodized salt)	36	12
				Unknown (control)	34	30
Nicod, 1953 *(138)*	Switzerland	Multiple cross-sectional	Children (6-year follow-up Valais canton)	10	71.2	29.5
			Children (30-year follow-up Vaud canton)	10	Avenches: 78.9 Moudon: 73.5 Payerne: 78.0	7.1 5.0 4.0
Wang et al., 2000 *(147)*	China	Multiple cross-sectional	School-age children	Unknown	Chaohu: 59.6 Dabeisan: 28.5 Hefei: 4.6	22.0 11.9 9.5
Yusuf et al., 2008 *(154)*	Bangladesh	Multiple cross-sectional	Children	45–50	49.9	6.2
			Women	45–50	55.6	11.7

ppm: parts per million; RCT: randomized controlled trial.

Annex 4. Summary tables: urinary iodine excretion with and without iodized salt

Randomized controlled trials and non-randomized controlled trials

Study ID	Study design	Country	Age group	Concentration of iodine in salt, ppm	Without iodized salt			With iodized salt		
					n	Median	Units	*n*	Median	Units
Hintze et al., 1988 *(53)*	RCT	Germany	Children	20	160	45.1	µg iodine/g creatinine	126	60.1	µg iodine/g creatinine
I'Ons et al., 2000 *(57)*	Non-RCT	South Africa	Children	>40	69	94	µg iodine/L urine	39	216	µg iodine/L urine
Pongpaew et al., 1998 *(58)*	Non-RCT	Thailand	Children	>40	93	Baseline 129 Follow-up 302	µg iodine/L urine	98	96 195	µg iodine/L urine
Romano et al., 1991 *(54)*	RCT	Italy	Adults	20	18	50.0	µg iodine/24 h	17	100.0	µg iodine/24 h
Saowakhontha et al., *1994 (59)*	Non-RCT	Thailand	Adults	50	Values reported were a factor of 10–1000× greater than expected and therefore considered not reliable and not included here					

ppm: parts per million; RCT: randomized controlled trial.

Urinary iodine excretion in cohort observational studies

Study ID	Country	Age group	Concentration iodine in salt, ppm	Without iodized salt			With iodized salt		
				n	Median	Units	*n*	Median	Units
Foo et al., 1996 *(95)*	Malaysia	All	>40	33 (aged ≤6 years) 48 (women)	28.1 36.8	µg iodine/L urine	33 48	33.4 168.2	µg iodine/L urine
Guo, 1984 *(97)*	China	All	20	31 (goitre adults) 30 (normal adults) 33 (children with cretinism) 13 (normal children)	16.5 24.5 30.0 34.1	µg iodine/g creatinine	31 32 33 13	99.7 99.2 131.2 170.6	µg iodine/g creatinine
Weber and Manz, 1987 *(107)*	Germany	All	20	NR	Men 55 Women 39 6–12 years 21 <6 years 21	µg/day		63 49 33 28	µg/day
Yang and Zhang, 1984 *(109)*	China	All	<20	NR	Cretinism patients 3.9 Non-cretinism patients 19.9	µg iodine/g creatinine	NR	139.9 134.3	µg iodine/g creatinine
Yang et al., 1984 *(158)*	China	All	<20	158 Hebei 150 Pingliang 160 Guading	23.3 29.1 20.7	µg iodine/g creatinine	104 105 62	128.4 153.0 178.0	µg iodine/g creatinine
Zimmermann et al., 2004 *(111)*	Morocco	Children	25	159	18	µg iodine/L urine	159	181	µg iodine/L urine

NR: not reported; ppm: parts per million.

Urinary iodine excretion in multiple cross-sectional observational studies

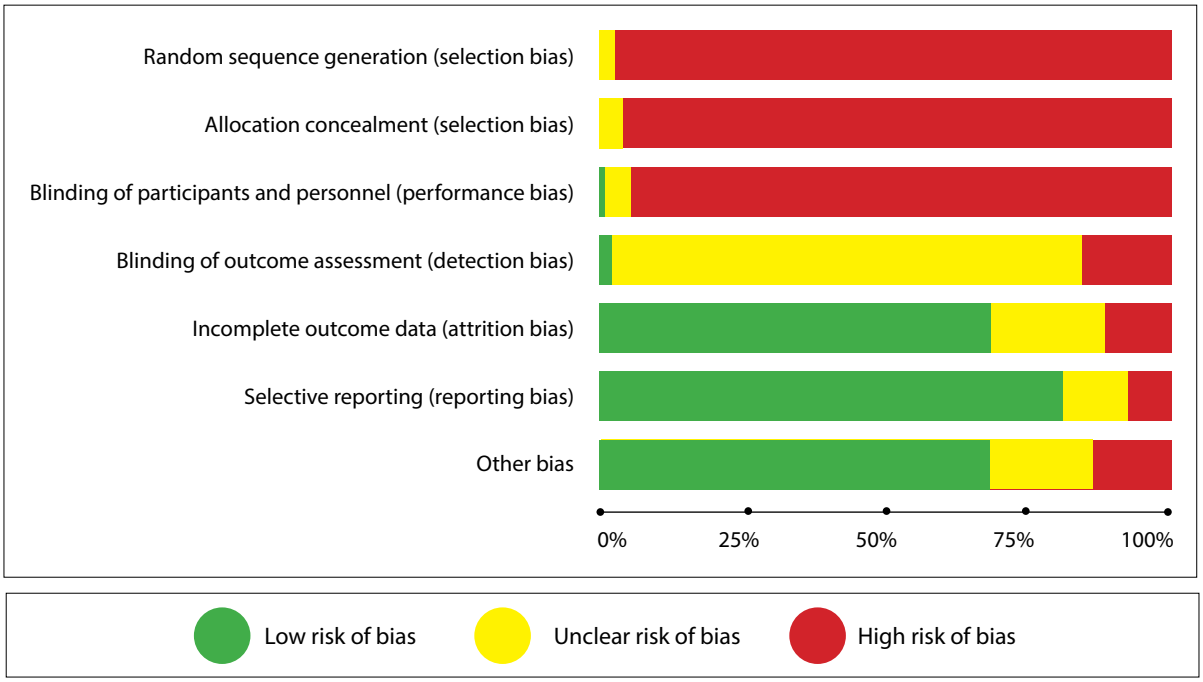
Study ID	Country	Age group	Concentration iodine in salt, ppm	Without iodized salt			With iodized salt		
				n	Median	Units	*n*	Median	Units
Baczyk et al., 2007 *(114)*	Poland	Children	30	NR	49	µg iodine/L urine	NR	107	µg iodine/L urine
Chen et al., 1999 *(121)*	China	Children	33	214	71.82	µg iodine/L urine	210	105.11	µg iodine/L urine
Chen et al., 2001 *(122)*	China	Children	33	210	60.10	µg iodine/L urine	210	103.4	µg iodine/L urine
Chen et al., 2002 *(123)*	China	Children	Unknown	147 (HAC) 64 (QGR)	68.53 61.25	µg iodine/L urine	147 63	140.11 99.69	µg iodine/L urine
Dai et al., 2008 *(124, 125)*	China	Children	Unknown	364 (city) 338 (suburb) 367 (rural)	137.5 102.12 94.66	µg iodine/L urine	257 210 210	271.12 240.42 198.14	µg iodine/g creatinine
Han et al., 2006 *(129)*	China	All	Unknown	1829	96.1	µg iodine/L urine	358	228.1	µg iodine/L urine
Hou et al., 2003 *(131)*	China	All	20–50	NR	187.6	µg iodine/L urine	NR	247.5	µg iodine/L urine
Jooste et al., 2000 *(134)*	South Africa	Children	>40	565	21.59	µg iodine/L urine	536	186.7	µg iodine/L urine
Lv et al., 2009 *(136)*	China	Children	35	360	160.1	µg iodine/L urine	362	212.3	µg iodine/L urine
Regalbuto et al., 2010 *(139)*	Italy	Children	30	NR	mean (SD) Bronte: 129.3 (16.6) Maniace: 68.2 (12.6)	µg iodine/L urine	NR	192.0 (117.2) 160.8 (79.5)	µg iodine/L urine

Study ID	Country	Age group	Concentration iodine in salt, ppm	Without iodized salt			With iodized salt		
				n	Median	Units	*n*	Median	Units
Wang et al., 2009 *(148, 149)*	China	Children	35	362	119.9	µg iodine/L urine	356	191.8	µg iodine/L urine
Yang and Zhang, 1984 *(109)*	China	All	<20	NR	cretinism patients 3.9 non- patients 19.9	µg iodine/g creatinine	NR	139.9 134.3	µg iodine/g creatinine
Yang and Yang, 2011 *(152)*	China	Children	35	100	109.4	µg iodine/L urine	100	216.9	µg iodine/L urine
Zhou et al., 2004 *(155)*	China	Children	<20	262	52.5	µg iodine/L urine	12	342.1	µg iodine/L urine
Zimmermann et al., 2003 *(156)*	Côte d'Ivoire	Children	30–50	419	28	µg iodine/L urine	526	104	µg iodine/L urine

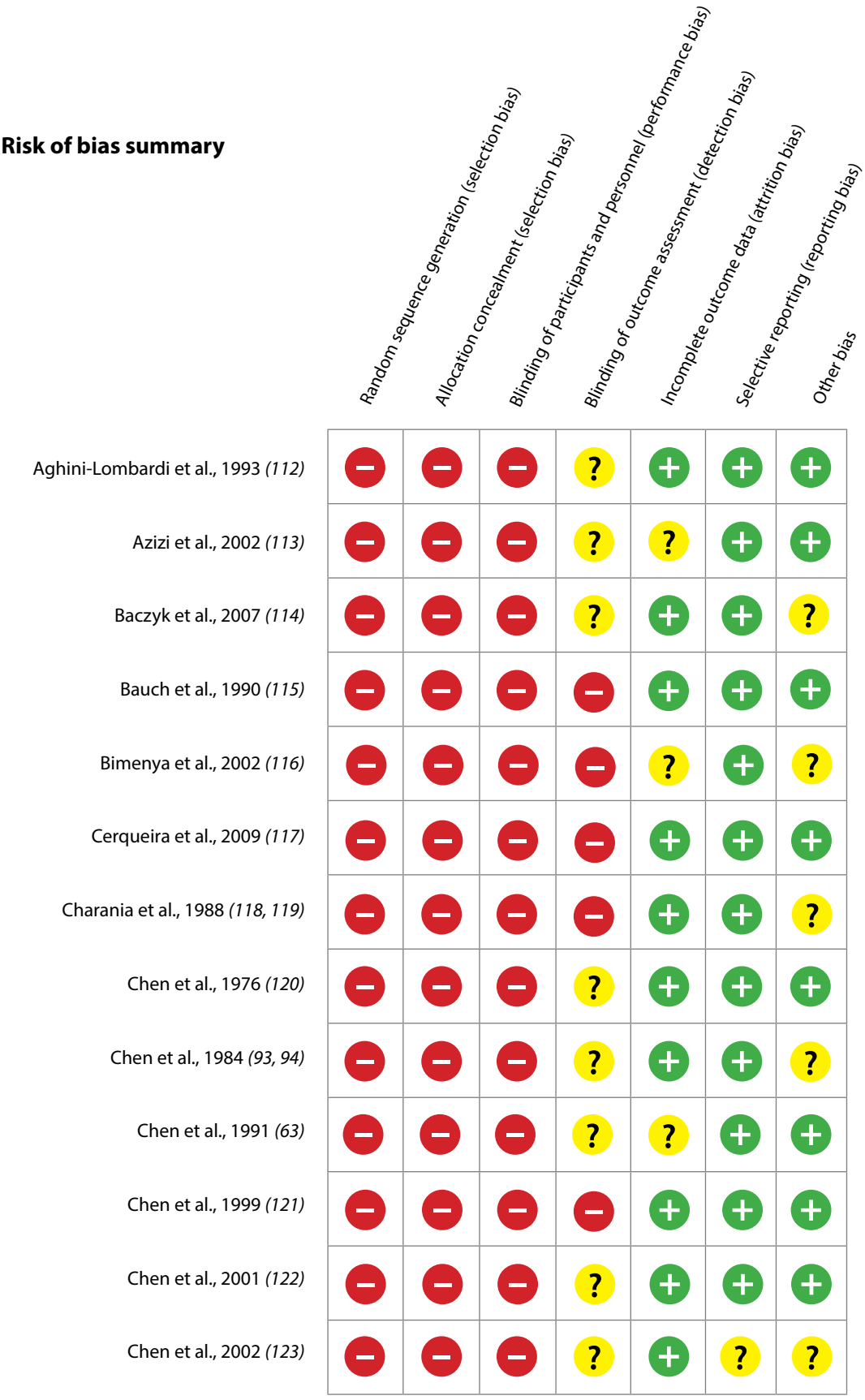
NR: not reported; ppm: parts per million.
Note: In the study conducted by Yusuf et al. in 2008 *(154)*, in children and adults in Bangladesh, the percentage of the population with urinary iodine excretion <10 µg/L decreased from 71.0% to 33.8% (children) and 70.2% to 38.7% (adults) from before the introduction of iodized to after the introduction of salt iodized at a concentration of >40 ppm.

Annex 5. Summaries of the risk of bias of included studies

Risk of bias graph: review of authors' judgements about each risk of bias item, presented as percentages across all included studies



Risk of bias summary



Risk of bias summary

Risk of bias summary

Risk of bias summary

Risk of bias summary

Risk of bias summary

Risk of bias summary

Annex 6. GRADE summary of evidence

Iodized salt and cognitive function

Patient or population: children
Settings: all settings
Intervention: iodized salt

Outcomes (study design)	Comparative values* and risks** (95% CI)		Relative effect*** (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt				
Cognitive function – (RCT)				0 (0)		
Cognitive function – (non-RCT)				0 (0)		
Cognitive function – (cohort)				0 (0)		
Cognitive function – (quasi-experimental) mean IQ	Mean IQ – in comparison group 80.39 points	Mean IQ – in intervention group 8.18 higher (6.71 to 9.65 higher)		12 995 (18 studies)	⊕⊕⊖⊖ low[1,2,3]	
Cognitive function – (multiple cross-sectional) mean IQ	Mean IQ – in comparison group 82.31 points	Mean IQ – in intervention group 10.45 higher (4.79 to 16.11 higher)		2262 (2 studies)	⊕⊕⊖⊖ low[1,3]	
Cognitive function – (quasi-experimental) IQ <70	107 per 1000	30 per 1000 (23 to 38)	RR 0.28 (0.22 to 0.36)	12 761 (16 studies)	⊕⊕⊖⊖ low[1,2,3]	
Cognitive function – (multiple cross-sectional) IQ <70	51 per 1000	12 per 1000 (4 to 41)	RR 0.24 (0.07 to 0.82)	509 (1 study)	⊕⊕⊖⊖ low[1,2,3]	Only 1 study

*Mean value for the comparison group and the group exposed to iodized salt.
**The assumed risk for categorical variables is the risk in the group unexposed to iodized salt. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
*** Calculated as risk ratio.
IQ: intelligence quotient; CI: confidence interval; RCT: randomized controlled trial; RR: risk ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Many studies did not provide sufficient detail to assess risk of bias.
[2] Quasi-experimental studies.
[3] Large protective effect with iodized salt.

Iodized salt for iodine deficiency

Patient or population: children, adults, general population
Settings: all settings
Intervention: iodized salt

Outcomes (study design)	Comparative values* and risks** (95% CI)		Relative effect** (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt				
Iodine deficiency UIE <100 µg/L (non-RCT)	Study population		RR 0.42 (0.14 to 1.29)	233 (2 studies)	⊕⊕⊖⊖ low[1,2]	
	349 per 1000	147 per 1000 (49 to 450)				
Iodine deficiency UIE <100 µg/L (cohort)	Study population		RR 0.40 (0.26 to 0.60)	1118 (6 studies)	⊕⊕⊖⊖ low[2]	
	640 per 1000	256 per 1000 (167 to 384)				
Iodine deficiency UIE <100 µg/L (multiple cross-sectional)	Study population		RR 0.45 (0.34 to 0.59)	7252 (10 studies)	⊕⊕⊖⊖ low[2,3,4]	
	707 per 1000	318 per 1000 (240 to 417)				

* The assumed risk is the risk in the comparison group. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
**Calculated as risk ratio.
CI: confidence interval; RCT: randomized controlled trial; RR: risk ratio; UIE: urinary iodine excretion.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Non-RCTs.
[2] 95% CI crossed null.
[3] Many studies lack reporting to assess true risk of bias.
[4] Very large protective effect of iodized salt.

Iodized salt for urinary iodine excretion

Patient or population: general population
Settings: all settings
Intervention: iodized salt

Outcomes (study design)	Comparative values* (95% CI)		No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt			
UIE – (cohort) µg iodine/L urine	Mean UIE in comparison group 97.11 µg/L	Mean UIE in intervention group 59.22 higher (50.40 to 68.04 higher)	1307 (3 studies)	⊕⊕⊖⊖ low[1,2]	
UIE – (cohort)[3] µg iodine/g creatinine in urine	Mean UIE in comparison group 42.90 µg iodine/g creatinine	Mean UIE in intervention group 87.35 higher (49.74 to 124.97 higher)[3]	244 (2 studies)	⊕⊕⊕⊖ moderate[2]	
UIE – (multiple cross-sectional) µg iodine/L urine	Mean UIE in comparison group 68.62 µg/L	Mean UIE in intervention group 72.35 higher (44.54 to 100.17 higher)	6760 (5 studies)	⊕⊕⊕⊖ moderate[2]	
UIE – (multiple cross-sectional) µg iodine/g creatinine in urine	Mean UIE in comparison group 42.78 µg iodine/g creatinine	Mean UIE in intervention group 104.11 higher (55.28 to 152.94 higher)	1773 (4 studies)	⊕⊕⊕⊖ moderate[2]	

*Mean value for the comparison group and the group exposed to iodized salt.
CI: confidence interval; MD: mean difference; RR: risk ratio; UIE: urinary iodine excretion.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Many studies lacked detail needed to assess true risk of bias.
[2] Very large positive effect of iodized salt on UIE.
[3] The standard deviation for one of the two studies was 10-fold less than the other study and these values could not be verified; therefore, the data were not pooled. Both studies showed a significant increase in UIE with iodized salt (MD = 66 *(45, 87)*; MD = 105 *(104, 106)*.

Iodized salt for goitre

Patient or population: general population
Settings: all settings
Intervention: iodized salt

Outcomes	Comparative risks* (95% CI)		Relative effect** (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt				
Goitre – (RCT)	225 per 1000	238 per 1000 (155 to 365)	RR 1.06 (0.69 to 1.62)	286 (1 study)	⊕⊕⊖⊖ low[1,2]	Only 1 study
Goitre – (non RCT)	422 per 1000	249 per 1000 (152 to 401)	RR 0.59 (0.36 to 0.95)	32219 (3 studies)	⊕⊕⊕⊖ moderate[3,4]	
Goitre – (quasi-experimental)	19 per 1000	2 per 1000 (1 to 2)	OR 0.1 (0.08 to 0.13)	42 367 (1 study)	⊕⊕⊖⊖ low[3,5]	Only 1 study
Goitre – (cohort)	156 per 1000	47 per 1000 (36 to 64)	RR 0.3 (0.23 to 0.41)	754 387 (11 studies)	⊕⊕⊕⊖ moderate[5]	
Goitre – (multiple cross-sectional)	154 per 1000	28 per 1000 (22 to 34)	RR 0.18 (0.14 to 0.22)	1 963 247 (34 studies)	⊕⊕⊖⊖ low[5,6]	

*The assumed risk is the risk in the comparison group. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
**Calculated as Peto odds ratio or risk ratio.
CI: confidence interval; OR: odds ratio; RCT: randomized controlled trial; RR: risk ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Unclear randomization and allocation of concealment.
[2] 95% CI crosses null.
[3] Non-randomized.
[4] Though the results of one study suggested an opposite result of the others, there were too few events to generate a meaningful result (5 in intervention and 4 in control).
[5] Very large protective effect of iodized salt.
[6] Many studies lack sufficient detail to understand true risk of bias.

Iodized salt for cretinism

Patient or population: children
Settings: all settings
Intervention: iodized salt

Outcomes	Comparative risks* (95% CI)		Relative effect** (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt				
Cretinism – (RCT)				0 (0)		
Cretinism – (non-RCT)				0 (0)		
Cretinism – (quasi-experimental)				0 (0)		
Cretinism – (cohort)				0 (0)		
Cretinism – (multiple cross-sectional)	30 per 1000	4 per 1000 (2 to 6)	OR 0.13 (0.08 to 0.2)	8273 (2 studies)	⨁⨁⨁⊖ moderate[1]	

* The assumed risk is the risk in the comparison group. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
**Calculated as Peto odds ratio.
CI: confidence interval; OR: odds ratio; RCT: randomized controlled trial.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] The reduction in risk of cretinism was very large

Iodized salt for adverse effects

Patient or population: general population
Settings: all settings
Intervention: iodized salt

Outcomes	Comparative risks* (95% CI)		Relative effect** (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt				
Positive ATMA – (cohort)	49 per 1000	123 per 1000 (95 to 161)	OR 2.51 (1.93 to 3.27)	2848 (1 study)	⊕⊕⊖⊖ low	Only 1 study
Positive ATMA – (multiple cross-sectional)	31 per 1000	40 per 1000 (29 to 53)	OR 1.27 (0.94 to 1.71)	6172 (2 studies)	⊕⊖⊖⊖ very low[1,2]	
Elevated TgAb – (multiple cross-sectional)	33 per 1000	47 per 1000 (36 to 63)	OR 1.43 (1.08 to 1.89)	6172 (2 studies)	⊕⊖⊖⊖ very low[2]	
Elevated UIE – (multiple cross-sectional)	222 per 1000	300 per 1000 (236 to 387)	RR 1.35 (1.06 to 1.74)	722 (1 study)	⊕⊕⊖⊖ low[1,2]	Only 1 study

* The assumed risk is the risk in the comparison group. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
**Calculated as Peto odds ratio or risk ratio.
ATMA: anti-thyroid microsomal antibody; CI: confidence interval; OR: odds ratio; RR: risk ratio; TgAb anti-thyroglobin antibody; UIE: urinary iodine excretion.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Point estimates fall on both sides of null.
[2] Downgraded due to inconsistency, which caused imprecision and therefore not downgraded again for imprecision.

Iodized salt for thyroid hormones

Patient or population: general population
Settings: all settings (low-, middle-, high-income countries)
Intervention: iodized salt

Outcomes (study design)	Comparative risks* (95% CI)		No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt			
Thyroid-stimulating hormone – (cohort)	Mean thyroid-stimulating hormone in comparison group 11.7	Mean thyroid-stimulating hormone in intervention group 9.80 lower (10.85 to 8.75 lower)	60 (1 study)	⨁⨁⊖⊖ low	Only 1 study
Thyroid-stimulating hormone – (multiple cross-sectional)	Mean thyroid-stimulating hormone in comparison group 2.5	Mean thyroid-stimulating hormone in intervention group 0.18 higher (0.28 lower to 0.64 higher)	5645 (2 studies)	⨁⊖⊖⊖ very low[1,2]	
Thyroglobulin – (multiple cross-sectional)	Mean thyroglobulin in comparison group 10.9	Mean thyroglobulin in intervention group 8.73 lower (9.31 to 8.14 lower)	624 (1 study)	⨁⨁⊖⊖ low	Only 1 study

*Mean value for the comparison group and the group exposed to iodized salt.
CI: confidence interval.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Point estimates fall on both sides of the null.
[2] Downgraded for inconsistency, which caused imprecision and therefore not downgraded again for imprecision.

Iodized salt for hyperthyroidism

Patient or population: general population
Settings: all settings
Intervention: iodized salt

Outcomes (study design)	Comparative risks* (95% CI)		Relative effect** (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt				
Hyperthyroidism – (cohort)	2 per 1000	2 per 1000 (2 to 3)	OR 1.36 (1.12 to 1.66.	202 848 (2 studies)	⨁⨁⊖⊖[1] low	
Hyperthyroidism – (multiple cross-sectional	5 per 1000	4 per 1000 (4 to 5)	OR 0.96 (0.92 to 1.00)	1 999 998 (5 studies)	⨁⊖⊖⊖[1,2] very low	

*The assumed risk is the risk in the comparison group. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
**Relative effect measured using Peto odds ratio.
CI: confidence interval; OR: odds ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Body of evidence not downgraded for any reason.
[2] Downgraded due to imprecision.

Iodized salt for hypothyroidism

Patient or population: general population
Settings: all settings (low-, middle-, high-income countries)
Intervention: iodized salt

Outcomes (study design)	Comparative risks* (95% CI)		Relative effect** (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Comparison	Corresponding risk Iodized salt				
Hypothyroidism (cohort)	1 per 1000	1 per 1000 (1 to 1)	OR 1.14 (0.84 to 1.53)	203425 (4 studies)	⊕⊖⊖⊖ very low[1,2]	
Hypothyroidism (multiple cross-sectional)	43 per 1000	48 per 1000 (40 to 58)	OR 1.13 (0.94 to 1.36)	11375 (4 studies)	⊕⊖⊖⊖ very low[1,2]	

* The assumed risk is the risk in the comparison group. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
**Relative effect measured using Peto odds ratio.
CI: confidence interval; OR: odds ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Point estimates fall on both sides of the null.
[2] Downgraded due to inconsistency, which also caused imprecision and therefore not downgraded for imprecision.

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ISBN 978 92 4 150828 5