# Iodine deficiency
# The problem and the solution

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# Spectrum of IDD

- Fetus: abortion, stillbirth, congenital anomalies, perinatal mortality, endemic cretinism;
- Neonate: goitre, hypothyroidism, mental retardation;
- Child: goitre, (subclinical hypothyroidism), impaired mental function, delayed physical development;
- Adults: goitre with its complications, hypothyroidism, impaired mental function, spontaneous hyperthyroidism, iodine-induced hyperthyroidism

# Copenhagen Consensus 2008

## Costs and benefits of proposals for confronting ten great global challenges

| | |
|---|---|
| 1 Micronutrient supplements for children (vitamin A and zinc) (60) | Malnutrition |
| 2 The Doha development agenda (0) | Trade |
| 3 Micronutrient fortification (iron and salt iodization) (286) | Malnutrition |
| 4 Expanded immunization coverage for children (1,000) | Diseases |
| 5 Biofortification (60) | Malnutrition |
| 6 Deworming and other nutrition programs at school (27) | Malnutrition/Education |
| 7 Lowering the price of schooling (5,400) | Education |
| 8 Increase and improve girls' schooling (6,000) | Women |
| 9 Community-based nutrition promotion (798) | Malnutrition |
| 10 Provide support for women's reproductive role (4,000) | Women |

(Annual cost in million USD)

# Epidemiological criteria for assessing iodine nutrition (WHO, 2007)

| Median urinary iodine | Iodine intake (μg/L) | Iodine nutrition |
|---|---|---|
| From WHO/UNICEF/ICCIDD | | |
| < 20 | Insufficient | Severe iodine deficiency |
| 20-49 | Insufficient | Moderate iodine deficiency |
| 50-99 | Insufficient | Mild iodine deficiency |
| 100-199 | Adequate | Optimal |
| 200-299 | More than adequate | Risk of iodine-induced hyperthyroidism within 5-10 years following introduction of iodized salt in susceptible |
| > 300 | Excessive | Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid diseases) |

# Worldwide iodine nutrition (WHO, 2004)

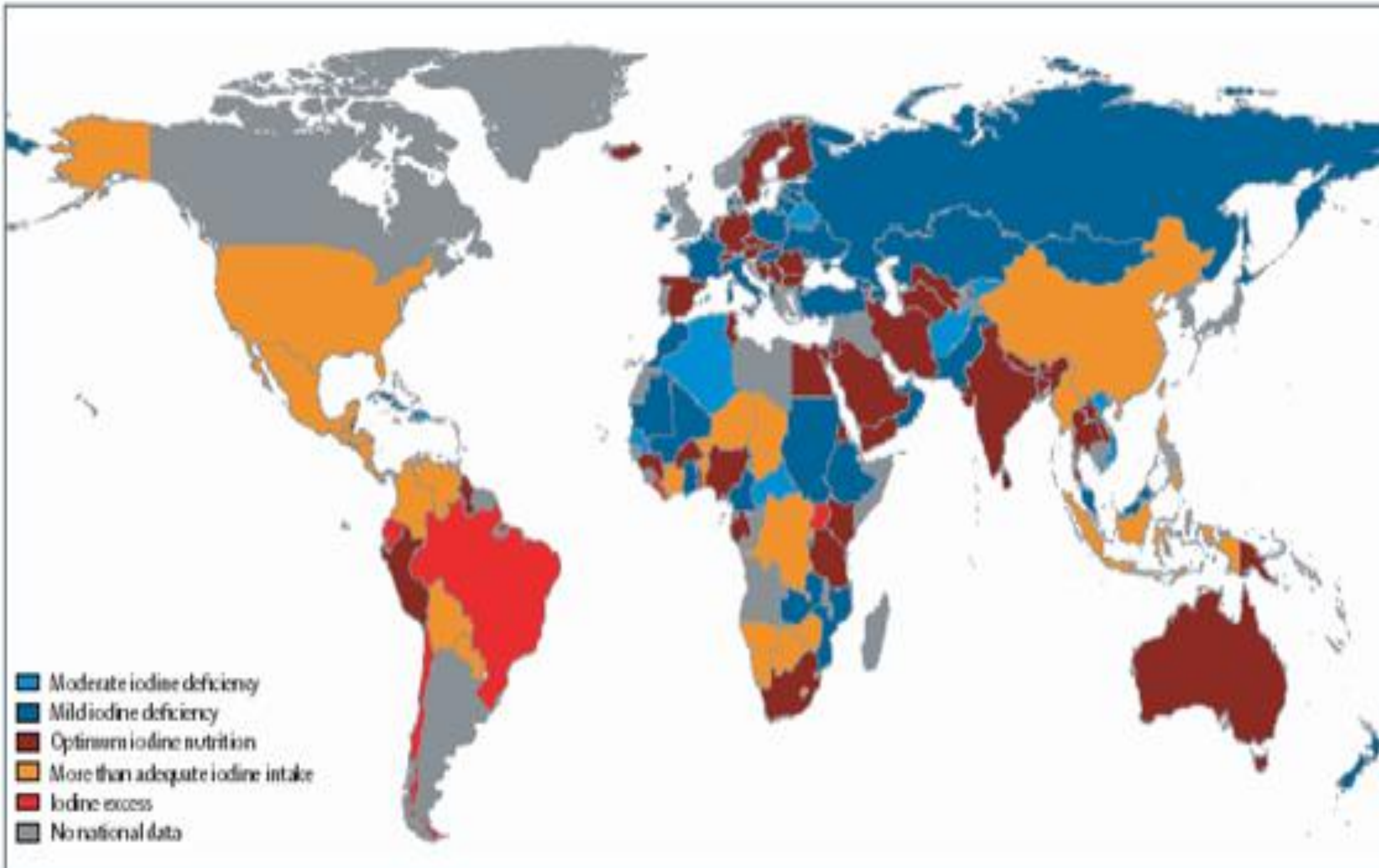
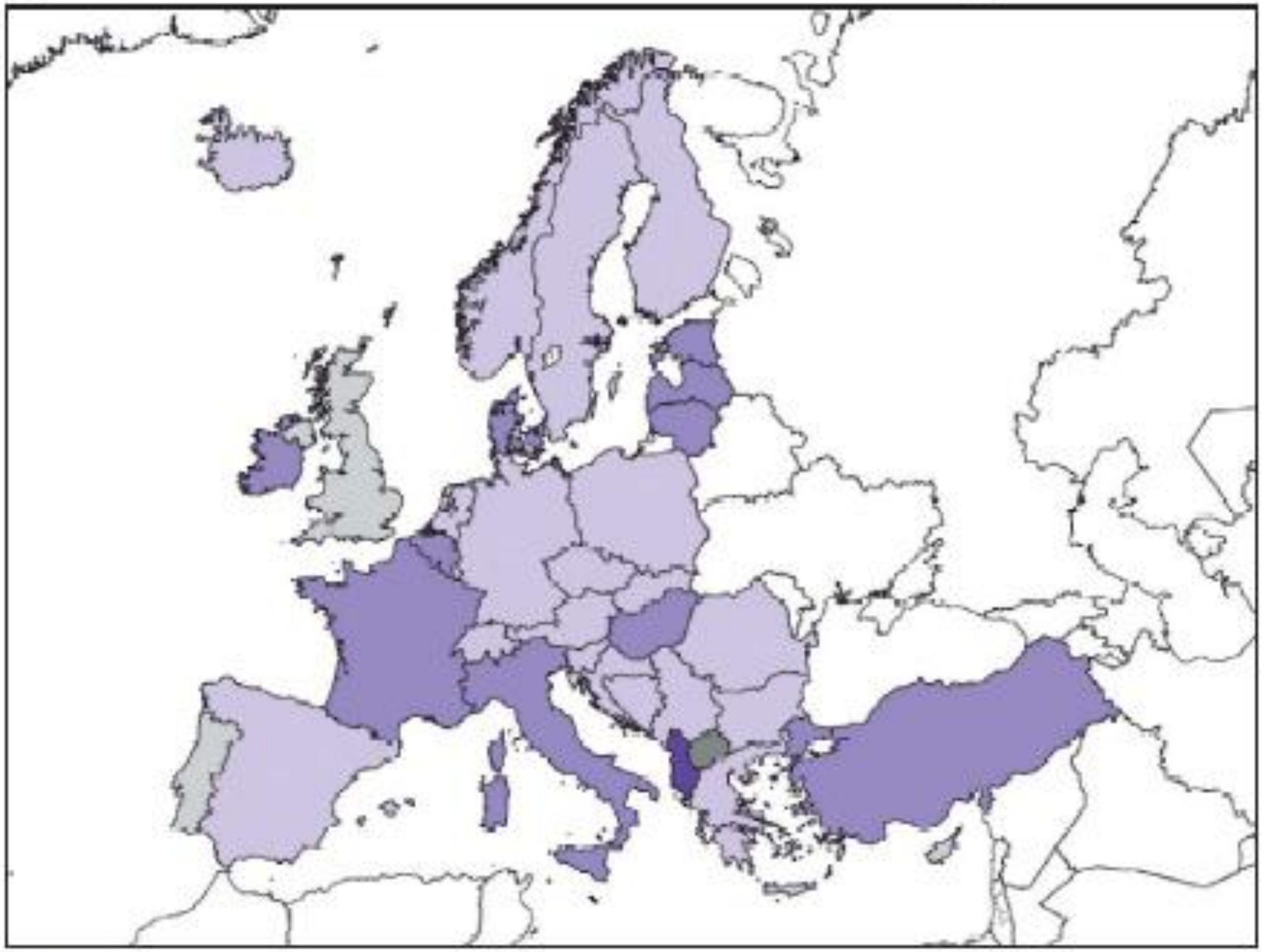


Figure 3.2: **National iodine nutrition based on median UI in Europe**



Moderate iodine deficiency (20-49 µg/l), 1 country

Mild iodine deficiency (50-99 µg/l), 10 countries

Optimal (100-199 µg/l), 20 countries

Risk of iodine-induced hyperthyroidism (200-299 µg/l), 1 country

No data

# UK iodine status – early studies

- 1924: Survey of 375,000 schoolchildren in England and Wales – Visible goitre in 30%
- 1948: MRC survey – Visible goitre in 50% adult women in Oxford, 43% girls in Dorset, 26% of children in St Albans, 2% in Essex
- 1958: Repeat MRC survey – goitre rates increased in girls in Oxford from 27% to 40%
- 1963-66: Surveys of goitre -Sheffield (12% men, 25% women), E Lothian (0.3% men and 4% women), Durham (1% men, 9% women)

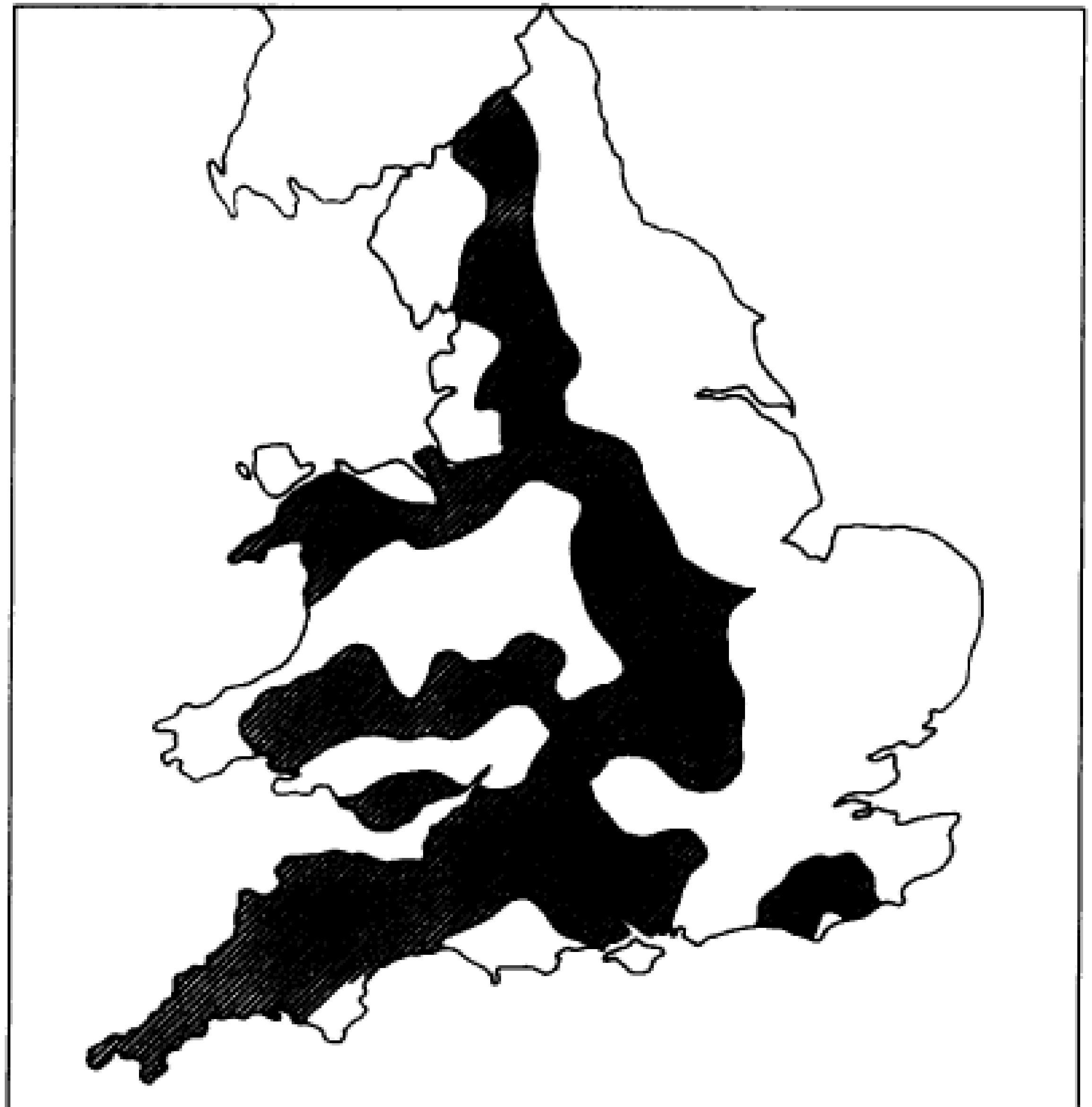


*Figure 1 Areas of England and Wales where endemic goitre has been prevalent in the past.*[24].

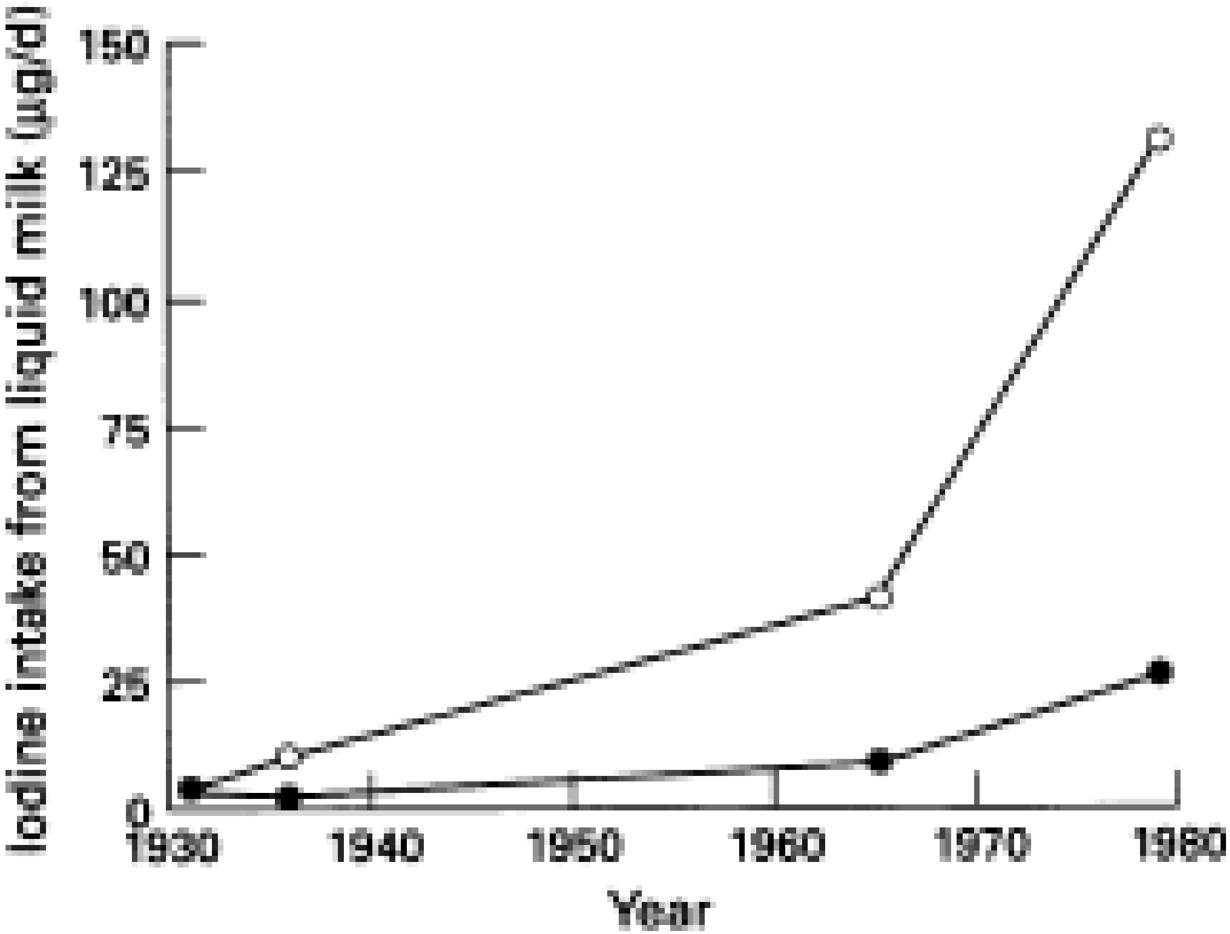
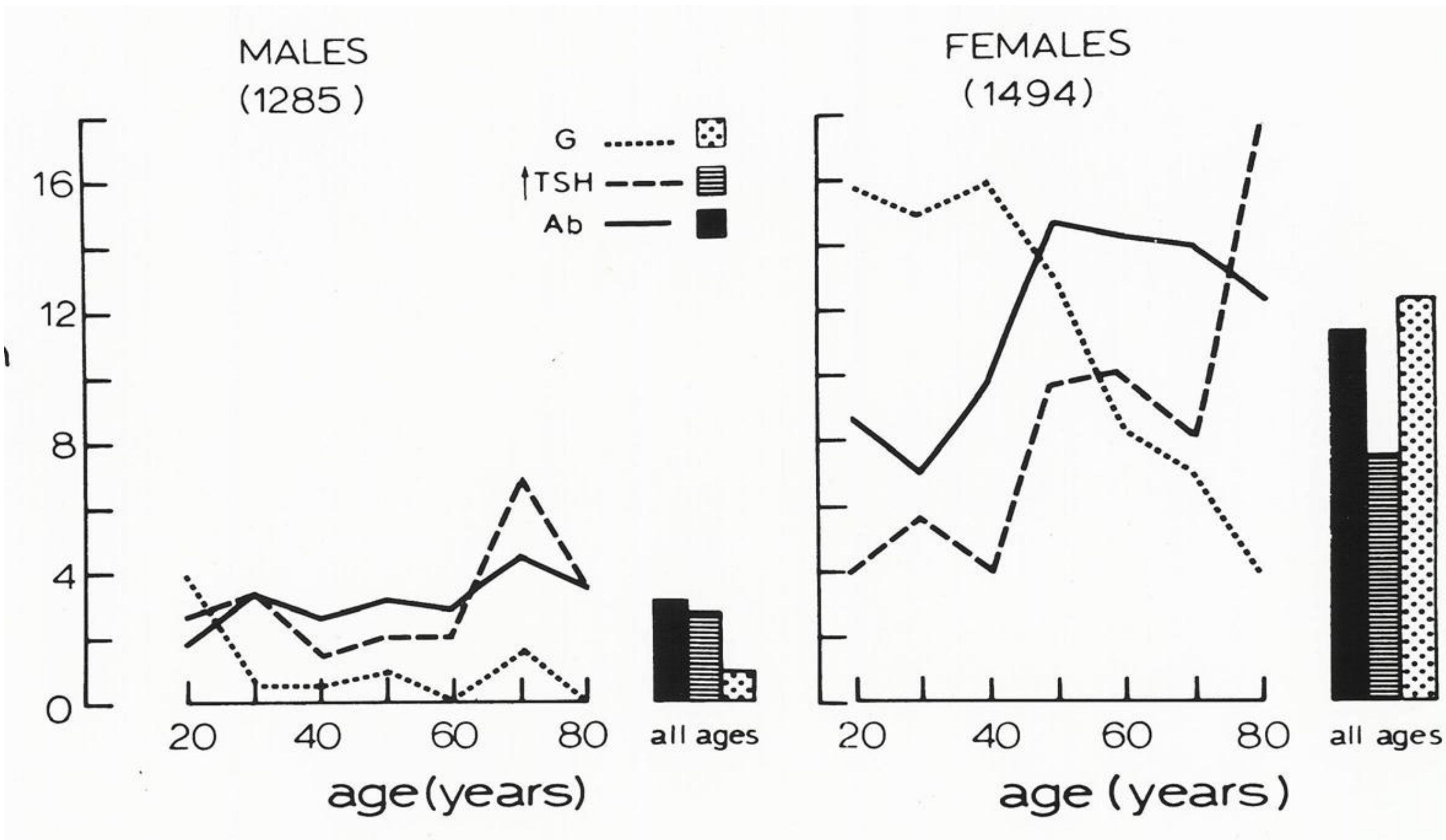



*Figure 2 Average daily iodine intake from milk in the UK based on surveys of milk intake* [14,24] *and the iodine content of milk* [13,22,23] *between 1931 and 1980. Closed circles represent Summer samples and open circles Winter samples.*

# “Accidental public health triumph”

- Changes in UK farming practice from 1940s with iodine-rich artificial feeds/disinfectants
- Rise in iodine content of milk especially in winter months
- UK governments post WWII encouraged compulsory milk consumption in schools
- Iodine content of milk alone sufficient to meet recommended daily requirement 150µg

# Whickham survey 1972-1974



# Whickham survey follow-up 1992-1994

- At 20-year follow-up 10% of women and 2% of men had goitre cf 23% and 5% at 1$^{st}$ survey
- Goitre not predictive of any clinical or biochemical evidence of thyroid dysfunction
- Weak association between goitre and thyroid antibody status in women at follow-up but not at 1$^{st}$ survey suggesting autoimmune aetiology
- Median urine iodine for random sample of 101 subjects aged over 38 years was 102µg/g creatinine (44-990)

# UK iodine status – recent studies

- 1990: Thyroid enlargement no longer detectable in schoolchildren in South Wales
- 1994: Median UIC 102μg/g at Whickham follow-up
- National monitoring to avoid concerns re iodine toxicity
- 2002-2009: up to 50% of pregnant women in small surveys (Middlesbrough, Dundee, Cardiff, Guildford) iodine deficient (median UI 66μg/L)
- 2006: Iodine deficiency noted in pregnant women in Ireland especially in summer months
- 2007: Survey of 36 household salt preparations in supermarkets for iodine – sufficient in only 2

# UK iodine status
# A national survey

British Thyroid Association

British Thyroid Foundation

Generously supported by

Clinical Endocrinology Trust

# Methods

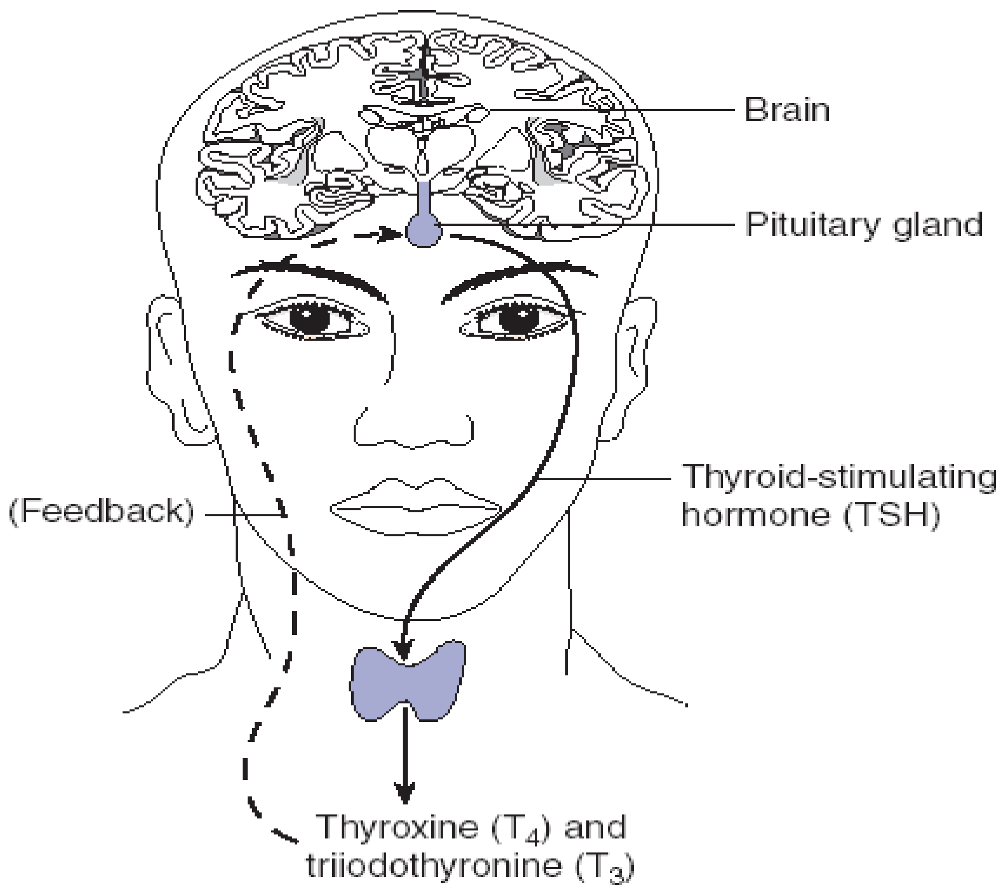
- 810 schoolgirls aged 14-15 recruited from 9 UK centres sampled in Summer and Winter 2009
- Sample size sufficient to estimate UI within 10µg/L
- UI measured using the ammonium persulphate digestion microplate method (Dublin)
- Spot urine sample 20mls
- Tap water iodine concentration from each centre
- Information on ethnicity, postcode, brief dietary questionnaire (milk, cheese, yoghurt, meat, eggs and fish products)


Aberdeen
Dundee
Glasgow
Newcastle/
Gateshead
Belfast
Sheffield
Birmingham
Cardiff
London
Exeter

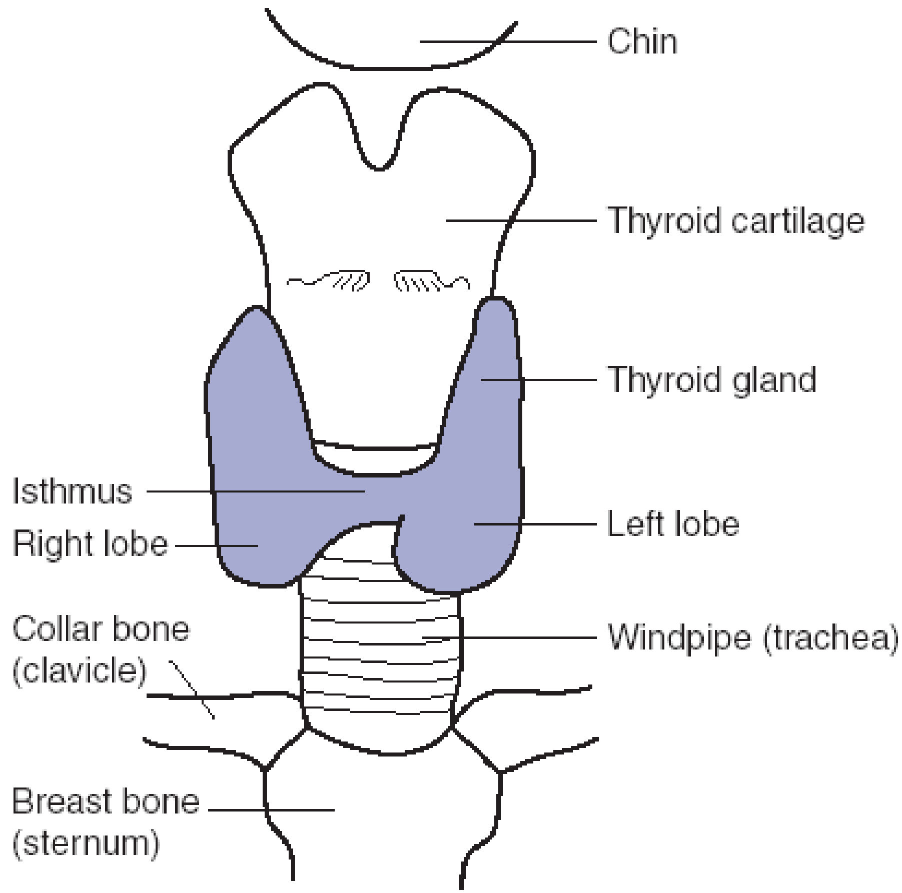
# Iodine

- An important element in the manufacture of thyroid hormones
- Most iodine is present in sea water which evaporates and returns to the soil in rain
- Low iodine levels are common in mountainous regions far away from the sea
- The major source is bread and milk

# Thyroid hormones

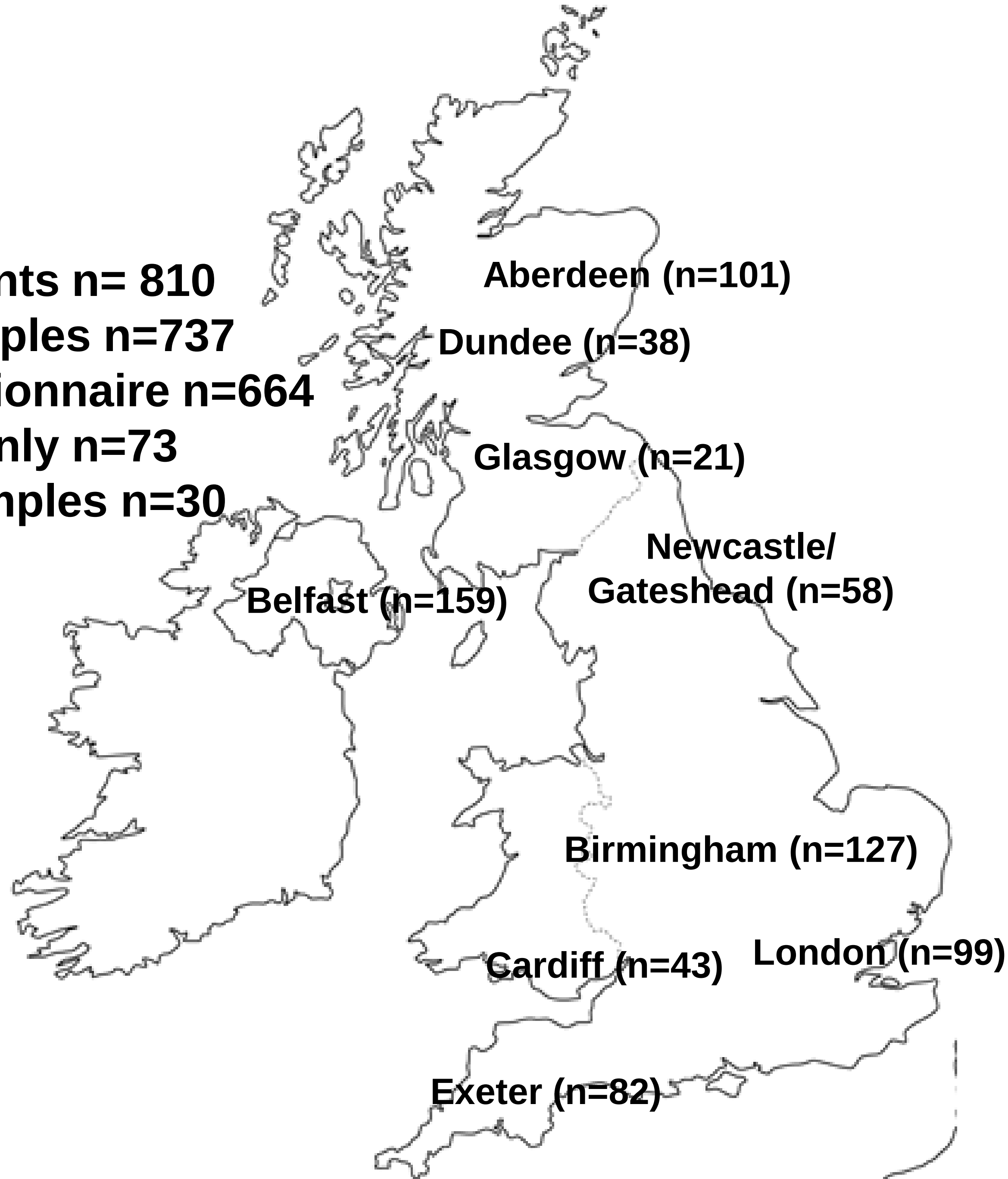


# The thyroid gland

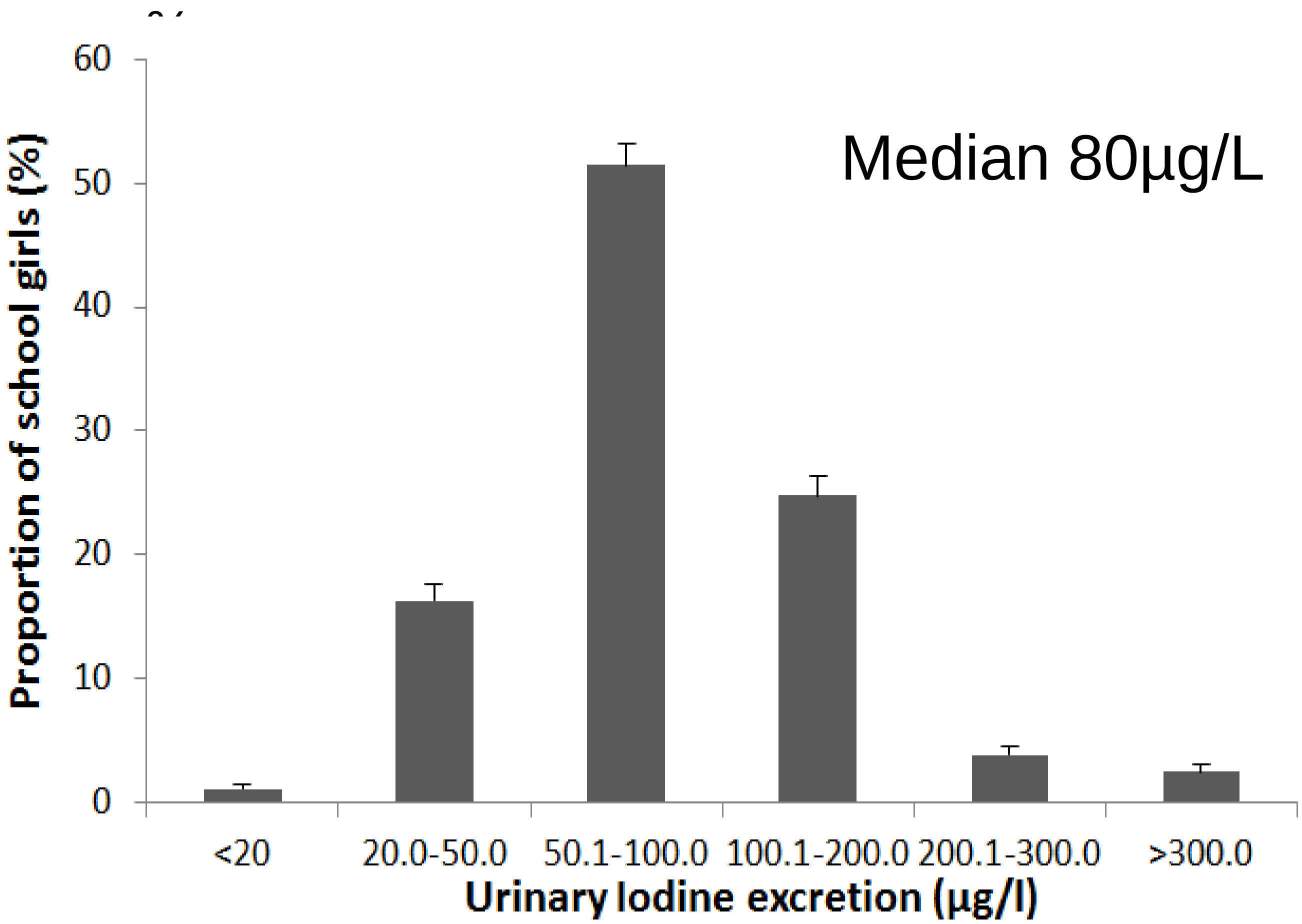



"YOUR COUNTRY NEEDS
YOU"

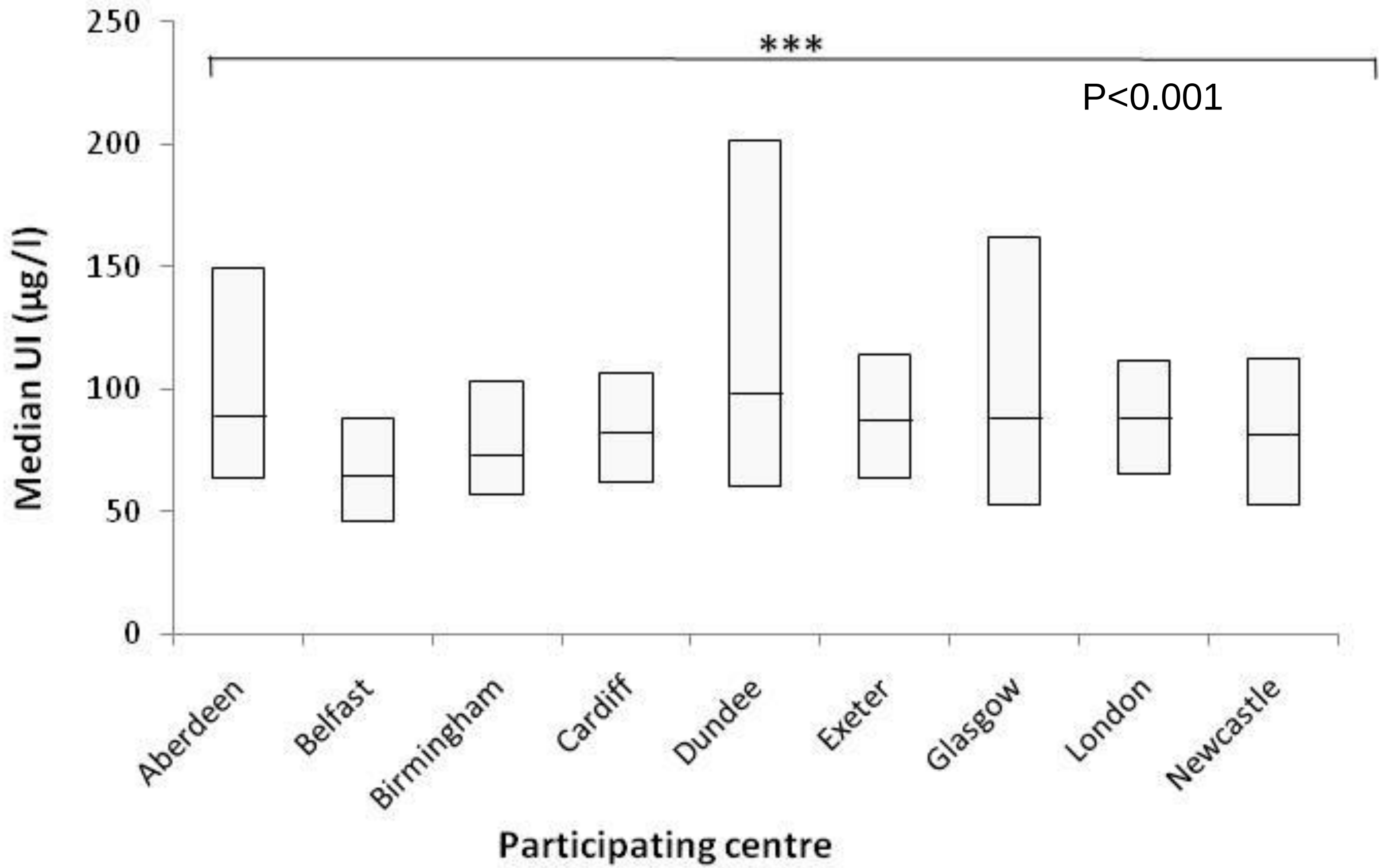
**Participants n= 810**
**Urine samples n=737**
**Urine + questionnaire n=664**
**Urine only n=73**
**Water samples n=30**



# UI concentrations in UK schoolgirls (n=737)



# Box plots of median UI for various participating centres



# % UK schoolgirls with iodine deficiency by centre

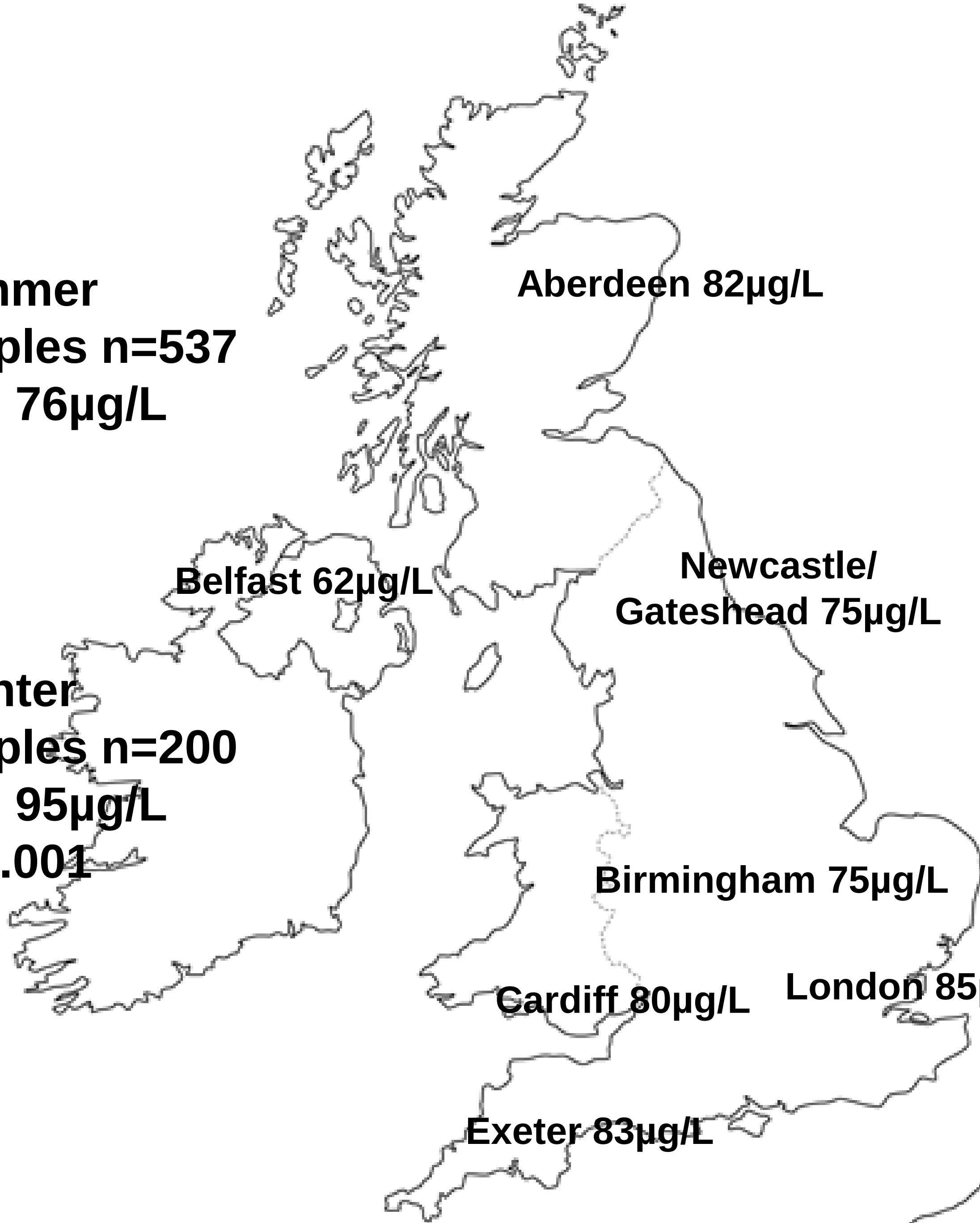
| Centre | Number of participants | % of participants with iodine deficiency (UI < 100 µg/l) | % of participants with mild iodine deficiency (UI 50-100 µg/l) | % of participants with moderate-severe iodine deficiency (UI < 50 µg/l) |
|---|---|---|---|---|
| Aberdeen | 110 | 59% | 49% | 10% |
| Belfast | 159 | 85% | 54% | 31%*** |
| Birmingham | 127 | 72% | 55% | 17% |
| Cardiff | 43 | 67% | 56% | 12% |
| Dundee | 38 | 53% | 40% | 13% |
| Exeter | 82 | 65% | 65% | 12% |
| Glasgow | 21 | 52% | 38% | 14% |
| London | 99 | 66% | 56% | 10% |
| Newcastle/Gateshead | 58 | 64% | 41% | 22% |
| **All Centres** | **737** | **69%** | **51%** | **17%** |

# Likelihood of iodine deficiency in Belfast vs. other centres

| Participating Centre | Likelihood of iodine deficiency (UI<100 µg/l) (AOR [95% CI], p-value) | Likelihood of mild iodine deficiency (UI 50-100 µg/l) (AOR [95% CI], p-value) | Likelihood of moderate/severe iodine deficiency (UI<50 µg/l) (AOR [95% CI], p-value) |
|---|---|---|---|
| Belfast | 1.0 | 1.0 | 1.0 |
| Aberdeen | **0.26 [0.14-0.84], p<0.001** | 0.82 [0.50-1.33], p=NS | **0.25 [0.12-0.51], p<0.001** |
| Birmingham | **0.47 [0.26-0.84], p=0.01** | 1.04 [0.65-1.67], p=NS | **0.47 [0.27-0.83], p=0.009** |
| Cardiff | **0.37 [0.17-0.80], p=0.01** | 1.07 [0.54-2.11], p=NS | **0.30 [0.11-0.80], p=0.02** |
| Dundee | **0.20 [0.09-0.43], p<0.001** | 0.55 [0.27-1.14], p=NS | **0.34 [0.13-0.92], p=0.03** |
| Exeter | **0.32 [0.17-0.61], p<0.001** | 0.94 [0.55-1.60], p=NS | **0.31 [0.15-0.65], p=0.03** |
| Glasgow | **0.20 [0.07-0.51], p=0.001** | 0.52 [0.21-1.33], p=NS | 0.37 [0.11-1.33], p=NS |
| London | **0.34 [0.19-0.62], p<0.001** | 1.06 [0.64-1.76], p=NS | **0.25 [0.12-0.53], p<0.001** |
| Newcastle/ Gateshead | **0.31 [0.16-0.62], p=0.001** | 0.60 [0.33-1.10], p=NS | 0.65 [0.32-1.31], p=NS |

**Summer**
**urine samples n=537**
**Median 76µg/L**

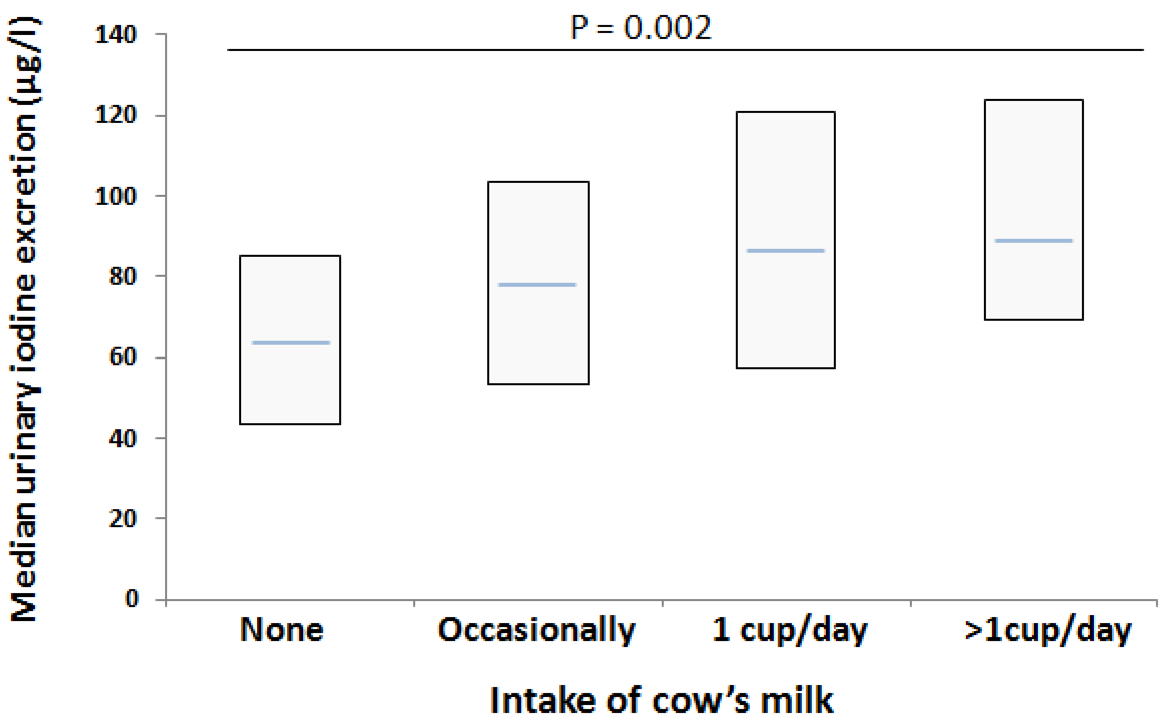
**Winter**
**urine samples n=200**
**Median 95µg/L**
**P<0.001**



# UI according to dietary habits

| Dietary habit | No of participants | Median UI conc ± IQR (µg/l) | P-value |
|---|---|---|---|
| Cow's milk | 660 | | |
| None | 54 (8.2%) | 61.95 [43.50-85.00] | |
| Occasionally | 254 (38.5%) | 76.60 [53.26-103.45] | **0.002** |
| 1 cup/day | 244 (37.0%) | 84.95 [57.55-120.85] | |
| ≥ 2 cups /day | 108 (16.4%) | 87.56 [69.10-123.65] | |
| Yoghurt | 659 | | |
| None | 149 (22.6%) | 74.60 [50.60-104.55] | |
| 1 pot /week | 305 (46.3%) | 83.70 [58.35-117.45] | 0.08 |
| >1 pot/week | 205 (31.1%) | 78.20 [57.95-108.05] | |
| Cheese | 661 | | |
| None | 97 (14.7%) | 81.40 [54.25-120.20] | 0.31 |
| once/week | 287 (44.9%) | 83.20 [58.90-115.78] | |
| >once/week | 277 (41.9%) | 75.80 [55.45-103.60] | |
| Beef | 661 | | |
| None | 144 (21.8%) | 85.50[58.68-111.08] | |
| once/week | 288 (43.6%) | 80.09 [55.90-118.90] | 0.76 |
| >once/week | 229 (34.6%) | 78.20[54.95-106.65] | |
| Chicken | 661 | | |
| None | 51 (7.7%) | 73.20 [50.60-112.70] | |
| once/week | 252 (38.1%) | 81.30 [56.90-107.13] | 0.74 |
| >once/week | 358 (54.3%) | 78.69 [56.30-111.41] | |
| Eggs | 660 | | |
| None | 176 (26.7%) | 83.80 [57.70-132.05] | |
| once/week | 394 (59.7%) | 78.10 [55.65-107.40] | 0.21 |
| >once/week | 90 (13.6%) | 71.00 [52.66-101.11] | |
| Fish | 660 | | |
| None | 235 (35.6%) | 83.30 [57.80-118.00] | |
| once/week | 362 (54.9%) | 76.60 [56.90-107.53] | 0.58 |
| >once/week | 63 (9.6%) | 85.20 [45.60-110.90] | |

# Milk intake



P = 0.002
140
120
100
80
60
40
20
0
Median urinary iodine excretion (µg/l)
None
Occasionally
1 cup/day
>1cup/day
Intake of cow's milk

# Multivariate analyses

- General linear model
- Performed following logarithmic transformation after exclusion of 5 highest and lowest UI measurement to ensure normal distribution
- Season of sampling (summer v winter)
- Dietary habits (intake of milk, yoghurt, cheese, eggs, beef, chicken and fish)
- Ethnicity
- City of origin
- Tap water iodine concentrations

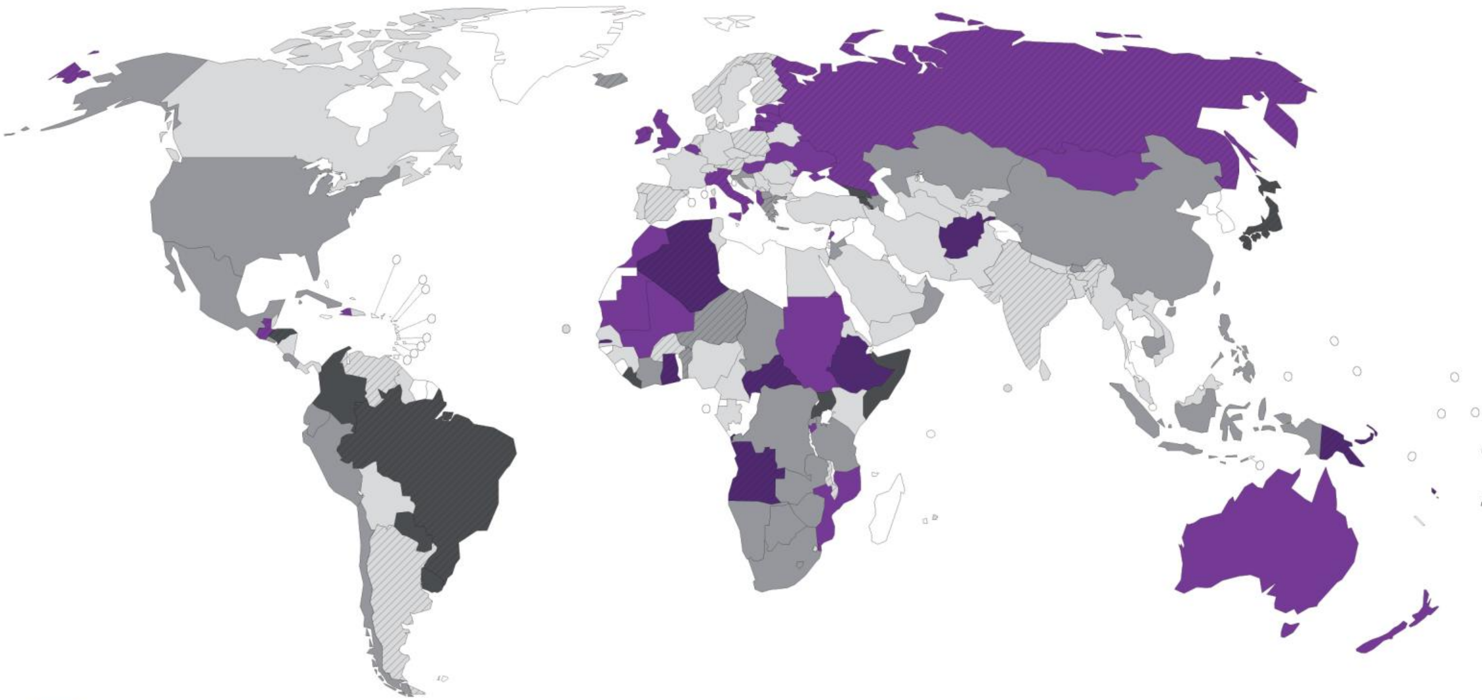
# Multivariate analyses: Results

- $R^2$ value for overall analyses 11.9%
- Sampling during summer vs. winter $p<0.001$
- Geographical location Belfast vs. others $p<0.001$
- Lower intake of milk $p=0.03$
- No association between milk intake and season
- Higher intake of eggs $p=0.02$
- During winter UI excretion higher in those who did not eat eggs
- No association with tap water iodine, ethnicity or other dietary habits

# Summary

- Median UI 80µg/L in total sample
- 51% 50-100µg/L, 16% 20-50µg/L, 1% <20µg/L
- Median UI levels significantly lower in Belfast (65µg/L) with 85% 50-100µg/L and 31% <50µg/L
- Influence of summer sampling (median UI 76µg/L) v winter (median UI 95µg/L ($p<0.001$))
- Independent association with lower milk intake ($p=0.03$) and higher egg intake ($p=0.02$)
- No positive correlation with tap water levels
- No correlation between UI and ethnicity

# National iodine status based on UI in schoolchildren (WHO, 2011)



- Moderate iodine deficiency (UIC 20-49 μg/L)
- Mild iodine deficiency (UIC 50-49 μg/L)
- Optimal iodine nutrition (UIC 100-199 μg/L)
- Risk of iodine induced hyperthyroidism (UIC 200-299 μg/L)
- Risk of adverse health consequences (UIC > 300 μg/L)
- Subnational data [a]
- No data

[a] The country estimates in the cross-hatched countries are based on subnational data. The national coverage of iodized salt in these countries is incomplete, there are large variations in the iodine intake and some regions likely remain deficient.

**Source**: Andersson M, Karumbunathan V, Zimmermann MB. Global iodine status in 2011 and trends over the past decade. J Nutr. 2012 Feb 29. [Epub ahead of print]

**Figure 1:** Proportion (%) of school-aged children at risk for mild, moderate and severe iodine deficiency, by WHO region, 2011.

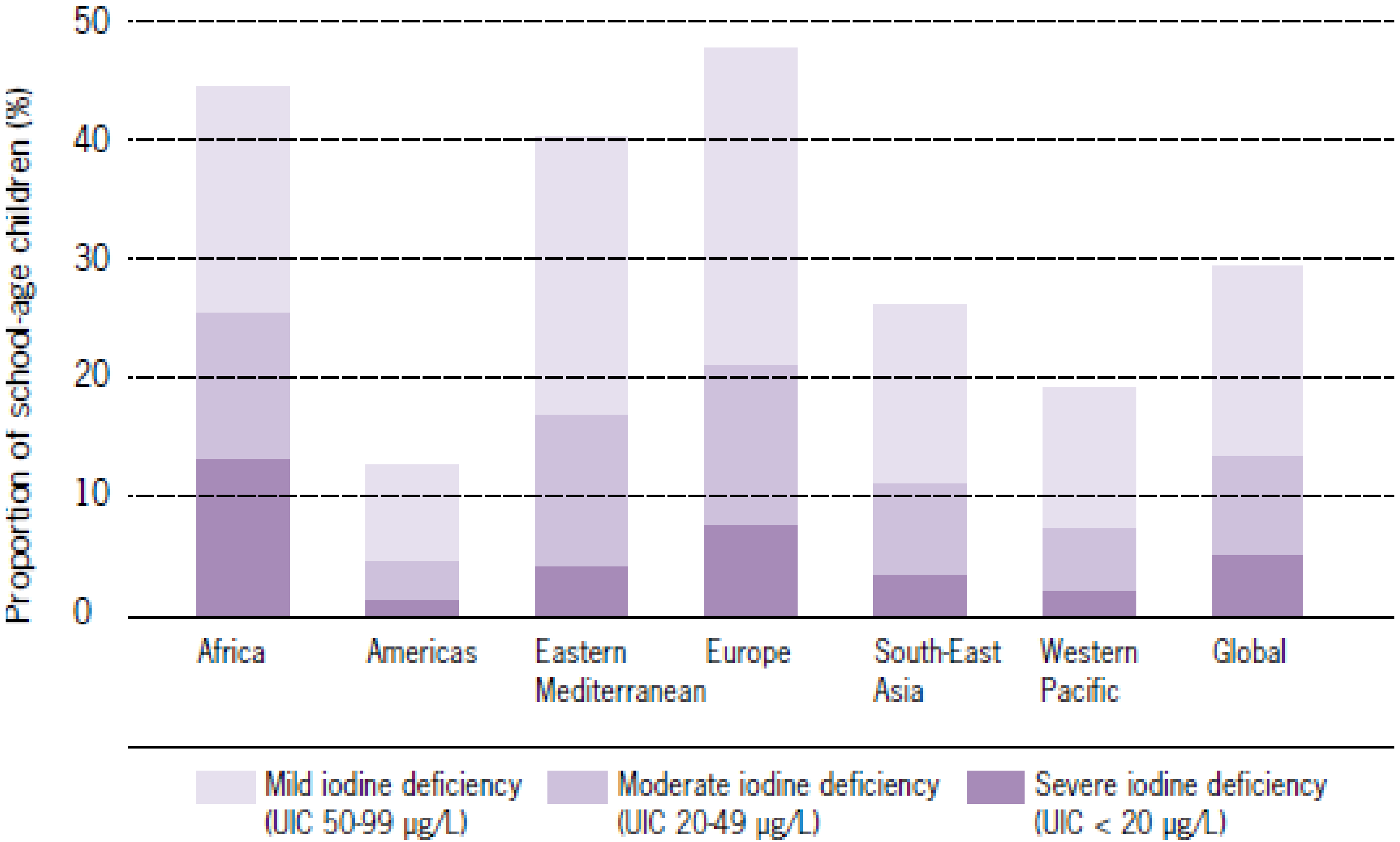
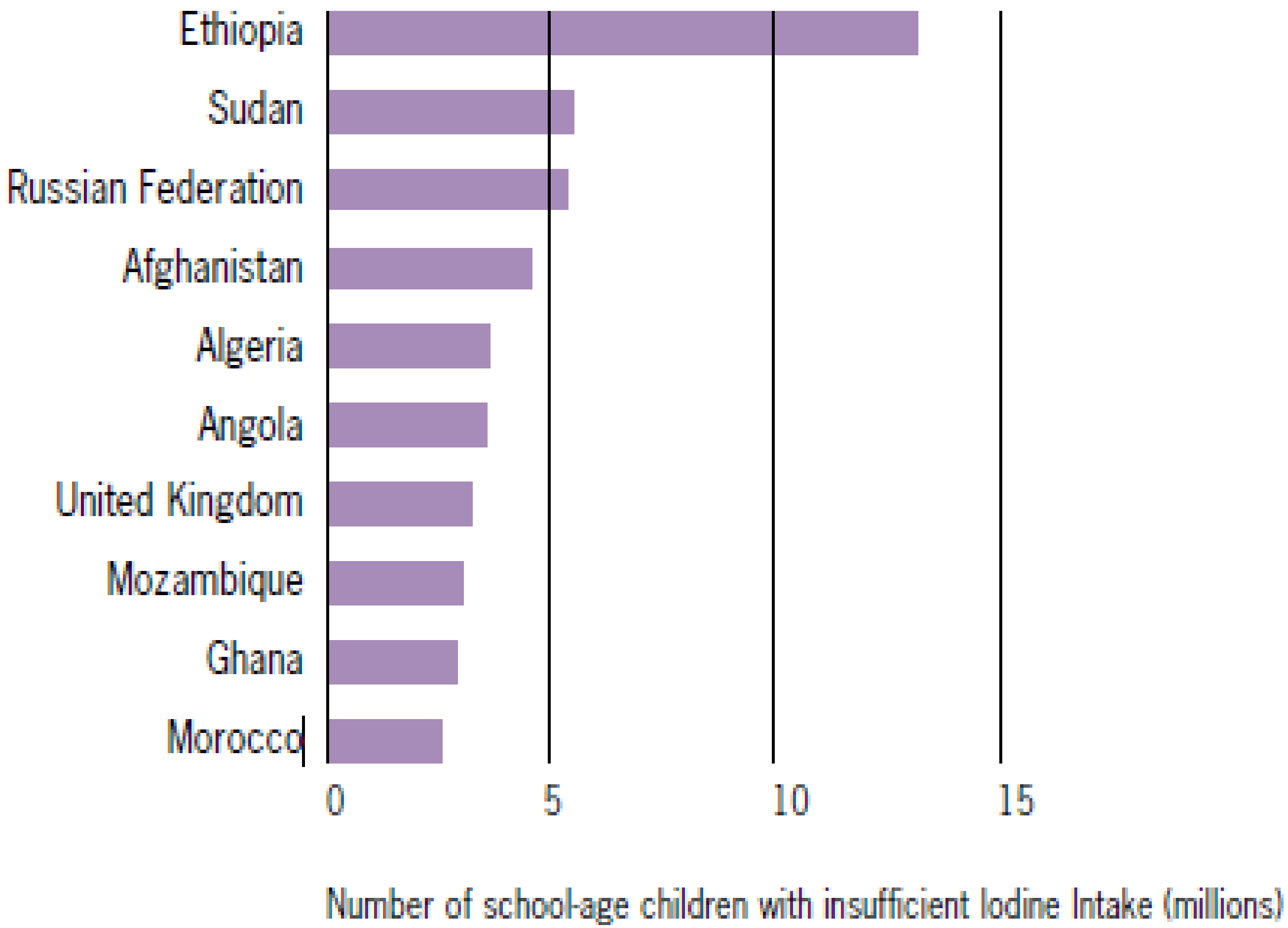


**Figure 2:** The top ten iodine-deficient countries (based on national median UIC <100 µg/L) with the greatest numbers of school-age children with insufficient iodine intake in 2011.



# Impact of mild-moderate iodine deficiency

- Hypothyroxinaemia rather than raised TSH
- Maternal T4 crucial before 13 weeks gestation
- Children born to women may have psycho-neurological deficits and delayed mental function compared with controls
- Randomised placebo-controlled trial in 184 children aged 10-13 in NZ (UIC 63µg/L) – iodine supplementation (150µg daily) for 28 weeks improved perceptual reasoning

# Current issues in UK

- Strong public health objective to lower salt intake to reduce risk of hypertension
- 10% of UK salt intake is added to food at table
- Cow's milk intake up to 50% and although milk iodine stable but evidence consumption falling
- Dialogue with food/salt industries ?feasibility of adding iodised salt to processed foods
- Are data required to provide reassurance at population level?

# Fear of correcting iodine deficiency

- Mild iodine deficiency associated with decreased risk of hypothyroidism/AIT and increased risk of non-toxic nodular goitre
- Sudden increase in iodine supply may enhance thyroid autoimmunity, hypothyroidism in those with damaged glands and hyperthyroidism in those with underlying nodular disease/Graves' disease
- Unlikely if deficiency not severe and increase relatively small

# Denmark epidemiological studies

- Iodized salt in a mildly deficient population
- Initial voluntary programme not successful
- Mandatory iodine fortification programme of bread salt and household salt in 2000
- Population median UIC increased from

  55-68µg/L to 93-108µg/L
- Positive benefits – goitre prevalence and hyperthyroidism
- Small increases in thyroid antibodies/TSH

# How to correct iodine deficiency?

- WHO recommend that salt iodisation is safe, equitable, self-financing and extremely cost-effective in industrialised country
- Alternative strategy is daily oral potassium iodide supplements for most susceptible groups eg women pre-pregnancy
- Only 50% of pregnancies in UK pre-planned
- Iodine supplementation is required for at least 3 months pre-conception

# Conclusions 1

- UK is mild-moderately iodine deficient
- Association between lower UI with summer sampling, Belfast location and reduced dietary intake of milk
- Similar trend observed in Australia/NZ
- Study focused on young women of child-bearing age as most susceptible group to the adverse effects of iodine deficiency

# Conclusions 2

- Mild perturbations of fetal and maternal thyroid function have impact upon neurodevelopment so these findings are of public health importance
- Need for a comprehensive investigation of the iodine status in the UK population
- Evidence based recommendations to health authorities required on the need to implement a policy of iodine prophylaxis

# The UK Iodine Survey Team

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British Thyroid Foundation

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