Universal salt iodization provides adequate iodine in the first 1,000 days of life

Globally-implemented, national programs of mass fortification of salt with iodine have been extremely effective at improving iodine intakes around the world: the number of countries with iodine deficiency in school-age children has decreased from 54 in 2003 to fewer than 20 at present (1). UNICEF estimates that iodized salt is currently available in 87% of households worldwide.

Is USI the optimal solution for all populations?

The baseline iodine requirement of a non-pregnant adult increases by 50% during pregnancy and by 100% during lactation (2). Most countries today report improved iodine intakes overall, and optimal iodine nutrition in school-age children (SAC). However, many countries with available data report iodine deficiency in pregnant and breastfeeding women (1). Low iodine intakes are particularly problematic in pregnant women, who need to synthesize additional thyroid hormone to cover maternal and fetal needs. Uncertain whether salt iodization alone can cover their needs, several countries recommended iodine supplementation targeted to pregnant and lactating women.

Program managers were also concerned that any attempts to increase the level of iodine fortification, to ensure adequate iodine nutrition in all population groups, would potentially increase the risk of excess iodine intake in school-age children. Moreover, there were reports of low iodine intake in infants, and concern that infants being weaned from breast milk may not be covered by iodized salt and, therefore, be at particular risk for iodine deficiency (3). The native iodine content in homemade complementary foods is generally low, and paediatric guidelines recommend that no salt be added to infant foods during the first year of life (4).

In this context, a study entitled “Salt Iodization: Meeting the needs of Pregnancy, Lactation and Infancy” (SIMPLIFY for short) was designed to evaluate whether USI, when truly universal, can meet the dietary iodine requirements of pregnant and breastfeeding women, and weaning infants.

When is USI truly universal?

WHO recommends that salt iodization should be universal, which is contingent on the following (2):
1) sufficient iodine (20–40 mg/kg) should be added to all food-grade and livestock salt, including salt used by the processed foods industry, and
2) more than 90% of households should have access to and consume adequately iodized salt (≥15 mg/kg). This goal is based on the assumption that typical salt consumption of 10 g/day fortified with 15 mg of iodine/kg will provide 150 μg of iodine, or the RDA of an adult.

The impact of salt iodization on population iodine status is monitored by measuring urinary iodine concentration (UIC) in spot urine samples. It is generally assumed that the iodine requirements of all population groups are covered in settings where universal salt iodization (USI) has been successfully implemented for ≥2 years, and the median UIC in school-age children (6–12 years of age) is adequate (≥100 μg/L).

Each site met three out of the following four eligibility conditions: 1) mandatory USI legislation; 2) access to adequately iodized salt (≥15 mg/kg) for ≥2 years; 3) ≥90% assumed household coverage of adequately iodized salt; 4) adequate iodine status in schoolchildren (median UIC of 100–300 μg/L). At each site, the following population groups were recruited: 1) SAC (aged 6–12 years); 2) non-pregnant non-lactating women of reproductive age (18–44 years); 3) pregnant women (18–44 years); 4) lactating women (18–44 years); 5) 0–6-month-old infants; 6) 7–24-month-old infants. The study assessed their iodine status, thyroid function, and access to iodized salt.

**USI and thyroid function**

The prevalence of thyroid dysfunction was overall low in all population groups, except for isolated hypothyroxinemia, present in 12.5% of pregnant women in Zagreb.

The estimated average daily iodine intake in non-pregnant women ranged from 280 to 350 μg/d, well above the RDA of 150 μg/d (4). Habitual iodine intake at this level is likely sufficient to build up thyroidal iodine stores, which may act as a buffer during pregnancy when the need for iodine increases. WHO does not recommend iodine supplementation during pregnancy in countries with effective salt iodization programs, and these findings support this position (6). The WHO position is also supported by findings from a recent controlled intervention trial in mildly-iodine deficient pregnant women (7), which did not find benefits to child development measured up to 6 years.

Universal salt iodization also appears to provide sufficient dietary iodine during lactation, when the iodine requirements are even higher than during pregnancy. In a secondary analysis of the SIMPLIFY study, it was shown that breast milk (BM) concentration is a more accurate marker of iodine status in lactating women than UIC (8). The BM iodine concentration in the study was adequate, and the estimated median iodine intake in breastfed infants ranged from 100 to 150 μg/d, exceeding the recently estimated RDA of 80 μg/d for young infants (9). Iodine sufficiency was also confirmed in infants (both age groups).

**Coverage of iodized salt and other sources of dietary iodine**

The measured salt iodine concentration was optimal in most samples in Linfen and Zagreb, but in Tuguegarao over 44% of samples were under-iodized, and almost 20% over-iodized (Table 1). The consumption of iodine-containing dietary supplements was ≥3% in all groups, except for pregnant and lactating women in Croatia (≥9%). Cows’ milk and water contributed additional dietary iodine in Croatia and China, respectively.

**USI and urinary iodine concentration**

The UICs reflected adequate iodine nutrition in all six population groups, except for excessive iodine intake in SAC in the Philippines (mUIC = 375 μg/L) and borderline low intakes in pregnant women in Croatia (mUIC = 129 μg/L) (Figure 1). It is possible that iodized salt used in the production of processed foods and condiments in the Philippines compensates for the poor household coverage of adequately iodized salt (5).

The median UIC in women of reproductive age was lower than in school-age children at all study sites (P < 0.05), but higher than in pregnant women in Zagreb and Tuguegarao (P < 0.05 for both).

### Table 1: Median iodine concentration in household salt at each study site reflects high coverage of adequately iodized salt in China and Croatia, with the Philippines lagging behind.

<table>
<thead>
<tr>
<th>Study Site</th>
<th>Median (IQR) iodine in salt* (mg/kg)</th>
<th>% samples</th>
<th>% samples</th>
<th>% samples</th>
<th>% samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linfen (China)</td>
<td>25.2 (23.3, 28.0)</td>
<td>1%</td>
<td>2.7%</td>
<td>96.3%</td>
<td>1.0%</td>
</tr>
<tr>
<td></td>
<td>n=402</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuguegarao (Philippines)</td>
<td>26.0 (14.6, 36.6)</td>
<td>11%</td>
<td>33.6%</td>
<td>48.4%</td>
<td>18.0%</td>
</tr>
<tr>
<td></td>
<td>n=1003</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zagreb (Croatia)</td>
<td>23.8 (22.1, 26.0)</td>
<td>0%</td>
<td>3.1%</td>
<td>96.4%</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>n=195</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* in salt iodized at ≥5 mg/kg
These results support USI as the main strategy to prevent iodine deficiency. We confirmed that salt iodization at an adequate level of fortification (−25 mg/kg), when it makes up a high proportion of the total amount of salt consumed, provides sufficient dietary iodine to ensure adequate iodine nutrition in all population groups including pregnant women, lactating women, and breastfed infants.

In the studied countries, the iodine status was adequate also in toddlers, suggesting that iodized salt may cover them indirectly through the consumption of breast milk and directly through the consumption of salt-containing complementary foods. However, as salt should be avoided in this age group, weaning infants may still be at risk for low iodine intakes.

The data also indicates that the risk of excess iodine intake from salt is minimal if it is fortified at the recommended level. However, large variations in salt iodine concentrations may increase the risk for both low and high iodine intakes.

Our findings imply that iodine deficiency in women of reproductive age and/or during pregnancy may be a sign that a national salt iodization program is underperforming, e.g., salt could be under-iodized and/or coverage of iodized salt could be poor. This underlines the importance of complete coverage of iodized salt. Equally, it is important to adapt the salt fortification levels to current salt intakes, and to strictly monitor the adherence to salt standards through salt quality assurance.

Another implication is the importance of iodine status monitoring in at-risk populations in addition to school-age children, to identify potential gaps in program delivery. This may be particularly relevant in countries with incomplete coverage of iodized salt, or where a large part of the salt comes from processed foods and data on the use of iodized salt in food production is limited.

Overall, the results support the recommendation that the impact of salt iodization should be monitored by measuring UIC, as this biomarker accounts for all dietary iodine sources. An exception is the period of lactation, when dietary iodine is sequestered into breast milk, making BMIC a more accurate indicator of iodine status, which should be used in preference to UIC.

Our results offer important guidance on the UIC levels in the different population groups that can be expected when the salt iodization program works well. We observed that in populations where USI covers the iodine requirements of pregnant women (i.e. the median UIC is >150 μg/L), the median UIC in other population groups is well above the WHO threshold of 100 μg/L (approximately 200 μg/L in schoolchildren and −160-200 μg/L in women of reproductive age). This makes sense, as this level of intake likely reflects optimal iodine intakes, whereas the WHO UIC thresholds were set to reflect intake levels below which goiter starts to develop.

The presence of normal thyroid function when the median UIC is in the range of 100–299 μg/L strengthens the evidence from previous studies that the adequate range could be widened without detriment to health (12). A large multi-center study coordinated by ETH Zurich and IGN, funded by UNICEF, is now ongoing to better understand the UIC thresholds corresponding to optimal iodine nutrition.

A large proportion of the 7–24-month-old infants were still partly breastfed, which means that iodized salt covered their iodine needs indirectly through BM, and directly through home-made complementary foods with iodized salt (4). Taken together, the existing body of evidence suggests that toddlers may be at risk of iodine deficiency in settings where: 1) they receive home-made complementary foods without salt; 2) the iodized salt coverage is poor and/or mothers’ breast milk iodine concentration is low (3,10); or 3) the breast milk and/or cow’s milk consumption is low (11). In such settings, iodine-fortified in-home fortification products targeted to weaning infants may be beneficial (6).

References
3. Andersson M et al. The Swiss iodized salt program provides adequate iodine for school children and pregnant women, but weaning infants not receiving iodine-containing complementary foods as well as their mothers are iodine deficient. J Clin Endocrinol Metab 2010;95:5217–24.