Salt iodization is the preferred strategy for IDD prevention and control. However, in some instances where salt is not the major condiment, alternate vehicles for iodine fortification have been considered.

The authors searched for published research papers and unpublished reports through a systematic database search and communication with experts and organizations working to address iodine and micronutrient deficiency until January 2018. The reviewers included randomized controlled trials and observational studies that examined the effects of fortification of a food, beverage, condiment, or seasoning with iodine alone, or in combination with other micronutrients versus the same unfortified food, or no intervention. The following measures were considered: death (all-cause), goiter, physical development, mental development, cognitive function and motor skill development, cretinism, hypothyroidism, adverse effects, urinary iodine concentration, thyroid-stimulating hormone (TSH) concentration, and serum thyroglobulin concentration.

Eleven studies met the criteria, providing 14 comparisons, and capturing data on 4317 participants. Seven studies were carried out among school children (N = 3636), three among women of reproductive age (N = 648), and one among infants (N = 33). The studies used diverse types of food as vehicle for iodine delivery: biscuits, milk, fish sauce, drinking water, yoghurt, fruit beverage, seasoning powder, and infant formula milk. The amount of iodine provided to participants ranged from 35 μg/day to 220 μg/day, and study duration ranged from 11 days to 48 weeks. Five studies examined the effect of iodine fortification alone, two against the same unfortified food, and three against no intervention. Six studies evaluated the effect of co-fortification of iodine with other micronutrients. Of the eleven studies, seven were assessed to be at high overall risk of bias. No study assessed the primary outcomes of death, mental development, cognitive function, cretinism, or hypothyroidism, or secondary outcomes of TSH or serum thyroglobulin concentration. Two studies reported the effects on goiter, one on physical development measures, and one on adverse effects. All studies assessed urinary iodine concentration.

Findings
The authors combined eligible data in a meta-analysis. The effects of iodine fortification compared to control on goiter prevalence (OR 1.60, 95% CI 0.60 to 4.31; 1 non-RCT, 83 participants; very low-quality evidence), and five physical development measures were uncertain (1 non-RCT, 83 participants; very low-quality evidence): weight (MD 0.23 kg, 95% CI -6.30 to 6.77); height (MD -0.66 cm, 95% CI -4.64 to 3.33); weight-for-age (MD 0.05, 95% CI -0.59 to 0.69); height-for-age (MD -0.30, 95% CI -0.75 to 0.15); and weight-for-height (MD -0.21, 95% CI -0.51 to 0.10). One study reported that there were no adverse events observed during the crossover trial (low-quality evidence). Pooled results from RCTs showed that urinary iodine concentration significantly increased after iodine fortification (SMD 0.59, 95% CI 0.37 to 0.81; 6 RCTs, 2032 participants; moderate-quality evidence). This is equivalent to an increase of 38.32 μg/L (95% CI 24.03 to 52.61 μg/L). This effect was not observed in the meta-analysis of non-RCTs (SMD 0.25, 95% CI -0.16 to 0.66; 3 non-RCTs, 262 participants; very low-quality evidence).

Conclusions
Overall, there is no clear evidence on the effect of the intervention on reducing the proportion of people with goiter, improving physical growth, or adverse events. However, these results show that adding iodine to foods likely increases urinary iodine concentration. Additional, adequately powered, high-quality studies on the effects of iodine fortification of foods on these, and other important outcomes, as well as its efficacy and safety, are required.