Controlling iodine deficiency disorders through salt iodation in Tanzania

By

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DEDICATION

'.... I have talked at length about this question of food because the foundation of development is people. A hungry person cannot bring progress. He is weak of the body and also weak of mind. This must always be remembered; especially, in relation to children. When a child is not well fed, he will not grow properly - he will be deformed, and his intelligence will be affected also; he will not reach his full potential.'

Mwalimu Julius K. Nyerere, the Tanzania's Father of Nation

'Iodine Deficiency Disorders constitute the single greatest cause of preventable brain damage in the foetus and infants, and retarded psychomotor development in young children. When elimination of IDD is achieved it will be a major and total public health triumph, ranking with small pox and poliomyelitis.'

Dr. Gro Harlem Brundtland, the ex-Director General of the WHO

This study is dedicated to all people suffering from IDD and the scientists who dedicated their lives, and those still working on, to the solutions of problems facing a sustainable global elimination of IDD.

CONTRIBUTORS

This thesis is the result of efforts towards freeing the next generation from the scourges of iodine deficiency in which 3 institutions played a key role in trying to meet the goal of sustaining the elimination of IDD in Tanzania.

Tanzania Food and Nutrition Centre (TFNC)

TFNC provided the candidate with a good atmosphere for conducting the studies in Tanzania.

International Maternal and Child Health (IMCH), Department of Women's and Children's Health, University of Uppsala, Sweden

IMCH provided two co-supervisors for the candidate, Associate Professor Stefan Peterson and Professor Ted Greiner.

Centre for International Health (CIH), University of Bergen Norway

CIH provided the main supervisor of the candidate, Professor Thorkild Tylleskär.

CONTENTS

LIST OF ABBREVIATIONS

APD	- Ammonium persulfate digestion
ANOVA	- Analysis of variance
CCM	- *Chama Cha Mapinduzi* (the Tanzania's ruling party)
CDC	- Centres for Disease Control and Prevention
CIH	- Centre for International Health
CV	- Coefficient of variation
DBS	- Dried blood spots
EAC	- East African Community
EQUIP	- Ensuring Quality of Urinary Iodine Procedures
FAO	- Food and Agriculture Organisation
FDGs	- Focus group discussions
ICCIDD	- International Council for Control of Iodine Deficiency Disorders
IDD	- Iodine Deficiency Disorders
IIH	- Iodine-induced hyperthyroidism
IMCH	- International Maternal and Child Health
IOC	- Iodinated oil capsules
IPICS	- International Programme in the Chemical Sciences
IQ	- Intelligent Quotient
IRLI	- International Resource Laboratories for Iodine
JICA	- Japan International Cooperation Agency
KAP	- Knowledge, attitude and practice
KI	- Potassium iodide
KIO_3	- Potassium iodate
MCH	- Maternal and child health
MDGs	- Millennium Development Goals
MEM	- Ministry of Energy and Minerals
MI	- Micronutrient Initiative
NBS	- National Bureau of Statistics
NCCIDD	- National Council for Control of Iodine Deficiency Disorders
NFCC	- National Food Control Commission
ppm	- parts per million (milligram/kilogram)
PT	- Proficiency testing
rT3	- reverse Tri-iodothyronine
RTK	- Rapid test kit
SCN	- Standing Committee on Nutrition
SCN^-	- Thiocyanate ion
Sida	- Swedish International Development Cooperation Agency
T_3	- Tri-iodothyronine
T_4	- Tetra-iodothyronine (Thyroxine)
TASPA	- Tanzania Salt Producers Association
TBG	- Thyroid binding globulin
TDHS	- Tanzania Demographic and Health Surveys
TFDA	- Tanzania Food and Drugs Authority
TFNC	- Tanzania Food and Nutrition Centre

TGP	- Total goitre prevalence
TISCO	- Tanzania Industrial Studies and Consulting Organisation
TRH	- Thyrotropin releasing hormone
TSH	- Thyroid stimulating hormone
μg/L	- Microgram per litre
UIC	- Urinary iodine concentration
UN	- United Nations
UNICEF	- United Nations Children's Fund
USI	- Universal salt iodation
USA	- United States of America
WHA	- World Health Assembly
WHO	- World Health Organisation

LIST OF PUBLICATIONS

Paper I

Assey VD, Mgoba C, Mlingi N, Sanga A, Ndossi GD, Greiner T, Peterson S. Remaining challenges in Tanzania's efforts to eliminate iodine deficiency. *Public Health Nutr.* 2007;**10**:1032-8.

Paper II

Assey VD, Greiner T, Mzee RK, Abuu H, Mgoba C, Kimboka S, Peterson S. Iodine deficiency persists in the Zanzibar Islands of Tanzania. *Food Nutr Bull*. 2006;**27**:292-9.

Paper III

Assey VD, Peterson S, Kimboka S, Ngemera D, Mgoba C, Ruhiye DR, Greiner T, Ndossi GD**,** Tylleskär T. Tanzania national survey on iodine deficiency: impact after twelve years of salt iodation. *BMC Public Health* 2009;**9**:319.

Paper IV

Assey VD, Peterson S, Greiner T. Sustainable universal salt iodization in low-income countries - time to re-think strategies? *European J Clin Nutr* 2008;**62**:292-4.

Paper V

Assey VD, Tylleskär T, Momburi PB, Maganga M, Reilly M, Mlingi NV, Greiner T, Peterson S. Improved salt iodation methods for small scale salt producers in low-resource settings in Tanzania. *BMC Public Health* 2009, **9**:187.

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ABSTRACT

Background: Iodine deficiency disorders (IDD) is a major public health problem worldwide, in which more than two billion people have insufficient iodine intake, including 285 million school-age children. In Tanzania, 41% of the population is at risk of IDD and 30% of perinatal mortality is estimated to be attributable to iodine deficiency. Iodine deficiency is the number one cause of preventable brain damage in children and an important cause of infant deaths. The most cost-effective health intervention to correct IDD is universal salt iodation (USI). Tanzania has adopted USI since the early 1990s, but not much is known about its impact on the population and the challenges that were met in implementing this programme in the developing world.
Objective: The iodine status of the population following iodine supplementation and salt fortification interventions, and performance of salt iodation technologies used to optimise intervention strategies for sustainable elimination of IDD in Tanzania, have been investigated.
Methods: Three cross-sectional surveys were carried out in: a) the most iodine deficient areas in 1999; b) low priority intervening areas of Zanzibar islands in 2001; c) a national survey in mainland Tanzania in 2004. These involved testing of salt consumed in the households, analysis of urinary iodine, and goitre assessment in >160 000 school-age children, and d) another survey in mainland Tanzania, which investigated the status of the salt iodation machines and the quality of the product at salt factories. An experimental study was also carried out to improve the local technologies for salt iodation.
Results: In the most IDD affected areas in Tanzania, total goitre prevalence (TGP) dropped from 65% in 1980s to 24% in 1999, with 83% of households consuming iodated salt. In Zanzibar islands where there was no intervention, TGP was 25.6%. Pemba Island had a higher TGP of 32% with almost no iodated salt consumed in the households. In mainland Tanzania, a marked improvement was observed in the national survey with a drop of 25% in TGP in school-age children in 1980s to 6.9% in 2004, and currently 94.5% of school children aged 6-12 years have no goitre countrywide. However, excessive iodine intake (>300 μg/l) was found in 35% of the urine samples, raising concern as to the effectiveness of quality control at the salt production factories. Interviews with salt workers indicated that the standard iodation machines previously serving 140 salt works had been abandoned due to high running costs. Instead, simple iodation techniques using sprayers and sprinklers had been adapted to iodinate the salt. However, 24% and 69% of the salt samples analysed from these local technologies were over-iodinated or under-iodinated. The local technologies needed to be evaluated if they were to sustain USI. Improved local iodation methods and procedures, achieved homogenous iodine concentrations with 96% of the salt samples falling within the recommended iodine level of 40-80 ppm.
Discussion: It has been demonstrated that a huge improvement in iodine status of large Tanzanian population has resulted from the USI. This might have prevented thousands of child deaths in the country and spared millions of school children from substandard IQ levels, which were both the correct policies. USI has to be extended

to cover the Islands of Zanzibar. Locally adopted salt iodation methods with low running costs need to be introduced and maintained in for sustainable IDD elimination. Efforts to enforce salt law and monitor the production and sales of iodated salt have to be stepped up throughout the country for each household to benefit from this cost-effective intervention.

Keywords: iodine deficiency, iodated salt, Tanzania, goitre prevalence, iodation technologies, sustainable IDD elimination

MUHTASARI (Abstract in Swahili)

Utangulizi: Madhara ya upungufu wa madini joto mwilini ni tatizo kubwa la kiafya linaloathiri zaidi ya watu bilioni mbili duniani wakiwemo watoto. Kwa Tanzania, karibu asilimia 41 ya watu wote wanaishi kwenye maeneo yenye upungufu wa madini joto na hivyo wapo hatarini kupata madhara yatokanayo na upungufu huo. Upungufu wa madini joto ndio kisababishi kikubwa cha kuharibika kwa ubongo na vifo vya watoto wachanga. Matumizi ya chumvi iliyochanganywa na madini joto ndio mkakati pekee wa kudumu na wa gharama nafuu unaotumika duniani kutokomeza athari zitokanazo na upungufu wa madini joto katika jamii. Tanzania iliridhia mkakati huu tangu miaka ya tisini, lakini takwimu za kuonesha mafanikio na changamoto zinazotokana na kuridhia mkakati huu zimekuwa hazijulikani na ndio kiini cha andiko hili.

Lengo: Kusudio la utafiti ulioelezwa katika kitabu hiki ni kuchunguza mafanikio ya kiafya yaliyopatikana baada ya kupata tiba ya vidonge vya madini joto, vikifuatiwa na matumizi ya chumvi yenye madini joto kwa maeneo yote yaliyo kuwa yameathirika na yasiyokuwa yameathirika, kujua maendeleo ya matumizi ya mitambo iliyotolewa kama pembejeo kwa wazalisha chumvi na changamoto wanazopata za namna ya kuboresha teknolojia inayotumika katika kuchanganya chumvi na madini joto. Vile vile utafiti mwingine ulilenga kuboresha teknolojia ya kienyeji iliyobuniwa na wazalisha chumvi wenyewe ya kunyunyuzia na kuchanganya chumvi na madini joto.

Matokeo: Majumuisho ya matokeo ya tafiti hizi yanaonesha kupungua kwa tatizo la uvimbe wa tezi la shingo kutoka asilimia 25 ya mwaka 1980 hadi kufikia asilimia 7 mwaka 2004. Asililimia 94.5 ya watoto wa umri wa miaka 6 – 12 kwa upande wa Tanzania bara walionekana kuwa wamekingwa na madhara ya upungufu wa madini joto. Kwa upande wa visiwani Zanzibar uvumbe wa tezi la shingo uliongezeka hadi kufikia asilimia 25 sawa na viwango vya Tanzania bara miaka ya 1980. Matumizi ya mitambo na vifaa vya kuzalisha chumvi bora ya madini joto viliyotolewa miaka ya tisini viliachwa kutumika, na badala yake matumizi ya vinyunyizia vya gharama nafuu vilibuniwa bila kuwa na ujuzi wa kuzalisha chumvi yenye viwango sahihi vya madini joto. Jaribio la kuboresha teknolojia hii rahisi ulionesha kuwa endapo

uchanganyaji utasimamiwa vizuri, viwango sahihi na salama (40 – 80 mg/kg) vya madini joto vinaweza kufikiwa.

Hitimisho: Utafiti huu umeonesha kuwepo kwa mafanikio makubwa ya kuwakinga mamilioni ya watoto kutokana na athari za upungufu wa madini joto, hasa vifo na uharibifu wa ubongo. Hatua za makusudi zinatakiwa kuchukuliwa ili kufuatilia uwekaji madini joto kwenye chumvi, usambazaji wake pamoja na kuimarisha utekelezaji sheria ya chumvi Tanzania bara na visiwani. Endapo ufuatiliaji na usimamiaji wa karibu utatekelezwa, teknolojia ya kunyunyuzia madini joto kwenye chumvi kwa kutumia pampu za mkono za gharama nafuu itasaidia sana wazalisha chumvi wadogo katika mikakati ya serikali ya kutokomeza madhara ya upungufu wa madini joto kwa jamii ya Tanzania na kwingineko duniani.

1. INTRODUCTION

1.1 Background to iodine deficiency disorders (IDD)

Iodine (atomic wt 126.9g/atom) is an essential component of the hormones produced by thyroid gland. Thyroid hormones and, therefore iodine, are essential for mammalian life, including humans [1]. Iodine is a trace element found naturally and unevenly distributed in soil. It is very volatile and sublimates easily, i.e. passes from a solid state directly to gas form (I_2). It is also water soluble. Access to iodine on a daily basis is through drinking water and consuming food originating from crops and plants grown on the earth [2]. For instance, people living in the islands or coastal areas have access to marine foods, including fish and seaweeds that are known to be rich in iodine [2, 3]. The foods grown on iodine-deficient soil have lower iodine content than those produced in iodine-rich soil [4], and man and animals consuming water and crops from the area of iodine-deficient soils themselves become deficient in iodine [5].

IDD is a globalising name for a spectrum of disorders caused by iodine deficiency, manifested by enlargement of thyroid gland, also referred as goitre [6]. Brain damage and irreversible mental retardation are the most important disorders induced by iodine deficiency. Cretinism - a condition resulting from extreme form of iodine deficiency in utero - and endemic goitre have been recognised as public health problems for centuries. The primary etiologic factor, iodine deficiency, was hypothesized in 1851 as the cause of goitre [7], although goitre had been recognised in the earliest of ancient history and was treated by giving seaweeds or burnt sponges to eat [8].

The modern history of global efforts to eliminate goitre and cretinism started after the long debate in 1932, when scientists meeting in Bern, Switzerland, correctly identified the cause of the problem as iodine deficiency and consensually advocated iodine prophylaxis on a national scale [9]. Today, control of iodine deficiency is an integral part of the most national nutrition strategies [7]. More than 120 countries were implementing salt iodation programmes by 2006 compared to 90 countries in 2000 [10].

Several interventions of proven high efficacy are being used. Iodized oil capsules (IOC) are used as a short-term or complementary measure in severely IDD affected areas, while universal salt iodation (USI) is a long-term measure to control IDD globally. To achieve the overall goal of elimination of IDD, a good and multipronged monitoring system is essential to ensure target groups are protected from iodine deficiency as well as from excessive consumption [11, 12].

Tanzania, a country with an estimate of 41% percent of its population living in iodine-deficient areas, and therefore at risk of IDD, has been intensively implementing a combination of these two interventions since the mid-1980s, coordinated by the Tanzania Food and Nutrition Centre (TFNC) [13, 14]. Spot assessment studies conducted in the most iodine-deficient areas indicated a positive trend towards reducing the prevalence of goitre and increasing coverage of households consuming iodated salt [15, 16]. Since most efforts were directed towards goitre endemic areas, no evaluation studies were conducted on a national scale to assess the impact and weaknesses of USI, making it impossible for the Tanzania to know whether it had achieved the goal of iodine deficiency elimination that was set for 2000 and later revised to 2005 [11, 17]. The results of studies into this concern form the basis of this thesis.

1.2 Iodine in the human body

Importance of iodine and dietary requirements

Iodine is an essential micronutrient required for normal growth, development and functioning of the body. It is used in a single metabolic pathway; it is a constituent of the thyroid hormones, thyroxine (T_4) and tri-iodothyronine (T_3). Thyroid hormones are important for the regulation of the body metabolism. The healthy human adult body contains 15-20 mg of iodine of which 70-80% is stored in the thyroid gland. The gland weighs only 15-25 g, highlighting the its importance in the overall metabolism of iodine [2].

The recommended dietary allowance of iodine is 50 μg/day for infants in first 12 months of age, 90 μg/day for children of 2-6 years, 120 μg/day for school children of 7-12 years, 150 μg/day for adolescents and adults, and 200-300 μg/day during pregnancy and lactation [5, 18]. In constant iodine intake situations, the amount of iodine excreted in urine correlates well with the iodine intake, thereby serving as an estimate marker of iodine intake. Less than 10% of human iodine is lost via egestion and excretion in faeces [19], sweat [20] and milk [21].

Thyroid hormones synthesis and secretion

The synthesis of thyroid hormones requires two principal raw materials [22]. First is the amino acid, tyrosine, provided by a large glycoprotein scaffold called thyroglobulin. A molecule of thyroglobulin contains 134 tyrosines, but only some of these are used to synthesize T_4 and T_3. The second raw material is iodine, or more accurately iodide (I^-). Iodine is absorbed rapidly as either 'iodate' (IO_3^-) or 'iodide' (I^-) in the stomach and upper small intestine.

When iodine is ingested in the form of iodate, it is normally reduced to iodide, and transported in the bloodstream to the thyroid gland where it is avidly taken up by thyroid epithelial cells. These have a sodium-iodide symporter, also known as '*iodine trap*', on their outer plasma membrane. Once iodide is inside the thyroid cell, it is transported into the lumen of the follicle along with thyroglobulin to synthesise thyroid hormones [5]. About 60 μg of iodine needs to be trapped daily to maintain an adequate supply of thyroid hormones for normal body function, and the efficiency of the trapping mechanism is regulated by thyroid stimulating hormone (TSH), which therefore depends on the availability of iodine and the thyroid gland's activity [4].

Thyroid hormone synthesis is catalyzed by the enzyme, thyroid peroxidase, through two sequential reactions (**Figure 1a & b**): the organification of iodide occurs first, where tyrosines on thyroglobulin are iodinated to form mono- and di-iodotyrosines. And second comes the coupling process, which is also a peroxidase-dependent process, where two molecules of di-iodotyrosines form thyroxine (T_4) or one mono- and one di-iodotyrosines molecules form triiodothyronine (T_3) and a tiny amount as a reverse-T_3 (rT_3) (**Figure 1b**). T_4 made by the thyroid gland circulates throughout the body and is converted into T_3 and a tiny amount of reverse-T_3.

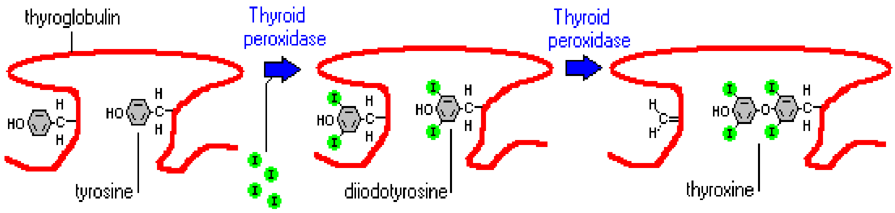


Figure 1a: Synthesis of thyroxine [22]

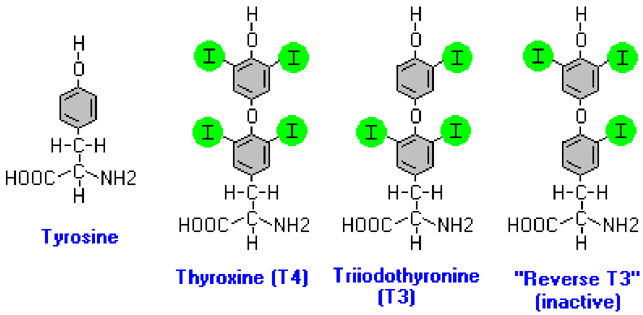


Figure 1b: The chemical structure of tyrosine and the thyroid hormones [22]

Most of the biological activity of thyroid hormones is due to T_3, which has a higher affinity for thyroid receptors and is ~4 times more potent than T_4 [18]. Thyroxine is, therefore, generally transformed to T_3 prior to exerting its biological action with the help of a selenium containing enzyme, 5'-deiodinase [23]. About 80% of serum T_3 is derived from T_4 in tissues such as the liver and kidney, and therefore T_4 is both a hormone and a pro-hormone.

Organification is normally reduced when the amount of iodine is greatly increased, the so-called Wolff-Chaikoff phenomenon [24]. Reverse-T_3 (a mirror image of T_3), however, is produced in small amounts, and is an antagonist of T_3. It can bind to thyroid receptors blocking the action T_3, but producing no thyroid response. In a situation where reverse-T_3 dominance exists, functional hypothyroidism may become manifest, with most of the hypothyroid symptoms, even though circulating T_4 and T_3 levels appear normal. Thus reverse- T_3 acts as a metabolic brake.

The processes of hormone synthesis and secretion are stimulated by thyroid-stimulating hormone (TSH, also called thyrotropin) from the anterior pituitary gland. The secretion of TSH is modulated by thyrotropin-releasing hormone (TRH) from the hypothalamus, being the regulator of iodine metabolism in a feedback mechanism [22]. A low concentration of thyroid hormones elicits an increase in TRH, which in turn increases TSH. Binding of TSH to its receptors on thyroid epithelial cells stimulates synthesis of the iodine transporters, thyroid peroxidase and thyroglobulin, which in turn incites production and release of more thyroid hormones from the thyroid gland to the bloodstream.

As thyroid hormone levels rise, the pituitary gland responds via a feedback mechanism which decreases TSH secretion. At high TSH levels, the thyroid will preferentially produce more biologically active T_3. Thyroid hormones regulate the speed or the rate of the metabolism of target organs by entering cells of the peripheral tissues and binding to the nuclear chromatin via a thyroid hormone receptor, which in turn affects transcription [25]. The levels of T_4 and T_3 in the blood can be used as an indirect measure of iodine status of individuals.

Sustained TSH levels stimulate an increase in the size and the number of follicular cells, an increase in vascularisation, and consequently thyroid hypertrophy, which leads to a better iodine capture. Hypertrophy of the thyroid is regarded as ‘goitre’ [6]. In addition, persistent stimulation may also cause the formation of thyroid nodules.

Thyroid hormones are poorly soluble in water, and >99% of the T_3 and T_4 circulating in blood is bound to carrier proteins. The principle carrier of thyroid hormones is thyroxine-binding globulin (TBG), a glycoprotein synthesized in the liver. Two other carriers of import are transthyretin and albumin. Carrier proteins allow the maintenance of a stable pool of thyroid hormones from which the free active hormones are released for uptake by target cells.

1.3 Aetiology of iodine deficiency

Millions of years of rainfalls and glaciations in the hills and floods in the river valleys had removed the iodine from the soil by erosions and leaching, making vast areas of the planet’s soil iodine-deficient. Iodine accumulates in the lowlands, lakes and oceans, thereby making seafood, e.g. seaweeds and fish products, iodine-rich foods [26]. Although some iodine is returned to the soil by rain, this is insufficient and soils remain persistenty iodine-deficient. On an iodine-deficient soil, all forms of plant life themselves become iodine-deficient and consequently animals and humans become iodine-deficient. Hence populations living in systems of subsistence agriculture on iodine-deficient soils, especially in low-income countries, are the people most at risk of iodine deficiency [6]. Iodine-containing animal feeds and antiseptics commonly used in the dairy industry resulting in iodine-rich milk are an important source of iodine in many countries [27]. However, food alone is generally not sufficient to provide adequate iodine intake.

Effect of goitrogens

While iodine deficiency is caused by insufficient dietary iodine intake, other substances known as goitrogens interfere with the proper functioning of the thyroid hormones synthesis and their utilization [28]. The natural occurring goitrogens are found in the following frequently consumed foods: cyanogenic glycosides and cyanohydrins in cassava, thiocyanates and isothiocyanates from cabbages predominantly of genus *Brassica* (Cruciferae family), and C-glycosylflavones from pearl millet – a staple food in semi-arid areas. Thiocyanate is formed in the body from cyanogenic glycosides, cyanide from tobacco smoking or from cyanogenic substances in insufficiently processed cassava. These cyanogens are detoxified to thiocyanate [29-31]. The pseudo-halide ion, thiocyanate (SCN^-), interferes with the uptake and metabolism of iodine by the thyroid gland through competitive inhibition [32, 33].

In the human body, most of the cyanide is enzymatically converted to thiocyanate, which at physiological levels is slowly excreted in the urine. In many countries, the high prevalence of goitre has been attributed to the combined effect of iodine deficiency and thiocyanate exposure due to cassava consumption [34-36]. The complication of thiocyanate in IDD has led to calls to reduce cassava consumption [37-39]. Yet, other observations suggest that an adequate iodine intake prevents hypothyroidism or goitre developing even in the presence of high thiocyanate loads [40, 41]. In addition, it is only during inadequate protein nutrition that thiocyanate aggravates endemic iodine-deficient disorders [42]. Calls to limit cassava to control IDD do not, therefore, appear to be justified; however, it is emphasized that improving the processing methods of cassava can reduce cyanide levels [43, 44].

Effect of other micronutrients on iodine metabolism

Multiple micronutrients in the bodily metabolism operate synergistically so that supplying several micronutrients may assist in reducing the prevalence of iodine, iron and vitamin A deficiencies in school-age children [45, 46].

Iron deficiency impairs thyroid hormone metabolism because of the two first steps in the thyroid hormone synthesis catalysed by thyro-peroxidases, which are iron-requiring enzymes. Concurrent iron deficiency anaemia impairs the therapeutic response to iodine supplementation, possibly mediated via decreased T_4 to T_3 conversion or through decreased thyroperoxidase activity impairing iodide organification [47]. Iron deficiency lowers plasma T_3 and T_4 concentrations, reduces conversion of T_4 to T_3, and increases thyrotropin concentration. Because of these impairments in iodine metabolism, goitre in anaemic individuals may become less responsive to iodine treatment. Combining iodine and iron supplements can reduce goitre more rapidly than iodine alone [48].

Selenium is an essential component of the enzyme, Type 1 deiodinase, which also catalyses the conversion of T_4 to T_3 [49]. Combined iodine and selenium deficiencies may cause the myxoedematous form of goitre [23], and thus explain the link between iodine and selenium deficiency [50, 51]. High selenium intake also affects thyroid function by reducing the production of T_3 to T_4 [52].

Vitamin A supplements can be effective in treating Vitamin A deficiency in areas of mild iodine deficiency children and have an additional benefit through suppression of the pituitary *TSH- β* gene, decreasing excess TSH stimulation of the thyroid, and ultimately reducing the risk of goitre and its sequelae [53]. Thus global control of micronutrient deficiencies i.e. iron, iodine, vitamin A and other minerals and vitamins requires an integrated approach that includes dietary diversification, targeted supplementation, and food fortification [54].

Tanzania has given priority in tackling the three major micronutrient deficiencies, i.e. iron, vitamin A and iodine; but only iodine and vitamin A deficiencies have made a substantial progress through universal salt iodation and vitamin A supplementation, respectively [55, 56]. The problem of iron and other micronutrient deficiencies have not yet been fully addressed because there is no common identified vehicle in Tanzania's setting that can deliver these micronutrients throughout the population [57]. However, the de-worming programme for the 2-5 year olds has been carried out concurrently with vitamin A supplementation twice yearly, which may have contributed to reducing nutrition anaemia [55]. However, dietary diversification is being emphasized that includes consumption of a balanced diet containing vitamins, proteins and minerals. In tackling iodine deficiency, 74% of households in the country were reported in 2004 to have access to iodated salt, but it was also estimated that 1.6 of the 3 million children under the age of two in Tanzania were living in households where inadequately iodated salt was being consumed [58, 59].

1.4 Iodine deficiency disorders

The most apparent manifestation of iodine deficiency is goitre, an enlargement of the thyroid gland, but the spectrum of diseases associated with iodine deficiency is much greater. The most prominent manifestation of iodine deficiency is the effect on brain function that may occur at all stages of life, from early foetal damage to hypothyroidism in the neonate, childhood, or adulthood [6, 60] (**Table 1**).

Pregnant women exposed to severe iodine deficiency, are unable to produce the extra thyroid hormones required to supply the fetus across the placenta during the first half of pregnancy [61]. At this time, rapid growth of the fetal brain is taking place. Sufficient maternal thyroid hormone is essential to secure the process of early growth and development of most organs, and especially the brain [62-64]. Deficiency of iodine causes maternal hypothyroidism, leading to irreversible fetal brain damage; the clinical consequence will be mental retardation (impaired intellectual development) and impaired physical growth, which can totally be prevented by correction of any iodine deficiency before pregnancy [2, 63, 65].

Table 1: Spectrum of iodine deficiency disorders (IDD)

Age groups	Health consequences of iodine deficiency
All ages	Reduced mental capacity (reduced IQ) Goitre Reduced work capacity Reduced economic potential
Foetus and neonates	Increased mortality: - Spontaneous abortions, foetal loss, stillbirths, - Increased perinatal and infant mortality Congenital anomalies Cretinism, including severe mental retardation with a mixture of mutism, spastic diplegia, squint, hypothyroidism and short stature
Children and adolescents	Impaired mental function Delayed physical development Goitre Iodine-induced hyperthyroidism (IIH), if iodine suddenly is provided
Adults	Impaired mental function Goitre Iodine-induced hyperthyroidism (IIH), if iodine suddenly is provided

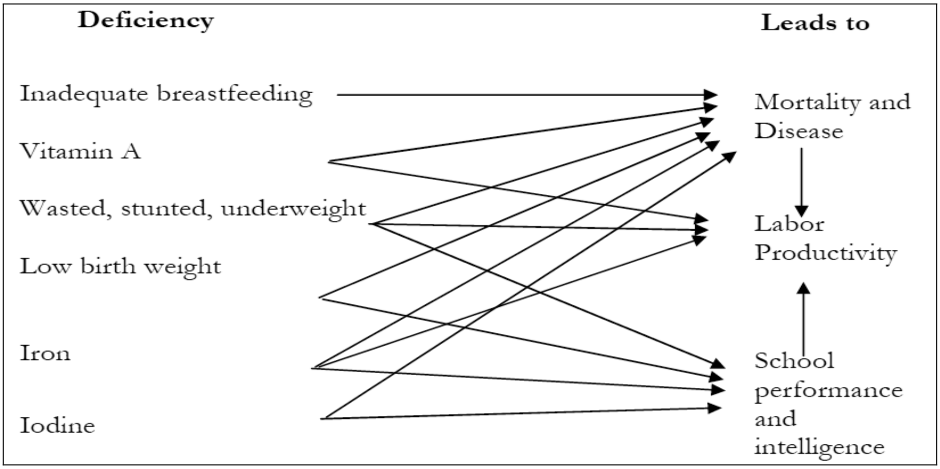
[a] Adapted from BS Hetzel [6]

The extreme consequence of iodine deficiency is death in the form of fetal loss, stillbirth, and increased perinatal and infant mortality. Others include congenital anomalies, hearing impairment, endemic cretinism, and a wide range of physical and mental anomalies [6, 66, 67]. Even with mild iodine-deficient, individuals usually experience moderate mental retardation, which decreases work capacity and economic potential. Cretinism caused by severe deficiency in early life is associated with extreme mental retardation [68].

Meta-analysis of studies has revealed that the mean score for the iodine-deficient population is 13.5 IQ points below that of the non-iodine-deficient population [61, 69]. In humans, there is reduced school performance in children, which later leads to reduced economic productivity and quality of life in adulthood [69, 70]. The problem of IDD exists worldwide, but its major devastation is in developing countries, despite the availability of the technology for prevention, which makes iodine deficiency the most amenable to quick and effective control [6].

Micronutrient deficiencies, including iodine, iron and vitamin A, all affect health, survival, intelligence in different ways, and consequently the productivity of individuals and the nation as a whole (**Box 1,** [54, 71]). The pathway from malnutrition to educational outcomes is via the capacity to learn, a direct consequence of the impact of poor nutrition on cognitive development. Iodine deficiency is an example that has negative and irreversible effects on the cognitive functioning of the fetal brain. Iodine deficiency can also become manifest in later in life, and is also associated with cognitive deficits [54].

Box 1: An overview of how nutrition deficiencies affect the prospects of young children



Source: [71]

Adverse effects of excess iodine intake

An adverse effect of exposure to excess iodine was reported about fifty years ago. Excess iodine causes an inhibition of thyroidal organic iodation in response to a marked elevation of plasma iodide, a phenomenon known as the Wolff-Chaikoff effect [24]. This acute iodide blockade spontaneously disappears, despite continued administration of iodide (escape phenomenon). Intake of iodine from a variety of supplements, salt and water-diffusers may pose a risk of iodine excess in some individuals [72].

Manifestations of excess iodine intake include thyroiditis, goitre, hypothyroidism, hyperthyroidism and sensitivity reactions. Exposure to excess iodine during pregnancy may lead to transient hypothyroidism in newborn infants [73]. Fetal goitre may also occur and in rare instances can give rise to respiratory problems [74, 75]. Nearly 100% of genetically susceptible animals fed with high iodine diet become positive for thyroglobulin antibodies [76]. Even a daily supplementation of 150 µg iodide in women with autoimmune thyroiditis was found to aggravate the disease [77].

An increase in the incidence of thyrotoxicosis may occur after introduction of iodated salt, as seen in Zimbabwe and the Democratic Republic of Congo [78, 79]. However, this side effect of iodation of salt is rare and usually mild, being associated to a rapid increase in iodine intake and a state of acute iodine overload [60]. Some persons tolerate high doses without side effects, while others respond adversely to levels close to recommended intake [60]. Increased prevalence of autoimmune disease after elimination of iodine deficiency has also been reported elsewhere in school-children [80].

High prevalence of thyroglobulin antibodies in school-children reflecting excessive iodation of thyroglobulin that lead to increased immunogenicity has been indicated, but without any cases of iodine-induced thyrotoxicosis being noted [81]. Furthermore, it was reported elsewhere that excessive iodine intake (median urinary iodine ≥500 µg/L) is a risk factor for autoimmune-prone subjects to develop hypothyroidism. Both extremely low and high iodine intakes correlate with an elevated tendency for thyroid autoimmune abnormalities [82].

Specific population groups, like pregnant and lactating women, however, require higher iodine levels than recommended for the normal healthy adult person. They should have median urinary iodine within the range 200-299µg/L, which is their normal requirement [83]. Based on the tolerance of huge doses of iodine in healthy iodine-replete adults, World Health Organisation (WHO) stated that; '*Daily iodine intake of up to 1 mg...appears to be entirely safe*' [11]. This statement does not include neonates and infants who have different iodine requirements [84-86]. Iodine excess is less of a health problem than iodine deficiency, but it is unnecessary, undesirable, and avoidable.

1.5 Global action towards prevention and control of IDD

WHO published (1960) the the first global review on the extent of endemic goitre that demonstrated the scale of the public health problem of IDD [87]. In the 1980s, the international community committed itself to the elimination of IDD through a number of declarations and resolutions. More countries continued to map the problem, and by the 1990s, the estimates of the global numbers of subjects affected by some of the IDD conditions had been established (**Figure 2;** [11, 88, 89]).

Global efforts were initiated in 1990 when IDD was recognised by the World Health Assembly as a problem of public health significance and a resolution was accordingly passed (WHA43.2), which adopted the goal of iodine deficiency elimination in all countries by the year 2000. WHO, United Nations Children's Fund (UNICEF) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) recommended Universal Salt Iodation (USI) as a safe, cost-effective and sustainable strategy to ensure sufficient intake of iodine by human and animals [88, 90].

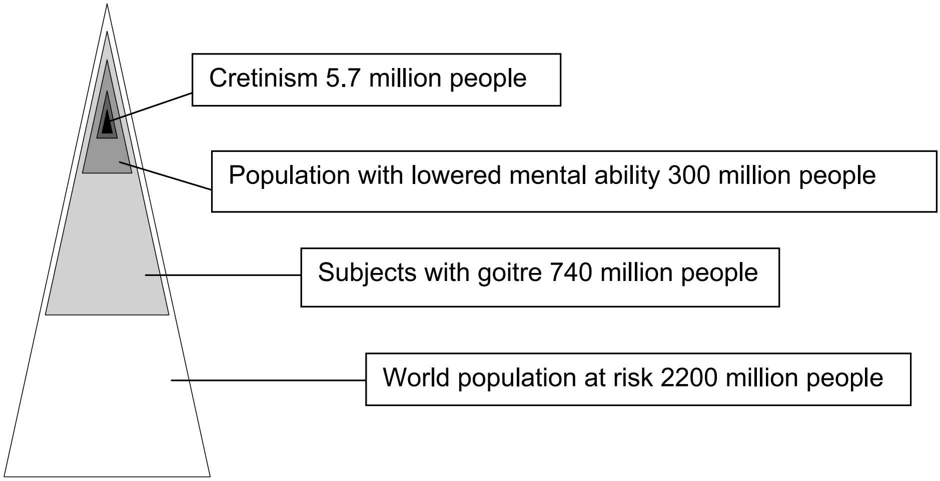


Figure 2: Global burden of iodine deficiency disorders (Adjusted from UNICEF 1995) [88]

For prevention and control of IDD, WHO recommended to:
'Iodize all salt for human and animal consumption (including salt for food processing), i.e. Universal Salt Iodization in all countries where iodine deficiency disorders (IDD) are a public health problem; where full salt iodization is impossible in areas in which IDD is a severe public health problem, supplementation with oral or injected iodized oil will be recommended as a temporary measure' [12].

The World Bank estimated that each dollar dedicated to the prevention of IDD would in return yield a productivity gain of US$ 28, supporting the widely held view that elimination of iodine deficiency is one of the most cost-effective nutrition-health interventions [91], and a smart thing to do. Moreover, while investing in nutrition such as in controlling IDD which will certainly give economic returns, it should also be considered as a human right [92].

Political commitment for the elimination of IDD
Investing in iodine nutrition requires conducive political, economic, technological and social environments [93]. The World Summit for Children in 1990 with support of the United Nations (UN) system raised the political commitment from the world leaders by aiming at the virtual elimination of iodine deficiency as part of the Plan of Action for Child Survival, Protection and Development [94]. Although the goal was not achieved in the year 2000 as planned, these commitments have led to strong political support by heads of state, and some progress has been made, even in Tanzania based on the UN milestones for elimination of global iodine deficiency summarised in **Table 2** [10, 87].

Table 2: Milestones for programmes for elimination of iodine deficiency and progress globally and in Tanzania

Year	Milestones	Programme progress globally	Progress in Tanzania
1990	Declaration of the World Summit for Children includes goal of virtual elimination of iodine deficiency disorders 43rd World Health Assembly accepts IDD elimination by 2000 as a major public health goal for all countries	Accelerated programme initiation and a shift from supplementation to salt iodization	- Peaked iodine supplementation - Feasibility studies and salt iodation programme started - Salt regulations prepared, gazetted and trainings for program monitoring
1994	UNICEF-WHO Joint Committee on Health Policy endorses universal salt iodization as a safe, cost-effective and sustainable strategy to ensure sufficient intake of iodine by all individuals	IDD prevention and control through expansion of salt iodization programmes	- Inauguration of salt iodation programme - Advocacy to raise consumption of iodated salt - Salt regulations effected
2002	UN General Assembly Special Session on Children adopts *A World Fit for Children*, the declaration that set the goal of sustainable elimination of IDD by 2005	Programme maturation with improvements in enforcement, public education and advocacy, monitoring and partnership with salt industry	Programme maturation, with efforts to unveil low programme performing areas, inventory of small producers, enhance partnership with salt industry
2007	*A World Fit for Children* commemorative session reviews progress in achieving and sustaining IDD elimination through universal salt iodization programme	Enhancements in programme sustainability	- Plan of action for 2007/8-2011/2 prepared, - Review salt regulations - Close supervision to small scale salt producers

Source: [10]

These commitments were renewed in 2002 at the UN General Assembly Special Session on Children, at which the world leaders declared "*A World Fit For Children"* and reinforced to continue efforts towards sustained elimination of iodine deficiency by 2005 [95, 96].

The outcome document of that Special Session states:
'Achieve sustainable elimination of iodine deficiency disorders by 2005, and of vitamin A by 2010, reduce by one third the prevalence of anaemia, including iron deficiency, by 2010, and accelerate progress towards reduction of other micronutrient deficiencies, through dietary diversification, food fortification and supplementation' [96].

Table 3: Proposed major implementation phases of an IDD control programme and their status in Tanzania

Programme implementation	**Actions required**	**Progress made in Tanzania**
Assessment phase	- Complete a situation analysis. - Establish an understanding of the nature of the problem: brain development instead of goitre; its geographic distribution (urban and everywhere instead of just rural); and its magnitude (loss of cognitive capacity in all developing brains, not just causing cretinism and severe mental retardation). - Attain high level multi-sectoral sponsorship for the programme. - Prepare or update legislation and regulation. - Collect key information for an advocacy and marketing campaign. - Mobilise the salt importers, producers and traders, and strengthen public/private cooperation.	All actions listed in this phase were addressed in 1990s
Implementation phase	- Establish the legal mandate and regulatory environment to ensure implementation. - Establish the capacity of producers and distributors to begin iodation of all salt. - Implement a marketing plan. - Phase in monitoring activities to ensure that adequately iodated salt is being produced and reaches households. - Use action teams to find problem areas and implement solutions to these problems.	- Most of the action components in this phase have been fairly addressed - There still some weaknesses on the implementation of market plan and the monitoring system
Consolidation phase	- Amend regulations to ensure that only iodated salt is available everywhere. - Move to more routine monitoring with a greater reliance on established government inspection to ensure high compliance with the 'best practices' established by industry. - Undertake periodic assessment at the community level to ensure that IDD elimination has been reached and is maintained. - Ensure that the programme elements are incorporated as routine activities in both government and business	- Salt regulations reviewed in were done in 2006 - Periodic assessments plan to ensure IDD elimination is in place and practised - The rest of the actions have been addressed but not yet fully implemented in order to achieve and sustain IDD elimination

Source: Monitoring salt iodization programs [99]

To reinforce the implementation of IDD elimination worldwide, a Global Network Alliance for Sustained Elimination of Iodine Deficiency was founded in 2002.

Members of the alliance have a common interest, i.e. a commitment to assist countries, to reach the goal through salt iodation [96].

In the world today, iodine deficiency remains the most common preventable cause of brain damage and mental retardation, with 30% of world population at risk in 130 countries [70]. Globally, more than 100 countries had salt iodation programmes by the year 2000, with nearly 70% of households having access to iodated salt compared with only 20-30% in 1990 [70].

However, only a few countries had managed to reach the goal of IDD elimination by the year 2000 [87]. In 2003, the total goitre prevalence in the general population globally was 15.8%, whereas in Africa alone it was estimated at 28.3%, which included 59.7 million school-age children with insufficient iodine intake [97, 98]. The renewed commitment in 2002 requires every country to work towards meeting the goal that was set to eliminate IDD by 2005 [96].

According to the UNICEF report on the Progress for Children in 2006, only 34 out of 157 countries had achieved USI by having more than 90% of households consuming iodated salt, but there were still 36 countries where fewer than half of the households consumed iodated salt [97].

The reason for not achieving the goal is that each country needs a unique solution to sustaining IDD elimination through salt iodation, which is based on its size, economic resources, cultural and political context, and market structure. Although national iodation programmes are at different stages of implementation, they are all following the same common pathway (**Table 3;** [99]).

2. SALT FORTIFICATION

2.1 Salt iodation

Fortification of salt with iodine is considered the most appropriate measure for a long-term solution that will sustainably eliminate iodine deficiency [100, 101]. The advantage of supplementing with iodated salt is that it is used by all sections of a community irrespective of their social and economic status. It is consumed as a condiment at roughly the same amount throughout the year. Its production is often confined to a few centres, which means processing can occur on a larger scale and with better controlled conditions [100]. However, this is not always the case in low-income countries where there are different sources of salt, e.g. from salt lakes, certain kinds of plants, thermal evaporation from foothills, and seawater [102].

Dual or triple fortification of salt with essential micronutrients, i.e. iodine, iron and vitamin A, has already proved effective [45, 103]. If adopted, this approach has an additional advantage because of the beneficial interactions of iron, iodine, and vitamin A in metabolism; therefore, it could reduce significantly the burden of diseases related to micronutrient deficiencies, especially in low-income countries.

2.2 The cost for iodine nutrition intervention

The consequences of micronutrient deficiencies are much too high in comparison to the costs for investing in nutrition, such as salt iodation, which has a return of $28 per $1 invested [91]. Internationally the cost of salt fortification with iodine was approximately $0.03 per capita (range 0.02-0.07) [100]. This is far cheaper than iodine supplementation using iodized oil capsules, which globally has been estimated at $0.85 (range $0.8-2.75) [104].

Cost-analysis studies conducted in Tanzania have shown that the costs of iodine and vitamin A supplementation using iodised oil capsules and vitamin A capsules were about $0.53 (range $0.32-0.97) and $0.71, respectively [56, 105]. Notwithstanding, salt iodation is 10- 30 times cheaper compared to iodine supplementation.

2.3 Iodine compounds for salt fortification

Salt iodation is a process of mixing iodine in the form of potassium iodate (KIO_3) or potassium iodide (KI) and salt crystals. Potassium iodate is less soluble but more stable than iodide and is therefore preferred for hot and humid climates [100]. Potassium iodate has a low proportion of iodine (59.5%) when compared to other salt- fortifying iodine compounds that have >70% [100]. The “salt” with iodine was previously referred to as “iodised salt”, irrespective of compound used, but the ICCIDD has reviewed the terminology and now the salt is referred to as ‘iodated salt’ or ‘iodised salt’ for salt fortified with sodium/potassium iodate or iodide, respectively [18]. The joint FAO/WHO Expert Committee on Food Additives endorsed the use of potassium iodate and potassium iodide compounds since they had a long-standing and widespread history of use for fortifying salt without apparent adverse health effects [106].

2.4 Quality of salt for iodation

Quality of salt suitable for iodation on a dry basis, according to the Codex Alimentarius specifications for a food grade salt, should not be <98% sodium chloride (NaCl) by weight with <3% moisture content and 0.5% insolubles [100]. **Table 4** summarises the chemical analyses of different types of salt produced. In the less developed countries where IDD is more prevalent, the type of salt commonly consumed is usually the coarse crystalline type (solar).

Table 4: Different types of salt and their chemical content on dry basis in percent.

Type of salt	NaCl	Magnesium	Calcium	Sulfates	Insolubles
Pure vacuum evaporated salt	99.95	0.0001	0.002	0.04	trace
Vacuum salt	99.70	0.01	0.01	0.2	trace
Refined salt	99.0	0.05	0.06	0.2	0.02 - 0.3
Solar salt	96 - 99	0.01 - 0.17	0.04 - 0.3	0.11 - 2.0	0.05 - 0.6
Rock salt	90 - 99	0.01 - 0.17	0.04 - 1.1	0.2 - 1.3	0.0 - 5.0

NB: Figures are %

Crude salt is commonly used for industrial purposes, livestock and even for humans in low-income countries.

2.5 Salt iodation methods

There are two methods commonly used for salt iodation; one is dry mixing where the dry potassium iodate or iodide salt in the form of powder is mixed with an anti-caking agent at a given ratio to form a premix that is sprinkled over dry salt. The other method is wet mixing, in which a concentrated solution of potassium iodate/iodide with known strength is added to the salt by spraying or dripping. For Tanzania, a wet mixing method is very common, which entails the use of pressurised tanks with calibrated iodation machines.

Dual and triple fortification of salt with major micronutrient in the form of micro-encapsulation is another advanced method expected to cost less than carrying out separate single fortification programmes [45, 53, 107].

Other food items fortified with iodine

In developed countries, such as in Europe and North America, different food items are fortified with iodine. These include fortification of bread with iodine, which has been successful in The Netherlands, Tasmania and Russia [108-110]. This is applicable only if bread is part of a staple food. Bread manufacturers add salt premixes containing not only iodine, but also iron, niacin, riboflavin and thiamine hydrochloride to their dough [100].

Milk is another source of iodine in the USA, Canada, United Kingdom and Northern Europe, mostly originating from iodophores that is used as a disinfectant agent in the milk industry. For instance, milk products, fish and fish products are the main source of iodine, contributing 80% of the iodine intake in the Norwegian diet [111, 112], and the same of their neighbours, Sweden [113].

In other countries such as Mali, iodised water has been used and has some of the advantages of salt as a vehicle for iodine fortification [114]. Both are daily necessities and thus their iodization will reach the most vulnerable groups – the poor and the isolated groups. Iodization of water is only of an advantage if water supplies are centrally controlled. ICCIDD has also recommended the use of water as an efficient vehicle in controlling iodine deficiency where resources are available, but it should be properly monitored [115].

2.6 Storage of iodated salt

One of the main objectives of any salt iodization program is to ensure that iodine levels in the salt are maintained at recommended levels up to the time of consumption [18]. The quality of salt, the compound used for fortification, the type of packaging materials and the climatic conditions are some of the factors which determine iodine retention in salt, remembering that salt is hygroscopic at a relative humidity above 76% [100].

When improperly packed iodated salt is transported over long distances under humid conditions, it will attract moisture and becomes wet, dissolving and carrying the iodate to the bottom of the bag, and finally it can be lost if the bag is porous to water [5, 100]. Salt packed in such materials may loose as much as 75% of its iodine content over nine months. High density polyethylene bags and polyethylene laminated bags are recommended for bulk packaging purposes. When jute/sisal bags are used, they should have inner linings of low density polyethylene sheet (**Figure 3**).

For high-income countries, air-tight containers are used for salt packaging, and the quality of the salt remains very high compared to raw salt used in many low-income countries [116]. Exposure to heat or sunlight can increase iodine evaporation in the form of iodine gas (I_2). Other iodine losses also occur from improper handling of iodated salt, such as failing to keep it in air-tight containers, washing it or not covering pots during cooking processes [116, 117].

2.7 Iodation levels

In order to iodise salt, the per capita salt consumption in an area should first be taken into account to determine the concentration of iodine required to meet daily iodine intake requirements. If the *per capita* salt consumption is high, then the iodine level

Figure 3: Inner lining for bulk salt packaging to prevent iodine losses

should be reduced and vice-versa for low salt intake areas [100]. Previously accepted levels of salt consumption were in the range 10-15 g per day, but now this is regarded as excessive because of the increased risk of hypertension [118, 119]. For this reason, salt levels in the range of 3-6 g per day are now recommended [120, 121].

Box 2: Sample calculation for fixing the level of salt iodation using KIO_3

* Assume daily requirement per capita as the of iodine is 200 µg;
* Assume that the per capita salt consumption is 10 g per day.
* Level of iodine required in salt is 200 µg per 10 g (1 g = 1 million µg) or 20 parts per million (ppm);
* Assume that half of the iodine may be lost in transit and storage;
* Then the level of iodation required: = 40 ppm iodine;
= 40 x 1.685 ppm KIO_3;
= 67 ppm KIO_3.

Source [100]

In Tanzania, the mean salt consumption was 8.1 g per person per day (range 6.4-9.4 g) being higher in urban (9 g per person per day) than in rural areas (7 g per person per day) [117]. Iodated salt is also needed as a feed supplement for the livestock living in the iodine deficient areas. In some developed countries, salt for cattle is also used as a carrier for trace minerals apart from iodine such as manganese, zinc, copper, iron, cobalt and magnesium [100]. WHO has recommended salt iodine levels of 20-40 ppm as adequate as the daily requirement of 150-200 µg iodine per person for adults [5]. The setting of iodation level for salt at production level has to be sufficient to cover this factor and the severity of IDD in the areas, together with other requirements mentioned earlier - iodine losses in transit from the point of production to the point of utilization - including the expected shelf life (**Box 2**).

Tanzania had its iodine levels reduced from 75-100 ppm in the 1990s (The United Republic of Tanzania 1994), and to 60 ppm iodine (40-80 ppm) in 2006 [122]. The recommended iodation levels for Tanzania are slightly higher than those recommended by WHO because of losses during salt handling/storage and utilization, which can be above 50% at each point [5, 117].

3. MONITORING OF A NATIONAL IDD CONTROL PROGRAMME

3.1 The 'Wheel Model' for implementing IDD control programme

For a smooth running of IDD intervention programme, the term partnership evaluation has been adopted by ICCIDD to describe the independent monitoring of implementing procedures and other aspects of the national IDD control programmes, in collaboration with the UN agencies, national government representatives and the private sector [70]. ICCIDD has represented the various components of the social process as a 'wheel model', suggesting that the wheel must keep turning with continuous assessment followed by the remedial actions as a measure of the effectiveness of the programme. The wheel represents the continuous 'feedback' process involved in the national IDD elimination programme, and it requires all participants to understand the whole concept of the social process and find its weaknesses in order to undertake corrective measures (**Figure 4**) [70]. The country's IDD programme coordinating body should oversee that each member or partner institution is playing his or her role successfully with available resources.

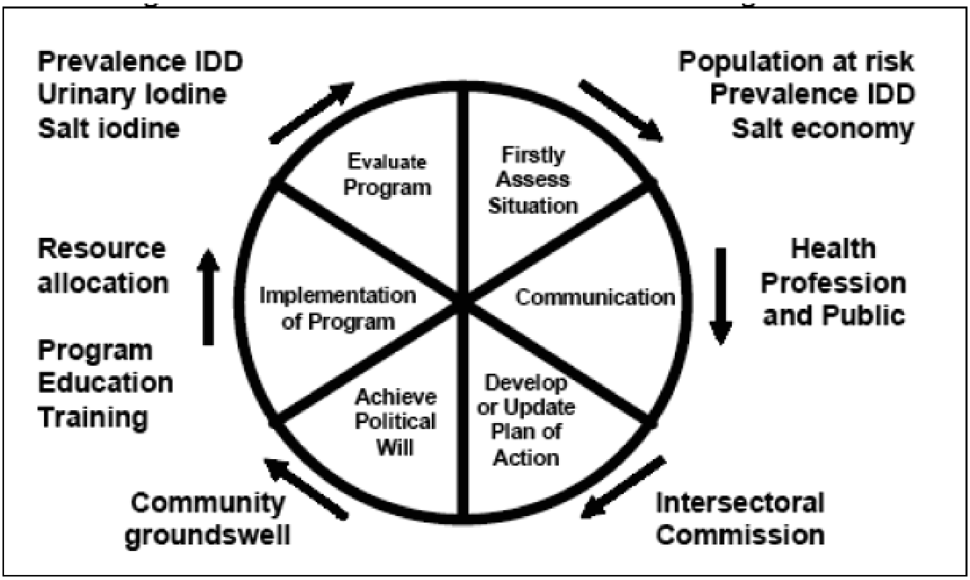


Figure 4: The 'Wheel Model' for an IDD Elimination Programme
Source:[123]

__1. Assessment__ of the situation requires baseline IDD prevalence surveys, including measurement of urinary iodine levels, identify population at risk and an analysis of the salt economy. __2. Communication of findings__ to health professionals and the public is necessary, so that there is full understanding of the IDD and the potential benefits of eliminating this most common preventable cause of brain damage. A community education campaign is required to educate all age-groups about the effects of iodine deficiency with particular emphasis on the brain. __3. Development of__

***a plan of action** includes the establishment of an intersectoral committee or coalition on IDD and the formulation of a strategy document on achieving the elimination of IDD. **4. Achieving political will** requires intensive education and lobbying of politicians and other opinion leaders. **5. Implementation** needs the full involvement of the salt industry. Special measures, such as negotiations for monitoring and quality control of produced and imported iodized salt, are required. It will also be necessary to ensure that iodized salt delivery systems reach all affected populations, especially the neediest. In addition, the establishment of cooperatives for small producers, or restructuring to larger units of production, may be needed. Implementation will require training at all levels in management, salt technology, laboratory methods and communication. **6. Monitoring and evaluation** is dependent on the establishment of an efficient system for the collection of relevant scientific data on salt iodine content and urinary iodine levels. This includes the establishment and the maintenance of suitable laboratory facilities.*

To guarantee that correct and safe iodine levels are reaching the consumers, monitoring of the iodine content in salt at production and import sites before the salt enters local markets in the country has been emphasized [124]. Both national laboratories and mini-laboratories are required to quantify the iodine concentration of produced or imported salt confirm that the specified standards are met and also to assist in speeding up the legal actions against non-compliant salt producers/traders.

The national monitoring program also requires sentinel sites to carry out periodic surveillance of salt iodine levels in retail shops and households, using rapid test kits, measuring urinary iodine regularly, and conducting occasionally goitre prevalence surveys. WHO has recommended high IDD risk communities as priority areas for establishing the surveillance system to prevent the scourges of IDD [5].

In high goitre endemic areas, iodine supplementation using iodinated oil capsules (IOC) as a short-term measure should be applied with carefully monitoring to ensure compliance and high coverage, while long-term measures are being sought [17, 105]. It is also important that the most IDD vulnerable groups, i.e. pregnant, lactating women and children under 2 years, are assessed as per WHO recommendation to ensure their iodine status before declaring sustainable IDD elimination [86, 125].

3.2 Iodine status indicators

WHO/ICCIDD has recommended three indicators to be used to assess the progress of implementing the IDD control programme [5].

3.2.1 Process indicators: These are used for monitoring and evaluating the salt iodation process at production, importation ports, retail shops and at the consumer level. In these cases, determination of iodine content at various points of salt handling is carried out to establish the coverage of adequately iodated salt (≥90%) in those areas. The assessment of household use of iodated salt also provides information that predicts both the probable iodine intake and status, making it easier to distinguish between difficulties with the iodated salt quality and use [5].

3.2.2 Impact indicators: These are meant to assess the magnitude of IDD as a public health problem and monitor the effects of intervention on the iodine status within a population [5]. The commonly used impact indicators include biochemical indicators, such as urinary iodine concentration, thyroid function hormones (TSH, thyroglobulin, T_4 and T_3), and total goitre prevalence/thyroid volume (a clinical indicator).

Urinary iodine

Most of the excess iodine absorbed by the body is excreted, making the urinary iodine concentration (UIC) a good marker of recent dietary iodine intake [126]. Median UIC is recommended for defining the population iodine status through a specific group of people, such as pregnant women, lactating women, infants and school-age children [5]. UIC assesses iodine nutrition status only at the time of measurement, whereas thyroid size reflects iodine nutrition over months or years. Therefore, goitre may still persist, even in children, although the population overall may have attained iodine sufficiency based on median UIC [48].

If a sufficient number of specimens is collected, profiles of iodine concentration in the morning, or from other casual urine specimens, will provide an adequate assessment of a population's iodine nutrition [126]. Thirty determinations of iodine in urine from a defined sampling group is sufficient [5]. In individuals, urinary iodine excretion can vary from day to day, and even within a given day, making it not normally distributed in a population. Thus, median urinary iodine is used rather than the mean to measure the central tendency. Likewise, percentiles rather than standard deviations are used to indicate better the spread [90].

The recommended assay methods for UIC are not difficult to use, but requires meticulous attention to avoid iodine contamination at all stages of specimen collection and analysis [5]. Quality control and reference laboratories have been established as part of International Network of Resource Laboratories of Iodine (IRLI) network to Ensuring Quality of Iodine Procedures (EQUIP) [127, 128]. This initiative is a step towards ensuring reliable measurements of urinary iodine, provision of technical training, and supervision for sustainability of iodine sufficiency globally.

The normal urinary iodine range has been extrapolated by WHO to include pregnant and lactating women (**Table 5**). The UIC suggested normal range for pregnant and lactating women reflects their additional needs to avoid the risk of iodine deficiency to fetuses, neonates and themselves [5, 61]. Intake of iodine >300 μg/L per day has been discouraged, particularly in areas where iodine deficiency has previously existed [5].

Table 5: Criteria for assessing iodine nutrition based on median urinary iodine concentrations of school-age children (≥6 years) [5]

Median UIC µg/L	Iodine intake	Iodine nutrition status	Traffic light colour
<20	Insufficient	Severe iodine deficiency	Red
20 – 49.9	Insufficient	Moderate iodine deficiency	Orange
50 – 99.9	Insufficient	Mild iodine deficiency	Yellow
100 – 199.9	Adequate	Adequate iodine nutrition	Green
200 – 299.9	Above requirements	Likely to provide adequate intake for pregnant /lactating women, but may pose a slight risk of more than adequate intake in the overall population	Light purple
≥300	Excessive intake	Risk of adverse health consequences (iodine-induced hyperthyroidism-IIH, autoimmune thyroid diseases)	Dark purple

Thyroid stimulating hormone (TSH)

TSH, a sensitive IDD indicator only in the neonatal period, is used for screening newborn babies for the identification of IDD and its control. At a population level, TSH levels indicate iodine deficiency and hypothyroidism. Increasing the levels of TSH compensates for iodine deficiency. TSH levels in the fetus and newborn are of special concern since TSH levels signal an insufficiency of thyroid hormones, which can lead to brain damage [5, 129]. However, difficulties in interpretation of the TSH level remain beyond the neonatal period because of inconsistent relationships between population TSH levels and iodine status [90].

TSH is first detected in the fetal blood in the 11th week of gestation. TSH levels rise sharply to a maximum at 24h after at birth and decrease gradually over the first 3-4 days as the infants T4 levels start to rise [130]. Therefore, neonatal blood sampling for TSH is recommended from cord blood or from heel-prick after 72 hours.

Where iodine intake is adequate, TSH is capable of identifying approximately 1: 4000 neonates suffering from congenital hypothyroidism [5]. In countries with universal screening, such as Italy, an incidence of 1:2000 indicates mild iodine deficiency [131, 132]. Measurement of the distribution of TSH levels in a sample of neonates can give a picture of the iodine status in the population [90, 133, 134]. Increase in the number of neonates with moderately elevated TSH concentrations (>5 mU/L whole blood) is proportional to the degree of iodine deficiency during pregnancy [5].

When a sensitive TSH assay is used on samples collected 3-4 days after birth, a frequency of <3% of TSH values >5 mU/L indicates iodine sufficiency in a population [135]. However, the cost of implementing a national TSH screening programme is too high for most low-income countries.

Thyroxine (T_4)
Thyroxine is the primary output of the thyroid gland, which is de-iodinated in the peripheral cells to T_3 making it the most active hormone (See Figure 1, [2]). In severe iodine deficiency, T_4 levels may decrease, but de-iodation following increased levels of TSH maintains adequate levels of T_3. Total T_4 depends on the amount of carrier proteins in the blood. Thus it is better to measure the levels of thyroxine that are unbound in the serum, the so-called free T_4. T_4 can characterize a finding of abnormal TSH values in patients [89, 129]. However, T_4 is not considered a suitable indicator for assessment of iodine deficiency at the population level [90].

Thyroglobulin (Tg)
The thyroglobulin is a precursor protein that is used in the synthesis of thyroid hormone, and is found in small quantities in the blood of normal healthy subjects. Thyroglobulin is a sensitive indicator of iodine deficiency in school-aged children which can be used to monitor improvement of thyroid hormone status after iodine repletion. In areas of endemic goitre, elevated serum thyroglobulin reflects thyrotropin hyperstimulation and thyroid hyperplasia [5]. In contrast to TSH which normally reflects more recent iodine intake status, serum thyroglobulin levels reflect iodine nutrition over a period of months or years. The dried blood spots (DBS) samples collected for Tg using recommended quality filter papers can be stored for up to one year at temperatures ≤ -20 °C. The DBS Tg reference interval for iodine-sufficiency in school-aged children has been established (4-40 µg/L) [136]. Both TSH and thyroglobulin are useful indicators of thyroid function.

Goitre assessment
Goitre assessment by palpation or ultrasound (thyroid volume) is a useful indicator of thyroid function, but because thyroid size decreases only slowly after iodine repletion, goitre in children may not reflect correctly the current iodine situation in a population until several years after the introduction of iodized salt [137, 138].

In areas of mild to moderate iodine deficiency, the sensitivity and specificity of palpation are poor, ultrasound being preferable [5]. Ultrasound provides a more precise measurement of thyroid volume [139], especially when the prevalence of visible goitres is small, and where thyroid volumes are expected to decrease over time when monitoring iodine control programmes. New thyroid volume references for the age of 6-12 year-olds with long-term iodine sufficiency have been established, covering all major ethnic groups globally [140].

School-age children 6-12 years are the preferred group for goitre assessment, usually being easily accessible [5]. However, since the highest prevalence of goitre occurs during puberty and around the childbearing age, other studies have been designed to focus on children 8-10 years-old to minimize the influence of adolescence. Pregnant and lactating women are of particular concern. Of the most vulnerable groups, pregnant women are a prime target group for IDD control activities, because they are sensitive to marginal iodine deficiency [83]. WHO reviewed and gave new guidelines for goitre grading and rating of the severity of IDD (**Table 6 & 7**).

Table 6: Simplified classification of goitre[a] by palpation [5]

Grade 0	No palpable or visible goitre
Grade 1	A goitre that is palpable but not visible when the neck is in the normal position (i.e., the thyroid is not visibly enlarged). Thyroid nodules in a thyroid which is otherwise not enlarged fall into this category
Grade 2	A swelling in the neck that is clearly visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated.

NB: [a]A thyroid gland is considered goitrous when each lateral lobe has a volume greater than the terminal phalanx of the thumbs of the subject being examined.

Table 7: The rating criteria for severity of IDD using goitre prevalence in school-age children (≥6 years)

Prevalence of goitre	Severity of IDD	Traffic light colour
0.0 – 4.9%	No public health significance	Green
5.0 – 19.9%	Mild iodine deficiency	Yellow
20.0 – 29.9%	Moderate iodine deficiency	Orange
≥30%	Severe iodine deficiency	Red

Source: [5].

3.2.3 Sustainability indicators

WHO has proposed 10 programmatic indicators for sustainability; aimed at assessing whether iodine deficiency has been successfully eliminated and whether the achievements that have been realized can be sustained and maintained for coming decades [5]. The status of these indicators is illustrated in **Table 8** that also shows the progress made on these indicators in Tanzania's IDD control program.

4. IODINE DEFICIENCY CONTROL IN TANZANIA: A BRIEF HISTORY

4.1 Establishing the magnitude of IDD in Tanzania

The Republic of Tanzania is composed of mainland Tanzania and the Islands of Zanzibar covering a total of 945,000 km^2. Mainland Tanzania has a large landmass with coastline, highlands, mountains and floodplains. Zanzibar is composed of two islands, Unguja (also referred as Zanzibar), which is mostly flat, and Pemba island, which is hilly in many areas.

Goitre as a public health problem in mainland Tanzania has been documented in the Ministry of Health records since 1912 and in 1953 the first community based goitre survey was conducted and reported for the first time the total goitre prevance of 22.2% in Njombe district, Southern Tanzania [141, 142]. Efforts to address the problem of IDD started in 1960 when the first proposal to iodate salt was made, but due to lack of expertise, the efforts to launch IDD interventions did not bare fruit until after the formation of the TFNC in 1973, an institution mandated by the government to assess and address all nutrition problems in the country, and to provide nutrition policy advice to the government for further action [15].

A national coalition body, the National Goitre Expert Committee (made up of medical professionals), was formed in 1977 to spearhead the assessment of the magnitude of IDD nationwide. The Committee was later expanded to include other sectors apart from health that were thought to play a role in the prevention and control of IDD. In 1986, the newly formed coalition was renamed the National Council for Control of IDD (NCCIDD), and since then it has cated as the programme steering committee and policy-making body [15].

The inception of the national IDD control programme in Tanzania in the mid 1980s was an outcome of the first district goitre surveys conducted between 1980 and 1990 [15]. Based on the goitre rates established from school surveys, it was estimated that in mainland Tanzania alone, 41% of the population (equivalent to 10 million people) are living in iodine deficient areas and therefore at risk of IDD. The potential number of IDD control programme beneficiaries estimates based on population projections, approximates at about 6 million children under the age of 5 years, about 3 million of these being under 2 years [58].

Moreover, 5 million people suffered from endemic goitre, 160,000 from cretinism, 450,000 from cretinoidism (a condition with some but not all the full features of cretinism), making a total of 5.61 million inhabitants (equivalent to 25% of the population according to the 1988 census population) suffering from IDD. It was also estimated that 30% of the total perinatal mortality was attributed to iodine deficiency [143]. In some areas of the Southern highlands of Tanzania, the prevalence of goitre reached as high as 90%, and about 50% of school children had hypothyroidism [133].

4.2 IDD interventions

The NCCIDD adopted and implemented two major IDD intervention strategies; one was iodine supplementation. This entails distributing iodinated oil capsules (IOC) to the population group 1-45 years of age living in the highest goitre endemic areas, being a short-term measure from 1985 to 1996, and continued in some few pockets until 2000 when IOC was completely phased out. The second was the adoption of USI as a long-term measure from early 1990s [11, 89]. **Figure 5** shows the conceptual framework approach involved and its expectations.

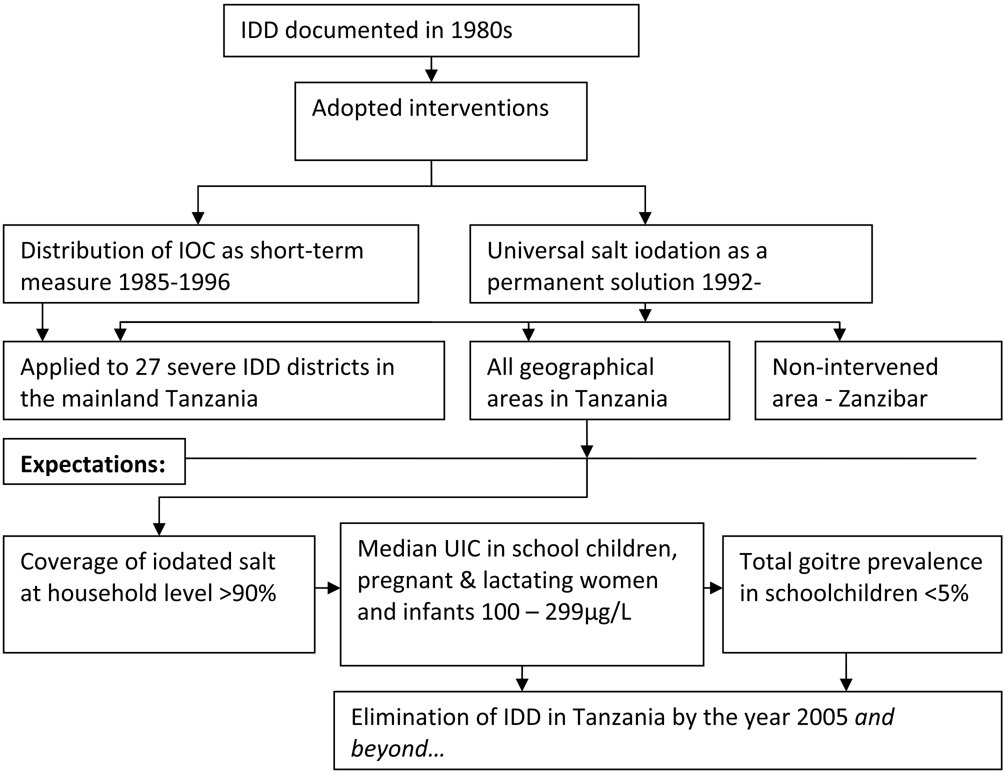


Figure 5: Conceptual framework used in controlling IDD and the expectations of the programmes

Iodine supplementation

The short-term intervention measure covered the 27 districts categorised as the most severely IDD affected (total goitre prevalence ≥30%), mostly located in the southern and western highlands of Tanzania (**Figure 6)** but later due to political and public pressure the number was extended to 30 districts based on a modification of the criterion of 10% visible goitre combined with goitre grade 1b [15].

This strategy was mainly supported by the Swedish Government through the Swedish International Development Cooperation Agency (Sida), which first required proof that USI was going to occur before they released funds for IOC implementation support. Sida was worried about the IOC project becoming a permanent temporary measure, similar to vitamin A capsules (personal communication with Ted Greiner in 2008). The Dutch government agreed to fund the USI via UNICEF in 1986, while in fact IOC distribution had already started in 1985 [15]. Further support came from UNICEF and the Government of Japan through its International Cooperation Agency (JICA) in the late 1990s (unpublished TFNC reports).

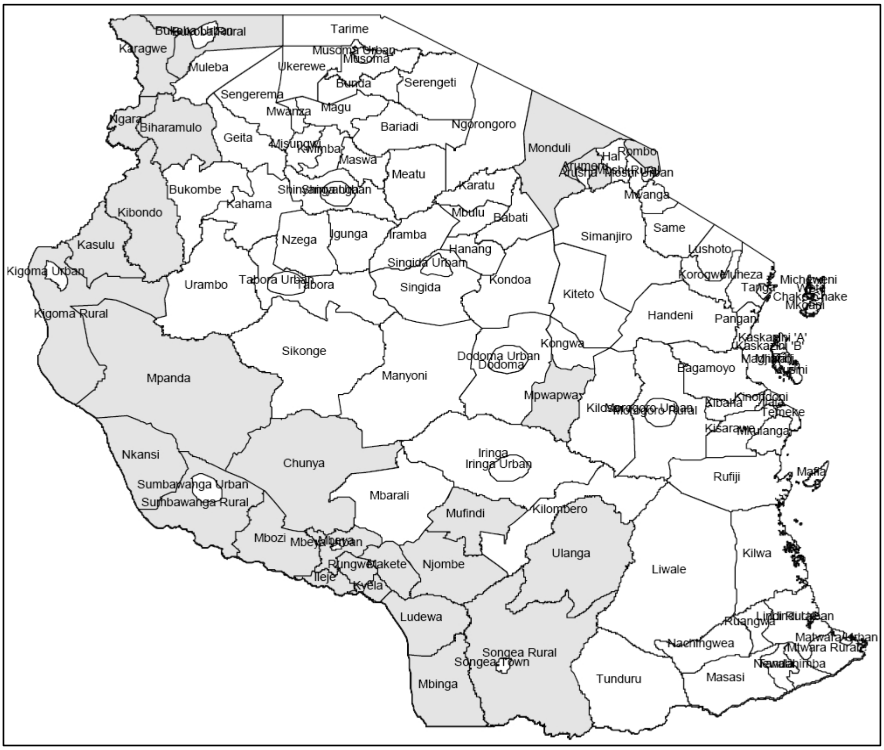


Figure 6: Severely IDD affected districts (coloured) that benefitted from IOC distribution from the mid 1980s to the 1990s

IOC dosage and distribution

Iodinated oil capsules were ordered from Guabert Laboratories Ltd, France, each gel capsule containing 200 mg iodine (**Figure 7**). In the IOC distribution, adults were given a dose of 400 mg iodine (2 capsules per person) and children aged 1-5 years 200 mg (one capsule) every second year. The capsule distribution was done through the Primary Health Care (PHC) system or in a campaign form using schoolchildren, community leaders and CCM Party (the ruling party) infrastructure for mobilization and compliance [15]. To avoid IOC losses, the dose of IOC was given and swallowed at the point of distribution (**Figure 7)** The mean IOC coverage in these districts during the period 1986-1994 was 64% (range, 24- 94%) [105]. By 1998, over 16 million capsules had been distributed, benefiting more than 6 million people living in the highest IDD risk areas in the country.

Figure 7: Iodinated oil capsules (right side) and a schoolchild taking a dose of IOC

An impact evaluation study conducted in 1991 in three goitre-endemic districts after 5 years of implementing iodine supplementation through IOC distribution showed 57% and 28% reduction in visible and total goitre prevalence, respectively [15]. However, to reduce dependency on this expensive iodine supplementation programme and possibly poor compliance in some areas, efforts were directed at the adoption of universal salt iodation as a long-term solution [144, 145].

The interventions were targeted at highest risk areas, which meant that some areas, previously considered as low-risk for IDD, went without intervention for some years, expecting to be covered by the USI plan. Investigations found that some of these areas were severely iodine deficient as goitre prevalence reached over 30% [146, 147]. The survey conducted in Mbinga and Songea districts in the early 1980s categorised the district as mild to moderately affected, but by the mid 1990s the total goitre prevalence was over 70%, and had become a very serious matter [148].

It has been argued that district goitre surveys in the 1980s were done by different people who probably lacked the necessary skills to palpate goitres, leading to under- or over-estimation of goitre prevalence in some districts, which later denied the rights for some districts to be categorised as requiring IOC intervention [145] (personal communication with Ted Greiner 2008). Despite of this argument, the numbers of iodine deficient subjects were also increasing, since there was no intervention taken to correct the problem in their areas.

Universal salt iodation

Tanzania adopted the global USI strategy and implemented it in the 1990s after a series of events to establish the existence of IDD that had started from the 1960s onwards (**Figure 8**).

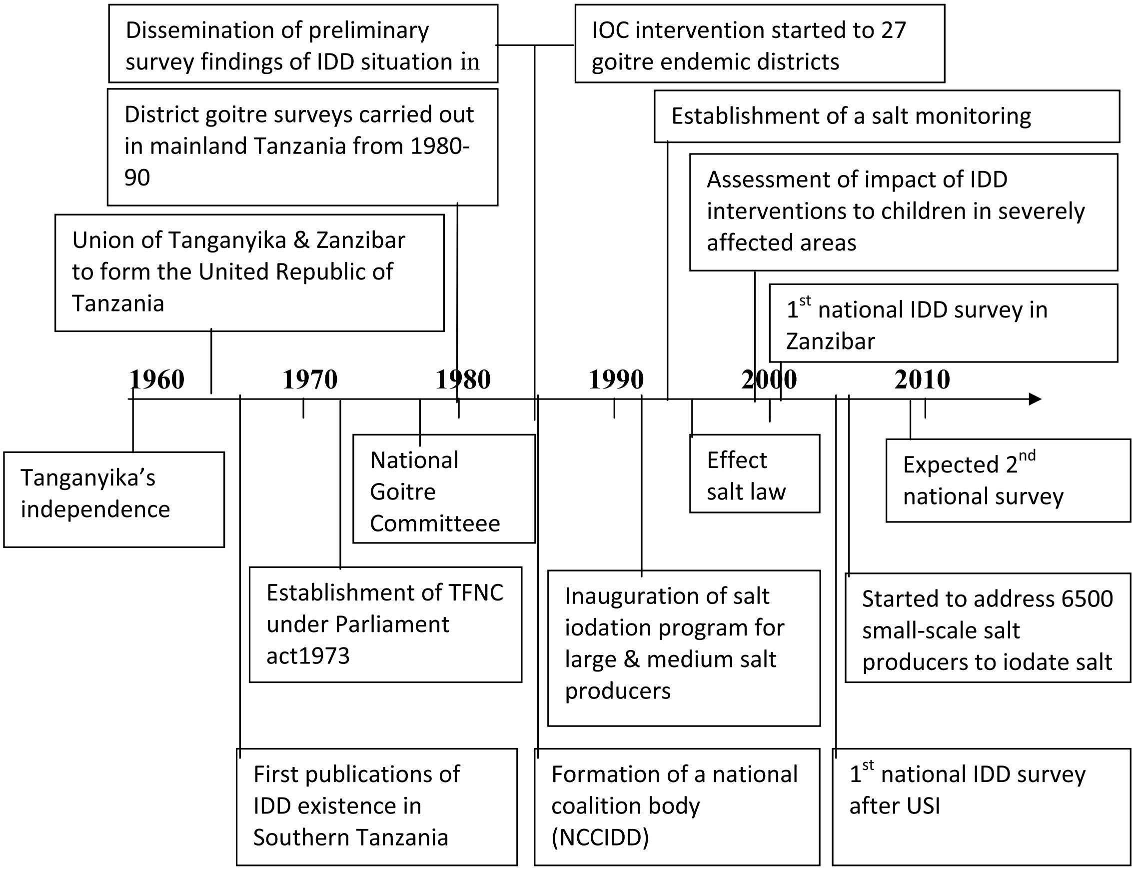


Figure 8: Time-line of the IDD control programme implementation in Tanzania

The feasibility study conducted in 1990 reported 4 major salt sources in the country: i) sea salt from water along the coastal belt of Indian Ocean; ii) thermal salt, originating from evaporation of underground brine (at Uvinza in Kigoma); iii) salt evaporites in the soil from the foothills and salt lakes within the Great Rift Valley; and (iv) rock salt (at Mandawa in Kilwa, a district not yet explored) [149].

Procurement of 72 salt iodation machines, distribution and installation to specified large and medium salt producers making salt from sea water and underground brine was carried out from the early 1990s [15]. Knowledge and skills of the operation of the iodation machines were given to the same salt producers, along with training on the quality control of iodated salt [145].

A salt monitoring system was also set up after training of health inspectors, who were mandated to take legal action against producers and traders who were not complying with the salt regulations [122]. This remains the case today (2009).

Apart from testing iodine in salt using rapid test kits, iodine laboratories were established (under NFCC) at eight salt factories and another 12 satellite laboratories in the different regions to carry out quantitative iodine determination. Technicians from the salt factories and the peripheral regions were trained and equipped with all the necessary laboratory facilities for testing salt by titration.

The supply of iodated salt from salt factories increased from almost zero in 1990 to 18.6% of the national salt demand (73,000 metric tons) for edible salt in 1992 [15]. Salt regulations under the Food Safety & Quality, and the Mining Acts (*Salt Acts*), requiring all salt for human and animal consumption to be iodinated, were passed in 1992 and 1994, respectively, but they were only officially in effect from January 1995 after the initiation of the salt iodation project [150].

Moreover, it was hoped that the importation of salt would encourage the national salt producers to improve on the quality of their salt in order to compete with imported salt in the long term. But the national salt producers wanted the government to ban the importation of salt to safeguard their own local market. However; according to the Ministry of Energy and Minerals (MEM), the government followed an open market policy, making it impossible to implement their request for a total ban [145].

4.3 The IDD control programme monitoring system

There are three major areas that are focused for monitoring the IDD control programme in Tanzania: one is salt monitoring at production sites and importation ports to ensure that all salt produced or imported is iodinated; the second is monitoring at the selling points (wholesale and retail shops) to ensure salt reaching the communities is adequately iodinated; and the third is monitoring at the community/household level to assess the coverage of iodated salt and its impact on IDD in the population[15].

The NCCIDD assigned the programme monitoring responsibilities to the government and non-government institutions as follows: (i) the monitoring of salt at the factory level was initially under the MEM, but it was realised after about 5 years that it was not functioning properly due to other ministry priorities, and therefore it was transferred to Tanzania Food and Drugs Authority (TFDA; formally the National Food Control Commission or NFCC) [145]. However, MEM continues to control salt mining and production licensing, with the restriction that the salt be iodinated, whilst providing support to salt producers as miners. (ii) TFDA was assigned the responsibility of monitoring salt both at factory level, importation sites and commercial outlets, concurrent with enforcing the salt law in collaboration with Local

Table 8: Status of programmatic indicators towards sustaining USI Tanzania

Programmatic indicator[5]	**Country situation**
1. Presence of a national multi-sector coalition responsible to the government for the national programme for the elimination of IDD reflecting:- national stature, all concerned sectors, including the salt industry, with defined roles and activities; - convenes at least twice yearly.	The national multi-sector coalition exists in form of: i) The NCCIDD, comprising members from 15 different stakeholder institutions. This has been the policy-making and steering body for the IDD control programme in Tanzania. ii) TFNC – the technical arm of the Ministry of Health and Social Welfare for nutrition issues (including control of IDD).
2. Demonstration of political commitment as reflected by: – Inclusion of IDD in the national budget (either as specific programme funds or through inclusion in existing programme funds) particularly with regard to procurement and distribution of potassium iodate ($KI0_3$).	- Tanzania's ex-Presidents and the current President had all, in one way or another, contributed to the efforts for establishing the USI. The 2nd phase President, Ali Hassan Mwinyi, at the World Summit for Children in 1990 made a commitment to work for the elimination of IDD and in 1993 inaugurated the salt iodation programme in Tanzania. - The Government convened a seminar for Members of Parliament to sensitize them to the prevention and control of IDD through USI, and the need to pass legislation to that effect. In the World Summit for Children (2002) in New York, the Vice President, Dr. Mohammed Ali Shein, reiterated the country's commitment to the elimination of IDD by 2005. During the Parliament session in July 2006, the Government promised to waive some of the taxes imposed on the salt industry.
3. Enactment of legislation and supportive regulations on USI, which establishes a routine external quality assurance.	Salt iodation regulations were effected since January 1st 1995, and were revised in 2006, pending ratification by the ministries concerned (MOHSW and MEM).
4. Establishment of methods for assessment of progress in the elimination of IDD as reflected by: – Reporting on national programme progress every 3 years.	Assessment and reassessment progress in the elimination of IDD has been going on since mid 1980s. National progress reports are now available from 1999, but not before, making this one of the weakness of the programme in the 1990s.
5. Access to laboratories as defined by: laboratories able to provide accurate data on salt and urinary iodine levels and thyroid function.	The programme has its own iodine laboratory since 1995; capable of carrying out analysis for thyroid hormones, urinary iodine and salt iodine content. In 2005, it was announced as the reference iodine laboratory for East Africa.
6. Establishment of a programme of education and social mobilization as defined by: – Inclusion of information on the importance of iodine and use of iodized salt, within educational curricula.	- The programme has collaborated with the Ministry of Education to incorporate component of iodine deficiency and its prevention in primary school curriculum. - Salt surveillance at community level is carried out in 68 severe and moderate iodine deficiency districts by primary schools - IDD reader materials and mass media are widely distributed, and used for public education.
7. Routine availability of data on salt iodine content as defined by: availability at the factory level at least monthly and at the household level at every 5 years.	This has not been operational. Mini-laboratories established in the 1990s in various salt factories and peripheral areas as satellite laboratories ceased to function, mainly due to poor management and lack of commitment. Effort to revive these laboratories is on-going
8. Routine availability of population-based data on urinary iodine every 5 years.	Data on urine iodine content of school children do exist, but are not available on a regular basis.
9. Demonstration of on-going cooperation with salt industry: quality control measures and absorption of the cost of iodate.	There is adequate cooperation with the salt industry, but the issue of quality control is not yet being adequately addressed.
10. Presence of a national database for recording of results of regular monitoring procedures iodated salt coverage, urinary iodine and other indicators of iodine status.	The database exists, but the weaknesses in data collection mentioned above render this aspect inadequate as well.
Programmatic indicators achieved	6 out of 10 (Goal: at least 8 out of 10 indicators)

Governments. (iii) The Tanzania Bureau of Standards took the responsibility of setting iodation standards and ensuring that the iodated salt product meets the required standard specifications. (iv) The formation of Tanzania Salt Producers Association (TASPA) in 1994 added another important stakeholder to facilitate mobilization of salt producers and improve the salt industry's performance, particularly in iodinating salt [145]. (v) The Tanzania Food and Nutrition Centre had the responsibility of monitoring the salt situation (salt coverage) and its biological impact (urinary iodine, thyroid hormones, goitre) in the population, to create awareness among the public of IDD, and its prevention and control through consumption of iodated salt, and lastly to coordinate the programme as a secretariat for the national coalition [15].

The inspiring statement from one of the Sida evaluation reports entitled 'Thoughts for Food' stated the following with regard to implementation of IDD control programme in Tanzania:

'We are impressed that Tanzania leads Africa in terms of iodine capsule distribution and is seen by WHO as a model for the continent; we are full of praise for the role of TFNC in getting so close again to iodation of salt for a sizeable proportion of the Tanzanian population; we are pleased that there is international recognition of TFNC's efforts to control IDD; and finally we are glad to see that research is underway, and monitoring and evaluation are planned….' [151].

Mainland Tanzania already has fully or partially fulfilled most of the WHO proposed programmatic indicators for sustainable IDD elimination. **Table 8** summarises the progress of each proposed indicator towards sustainability of IDD elimination in Tanzania [5].

While the implementation of the IDD interventions were ongoing, with its marked impact in the mainland Tanzania, no action was taken in the Islands of Zanzibar **(Figures 5 & 8)**.

In 1998, 31 cases were reported after a random screening of subjects in Pemba South district, of whom 84% were women. The Minister of Health and Social Welfare reported the findings to the Zanzibar Revolutionary Council's House of Representatives in 1999. The Council resolved to carry out an immediate survey to establish the magnitude of the iodine deficiency problem in Zanzibar and consider the possible remedial actions needed to be taken [152].

5. RATIONALE, AIM AND OBJECTIVES OF THE STUDIES

5.1 Rationale of the studies

In the past decades, extensive research has been carried out on the epidemiology of iodine deficiency, causative factors and impact of interventions including the use of iodated salt [70]. The global initiative to eliminate iodine deficiency mainly through universal salt iodation pushed the agenda from physiology to programme implementation and evaluations of the impact of the applied interventions. Countries were urged to achieve sustainable elimination of iodine deficiency disorders goal by the year 2000, which later was revised to the end of 2005 [95].

However, not all countries on the African continent have been able to establish a national iodine deficiency control programme, and progressively make follow-ups on the process and impact of the applied interventions, although guidelines had been provided [5]. For Tanzania, feasibility studies, covering efficacy and safety of iodinated oil capsules (IOC) and iodated salt, potentials of salt production, marketing and salt consumption patterns, were done before implementation of both IOC and universal salt iodation strategies [15, 117, 149, 153].

Some sporadic spot surveys reported on the progress of the IDD interventions, but there was no nationwide data that was representative of the effective size of the interventions applied [154]. Lack of such data triggered the need to have a sequential operational and evaluation studies to establish the outcomes of the intervention strategies adopted by the NCCIDD since 1986 [15, 145]. After implementing the IOC from 1985-1996 and USI from the 1990s, the following remained unknown:

- The impact of intervention strategies (IOC & USI) applied to the most goitre-endemic areas in the country
- The status of the IDD in the Islands of Zanzibar, an area regarded as a low priority area for IDD intervention strategies
- The magnitude of IDD and the iodine status after 12 years of implementing USI to the general population in the entire country
- The status of supplied salt iodation machines, existence of locally devised iodation methods, and weaknesses in implementing salt iodation strategy in the country
- Whether existing locally devised salt iodation technology could be used as an appropriate technology to sustain USI among small scale salt producers in low-income settings

These studies were designed to addess and resolve some of these knowledge gaps.

5.2 Overall aim

To investigate the iodine status in the population following iodine supplementation and salt fortification interventions, and the performance of salt iodation technologies used to optimise intervention strategies for sustainable elimination of IDD in Tanzania.

5.3 Specific aims

1. To describe the impact of IDD interventions in school-age children living in severely iodine deficient areas (**Paper I**)

2. To investigate the hypothesis that the population living in the islands of Zanzibar was not affected by iodine deficiency (**Paper II**)

3. To determine the use of iodated salt and its impact on the school-age children in mainland Tanzania (**Paper III**)

4. To describe the functional status of the previously supplied salt iodation machines, salt producers' experiences on salt iodation, and the quality of salt they produce (**Paper IV**)

5. To optimise the performance of the locally-used hand and knapsack sprayers for salt iodation in Tanzania (**Paper V**).

6. MATERIAL AND METHODS

6.1 Study areas

The studies of this thesis were conducted in the United Republic of Tanzania, which has an estimated total population of 35 million in 2004, of which about one million inhabited the islands of Zanzibar [58]. The growth rate was 2.9% and the projected overall population in 2009 was estimated to be around 40 million people. A summary of study areas where the data was collected is shown in **Figure 9**.

The data for **Paper I** (red) were obtained from the highland areas (over 1000 metres above sea level) where the population was assumed to be at high risk of IDD [6].

Figure 9: Study sites for each of the papers in the thesis

Paper II (green) was conducted to establish the magnitude of iodine deficiency in the low priority intervention area of Zanzibar Islands (Unguja and Pemba). Zanzibar has its own Ministry of Health and Social Welfare; therefore its health priorities are not necessarily the same as those of mainland Tanzania. The status of the IDD after interventions in the population of mainland Tanzania is dealt with in **Paper III** (orange).

The status of the salt iodation machines, the experience of the salt producers, and the quality of salt iodation in the salt-producing areas along the coastal strip of the Indian Ocean were investigated in **Paper IV** (areas in deep blue). The coastal strip of the Indian Ocean hosts most of the large and medium-scale salt producers, and it is where approximately 60% of all the salt consumed in the country is produced [155]. The study also covered areas in the basements of the Rift valley arms in Central and Western Tanzania, where most of the small-scale salt producers operate and produce the rest of the salt consumed in the country. To establish whether locally devised salt iodation methods could be used to sustain USI, a study presented in **Paper V** (yellow) was conducted in Bagamoyo district, located 45 km North of Dar-es-Salaam city. In this district, a combination of large, medium and small-scale salt producers operate and this combination met the needs for the study.

6.2 Study designs and subjects

A summary of the study designs, data collection methods and analyses used for each study (paper), and the main outcome indicators in this thesis are given in **Table 9**.

Papers I-III were all cross-sectional surveys targeting school-children aged 6-18 years of age in mainland Tanzania and Zanzibar. Combinations of qualitative, epidemiological and biostatistical methods were used. The multi-stage sampling procedure was applied, followed by systematic sampling of schools and children from identified strata/schools. **Figure 10** illustrates the stages applied to all 3.

Owners of salt factories and salt-workers were targeted (**Papers IV and V),** with one cross-sectional and one experimental study design. In addition to the quantitative data, qualitative data was also collected from observations, interviews and focus-group discussions (FGDs), and used for triangulation. Random or convenience sampling of salt was used for determination of iodine content levels.

In **Paper IV,** moisture and water-insoluble matter were analysed to reflect other basic aspects of the quality of salt required by the salt law [122]. Both salt and urine samples were collected according to the standard operating procedures of WHO [5].

Table 9: Summary of study areas, time, designs, data collection methods and outcome indicators and analyses applied in the studies

Paper	Area of study & year	Study design	Data collection methods	Main outcome indicator(s)	Main analysis
I	Highlands and flood prone areas in Tanzania 1999	Cross-sectional	- Salt iodine by RTK[a] & titration - Urinary iodine by APD[b] - Goitre palpation	- Proportion of households with iodated salt - Proportion of children with adequate iodine intake - Prevalence of school-children without goitre	- Descriptive statistics & Mann-Whitney *U*-test
II	Islands of Zanzibar (Unguja & Pemba) 2001	Cross-sectional	- Salt iodine by RTK & titration - Urinary iodine by APD - Goitre palpation - Interviews - FGDs	- Proportion of households with iodated salt - Proportion of children with adequate iodine intake - Prevalence of school-children without goitre - Knowledge of IDD among the public	- Descriptive statistics & Mann-Whitney *U*-test - Inductive latent content analysis
III	All districts of the mainland Tanzania 2004	Cross-sectional	- Salt iodine by RTK - Urinary iodine by APD - Goitre palpation	- Proportion of households with iodated salt - Proportion of children with adequate iodine intake - Prevalence of school-children without goitre	- Descriptive statistics & Mann-Whitney *U*-test
IV	Salt producing sites in mainland Tanzania 2003/4	Cross-sectional	- Observations - Interviews - Salt iodine by RTK & titration	- Status of UNICEF supplied iodation machines - Quality of salt and iodine content in salt	- Descriptive statistics & Mann-Whitney *U*-test - Manifest content analysis
V	Bagamoyo district in Tanzania 2004/5	Experi-mental	- Observations - Interviews - FGDs[c] - Salt iodine by RTK & titration	- Performance of salt workers using improved local iodation technology - Quality & iodine homogeneity in salt	- Descriptive statistics & Anova - Inductive latent content analysis

[a]RTK= rapid test kits, [b]APD= Ammonium persulfate digestion method, [c]FDGs = focus group discussions

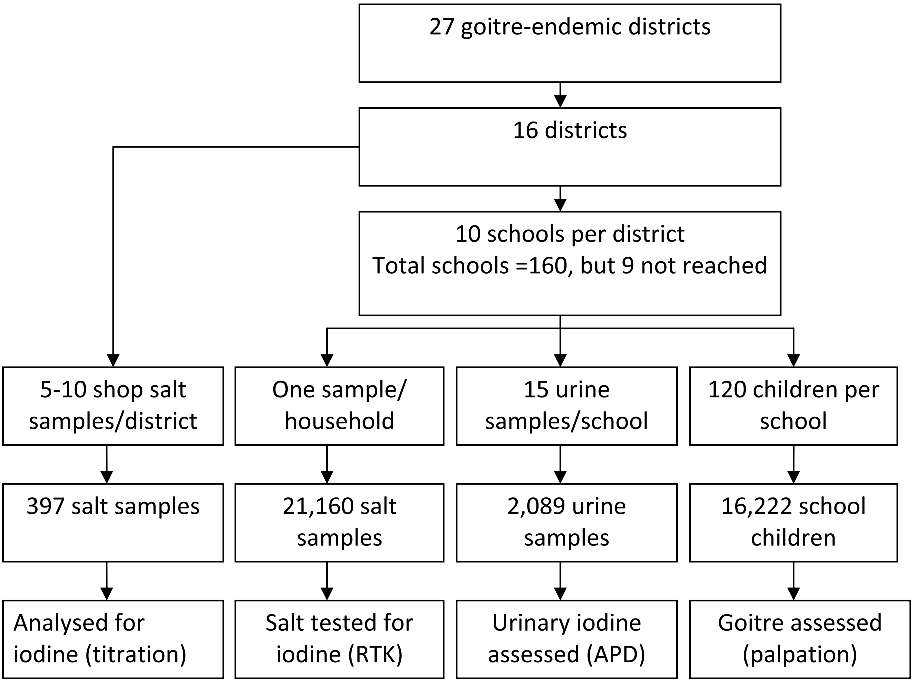


Figure 10: Multi-stage sampling procedure for the severely IDD affected areas (Paper I)

6.3 Data collection methods

Tools (**Appendices I-VI**) for data collection were used to collect the necessary information of indictors that could reflect the progress and constraints in the programme implementation.

Iodine in salt

All households represented by schoolchildren in the selected schools were tested for iodine. One child from each household represented in the schools was requested to bring a salt sample (a teaspoonful), wrapped in dry white paper to be tested for the presence of iodine using RTKs (Madras, India).

RTKs were of the same brand (MBI) as supplied for each investigator. One to two drops of the RTK solution on the salt sample will turns the colour from white to blue/purple, indicating the presence of iodine to threshold of ≥15ppm **(Figure 11)**.

For alkaline salt samples or salt with high moisture content, addition of one drop of recheck solution (the pink coloured vial in **Figure 11**) was important, followed by starch solution (the white coloured vial) drop in order to develop the blue/purple colour, showing whether iodine is present in the sample. Salt samples with dubious colour changes were disregarded as positive.

Figure 11: Testing salt for iodine using the rapid test kit

For all studies, except **Paper III,** salt samples from households, retail/wholesale shops and salt factories (random or convenience sampling) were further analysed by iodometric titration method [5] to determine the iodine content against recommended levels [122, 150].

Urinary iodine concentration
To determine urinary iodine concentration, a sub-group of schoolchildren palpated for goitre prevalence was systematically sampled per school, each chosen at an equidistant interval for each study, i.e.in **Papers I** and **Paper II,** 15 and 10 children were sampled, respectively, while in **Paper III,** 70 children per school were sampled, in which 10 children per class were selected on the basis of there being an equal number of boys and girls. Each child was asked to provide a 5-15 ml urine specimen. Instructions were given to each child on how to handle the urine sample to avoid contamination. The total number of urine samples for each study is summarised in **Table 10**.

Table 10: Summary of sample size of major indicators by study paper

Paper	Area	No.of districts covered	No. of schools surveyed	No. of shops tested for salt	No. of salt samples tested from households	No. of urine samples analysed	No. of children assessed for goitre
I	Severe ID districts	16	160	397	21 160	2 089	16 222
II	Zanzibar Islands	10	60	121	15 824	559	11 967
III	Mainland Tanzania	106	318	N/A	131 941	4 522	140 758

N/A = salt testing in shops not included in the study

The determinations of UIC (**Papers I, II and III**) were carried out spectrophotometrically at 405nm, using ammonium persulfate digestion (APD) based on the *Sandell Kolthoff reaction* [5, 156]. The UIC data was interpreted according to WHO criteria, previously indicated in **Table 5** [5], where median UIC within the range 100- 200 µg/L signals optimal iodine intake.

Salt experiment
Qualitative data assisted in identifying areas of weakness in the salt iodation procedures and the planning of the salt experiments to modify existing local methods. A series of experiments in **Paper V** were carried out on local methods of salt iodation and mixing procedures to identify the weaknesses of the iodation processes and how to improve on them. The experiment process is outlined in **Figure 12**.

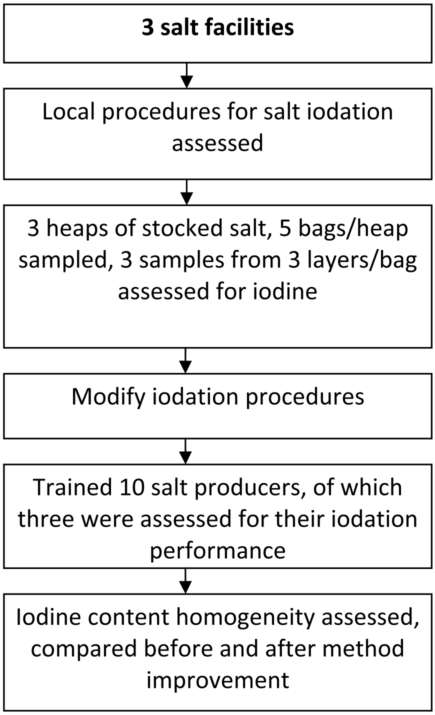


Figure 12: Summary of the experiment process in Paper V

The improved method that was found to deliver the right iodation levels was further tested without supervision by three of ten salt workers (randomly selected) who were trained on the improved method procedures (**Figure 13**). Their performance was assessed and the results compared to the unimproved method.

Figure 13: Salt iodation using knapsack sprayers with manual mixing

Quality control on iodine laboratory methods

The TFNC laboratory used for carrying out analyses of salt and urine samples from these studies is participating in the Proficiency Testing (PT) schemes for salt and urinary iodine carried out by East African Community (EAC) under coordination of Tanzania Bureau of Standards and Centres for Disease Control and Prevention (CDC), Atlanta, USA, respectively. Internal quality control of salt samples (externally evaluated) was used to track the performance of the titration method.

Quality Control (QC) is a measure of the precision, i.e. of how well the measurement system reproduces the same result over time and under varying operating conditions. Both internal and external quality controls are necessary to achieve the standards and the validity of these measurements [128].

The results of the internal quality control sample material show that the titration method has a coefficient of variation of <15%, recovery of 95%, and a detection threshold of <5 ppm iodine, similar to findings elsewhere [157] that met the WHO criterion [5]. The TFNC laboratory is also a member of the International Resource Laboratories for Iodine (IRLI) network, participating in the urinary iodine proficiency testing scheme, which is run on a quarterly basis by the CDC to ensure the quality of urinary iodine procedures (EQUIP) [128]. The coefficient of variation (CV) obtained by the urinary iodine laboratory method for all three studies were within the desirable threshold (≤10%) recommended by CDC [127, 128].

Assessing goitre prevalence
To establish the goitre prevalence **(Papers I and II)**, palpation and grading was done according to the WHO goitre classification of 1960 [158], in order to have comparable uniform data to those obtained in the 1980s **(Figure 14)**.

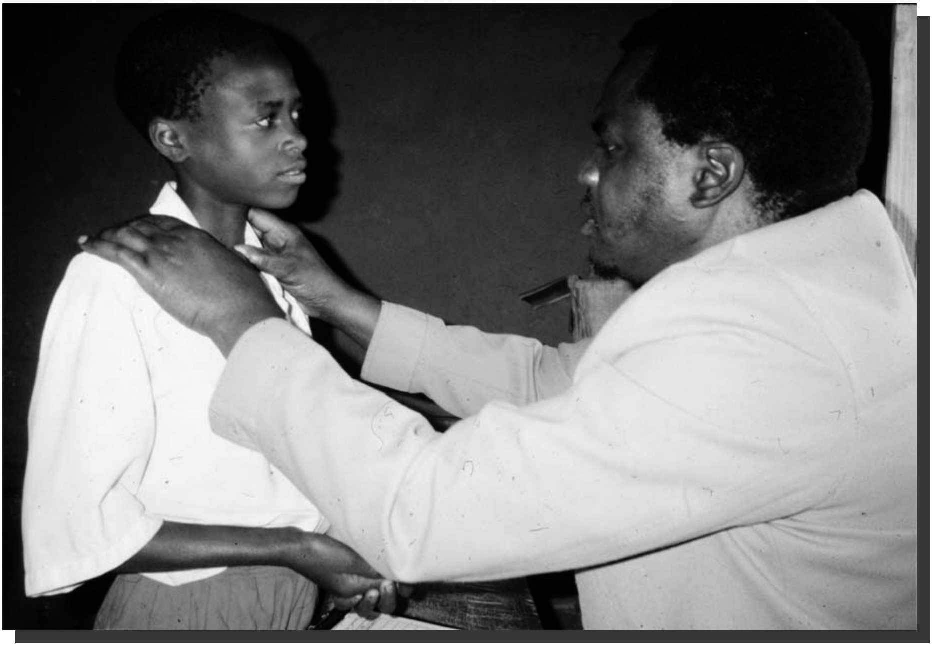


Figure 14: Schoolchild being examined for goitre by palpation

In additional, the WHO simplified criteria for the goitre classification system[90] (**Table 6)** has been criticised as having a decreased specificity, but with increased sensitivity, when compared to the old goitre classification system [139]. However, the criteria were used in **Papers II&III** as landmarks for future comparisons of the IDD control programmes. Training on goitre palpation and the study protocols, including pre-testing of the questionnaires and checklists, were provided for the team prior the studies (**Papers I, II&III**).

The sample size for goitre prevalence estimation varied from one study to another, but all were school-based surveys with unknown enrolment proportions (**Paper I - III**), as recommended [5]. In **Papers I &II**, 10 and 6 schools, respectively, were covered in each district, stratified into highlands, lowlands and townships. During the analysis and data interpretation, these strata were combined to reflect rural and urban areas. The sample size was 120 and 200 school-children per school selected in each district (i.e. 1200 children/district) in **Papers I and II**, respectively. In **Paper III,** three schools per district in all 106 districts on mainland Tanzania (districts with Area Commissioners as a top political leader - covering 1-2 councils). All the children attending school on the day of the survey were assessed for goitre (summarized in **Table 10)**. The gender balance was taken into account in all 3 studies.

For the purpose of minimizing intra- and inter-observer errors, the goitre assessment for **Papers I & II** was done by one and two experienced medical staff, respectively, while **Paper III** covering the entire mainland Tanzania involved 21 trained medical staff (regional investigators), i.e. one for each region. Moreover, in **Paper III,** goitre for the age group 6- 9 years was assessed to improve our understanding of the goitre status at the younger ages. The WHO epidemiological criterion for interpretation of the severity of total goitre prevalence in school-age children was used, as indicated in **Table 7.**

Qualitative data

The qualitative data **(Papers II, IV&V)** were obtained from observations, interviews and focus group discussions in triangulation (**Figure 15**). This allows for greater accuracy and enriches the quantitative data in drawing conclusions [159].

Figure 15: Researcher carrying out interviews (top-left) with small-scale salt producers, while the assistant researcher inspects the quality of the salt

Observations and interviews

Observing and interviewing is an evolving process during which the observers and interviewers acquire new insights into the phenomenon of the study that can influence follow-up questions or narrow down the focus of observation [160]. Dahlgren and colleagues [161] stress the compatible nature of observation and interview, arguing that observation guides researchers to some of the important questions to be asked, and interviewing helps to interpret the significance of what researchers are observing.

Observing, listening to and asking questions of subjects, i.e. members of the community and salt workers (**Papers II, IV& V),** provided a unique window into the thinking, problems solving, and in-depth of understanding of their abilities and attitudes towards iodine deficiency and salt iodation practices. It also helped to identify gaps or misconceptions in their knowledge. The approaches inspired scientific investigation, and the search for evidence to make sense of the data. For example, the iodation machine is in good condition in **Figure 16**; *'why not in use?'*

Figure 16: One of the iodation machines in perfect condition but not in use (discussion with leadership of salt producers and district leaders)

Individual interviews

To carry out the interviews, prepared check-lists of questions were used, followed by probing tactics. The subjects interviewed were village leaders, teachers, community health workers and shopkeepers (**Paper II)**. School-children were also assessed for awareness using two structured questions with closed answers '*Yes'* or '*No*'. These questions were: (i) had they ever heard of iodine deficiency and (ii) had they ever heard of iodated salt. For **Papers IV&V,** individual salt workers and factory managers/foremen were interviewed **(Figure 15)**.

Focus group discussions
Focus group discussions (FGDs) are used to obtain information on concepts, perceptions and ideas of a group, assuming that the participants can and will discuss the subject freely, and to add to each other's comments. FGDs can potentially produce a considerable amount of information in a short space of time [162]. The FGDs involved two groups of 8-10 people over 18 years of age, one with men and another with women, recruited from the village in selected schools for IDD surveys, and in the three salt factory facilities (**Papers II&V)**. A check-list of questions and probing tactics were applied to generate the information for specific areas of the topics.

Analysis of qualitative data
Qualitative data were documented on notebooks and semi-structured questionnaire forms, and were later analysed using manifest and inductive latent content analysis [159, 160]. This dealt with knowledge, attitudes and practices related to IDD, and with iodated salt use and salt iodation methods and procedures. *Manifest* and *inductive latent* content analysis was used that included identification of units of analysis, coding, and definitions of categories from the texts.

Manifest content analysis deals with the surface content aspect that describes visible and obvious components. In **Paper IV,** this type of analysis assisted in revealing the status of salt iodation equipments supplied to large and medium salt producers. It was also used to explore the existing alternatives for salt iodation, and to focus on the problem areas in salt iodation methods, weaknesses of equipment found in use, and quality of iodated salt produced.

Inductive latent content analysis, which is an immersion into the details and specifics of the data to discover important categories, dimensions and interrelationships by exploring genuinely open questions, was used in **Papers II&V**. In **Paper V,** this analysis was used to identify problem areas in the methods, use of equipment and procedures for salt iodation. It was also applied to the texts from the FGDs and key informants from individual interviews.

Credibility and validity of qualitative data
For credibility and validity of the qualitative data, we read carefully and re-read the hand-notes and made comments on the margins of the text for the important categories. These were linked to the study topics and the quantitative data. Finally valid conclusions were drawn, from which recommendations for intervention and sustaining USI in Tanzania were made.

6.4 Statistical data analysis
Epi-info (CDC WHO, Atlanta Georgia, USA) and Excel programmes were used for data entry and validation. Data analysis was carried out using Statistical Package for the Social Sciences - SPSS versions 9.0 – 15.0 (Chicago, Illinois, USA) for **Papers I, II & III**, with Excel being used for **Paper IV**. Intercooled Stata version 9.2 (College Station, Texas, USA) was used for **Paper V**, which compared the performance of the

different salt iodation methods. The main statistical methods of analysis employed were descriptive statistics; Mann-Whitney *U*-test and analysis of variance (ANOVA).

6.5 Ethical considerations

The protocols for conducting surveys were presented and approved by the research committees of Tanzania Food and Nutrition Centre (**Papers I, III, IV & V)** and the Ministry of Health and Social Welfare, Zanzibar (**Paper II**). The ethical risks in these studies might otherwise have been the breaching of confidentiality, such as disclosure of sample findings of the individual, disclosure of household iodine status, and information on products of the salt factorys. Parents of schoolchildren were informed through school teachers and village leaders on the nature of the intended studies. By doing so, parents allowed their children to participate and provide them with salt samples for the studies. Furthermore, only those children who gave oral assent participated in the studies. Request letters to carry out the study for **Paper V** were sent to the salt factory owners, who gave permission for the study team to carry out its work and interact with salt workers.

7. SUMMARY OF KEY FINDINGS

7.1 Paper I: Challenges in Tanzania's efforts to eliminate iodine deficiency

We surveyed in this paper 16 of the most iodine deficient districts in the mainland Tanzania in 1999, checking on the iodine content of salt in retail shops and households, as well as urinary iodine and TGP among school-children. Of the salt samples from retail shops and households, 94 and 83%, respectively, contained iodine within the threshold of 15 ppm. The median iodine of a sub-sample of 146 out of 397 salt samples obtained from shops was 37.0 ppm (range 4.2-240 ppm). 49% of the samples were below the minimum recommended iodine level of 37.5 ppm iodine at retail level (range 37.5-100 ppm according to the 1990s salt regulations). Although a high proportion of these samples had iodine contents below the national recommended level, 17% of them were within the WHO recommendation of 20-40 ppm, and therefore contained enough iodine to contribute to the reduction of iodine deficiency. Moreover, 4.8% of the salt samples were over-iodinated and 30% were extremely under-iodinated, raising awareness of the possibility of inadequate quality control during the salt iodation or potential losses due to poor salt handling.

The median UIC was 235 µg/l (range by district 70-452 µg/L) with only 9.3% of the samples having an UIC <50 µg/L. This is an indication that the vast majority had a sufficiently high iodine intake. However, the iodine results surpassed the WHO optimal range for adequacy by having 56.2% of the samples with iodine levels >200 µg/L. The overall unweighted mean total goitre prevalence for all ages (6-18 years) was 24.3% (4.1-49.4%, n=16,222), indicating moderate IDD. There was a significant difference compared to the 1980s historical goitre data 65.4%, $p<0.05$. The overall visible goitre prevalence was 6.7% compared to 11% in 1980's, indicating significant reduction. The goitre prevalence in children of 6-12 years was 18% (mild IDD), while older age groups had goitre prevalences that indicated moderate IDD. The iodine content of salt purchased from shops was highly variable and excessive iodine intake was >50%.

7.2 Paper II: Iodine deficiency persists in the Zanzibar Islands of Tanzania

This paper reports the iodine situation in Zanzibar, an area that was not targeted for intervention for iodine deficiency in 1980s. This was due to the assumption that the population had access to seafood, which was believed to be rich enough in iodine to protect them from IDD. The overall results showed that only 30% of the households in Zanzibar Islands had access to iodated salt, with iodine levels of ≥15 ppm. On assessing the individual islands, Unguja had better coverage of the use of iodated salt (63.5%) compared to Pemba, which has only 1% coverage. In salt shops that had been surveyed, only 3.3% on Pemba Island were selling iodated salt whereas in Unguja 58.7% were selling it. Out of 80 salt samples that tested positive with RTKs and later on analysed by titration, only 10.1% were adequately iodinated, while 86.2% had low iodine levels (<37.5 ppm). The salt consumed in Pemba was reported to be almost exclusively produced locally, and there was no regulation in Zanzibar restricting the production or sale of non-iodated salt.

The median UIC for both Islands was 127.5 µg/L (95% CI: 99.8-155.1). Unguja alone had a median of 186.7 µg/L (95% CI: 145.5-226.4), while in Pemba the overall median UIC was 53.4 µg/L (95% CI: 22.1-83.9). The proportion of children with UIC <50 µg/L in Pemba was 47%, also indicating a severe iodine deficiency, while in Unguja it was only 8%, indicating adequate iodine intake.

The TGP in Zanzibar Islands was 25.6% (95% CI: 22.8-28.4) with the Pemba island being the worst affected by having goitre in 32% (95% CI: 27.0-36.9) of its school-children (district range 28.8-36.5%). Unguja island had 21.3% (95% CI: 17.9-24.7) goitre prevalence, an indication of moderate IDD (district range 15.0-28.7%). The large difference is likely to be due to the consumption of non-iodated salt produced in Pemba, while the population in Unguja consumes imported salt from mainland Tanzania, which in most cases is iodinated. The overall visible goitre prevalence was <10%, with highest prevalence in Pemba (8.8%). TGP was low (18.1%) in the age-group 6-12 years in comparison to 36.9 and 27.2% in the higher age-groups of 13-15 and over16 years, respectively. TGP found in Zanzibar was similar to findings reported in mainland Tanzania a decade ago.

Neither the school children nor the members of the community, including teachers, had any knowledge of iodine deficiency, its prevention and control measures. It was noted that seafoods were expensive, and not all Zanzibaris had access or could afford to eat fish often enough. The two scenarios of the findings from the two Islands of Zanzibar (one island supplied with iodated salt and other supplied with non-iodated salt) confirmed the importance of using iodated salt to alleviate the iodine deficiency in the population.

7.3 Paper III: Tanzania national survey on iodine deficiency: impact after twelve years of salt iodation

The findings in P**aper III** describe the status of iodine nutrition in the population of mainland Tanzania through school-children after more than a decade of implementing salt iodation. The coverage of households consuming iodated salt with iodine levels more than or equal to 15 ppm was 83.6% (95% CI: 83.4-83.8). In 58 (55%) out of 106 districts, over 90% of the households used iodated salt, while 48 districts (45%) had <90% coverage in the use of iodated salt, including 14 districts found with less than a 50% use of iodated salt.

The overall median UIC was 204 µg/L (95% CI: 192-215), with no significant gender difference *(p=0.973)*. The median UIC for children 6-12 years was 203.0 µg/L. The urban population had a higher median UIC (250 µg/L) compared to the rural population (182.3 µg/L), *p=0.0001*.

The overall proportion of individual UIC <100 µg/L and <50µg/L was 25 and 10.5%, respectively; they were all below the WHO thresholds of 50% and 20% for low iodine intake, respectively, and this agreed with the WHO recommendation for adequate iodine intake. However, 35% of the urine samples had iodine concentrations >300 µg/L, a sign that segments of the population may be at risk of the problems associated with excessive iodine intake (**Figure 17**).

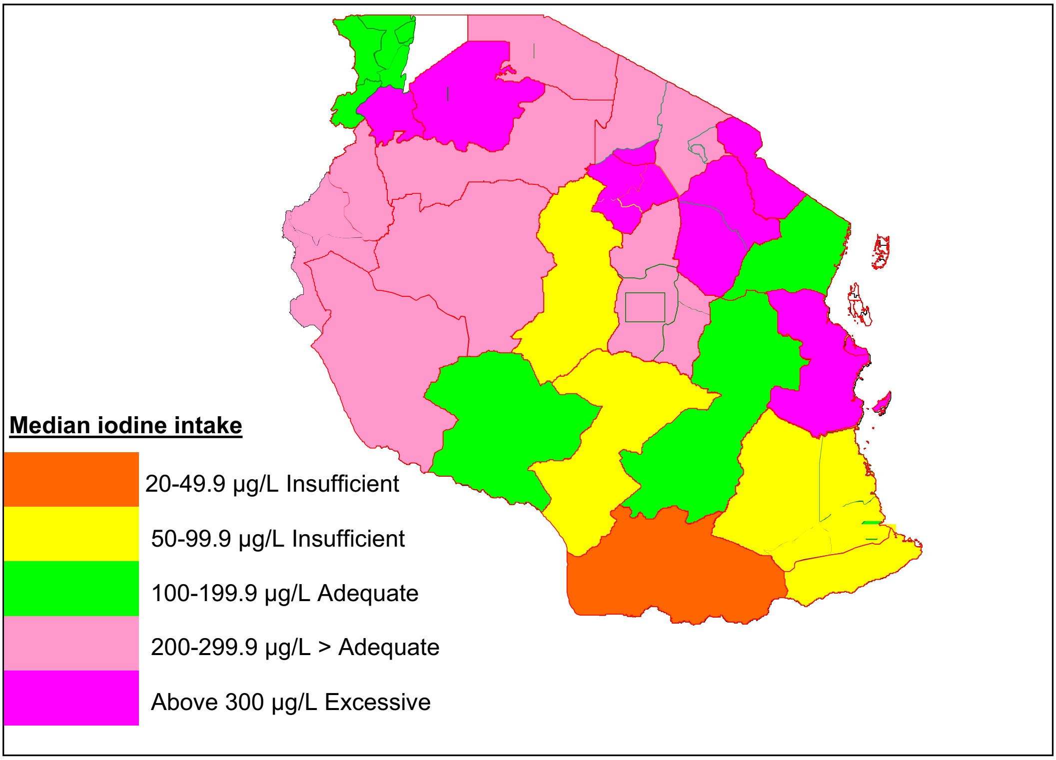


Figure 17: The median urinary iodine intake in school-children by regions, indicating areas with simultaneously under- and over-iodine intake in 2004

TGP in school-children was only 6.9% (95% CI: 6.8-7.1), with very low traceable or visible goitre prevalence (0.3%). Out of 21 regions, only 2 and 8 regions were found with moderate (20-29.9%) and mild (5.0-19.9%) IDD, respectively.

The overall TGP in the 6-18 year age group had decreased significantly from 25% in the 1980's to 6.9% in 2004 (**Figure 18**). In the age group 6-12 years, TGP had decreased to 5.5% (95% CI: 5.47-5.53), indicating that countrywide the population in 2004 had a mild iodine deficient problem.

However, TGP in the youngest age-group 6-9 years was 4.2% (95% CI: 4.0-4.4) indicating that iodine deficiency is no longer a problem of public health significance in the youngest generation in mainland Tanzania.

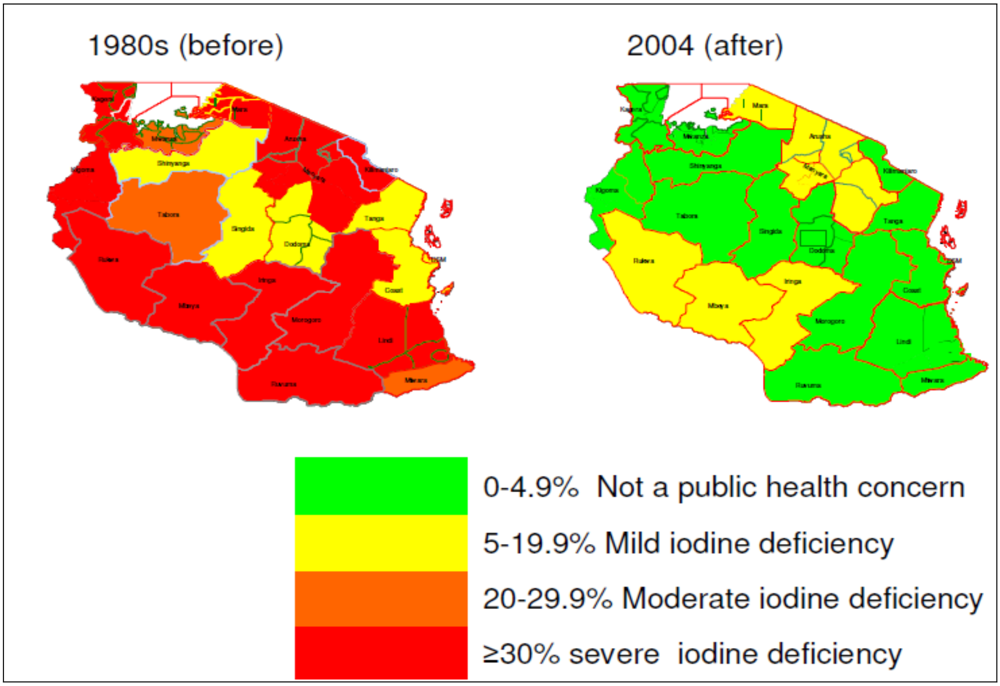


Figure 18: Total goitre prevalence by regions before and after USI intervention

The trend is shown in **Figure 19** of coverage of iodated salt at the household level against the impact indicators following school-children (6-18 years) surveys conducted in the previous goitre endemic districts from 1980s to 2004. In the previous 27 severely affected districts, the coverage of iodated salt at the household level increased from nearly zero in 1980s to 83% by 1999, and remains almost stalled (84%). However, the median UIC continued to increase beyond the upper recommended limit by 1999 and later started to decrease towards the optimal range in 2004. TGP decreased significantly from 61% (1980s) to 23.5% (1999), and finally to 12%, p=0.0001**(Figure 19)**.

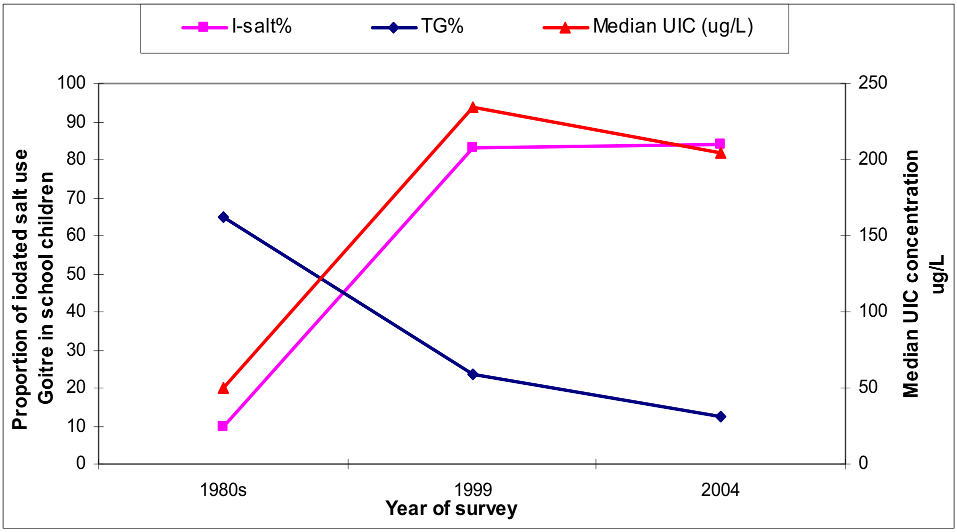


Figure 19: The trend of iodated salt use, median UIC and TGP in goitre endemic districts 1980s-2004

7.4 Paper IV: Sustainable universal salt iodization in low-income countries - time to re-think strategies?

This paper reports on the disappointment that salt producers in Tanzania were not using the iodation machines that had been supplied, but instead developed their own technology that fits their needs with extra benefits and at the same time supplying iodated salt to the people. The outcome of the study visits made to 140 salt works, previously supplied with 72 salt iodation machines in 1990's, revealed mostly that the machines had been abandoned due to high running and maintenance costs. Alternatively, a locally devised simple and rugged iodation technology has been widely adopted, i.e. based on simple gadgets requiring low labour input. The gadgets include knapsack, garden sprayers and sprinklers that replaced the iodation machines.

Assessment of iodine levels from the salt samples produced by the local technology shows high variability of iodine content levels, since only 7% of the samples (n = 85) met the then recommended iodine standard range of 75-100 ppm required at factory level. The rest of the salt samples were under-iodinated (69%) and over-iodinated (24%). However, the majority of the salt samples that were under-iodinated had levels of 20-74.9 ppm. This means that without meeting the national iodine specification, these levels may have contributed to the reduction of iodine deficiency. Moreover, salt producers complained of the responsible authorities not taking serious legal action against non-compliant facilities. This together with the reported low price of adequately iodated salt demoralized the producers/workers at the iodinating salt facilities. The study revealed the need to evaluate whether the iodation technologies were appropriate to sustain USI.

7.5 Paper V: Improved salt iodation methods for small scale salt producers in low-resource settings in Tanzania

This paper is based on observations, interviews and focus group discussions with salt producers and salt workers on the knowledge, attitude and practices of salt iodation. It showed that quality control was very poor, using locally devised iodation equipment. Salt workers had little or no skills/knowledge of salt iodation procedures. The overall median iodation in samples from salt previously iodinated using non-improved methods was 10.6 ppm (range from 1.1-110 ppm), far higher iodine levels being in the top layers of the salt bags compared to the middle and bottom layers ($p<0.0001$).

Salt iodation experimentation using knapsack sprayers and manual mixing led to improved methods that could reliably achieve the recommended level of 60 ppm iodine (±7.4 SD), using technologies and materials available on site. The improved methods had increased homogeneity between top, middle and bottom layers of the salt-sacks ($p=0.58$), with 96% of the salt samples ($n=45$) falling within the required 40-80 ppm iodine range in comparison to only 9% ($n=45$) before the experiment and training ($p<0.0001$). The use of a machine-mixer gave only a slight improvement in iodine levels and homogeneity in comparison to knapsack spray and manual mixing method ($p=0.05$).

8. DISCUSSION

The key findings from study **Papers I-V** will be briefly discussed in this section, in the light of the general objective of the studies. This has been to investigate the impact of universal salt iodation on the population of Tanzania, as reviewed through school children and salt iodation processes to reach the sustainable elimination of IDD. Each study is discussed in greater detail within the individual papers of this thesis. The discussion starts with reflections on some key methodological issues that are sometimes associated with limitations and biases, and therefore with their implications. They then continue with the successes and challenges, mostly with reference to the implementation of the IDD control programme in Tanzania. The discussion will be based on the study findings and role of indicators in the course of sustaining IDD elimination. Finally conclusions will be drawn and their policy implications briefly discussed.

8.1 Methodological issues

Study designs

The design of the studies, with particular attention to **Paper I & III**, was cross-sectional in nature. However, because of historical data from parts of the same populations, it became in some ways of 'before and after' study, in which the effect of iodated salt was assessed by comparing historical (pre-intervention) data with our post-intervention data. This design has its limitation because it gives a snap-shot view of a disease and its potential causal agents but does not show the sequence of events, the exposure, or the disease. To do so, longitudinal studies were needed to be done either prospectively or retrospectively along with measurements of IDD incidence [163]. The outcomes were assessed on two different groups of children of the same age group of 6-18 years pre- and post-intervention performed on the seventh and twelfth years after USI in **Papers I & III,** respectively.

In **Papers II, IV** (also with cross-sectional designs) & **Paper V** (an experimental design), a qualitative approach assisted in acquiring the contextual information with regard to knowledge, attitude and practices in relation to people's awareness of IDD and its control through the consumption of iodated salt. The experiences of salt workers on the different methods and procedures of salt iodation at the production facilities were deduced, analysed and improved.

Conducting the FGDs was one of the challenges we experienced, especially in **Paper V**, since it was difficult to organise the group discussions. Every salt worker was busy harvesting, iodinating or packaging salt to achieve the day's quota, which is what they were paid for by the salt factory/site owners. The only convenient time was during the lunch hours. Group interviews were often done by giving incentives, such as soft drinks and bites. In other areas, we joined the workers in the evening in local recreation clubs after working hours to get groups for discussion, during which we had to share with them a local coconut brew *(pombe ya mnazi)*.

Another design in our series of studies was an experimental approach. We controlled and evaluated various factors related to salt iodation and their effects on the resulting iodinated product. These include the different steps for iodation of salt using old and modified methods, training of salt workers on the right measurements and the control of sprayers during manual salt mixing with potassium iodate solution, the procedures in the laboratory methods, application of quality control procedures, and the use of reference materials to ensure reliability of reported results.

Validation of methods

Method for testing iodine in salt

Testing iodine in salt involved a semi-quantitative rapid test kits (RTK) recommended for iodated salt, which can give high output [5]. The test kit method is accurate, but lacks specificity, especially when applied by multiple observers, giving a large number of false-positives, which can create complacency [164]. However, positive salt samples for iodine prepared at the TFNC laboratory were given to each investigator as a reference material for evaluating the quality control performance of RTK on iodated salt before testing salt from households. This may have increased the validity of the RTK results, but not the correct amount of iodine added in the salt due to its low specificity, as has already been reported [164, 165].

Some salts produced in Tanzania, however, are alkaline in nature. The high pH of salt prevents the colour change. Therefore a drop of recheck solution (acidic media) has to be applied first to decrease the pH, before the ordinary starch test solution could be applied [164]. Although investigators were made aware of using the recheck solution, it cannot be ruled out that some did not observe this procedure due to high turnover of school children. In this case some positive salt samples may have been regarded as negative, thereby reporting a lower proportion of households accessing iodated salt. Some observers may have colour-blindness, which may also have affected the household coverage results.

A titration method is recommended for the correct determination of the amount of iodine present in salt [5, 166]. Different salt brands of refined and course salts previously known to be iodinated were pooled separately as reference materials and their iodine concentrations established by titration. The pooled reference salt materials were tested by RTKs to confirm positivity and negativity with iodinated and non-iodated salt, respectively. Salt with a known iodine concentration was used for internal quality control in the titration method. External quality control was assured by the participation of TFNC's iodine laboratory in the proficiency of iodine testing procedures. This strengthens the reliability of our results, since this method a precision of <15% on many occasions, similar to the findings of others using the same method on fortified salts [5, 157].

The titration method was used in all studies, except that reported by **Paper III**. This is seen as a weakness of this study because it would have been important to sample and analyse by titration salt samples from salt factories in the same way as for samples from wholesale and retail shops. The data would have increased the validity of the results obtained by the RTK at the household level. Nevertheless, very few (16% out of 131,941) salt samples from the households contained no iodine.

Method for determination of urinary iodine
The urinary iodine determination method has been evaluated through the global network of iodine laboratories, and correlate closely with reference chloric acid method (r = 0.994) [156]. The TFNC laboratory has gained experience from its participation in the urinary iodine proficiency testing scheme since the mid 1990s, and has demonstrated satisfactory accuracy and precision in the participated rounds [128]. Just as for the iodometric titration method, both internal and external quality control aspects were used on the validation of the urinary iodine method.

Method for assessment of goitre prevalence
For the goitre palpation method, the examiners were trained by the existing standardized trainers before the actual surveys were reported in **Papers I, II & III**. To minimise reporting errors, the questionnaires were standardized and pre-tested so that corrections could be made prior to the surveys. Additionally, the interviewers received training, under “blinded” conditions, about the expected outcome in order to minimise bias in the results. The intra- and inter-variations were not documented after training was given to the goitre examiners. By using the experience of the trainers and the results from their past experiences in a goitre standardization study [89, 139], they were able to caution investigators on the possible mistakes that could have made goitre palpation measurements unreliable.

To minimize errors in all the studies, validation of the data was done on daily basis during the study conducting processes and data analysis. We went through the questionnaires and documented information to clear any doubts found after understanding the logic behind some of the data. For instance, in some areas reported in **Paper III**, discrepancies were noted in two regions. This was remedied by repeating the goitre palpation; in another region collection of urine samples was repeated in one district. Such further validation may have strengthened some of our findings. On the other hand, a potential weakness in **Paper III** was that regional principal investigators were used, each conducting the study in his/her own region, thereby potentially creating possibility of a bias for all the regions taken together, either by under or over reporting of goitre.

In **Papers I & II,** only one or two trained and experienced medical officers did the goitre examination. These were from TFNC and had previously participated in studies for standardizing the goitre palpation method [139]. It is assumed that this would have minimized errors in these studies.

As an effort to bring about the differences in status of IDD in the 3 featured geographical patterns of the country, the aspect of stratifying schools in highlands, lowlands and townships in each district was used in the baseline surveys conducted in the 1980s [15]. This type of ‘relative highlands’ and ‘relative lowlands’ of different altitudes merged together in the analysis may not be particularly relevant. For example, the ‘highlands’ and ‘lowlands’ in a district located entirely at 1000 meters above sea level were grouped with ‘highlands’ and ‘lowlands’ from a district located entirely below 200 metres altitude. Analysis is only meaningful if *absolute* altitudes instead of relative altitudes are used for these divisions inside each individual district.

Alternatively, we categorised schools as urban and rural at a ratio of 1: 2 schools, respectively. The rural schools include one school from the district’s relative highlands and another school from the district’s relative lowlands area. Findings from these two categories (rural and urban) reported in **Papers I-III** clearly show this difference is pertinent.

Goitrogens: a potential confounding factor

A confounding occurs when the apparent effect of the exposure of interest is distorted because a third factor is mistaken for, or mixed with, the actual exposure [167]. The confounding factor can either overestimate or underestimate the observed associations, and must always be accounted for.

The naturally occurring goitrogens, such as thiocyanate, is a potential confounding factor for thyroid gland enlargement. The foods listed in item 1.3 as a source of goitrogens are staple food in many parts of the country where these studies were carried out, and all may have played a role in aggravating the existing iodine deficiency. This had previously been reported in Tanzania and Sudan [43, 168]. The effect of goitrogenic substances was not considered during the design of these studies. Goitrogenic effects are more pronounced in areas with frank or borderline iodine deficiency [169]. Therefore, their impact on the study results may have decreased with increasing iodine repletion.

Excess fluoride intake is another confounding factor, which occurs in some districts in Tanzania. The fluoride concentration in some waters can reach 95 mg/L where the rocks are rich in fluoride-containing minerals, and the prevalence of fluorosis in Tanzania was 33.6% in 2004 [15, 170]. Goitres observed in some areas were not in fact caused by any deficiency of iodine as commonly known, but perhaps relate to by an excessive intake of fluoride from all sources, water, food, and air [171, 172].

New evidence indicates that iodine metabolism is being disturbed in peripheral tissue through manipulation of the deiodinases, the three enzymes which delicately regulate thyroid hormone metabolism through external TSH/G-protein activation. Disturbances in thyroid hormone levels appear to be identical with those observed in IDD [173, 174]. During IDD surveys, this concern was not considered, thus possibly contributed to some falsely high goitre prevalence results in some areas that were not purely related to iodine deficiency.

Implications of the methodological weaknesses for future IDD surveys
In future IDD surveys, the gaps identified as limitations in these studies should be addressed. In our view, the semi-quantitative method (test-kits) will continue to be used since this is the best method available for testing large number of salt samples, which lead to some remedial action being taken on the spot [5]. The survey teams need to be standardized on the method before embarking on a survey.

The inclusion of salt sampling from salt factories and shops to determine iodine content is important for comparison with other IDD indicators (e.g. variability in urinary iodine) and in assessing whether USI is meeting the optimal iodine levels. In the case of the method for urinary iodine determination, we recommend researchers and programme managers continuing to use the same method, with application of both external and internal quality control as was done here.

For the goitre assessments, one additional quality control needs to be included prior to a survey, i.e. standardization of goitre palpation techniques among all goitre palpating members of the survey team. Elements of subjectivity - ‘single-person effects’ - can also be avoided by allowing investigators to move between regions.

For the USI programme at an advanced stage as in Tanzania, assessment of thyroid size has become less useful, especially the goitre palpation method, which will no longer be a method of choice. Instead a more sensitive method such as ultrasound (gold standard method) ought to be adopted in future goitre surveys [5]. Where resources do not allow this, a mix of the two with at least 5% of the school-children palpated for goitre and simultaneously being assessed by ultrasound to validate the palpation method would be helpful and assist in interpreting the results by comparison with other indicators, such as urinary iodine.

Thyroid volume is also a slow indicator of change in an evolving iodine nutrition landscape and instead biomarkers of thyroid function (TSH and thyroglobulin) have been proposed as indicators for iodine status. Their use in cross-sectional surveys has generated variable results [136, 138, 175]. Because of existing dubiety about the usefulness of both thyroid size and biological markers of thyroid function, future cross-sectional surveys may continue to rely on urinary iodine levels as the primary indicator of iodine status [101].

8.2 Major findings

Epidemiology of iodine nutrition in mainland Tanzania
An impressive improvement in iodine nutrition in Tanzania over the 12 years since the initiation of the USI has occurred, demonstrably by the fact that 84% of households now consume iodated salt. This has moved it from a situation where an estimated 25% of the population had iodine deficient conditions [143] to one in which 94.5% of the 6-12 year olds have no iodine deficiency. The iodine status of the 6-12 year olds living in the most of the high risk areas for iodine deficiency in the

country have also remarkably improved from severe iodine deficiency (TGP >60%) in 1980s [15] to mild iodine deficiency (TGP = 9%) in 2004.

The most encouraging result is that TGP is below 5% in the youngest age-group, the youngest generation in Tanzania having grown up with iodine replete conditions. This may have protected them from the risk of brain damage resulting from iodine deficiency [5].

The median UIC indicated adequate iodine intake irrespective of age, sex and location - a clear sign of the maturation of the IDD control programme. Areas previously categorised as severe iodine deficient are now regarded as mild iodine deficient, based on TGP, but with sufficient iodine intake based on median urinary iodine concentration.

Iodine deficiency in Zanzibar Islands

There was no IDD control programme in Zanzibar before 2001. The high coverage of iodated salt consumption reported in Unguja was an incidental finding since there was no USI programme. In Pemba Island, almost no iodated salt was consumed. This was confirmed by the prevalence of goitre found in both islands, but being much worse in Pemba Island that had TGPs indicative of severe IDD. Higher altitudes and lower availability of iodated salt in Pemba seem to have contributed in worsening of the IDD situation. These findings seriously challenged the common assumption that accessibility to seafood can protect a population from the risks of IDD [2]. The main factor that contributed to the high goitre prevalence in Zanzibar islands was inadequate dietary iodine intake, as had previously been emphasised [176] .

Three immediate reasons cause delay in implementing the IDD control programme in Zanzibar: first; a conventional top-down approach, in which local governments were not enabled to assess the existence of any iodine deficiency in their areas because they were also used to implement instructions from the central government as it was for mainland Tanzania.

Second, the lack of TFNC's input. Although TFNC reflects on Tanzania as a union, it was not mandated by the Revolutionary Government of Zanzibar, which also makes it difficult to initiate a follow-up of the use of iodated salt in those islands. TFNC is involved in formulating, initiating and promoting development policies, and planning regulations and legislation for improvement of nutritional status of Tanzania's community [15].

Third, the influence of a general belief that the population of the islands like Zanzibar had access to seafoods, assumed to be rich in iodine [6], also shared by the Ministry of Health and Social Welfare in Zanzibar. On this flawed basis, the government did not see the need to establish an IDD control programme. Zanzibar needs now to establish the capacity building for this programme, using the organised hierarchy of needs [177] and the ICCIDD *'wheel model'* for implementation of the IDD control programme [70].

Variability of iodine content in salt

Another important finding obtained in the studies was lack of uniformity in the salt iodine content due to the lack of standardized and calibrated machines for iodating and mixing salt. The local iodation methods adopted without proper knowledge and skills for quality control during the process were the main cause of the variability in iodine content that was also reflected as high variatiability in urinary iodine excretion levels. However, despite of shortfalls of the locally adopted methods, the approach initiated by salt producers has nevertheless brought the country to a situation where IDD is a mild problem, which has saved many children's lives, and protecting them from brain damage and other associated anomalies[61, 86, 102].

As a compliment to the efforts taken by salt producers, the interactions in studying and modifying the locally iodation methods and procedures has indeed led to improved iodine homogeneity in salt and achievement of the required iodation levels [122]. If the process of salt iodation using local technology is standardized and supervised, it will contribute to the efforts of achieving sustainable IDD elimination, especially in low-income countries with many smallscale salt producers (**Paper V**).

8.3 Why is USI not yet universal in the country?

Despite of the impressive achievements obtained in the past 12 years of implementing IDD programme in mainland Tanzania, the USI is not yet achieved. Conversely, Tanzania is already implementing most of the components in the 3 phases outlined in **Table 3** for IDD prevention and control [99]. The country's IDD control programme needs to be working within the implementation and consolidation phases to remove doubts where any weaknesses may exist. It also needs to refine the quality control of salt iodation at production sites to avoid variability of iodine concentrations reflected in **Paper I-IV** by meeting required iodine levels [5, 122].

During analysis of the findings in this thesis, we realised that the national IDD control programme most certainly had all the necessary requirements (capacity building for salt iodation) by mid 1990s. Nevertheless, the programme has not yet to reached the WHO intermediate goal and the ultimate goal of sustaining IDD elimination [87, 88]. The following may be the contributing factors: i) weaknesses in the organisation of the programme ii) problems relating to sustainability of USI and, iii) lack of integration of the IDD control programme activities with comprehensive health plans of the district council.

i) How might a national IDD programme be organised?

We have identified an article that we think can assist in understanding the strengths and the gaps existing in the IDD control programme in Tanzania. This article presents

Table 11: Relation of the nine component elements of the health systemic capacity building with those in the status of implementing IDD control programme in Tanzania

Systemic capacity	**Elements of systemic capacity building**	**Status of requirements to achieve USI & IDD elimination goals in Tanzania**
Performance capacity	Are the tools, money, equipment, consumables, etc. available to do the job? A doctor, however well trained, without diagnostic instruments, drugs or therapeutic consumables is of very limited use.	- Iodation supplies and monitoring facilities provided, - Inadequate funding
Personal capacity	Are the staffs sufficiently knowledgeable, skilled and confident to perform properly? Do they need training, experience, or motivation? Are they deficient in technical skills, managerial skills, interpersonal skills, gender-sensitivity skills, or specific role-related skills?	- Programme staff managers, inspectors and registered salt producers trained - But >6500 producers without iodation skills
Workload capacity	Is there enough staff with broad enough skills to cope with the workload? Are job descriptions practicable? Is skill-mix appropriate?	- Insufficient at district and community level
Supervisory capacity	Are reporting and monitoring systems in place? Are the lines of accountability clear? Can supervisors physically monitor the staff under them? Are there effective incentives and sanctions available?	- Salt regulations in place but their implementation is insufficient, - Weak monitoring
Facility capacity	Are training centres big enough, with the right staff in sufficient numbers? Are clinics and hospitals of a size to cope with the patient workload? Are staff residences sufficiently large? Are there enough offices, workshops and warehouses to support the workload?	- Manpower sufficient at institutional level; - Insufficient at some districts and at salt production levels
Support service capacity	Are laboratories, training institutions, bio-medical engineering services, supply organizations, building services, administrative staff, laundries, research facilities, quality control services available? They may be provided by the private sector, but they are required.	- There are six institutions that are key players with all necessary facilities provided - Inadequate quality control services
Systems capacity	Does the flow of information, money and managerial decisions occur in a timely and effective manner? Can purchases be made without lengthy delays for authorization? Are proper filing and information systems in use? Are staff transferred without reference to local managers' wishes? Is there good communication with the community? Are there sufficient links with NGOs?	- Insufficient as result of bureaucracy that still exist in some implementing sectors. - Poor data banking and insufficient communication
Structural capacity	Are there decision-making forums where inter-sectoral discussion may occur and corporate decisions made, records kept and individuals called to account for non-performance?	- Fairly sufficient, registered changes but not 100%
Role capacity	This applies to individuals, to teams and to structure such as committees. Have they been given the authority and responsibility to make the decisions essential to effective performance, whether regarding schedules, money, staff appointments, etc?	Insufficient at district level

a systematic approach to assess the systematic capacity of a health system that will be briefly summarised [177]. The authors of this article emphasise the importance of a systematic capacity building approach to achieve optimal system operation. They argue that *'the capacity building consists of meeting a hierarchy of needs which all need to be considered in a logical order if investments in developing are to pay off '* [177].

They also indicated that systematic capacity building consists of 9 individual but interdependent components (**Table 11),** forming a 4-tier hierarchy of capacity building requirements (**Figure 20)** [177]. To relate this argument with Tanzania's programme, an in-depth analysis of the current capacity building of the national IDD control programme is presented and also related with WHO programmatic indicators for sustaining IDD elimination, **Table 8** [5].

The authors indicate that the capacity development often consisted of inputs in terms of equipments, consumables and workshops for providing technical skills. The USI project for IDD prevention and control programme in Tanzania fulfilled the top two parts of the pyramid capacity structure (**Figure 20),** which covered performance capacity and personal capacity (**Table 11).** These provided an initial driving force for the two remaining capacity building components. The exceptional was the small-scale salt producers, which remained unknown until an inventory of their existence was carried out in 2003 [178].

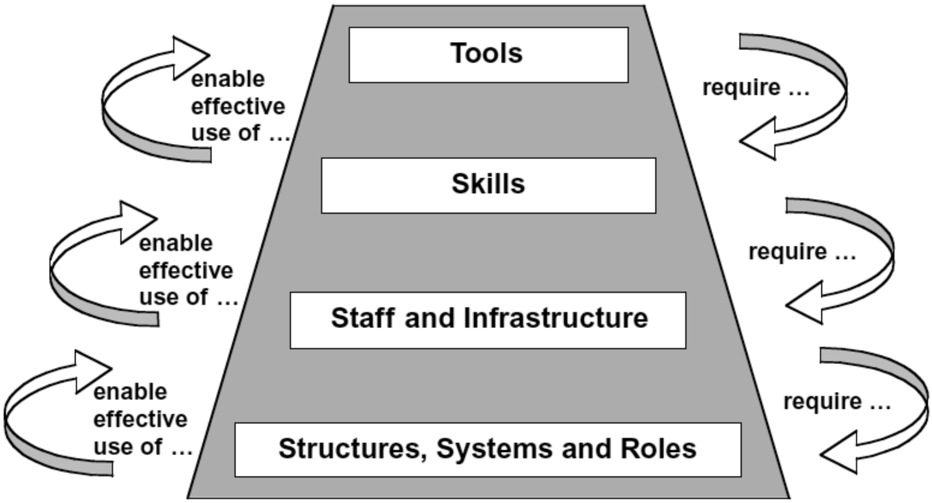


Figure 20: Pyramid structure denoting a systemic capacity hierarchy of interdependency action according to Potter and Brough [177]

It can be argued that despite the shortfalls indicated in other existing capacities, the successes reported in **Papers I&III** were possible because of IOC intervention in the most severely IDD affected districts, and thereafter through the fortification of about 60% of salt produced by medium and large salt factories since 1990s [155]. The restriction on the importation of non-iodated salt for human and animal consumption is also a factor in the success. Imported salt is about 10% of the salt consumed in the country, and is monitored well at the ports of entry [122, 149].

However, the shortfalls indicated in some of the systemic capacities as insufficient and fairly insufficient may denote that the inputs provided did not result in satisfactory improvement; they could have been noted earlier so that appropriate action could be taken. The possible reason for inaction could be complacency that may have arisen from the sporadic surveys or surveillance reports in the mid 1990s that were showing good progress [15, 154]. Everything for salt iodation and the monitoring system were "thought to be in place", and the coverage of iodated salt was on the increase and at the same time, TGP was decreasing fast, which assumed IDD would not recur' [179].
Subsequently, the momentum of inspection and follow-up gradually declined, except for some activities that were followed-up by TFNC [145]. Experience has shown that where national leadership and oversight were evident, iodine deficiency virtually disappeared [180], with the vice-versa also being true [181].

Potter and Brough cautioned that efforts to strengthen capacity should focus on the organisational system that:
'*is composed of a network of programmes of services, staff, facilities, structures (forums for discussion and collective decision making such as management boards, committees, etc), and processes of supervision, decision making, information passing, financial flows, and so forth. When the systems capacity is ignored, inputs are often wasted and results scarce'* [177].
Strategic assessment of the programme was necessary, especially in the mid 1990s, to finer tune each of the nine different interacting systems capacity shown in **Table 11,** and link the coverage indicators reported with quality and equity.

ii) Making USI sustainable
In the start-up phase, the national IDD programme had a high degree of donor dependency [15]. Donor support was necessary for providing the capital costs for establishing the salt iodation and supplying potassium iodate [10]. The support advocated by WHO, ICCIDD and UNICEF was also part of strategies and incentives for salt industry and countries to enable the take-off of the national IDD control programmes globally through the 1980s and 1990s. But at a certain point, this donor dependency was a weakness: where a donor hesitated, the programme activities were almost halted or considerably slowed down due to lack of funds, thereby questioning the sustainability of the programme [182].

To sustain USI as the programme advances, the financing needs to move from external to domestic funding, for which the government needs to do two things:
1) Ensure continued financing and running of the regulatory enforcement and monitoring aspects [10]. To date, monitoring and enforcement have been major weaknesses; by strengthening them now, improved output for each system capacity can be obtained, filling in some of the gaps indicated in **Tables 8 & 11**. The contribution of the government is still adequate to meet the tool requirements, which are fundamental for the other systemic capacity structures to operate [177].
2) Securing the provision of potassium iodate and salt monitoring tools for salt producers. These are not yet regularly available or easily accessed, especially by the

small-scale salt producers, most of whom are poor and operate in rather inaccessible areas [178]. There is a need for the government to work with the salt industry on how to include some of the costs as part of the price that can be absorbed by the consumer.

Sustainable acquisition of potassium iodate and other supplies for iodation

Two options might solve the current problems and achieve sustainability of the programme at the same time. One is to mobilise small-scale salt producers into working groups or co-operatives. They can then raise funds through their organisation to acquire potassium iodate through the controlled sale of salt produced in their area, while the national IDD control programme assures them access to potassium iodate when they need it.

In relating with previously proposed formation of cooperatives for salt iodation in 1990s, the focus at that time was mainly on medium and large scale salt producers [15]. Somehow the strategy failed due to disagreements among members of the proposed cooperatives or working groups on management of the iodation machines supplied and sharing of the salt iodation running costs [145].

At the moment, organisational working groups suggested in this report would be for small-scale producers, aiming at each producer or team of people to continue producing salt at individual/group level, but they should be a member of a big salt working group. In doing so, other technical aspects relating to improving salt production, iodation and monitoring can be easily provided rather than dealing with individual producers. This alternative, which was also recommended by ICCIDD [102], cherishes the already existing reimbursable revolving fund for sourcing potassium iodate that was established by TASPA in the early 2000s[183].

The second option is for the government to create or reinforce a (national) procurement and supply system, as is done for essential drugs, so that it to now includes the purchase of iodation equipment and supplies, and provides quality assurance support [123, 180]. However, although issues of sustainability have been discussed a lot at high policy level on global IDD programme implementation, not much has been done to relate potassium iodate acquisitions with vaccines, which are also used for mass interventions.

The need for parents to pay for vaccines has not often emerged as it has for potassium iodate, and governments and donor community are probably happy to continue to support it; so why should this not also be the case for potassium iodate, which is infinitely cheaper than buying vaccines for a country?

Assuring that existing and new vaccines are made available to all the children in the world is a global health priority [184]. However, despite their clear health needs and benefits, many countries have been unable to provide the 'new' vaccines, e.g. hepatitis B vaccine, for their populations. The limitation has been the inability of some governments to finance the vaccine because of a combination of factors including dependence on donors, donor policy, inadequate recognition by governments of the value of vaccines and, for some countries, the actual cost of the vaccines [185].

Acquisition of potassium iodate, though, is not a like getting a vaccine, but its purpose is very similar. It is required for protection of children from brain damage, which tends to occur before birth, which has an implication on the socio-economic development of nations and global as whole [68]. WHO/UNICEF/ICCIDD advocates self sustainability in countries implementing the IDD elimination programmes and the needs for consumers to contribute towards the cost of salt iodation. However, in countries where there are complexities of small-scale salt producers who cannot afford a kilo of potassium iodate, governments and donor communities need to think again about supporting this particular group as part of its overall poverty alleviation strategy [102].

Experience suggests that a positive outcome is more likely when the means of salt production is kept either under state control or through a limited number of large producers when an accountability framework is in place before a project is financed [186]. The existence of a multitude of small-scale salt producers in Tanzania competing for the market that was unknown earlier probably contributed in large measure to the programmes lagging behind in achieving USI due also to failure to develop an effective accountability framework.

The issue of iodation supplies remains as a challenge for the government, especially for the small-scale salt producers. The government also need to provide an enabling environment to attract the private sector to take over by investing in proper salt iodation machines, after the earlier supported iodation machines from UNICEF become defunct.

iii) Programme management at community level

From its inception in the mid 1980 to around 2000, the national IDD programme has been operating a top-down management approach, making the implementers of the IDD programme at the local government act only on instructions received from the central government (MOHSW represented by TFNC and TFDA).

The IDD programme was not integrated into district plans from the beginning, and therefore there were no forum or any other monitoring system within the districts that could identify local shortcomings of the programme and take action at this level. At that time, many government programmes, including health programmes, were vertical. It was not until sector reform (decentralisation) in 1990s that the local governments were mandated to address local problems and develop their areas [187]. The bottom-up monitoring approach has been very successful in China, where surveillance systems with action taken from the district, provincial, up to national level has seemingly eliminated the country’s IDD problem [188].

The effects of iodine deficiency affect the productivity and social well-being of the individuals, community and nation as a whole, starting at district level. Elimination of iodine deficiency has been shown to contributes to six of eight Millennium Development Goals (MDGs) agreed to by the UN Member States in 2000 (**Box 3)** [10].

Box 3: IDD AND MILLENNIUM DEVELOPMENT GOALS

Goal 1 – *Eradicate extreme poverty and hunger*: Eliminating IDD eliminates a 'hidden hunger' (= a nutritional deficiency) and increases the economic potential of the population

Goal 2 – *Achieve universal primary education*: Eliminating IDD improves the intellectual development and the learning potential, leading to improved school performance and reduced drop-out rates, thereby making better educated citizens.

Goal 3 – *Promote gender equality and empower women*: Eliminating IDD in women promotes gender equality in itself, and eliminating IDD in children reduces women's childcare burdens, frees up household resources, and allows women more time for work.

Goal 4 – *Reduce child mortality*: Eliminating IDD reduces the rate of neonatal and infant deaths.

Goal 5 – *Improve maternal health*: Eliminating IDD reduces rates of miscarriages, stillbirths and other pregnancy complications; it also improves the overall health of women of reproductive age and lowers the occurrence of thyroid diseases.

Goal 8 – *Develop a global partnership for development*: Programmes for sustainable elimination of iodine deficiency strengthen partnerships at global, regional and country levels. They also leverage resources and commitments through alliances of public organizations, civil society and the private sector.

Source: [10]

If the districts are aiming to achieve the UN-MDGs, the IDD control programme needs to be integrated with other district health priorities by allocating budget and taking action in terms of regulatory enforcement and monitoring of the USI, while other major issues – such as acquisition of potassium iodate and monitoring tools for salt producers (performance capacity) - need to be forwarded to the Central government for action (role capacity).

The district leaders need to support health inspectors in passing on the monitoring tools and skills (performance and personal capacity) already provided by them to the lower health cadres operating at ward/village levels (to strengthen workload capacity), as well as carrying out supervisions (supervisory capacity) and creating a feedback salt monitoring system (systems capacity) in which implementation progress can be discussed and decisions made for further actions in their locality (structural and role capacity).

By considering the varying processes of implementation, prevailing circumstances and conditions from district level up to the central government level (bottom-up approach), the national programme would be able to sustain IDD elimination.

8.4 The role of IDD indicators in influencing policy change/decision making

Urinary iodine

The studies (**Papers I&III**) in this thesis report a decrease in goitre prevalence with an increase in UIC, indicating that USI has been effectively working, reaching the population almost equally (depicted by there being no significant variations of the indicators by age and sex). These findings could potentially lead to the conclusion that iodine deficiency in the population is a problem of the past. The findings also identify some areas (**Figure 18 & Appendix VI**) that are still iodine deficient, similar to those reported in the global findings [98].

Different sub-groups (most disadvantaged) of the population tend to lag behind in the use of non-iodated salt and therefore remain iodine deficient [189]. For each 10 ppm (mg/kg) increase in salt iodine content, the UIC increase by 30-35 µg/L in school children. However, the increase was approximately 15-20 µg/ L in pregnant women, emphasizing on the need of pregnant women for additional iodine due to their physiological state [86]. Thus iodine status in schoolchildren using salt with 15-29.9 ppm provided the recommended optimal range, while at the same time the status of pregnant women living in the same households fell below the minimum desired level [189]. Reliance on assessment of UIC in school-children may be misleading in generalising about the iodine status of the population. Thus each vulnerable group needs to be assessed separately before declaring IDD elimination.

The percentage of individuals with high UIC levels (>300 µg/l) was on the increase in mainland Tanzania, raising concern on the possible risk of iodine-induced hyperthyroidism in some sectors of the population [190].

Reasons for excessive iodine intake

Excess iodine intake (≥300µg/L) was found in 35% of the urine samples analysed for UIC (**Paper I & III**). Five regions had a median iodine intake that was excessive and another seven regions had a median UIC that was more than adequate (200 to >300 µg/L; see **Figure 17).**

The possible reasons for excessive iodine intake could be due to improved salt packaging, especially for the people living close to salt factories and ports of entry, which receives iodated salt and where minimal losses occur before consumption. Inadequate quality control is another reason for over-iodation of salt and possibly also high intake of salted marine foods (using iodated salt), for instance in the lake region of Mwanza, and the Coast and Dar es Salaam regions along the Indian Ocean. The most common fish preservative used in these regions is salt, which in most cases is iodated, hence possibly adding up the amount of iodine consumed.

An excess iodine intake of >30% is not exceptional for Tanzania, and has been reported in other countries in Eastern and Southern Africa regions [180]. The figure for the proportion of excess intake is still low compared with Latin American countries where some countries have as high as 94% excess iodine intake, and hence it becomes a major challenge after attaining the IDD elimination.[191]. However, it has also been shown that people lacking evidence of an underlying thyroid disease remain euthyroid when exposed to excess iodine [192]. Nevertheless there is a need to improve the monitoring of the salt at production, at wholesale/retail sales level and at the ports of entry throughout the country, in order to avoid unnecessary risks of iodine-induced hyper- or hypo-thyroidism [78, 80, 193, 194].

The fear of possible cases of IIH occurring in some few people cannot be ruled. In the advanced stage reached by the programme, it may not be a threat to the population of Tanzania, since the majority of people are already experiencing intake of iodine daily. Their bodies are no longer thirsty for iodine due to severe iodine deficiency, which was a risk factor for IIH reported elsewhere [78, 195]. Although this subject was not part of this thesis, there is a need, however, to ensure that basic training programmes for medical practitioners are provided that include training in the symptoms and treatment of IIH, and probably start to consider identifying and offering special sources of non-iodated salt for a few cases that may be diagnosed. This entails developing IIH management guidelines for practitioners' use, and to provide public education.

Any policy change within the IDD control programme is likely to be based on the urinary iodine findings. In fact, this has already happened since the UIC indicator (**Papers I & III**) has been used by policy makers to review and lower the regulated iodation levels at the salt production sites in mainland Tanzania.

The same impact indicators (**Paper II**) had strongly pointed to the existence of IDD in Zanzibar and other similar islands despite the general belief that population in the Isles have adequate iodine intake from seafood [196, 197]. These indicators have begun to change the policy, requiring mandatory salt iodation now for all the population in Zanzibar and elsewhere.

Urinary iodine as a marker of a poorly performing IDD control programme

The urinary iodine marker has also identified high variability of UIC in some areas, which has brought into question the quality control of salt iodation, its monitoring, and probably the handling of iodated salt before it reaches the consumer.

The median urinary iodine levels were <100µg/l in 5 regions, indicating that their populations were consuming non-iodated or under-iodated salt (**Figure 17**). Lindi and Mtwara regions are the major suppliers of salt for the Southern highlands, which include Rukwa, Mbeya, Iringa and Ruvuma regions [15, 178]. These regions may be the source of insufficiently iodated salt that gave the low median urinary iodine levels, which could be attributed to: 1) existence of small-scale salt producers; a group which at the time of this study had not yet been addressed for salt iodation; 2) poor demand for iodated salt by the community; and 3) weak monitoring and regulatory enforcement of the salt regulations by local government and central authorities [178].

8.4.2 Goitre prevalence as an indicator for IDD

It has been claimed that goitre prevalence is not a good indicator for short-term IDD programme evaluations, thyroid size in children taking a long time to regress to normal after normalisation of the iodine supply [198, 199]. However, it is a good indicator for establishing baseline data of the magnitude of IDD in a non-intervened area, as we did in mainland Tanzania in the 1980s [143] and in Zanzibar. It is also a good indicator of the long-term follow-up of interventional areas (**Papers I & III**). A large reduction in goitre prevalence occurred, demonstrating that the USI programme in Tanzania has worked (**Appendix VI**), as in other countries [70, 143]. Nevertheless, the programme has not yet full eliminated iodine deficiency by this criterion [5]. The elevated goitre proportions observed in older children in these studies are possibly reminiscent of previous iodine deficiency, at least in part, and might take time to disappear.

The approach taken by the IDD control programme in Tanzania to combine distribution of OIC as a short-term measure to the most affected areas, followed by USI as a long-term measure, was a commendable initial approach, which no country in Africa has taken with such success [151]. It must be admitted that the vigour of USI has not been 100%, but nevertheless over 80% households in both urban and rural areas had access to iodated salt country-wide. This in turn had contributed to the achievement of an 80% reduction in goitres in the goitre-endemic areas (**Papers I&III**). China is one example among the few countries in the world that has used this approach of combined interventions, and by 1995 had succeeded in achieving the same 80% coverage of iodated salt at household level along with an 80% goitre reduction in the same way as was achieved in Tanzania in 2004 [200].

Increased goitre prevalence in the Island – a new environmental phenomenon?

Our findings of moderate to severe iodine deficiency in Unguja and Pemba Islands, respectively (**Paper II**) were unexpected as it contradicted the old idea that island populations are protected from IDD. But in fact, these findings and those from other island populations (The Maldives, Fiji and Canary islands [196, 201, 202]) have shown that island populations are not fully protected from IDD. The high endemicity of goitre reported in these Islands and elsewhere [196, 201] indicates that marine foods are not enough to protect the people living on the islands, as was previously assumed [2]. Poverty also makes most of the people unable to afford adequate marine food products often, which might otherwise have satisfied their daily iodine requirement [186, 203]. Environmental degradation and high rainfall may also have contributed to producing iodine-deficient soil, and hence food grown on it will remain iodine-deficient indefinitely [2].

Effect of stalled iodated salt coverage on impact indicators

There has been an significant inverse correlation in the trend regarding the findings of the process and impact indicators in severely goitre affected districts (**Figure 19)**. The findings were similar to reports from elsewhere of the relationship between measures of urinary iodine concentration and thyroid volume [204, 205]. However, the observed decline in median UIC in the later stages towards the optimal range may be due to efforts taken to re-address the quality control measures for salt iodation at medium and large production scales in the period of 2000- 2004 following the findings reported in **Paper I**. In the 5 years to come, if the iodated salt coverage in households is maintained within the range 80- 90%, goitre prevalence rates will no longer be a public health problem of any significance in all age-groups.

8.5 Sustaining IDD elimination

For sustainable control of iodine deficiency disorders, the appropriate iodine fortification recommended that should reach the entire population is through salt iodation [11]. WHO, UNICEF and ICCIDD had been facilitating the implementation of salt fortification by working with scientists, governments and the the private sector to reach a decision on the standard machines for salt iodation that will deliver the recommended iodation levels [11], i.e. that could be applied in Tanzania. However, the technology suggested by these high policy level decisions functioned well in some countries but did not last long in other low-income countries like Tanzania.

Papers I-IV report a high variability in iodine content in both salt and urine samples, showing that under and over intake of iodine co-exist, thus making the intervention programme more complex than before. One among the major contributing factors for the iodine differences was the avoidance by the salt producers of the standard salt iodation and mixing machines, which was previously not reported to the programme [178] (**Paper IV)**.

Another factor, apart from abandoning of the standard iodation machines, was the large number of small-scale salt producers operating in the informal sector that were not included in the USI efforts [155]. The salt produced by small-scale producers was usually consumed locally and did not enter the formal market system. Salt from small-scale salt producers reaches households by either *'bartering'* or through sales of salt from *'house to house'* at very low convenience prices. Such trade easily escapes salt monitoring authorities. It is estimated that over 13 million people may have access to foothill salt, which is just one type of salt produced by traditional dealers in the basements of the Central and Western arms of Rift valley [155].

Adopting local salt iodation technology as temporary measure

The approach taken by the IDD Control programme to undertake a study to improve on the effectiveness of self-initiated local salt iodation and mixing technologies by the salt producers was a major step towards sustaining elimination of IDD in Tanzania. The study successfully produced adequate and homogenous iodine levels according to recommended iodine levels [122]. Previously, the government regarded the local methods for iodation and mixing of salt as inappropriate (*TFNC Internal reports*). Indirectly, our data suggest that these methods had already contributed to the decrease of IDD, but the iodine concentration in the salt was not sufficiently homogenous due to the lack of quality control (**Papers I-IV**).

Working with the salt producers and sharing their understanding of salt iodation procedures to modify finally their own methods to deliver the correct iodine levels is a shift in policy. This could signal a starting-point for a renewed partnership with private enterprise – and also small-scale salt producers – taking a lead in tackling public health problems. Cooperation from the salt industry in maintaining quality control is possible when there is a good dialogue from the government side. The most important handicap has been the slow development of an efficient monitoring system for the national programme. This has also been observed by ICCIDD in other IDD country programmes [206].

The qualitative findings in **Paper V** indicated that *'the iodation procedure was carried out by inexperienced personnel with minimum knowledge on salt iodation and rationale for salt iodation'*. Salt workers in the factories and in the small-scale salt production sites in Tanzania are very transient and simply work to earn a daily pay. However, many of the salt factory owners and managers had been trained earlier to train the factory workers, and were expected to continue educating any new workers on the rationale for salt iodation and procedures for iodation. This is where more effort is needed to ensure adequately iodated salt is produced by properly trained personnel.

The registered salt producers/traders are granted a licence on the condition that they produce or import iodated salt, where it is meant for human and animals consumption [150]. Good salt producing practices with proper monitoring and enforcement in place, the iodation using improved locally standardised technologies can assist the programme in sustaining the IDD elimination in Tanzania, while better iodation technology, which is cheap and affordable, is sought.

Strategies to attain >90% coverage of quality iodate salt

1) Training salt producers on salt iodation

Training salt producers on this modified local technology and assessing the wider outcome performance of the method under close supervision is required. For instance, a DVD training video could be prepared and copies supplied to salt factories/sites and on the internet, to show workers regularly. The training should be accompanied by free supplies for the initial trials as an incentive for small-scale salt producers, with special emphasis to the salt producers to make replacement at their own costs when such capital supplies (equipments and chemicals) run out of stock. The global goal of >90% of households using iodated salt cannot be reached without the contribution of medium and small-scale salt producers.

2) Emphasis on salt iodation quality control

A manual for standard operating procedures (SOPs) for salt iodation and iodine testing needs to be developed, with small adaptations to fit each scale of salt producers and their needs for reference. It should also be in *Kiswahili* language, and preferably supplied in DVD form, and where possible on the internet. Quality control of iodine levels is the second major challenge after sustainability of iodation supplies. According to previous experience, not all salt producers had adhered to the standard operating procedures. In most cases they were given it verbally or in English manuals to large/medium salt producers, where only a few workers could remember the instructions or understand the language.

3) Revive sentinel/satellite iodine laboratories

Apart from using test kits, mini-laboratories for carrying out salt titration to determine iodine content levels are important in maintaining optimal iodine intake requirements. Field evaluation of iodine levels at factories, retailers, wholesalers and households has not been done on a regular basis, which is the next major challenge in achieving sustainable IDD elimination [207]. Simple portable iodine monitors can be used at satellite iodine laboratories for this purpose, stationed at district or regional level to easy provision of advice, and taking legal action to salt manufactures/traders who are not complying with the salt regulations.

The laboratories will be managed by TASPA branch offices and local government at the district level, with technical support provided by the national institutions responsible, i.e. TFDA, TBS, TFNC and Madini Laboratories (under MEM). The use of these mini-laboratories will be enhanced under the influence of law enforcement that indirectly requires salt producers (large, medium and group of small-scales) to have data on iodine levels of different batches of salt produced or sold. Compulsory monthly online reporting for each licensed producer is one way to overcome the logistic hurdles.

4) Regular monitoring of salt and urinary iodine

There is need to carry out regular surveillance to obtain data on the progress made regarding iodine intake and status. Lack of regular data is one of the weaknesses outlined in the WHO progress of programmatic indicators for Tanzania (**Table 8**). The use of school children is an effective means of getting data for both salt and urinary iodine as process and impact indicators, respectively [5]. It is also means of creating awareness among the communities on the importance of using iodated salt, i.e. once the children are sensitized during salt testing from households. This will then create demand of iodated salt at the consumer level, thereby increasing the coverage of iodated salt at retails shops and in households.

Mandatory salt iodation with surveillance in place to track the trend of iodine nutrition intake has been successful in many countries [5, 208, 209]. Where there is no mandatory salt iodization, as in the US, but iodized salt at 45-80 µg of iodine per gram of salt, decline has been reported in median urinary iodine excretion of adults from 320 µg/L in the early 1970s to 145 µg/L in 1988 -1994, and later on it was 168 µg/L in 2001-2002, suggesting marginal iodine intake [210-212].

5) Use of popular media
Promote consumption of iodated salt using popular media like songs, music, drama and educative radio programmes applied more often to reflect the importance of consuming iodated salt. This will contribute to creating a grater public demand for iodated salt.

8.6 Suggested protocol for the next national IDD survey

Based on the observations in this thesis, we suggest the future protocol for the national surveys should focus on the following four major areas to assess the fulfilment of the requirements of the organisational programme system capacity and that of the programmatic indicators for sustainable IDD elimination:

At the national programme implementation level – assess the adequacy of the organisational system that coordinates IDD control programme activities, the awareness and political commitment of the government in supporting the programme to attain sustainability, the programme monitoring system encompassing quality control, enforcement, and information flow, and its use for programme implementation and sustainability. There might also be a need to assess the cost effectiveness of implementing the national IDD control programme against the achievements realised.

At the salt production level – Assess the quality assurance system (including internal and external quality controls covering the quality of salt produced), the adequacy of iodation methods, iodine testing data and its use, the manpower and skills for salt iodation and handling, the frequency of supportive supervisions and its effects (by assessing the proportion of factories adequately iodating salt).

At the distribution level – assess monitoring system at local government level and responsibilities, the current status of districts in supporting the IDD control programme, the existence of external quality control, and the awareness of salt distributors on the rationale for trading of iodated salt, the coverage of shops selling iodated salt, and the adequacy of iodine levels reaching the community.

At the consumer level – assess consumer awareness of importance of consuming iodated salt, the coverage of households consuming iodated salt ≥15ppm iodine through school surveys as previously done. A nationwide survey of iodated salt coverage and urinary iodine, taking representative samples from each district, is required. Convenience sampling of urine from pregnant and lactating women also needs to be collected from the MCH clinics in the nearby Health Centres of selected schools, or by incorporating the susceptible groups into the national demographic health surveys.

The obtained data will enable the national programme to identify weak areas and make the appropriate corrections. At the same time, districts will be able to use the data to address IDD through integration with the comprehensive health plans. The data at the higher levels could also be used to correct weaknesses at the levels of national programme management and salt production factories.

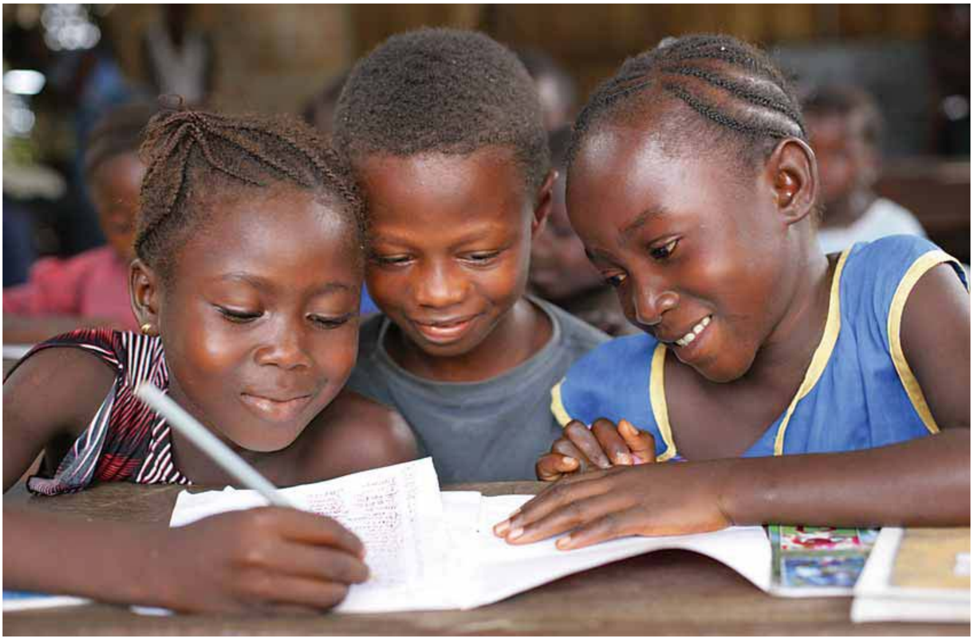


Figure 21: Children who are eager to learn in school are likely to make a more powerfully developed nation if protected from brain damage

8.7 Impact of IDD interventions on socio-economic development in Tanzania

The United Nations has agreed that elimination of iodine deficiency may contribute towards the achievement of a majority of the MDGs [180]. Not much is known about the impact of the IDD interventions applied in Tanzania on terms of socio-economic development. One area that can be used as a starting point of assessment is the intervention's impact on the population by considering the performances of children in schools, which is one aspect of socio-economic development. A number of factors may have contributed to any of the positive performances by our school children. However, it is known that iodine deficiency can rob children of an average of 13.5 IQ points, resulting in poor learning ability [2], and in turn lead to lower productivity in adulthood [6].

Studies in China and Iran following the introduction of USI have shown that the IQ score of children has gone up by 15-20% over 12 years! [200, 213, 214]. Furthermore, children born to iodine-supplemented mothers before pregnancy have higher IQs compared to those born with mothers supplemented after conception [215].

A study in the severely IDD endemic areas in Tanzania showed that reducing fetal IDD has significant benefits for the child's cognition; and protection from IDD *in utero* was associated with 0.36 years of additional schooling [14]. The study concluded that the IOC followed by USI interventions may well have contributed to improved enrolment of school children, especially girls [14]. For a child, IDD is a factor in the economic and social well-being for life. While efforts to sustain elimination of iodine deficiency continues, it will be of interest if future studies could quantify the socio-economic benefits in detail and from them project their future impact on economic development in Tanzania.

9. CONCLUSIONS AND POLICY IMPLICATIONS

These studies demonstrate a huge improvement in the iodine status of the large Tanzanian population, mainly due to the USI. This will have prevented thousands of child deaths in the country and spared millions of school children from loss of IQ points – really a smart thing to do.

USI needs to be made universal throughout the whole country; efforts to enforce the salt law, and monitor the production and sales of iodated salt needs to be stepped up so that every Tanzanian citizen can benefit from this cost-effective and smarter health intervention.

However, the findings in this thesis have brought up a number of implications based on the key findings summarised in **Table 12**.

Table 12: Summary of the key findings in the studies and their implications

Study, key findings and conclusions	Implication(s)
Papers I&III: - Iodine-deficiency is well on its way to be eliminated and is now a mild problem in mainland Tanzania. The challenges for sustaining IDD elimination are now two-fold: - to reach more areas that still have low iodated salt coverage, and - to reduce excessive iodine intake	The national IDD control programme needs to: - take action to increase iodated salt coverage - improve the monitoring of the salt at production and wholesale / retail sales level throughout the country - Perhaps introduce a surveillance system for screening inborns for hypothyroidism and for suspected cases of iodine-induced thyrotoxicosis, including provision of management guidelines.
Paper II: - Moderate iodine deficiency exists in the Zanzibar Islands, but Pemba Island is seriously affected and requires immediate attention. - The findings reported in Zanzibar Islands (supported by studies of similar islands) signal that the population is no longer – if ever – protected from IDD through an iodine- rich seafood diet alone.	- Assumptions should not be made that certain areas such as islands and offshore are free from iodine deficiency disorders, - Health planners need to implement USI as mandatory in all geographical areas. This finding underlines the need for iodine control measures like USI to be exactly that: universal.
Papers I-III: - Vulnerable populations, i.e. pregnant and lactating women and infants, were not sufficiently assessed	- Before declaring elimination of IDD, the national IDD control programme need to assess the impact of USI in targeted surveys of the most vulnerable groups, i.e. pregnant and lactating women, and infants in the country.
Papers I-IV: - The variability of iodine content was very high in both salt and urine samples	- The national IDD control programme in Tanzania needs to: - strengthen the quality control of salt iodation to avoid excessive iodine intake, and - carry out frequent monitoring of salt at production, importation points and at the consumer levels concurrent with effective enforcement of salt regulations, - Similarly health ministries need to review and enact of salt iodation regulations in mainland Tanzania and Zanzibar, respectively.
Paper IV: - The supplied iodation machines have been abandoned and new local devised methods are widely used for salt iodation, which has probably contributed to the reduction of iodine deficiency in Tanzania.	- The USI strategy is failing to protect the population in areas with small-scale salt production. This needs to be acknowledged and dealt with. The studies have demonstrated that local salt iodation and mixing technologies can be improved, thus providing a possible solution to this problem.
Paper V: - Supervised, standardized salt iodation procedures adapted to local circumstances can yield homogeneous iodine levels within the required range.	- International and national organizations need to revisit salt iodation strategies and consider including existing local technologies if and where appropriate, in order to sustain USI in low-income settings with small-scale salt production.

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