

1 **Iodine status in western Kenya: a community-based cross-sectional survey of urinary**
2 **and drinking water iodine concentrations**

3 Michael J Watts^{1*}, Daniel R S Middleton^{1,2}, Andrew Marriott¹, Olivier S Humphrey¹, Elliott
4 Hamilton¹, Valerie McCormack², Diana Menya³, Jessica Farebrother⁵ and Odipo Osano⁴

5 *1 Inorganic Geochemistry, Centre for Environmental Geochemistry, British Geological*
6 *Survey, Nottingham, UK*

7 *2 Section of Environment and Radiation, International Agency for Research on Cancer,*
8 *Lyon, France*

9 *3 School of Public Health, Moi University, Eldoret, Kenya*

10 *4 School of Environmental Sciences, University of Eldoret, Eldoret, Kenya*

11 *5 Human Nutrition Laboratory, ETH Zurich, Switzerland*

12 *Corresponding author Dr Michael J Watts*

13 *Email: mwatts@bgs.ac.uk*

14

15 **Abstract**

16 Spot urinary iodine concentrations (UIC) are presented for 248 individuals from western
17 Kenya with paired drinking water collected between 2016 and 2018. The median UIC was
18 271 $\mu\text{g L}^{-1}$, ranging from 9 to 3146 $\mu\text{g L}^{-1}$, unadjusted for hydration status/dilution. From
19 these data, 12% were potentially iodine deficient ($<100 \mu\text{g L}^{-1}$), whilst 44% were considered
20 to have an excess iodine intake ($>300 \mu\text{g L}^{-1}$). The application of hydration status/urinary
21 dilution correction methods were evaluated for UICs, using creatinine, osmolality and
22 specific gravity. The use of specific gravity correction for spot urine samples to account for
23 hydration status/urinary dilution presents a practical approach for studies with limited
24 budgets, rather than relying on unadjusted UICs, 24 hour sampling, use of significantly large
25 sample size in a cross-sectional study and other reported measures to smooth out the
26 urinary dilution effect. Urinary corrections did influence boundary assessment for deficiency-
27 sufficiency-excess for this group of participants, ranging from 31 to 44% having excess
28 iodine intake, albeit for a study of this size. However, comparison of the correction methods
29 did highlight that 22% of the variation in UICs was due to urinary dilution, highlighting the
30 need for such correction, although creatinine performed poorly, yet specific gravity as a low-
31 cost method was comparable to osmolality corrections as the often stated 'gold standard'
32 metric for urinary concentration. Paired drinking water samples contained a median iodine
33 concentration of 3.2 $\mu\text{g L}^{-1}$ (0.2-304.1 $\mu\text{g L}^{-1}$). A weak correlation was observed between UIC
34 and water-I concentrations ($R = 0.11$).

35 **Keywords:** Urinary Iodine Concentrations; iodine excess; hydration status corrections

36

37

38

39

40

41

42

44 Introduction

45 Approximately 2 billion people are estimated to be at risk of iodine deficiency disorders (IDD)
46 worldwide (WHO, 2004; Andersson et al. 2012), for which the most severe consequences
47 occur during foetal and early childhood development and can later manifest as goitre and
48 impaired cognitive development (Obican et al. 2012; Bath et al. 2013). The Iodine Global
49 Network estimated that 19 countries remain at risk of IDD whilst 10 countries have excess
50 iodine intake (IGN, 2017). Excess intake of iodine (I) can cause hyper- or hypo-thyroidism,
51 thyroid autoimmunity or euthyroid goitre (Burgi et al. 2010; Leung et al. 2014). Rohner et al.
52 (2013) provided a comprehensive review of health consequences of I-deficient or excess
53 intake and an evaluation of biomarkers to define I-status. The I-status of populations was
54 traditionally quantified based on the prevalence of goitres, but the the use of urinary iodine
55 concentration (UIC) measured in spot urine samples is now considered standard practice
56 given the subjective nature of goitre classification and the more widespread availability of
57 laboratories capable of urinary iodine analyses (UNICEF, 2007). In addition, over 90% of
58 ingested iodine is rapidly excreted in the urine over 24-48 hours allowing for reliable
59 estimates of iodine intake, as well as providing ease and cost effectiveness of collection with
60 few limitations (Zimmerman et al. 2008; Zimmermann & Andersson 2012; Rohner et al.
61 2013; WHO 2013). UIC are normally expressed as a population median in $\mu\text{g L}^{-1}$, since
62 assessment of individual status using single spot samples is not recommended due to high
63 intra-diurnal variations in iodine intake (Vejbjerg et al. 2009; Knudsen et al 2009; König et al.
64 2011; Zimmermann & Andersson 2012, Rohner et al. 2013).

65 The highest prevalence of iodine deficiency is in the African region, as measured using
66 school age children (SAC), at 39.3% (58 million) (Andersson et al. 2012). For example, in
67 Malawi, 35% of the population (calculated from SAC) present a UIC of $<100 \mu\text{g L}^{-1}$,
68 representing a population risk of inadequate iodine intakes, whilst the same 2010 Malawi
69 Demographic and Health Survey (NSO, 2012) also reported that 62% of households were
70 consuming adequately iodised salt. Further, Farebrother et al. (2018) described the history
71 of the successful salt iodisation programme in Kenya which recorded a national median UIC
72 in SAC of $118 \mu\text{g L}^{-1}$ in 2004, though regional variations in UIC were wide with values as
73 high as $477 \mu\text{g L}^{-1}$, which resulted in a reduction in salt-I concentration from 100 to 30-50 mg
74 kg^{-1} in 2010 (Kenya Ministry of Health, 2011). Yet, the Kenyan National Micronutrient Survey
75 reported in 2011 a median UIC of $208 \mu\text{g L}^{-1}$ in SAC, of which 30% were considered to have
76 excess-I intake at $>300 \mu\text{g L}^{-1}$ (Kenya Ministry of Health, 2011). These examples show that
77 often the success of salt iodisation strategies is not maintained through lack of consistent
78 and sustained monitoring of iodinated salt alongside UIC, which can be problematic for
79 assessment of both deficiency and excess I-intakes.

80 The Estimated Average Requirement (EAR) for iodine in children, adults and pregnant
81 women is 64, 107 and $143 \mu\text{g capita d}^{-1}$, respectively (WHO, 2004). The Tolerable Upper
82 Limit (TUL) is defined as the level of iodine intake at which there is no demonstrable
83 evidence of toxicity and for adults is 600 and $1,100 \mu\text{g capita d}^{-1}$ in the EU and USA,
84 respectively (Zimmerman 2008; Leung et al 2015). Excess iodine intake can result in thyroid
85 disorders, but little data is available of the effects in vulnerable groups (Farebrother 2018),
86 although a healthy thyroid can tolerate I-intakes in excess of the EAR (Burgi et al. 2010;
87 Leung et al. 2015; Katagiri et al. 2017). Reports identifying excess I-intake are becoming
88 more common, with I-intake now being a problem of both deficiency and excess in many
89 regions often at a local scale. For example, in some regions in Argentina (Watts 2009),
90 Algeria (Barikmo et al. 2011), Somalia (Kassim et al. 2014), Malawi (Watts 2015) and Ghana

91 (Simpson et al. 2016; Abu et al. 2018), although Farebrother et al. (2018) reported a
92 generally low prevalence of thyroid dysfunction across the study population in Kenya. On the
93 basis of I status defined as 'inadequate' if the median UIC is $<100 \mu\text{g L}^{-1}$, sufficient $100\text{-}300$
94 $\mu\text{g L}^{-1}$ and excess $>300 \mu\text{g L}^{-1}$ (WHO/ICCIDD 2007), Watts et al. (2015) reported 12 and
95 33% of a study in Malawi to have a risk of moderate deficiency ($50\text{-}100 \mu\text{g L}^{-1}$) and excess,
96 similarly in Lesotho, 18 and 47% at risk of deficiency and excess, respectively (Sebotsa et
97 al. 2005). The 2017 Iodine Global Scorecard (IGN 2017) classified 7 of 47 mainland African
98 countries as having 'more than adequate' I intake, 14 with no data and four as 'excessive' on
99 the basis of UIC in School Age Children (SAC). Such variances may be due to differences in
100 dietary intake given that plant based foods are generally low in I content compared to the,
101 consumption of iodised salt, increasingly processed foods (e.g. stock cubes) or availability of
102 I-rich fish (Rohner et al. 2013; Watts et al. 2015; Abizari et al. 2017). Additional uncertainty
103 could be derived from cooking processes, for example, 6 to 51% of I is reportedly lost from
104 iodised salt when cooking (Rana & Raghuvanshi 2013). A review of cross-sectional studies
105 by Katagiri et al. (2017) revealed the sources of excess I to be mainly from iodised salt or
106 drinking water. Rohner et al. (2013) also referred to studies reporting the contribution of I-
107 intake from groundwater sources in China and Algeria (Andersen et al. 2009; Henjam et al.
108 2010).

109 Drinking water-I can vary in concentration according to the source; Reimann et al. (2003)
110 reported $0.3\text{-}961 \mu\text{g L}^{-1}$ (median $11 \mu\text{g L}^{-1}$) from spring, well and river sources along the
111 Ethiopian Rift Valley. Aakre et al. (2015) reported a median water-I concentration of $102 \mu\text{g}$
112 L^{-1} ($80\text{-}255 \mu\text{g L}^{-1}$) in Algerian refugee camps, which correlated with UIC, but also coupled
113 with high milk-I and salt-I consumption resulted in thyroid dysfunction after excessive I-intake
114 over several years. Farebrother et al. (2018) reported median water-I concentrations of 92
115 $\mu\text{g L}^{-1}$ for Kenya, Tanzania and Djibouti although no correlation was observed with UIC.

116 Concentrations of spot urinary analyte concentrations, I included, require correction for
117 hydration-driven dilution variation (Middleton et al. 2016). However, corrections of UIC are
118 not commonly reported in the literature, with largely uncorrected UIC available for
119 comparison of datasets. The routine approach to dilution correction in the wider biomonitoring
120 discipline is creatinine correction, the validity of which has been questioned (Nermell et al.
121 2008). For a correction method to perform properly, it must satisfy a number of prerequisites.
122 Firstly, the metric used should be an accurate physicochemical marker of urinary dilution and
123 it has long been recognised that urinary osmolality, the proxy for which is specific gravity
124 (SG) is far more reliable than creatinine. Creatinine, the breakdown product of muscular
125 creatinine phosphate, is subject to appreciable variation, more so than osmolality (Yeh et al.
126 2015) from demographic factors, particularly in developing countries owing to varying intake
127 of protein and water and the existence of malnutrition, as well as age-sex cut-off points
128 (Knudsen et al. 2000; Vejberg et al. 2009; Jooste et al. 2010; Cockell 2015). Secondly, the
129 application of the metric must be mathematically robust and representative of underlying
130 physiological changes in analyte excretion in relation to fluctuations in urinary flow rate
131 (Araki et al. 1986). Several criteria have previously been proposed (Middleton et al. 2016) to
132 assess the performance of urinary dilution corrections, one of which is the removal of dilution
133 variation from samples, crudely assessed by plotting corrected concentrations against the
134 measurement used to correct them.

135 This paper aims to: (1) evaluate a sample population for I status using UIC measurements in
136 western Kenya; (2) comparatively assess the use of creatinine, osmolality and specific
137 gravity as effective dilution corrections in comparison to uncorrected UIC (as is commonly
138 reported) and potential influence on boundary assessment for deficiency-sufficiency-excess,
139 and (3) explore whether drinking water influences UIC.

140

141

142 **Methods**

143 *Study setting*

144 Sample collection was part of a wider project as described in Watts et al. (pending), which
145 collected soil, crops, drinking water and a urine sample from households. Each household is
146 shown in Figure 1, including Bomet, Bungoma, Elgoyo Marakwet, Kakamega, Kisumu, Nandi
147 Hills, Siaya, Uasin Gishu counties in Western Kenya.

148 *Collection of urine*

149 This paper describes the urinary iodine concentrations (UICs) and paired drinking water
150 iodine from each household. Adult and consenting volunteers at each site were requested
151 for a urinary sample following an explanation of the study and why samples were being
152 collected. In general, we attempted to collect from a minimum of 30 different sites that were
153 spread out evenly across each county, representing rural land-use, although the geographic
154 size and accessibility resulted in slight variation in numbers per county. One sample was
155 generally collected from each household, a second volunteer provided a sample in <10% of
156 households. Ethical approval was obtained from the Institutional Research and Ethics Board
157 of Moi University (000921). Volunteers above the age of 18 were requested. Pregnant and
158 lactating women excluded. Volunteers were asked to urinate into a 30 mL nalgene LDPE
159 bottle, which was hygienically capped and transported in a coolbox (Ca 4°C) and
160 subsequently filtered into an 8 mL nalgene LDPE bottle using a nylon 0.45 µm syringe filter
161 at the end of each day, followed by storage in a coolbox and freezing at -80°C on return to
162 the University of Eldoret laboratory in Kenya. Urines were transported frozen to the UK for
163 elemental analyses, including I and urinary dilution measurements for subsequent
164 corrections.

165 *Collection of water*

166 Generally, only drinking water was collected and filtered (nylon, 0.45 µm) on-site into a 30
167 mL nalgene LDPE bottle to be used for anion, organic carbon and pH/alkalinity
168 measurements and a 15 mL nalgene LDPE bottle to be acidified on return to the UK with 1%
169 HNO₃/0.5% HCl for elemental analyses by inductively coupled plasma mass spectrometry
170 (ICP-MS) (Watts et al. pending), although iodine analyses were performed on the filtered
171 unacidified portion owing to the requirement of an alkaline matrix (Tetramethylammonium
172 Hydroxide-TMAH). Additional data was collected regarding the source (rain, river, borehole,
173 well), any treatment, reliability and field parameters, including conductivity, pH, temperature
174 and total dissolved solids.

175 *ICP-MS analyses for iodine*

176 Urine samples were analysed with a x20 dilution in 0.5% TMAH solution prior to analyses by
177 ICP-QQQ-MS (Agilent 8900) with the collision cell in no gas mode, Rf power 1550 W,
178 nebuliser flow rate of 0.4 ml min⁻¹, providing a limit of detection (LOD) of 0.2 µg L⁻¹ (3SD
179 blanks). Tellurium was used as an internal standard to correct for minor signal drift.
180 Measurements below the LOD were attributed a value half of the LOD. Water samples were
181 analysed separately to urines, but using the same method. Certified reference materials
182 were measured giving iodine concentrations of 114 ± 2 µg L⁻¹ (recovery: 109%; n = 15) for
183 Seronorm™ Trace Elements Urine L-1 (Sero, Norway) and 39.7 ± 3.0 µg L⁻¹ (recovery: 99%;
184 n = 21) for a spiked SLRS-2 Riverine Water.

185 *Urinary dilution corrections*

186 Urinary creatinine was determined using a Randox liquid assay kit and a Randox RX Imola
187 chemistry analyser. Osmolality was measured by freezing-point osmometry using a
188 Gonotect Osmomat 030 (Gonetec, Germany). Specific gravity was measured with a PAL-10-
189 S digital refractometer (Atago, Japan) prior to filtration. Creatinine, SG and osmolality
190 corrections were performed using Equation 1:

191

$$192 \quad UIC_{cor} = UIC_{vol} \times (D_{ref})/(D_{meas}), \quad (1)$$

193 where UIC_{cor} is dilution corrected urinary iodine concentration; UIC_{vol} is the measured,
194 volume-based urinary iodine concentration (in $\mu\text{g/L}$); D_{ref} is the reference value to which UIC
195 concentrations are scaled to and D_{meas} is that measured in the given specimen (note: $D_{ref}-1$
196 and $D_{meas}-1$ are used for SG correction). D_{ref} was 1 g L^{-1} for creatinine – synonymous with
197 the conventional division-based correction and yielding results in $\mu\text{g g creatinine}^{-1}$; and, for
198 both SG and osmolality, the study group medians were selected: 1.017 (unitless) and 581
199 mOsm kg^{-1} , respectively.

200

201 *Statistical analysis*

202 Summary statistics (arithmetic mean, median, standard deviation (SD), minimum and
203 maximum) were calculated for UICs – uncorrected and corrected by various dilution metrics.
204 Pearson correlation coefficients (R) and significance tests (P-values) were calculated on
205 natural log-transformed variables due to the positively skewed distributions of UIC
206 concentrations. All statistical analyses and graphics were performed in R version 3.4.3 and
207 the RStudio GUI.

208 **Results & Discussion**

209 *Urinary iodine concentrations*

210 Urinary iodine concentrations (UIC) for 248 adults are summarised in Table 1. Uncorrected
211 UIC values, which are commonly compared across studies provided a mean of $321 \pm 280 \mu\text{g}$
212 L^{-1} and median of $271 \mu\text{g L}^{-1}$, with a wide range of UIC values from 9-3146 $\mu\text{g L}^{-1}$. Whilst only
213 12% of the measured population were considered to be iodine deficient ($<100 \mu\text{g L}^{-1}$)
214 according to UIC, 44% were above $300 \mu\text{g L}^{-1}$, indicating excessive iodine intake. These UIC
215 data are comparable to other studies reporting the prevalence of excess I intake, according
216 to UIC and other urinary biomarkers. For example, Farebrother et al. (2018) reported
217 uncorrected median UICs in non-pregnant, non-lactating women elsewhere in Kenya of 289
218 $\mu\text{g L}^{-1}$ (IQR 173, 458 $\mu\text{g L}^{-1}$), and coastal Tanzania, of $473 \mu\text{g L}^{-1}$ (IQR 321, 689 $\mu\text{g L}^{-1}$).
219 Median uncorrected UIC's reported in Malawi (Watts et al. 2015) were $221 \mu\text{g L}^{-1}$ (141-344
220 $\mu\text{g L}^{-1}$); in Port Sudan 464 and $561 \mu\text{g L}^{-1}$, Medani et al. (2012) and Hussein et al. (2012),
221 respectively. In Somalia non-pregnant women provided a median of $329 \mu\text{g L}^{-1}$ (Kassim et al.
222 2014) and in Lesotho median UIC of $280 \mu\text{g L}^{-1}$, with 21 and 47% of women considered
223 either deficient or excess following two years after introducing a salt iodisation programme
224 (Sebotsa et al. 2005). Additionally, the median uncorrected UIC of $271 \mu\text{g L}^{-1}$ in this study is
225 high when compared to data summarised in the Iodine Global Scorecard (IGN, 2017),
226 median uncorrected UICs were 215, 175, 66 and $118 \mu\text{g L}^{-1}$ for Lesotho, Malawi, Sudan and
227 Kenya, respectively in the general population.

228 **Table 1:** Summary statistics for uncorrected and dilution corrected urinary iodine
 229 concentrations (UIC), comparison to World Health Organisation (WHO) guidance values and
 230 to the Hays et al. (2018) Biomonitoring Equivalents (BE) – displayed as number of
 231 individuals and in brackets as (%) of group below BE.

| UIC ($\mu\text{g L}^{-1}$) | Uncorrected | Osmolality-corrected | Creatinine-corrected | Specific Gravity-corrected |
|--|-------------|----------------------|----------------------|----------------------------|
| <i>n</i> | 246 | 242 | 230 | 246 |
| Median | 271 | 285 | 232 | 299 |
| Arithmetic mean | 321 | 325 | 395 | 321 |
| SD | 280 | 278 | 655 | 279 |
| Range | 9-3146 | 14-3870 | 6-4771 | 9-3149 |
| Percentiles (25, 75) | 163, 403 | 205, 382 | 149, 359 | 190, 404 |
| Number | 246 | 242 | 230 | 246 |
| WHO Values, <i>n</i> (%) | | | | |
| Extreme deficiency ($<50 \mu\text{g L}^{-1}$) | 9 (4) | 1 (0) | 9 (4) | 8 (3) |
| Mild deficiency ($<100 \mu\text{g L}^{-1}$) | 30 (12) | 6 (2) | 23 (10) | 30 (12) |
| Sufficient ($100\text{-}300 \mu\text{g L}^{-1}$) | 107 (43) | 129 (53) | 130 (57) | 106 (43) |
| Excess ($>300 \mu\text{g L}^{-1}$) | 109 (44) | 107 (44) | 78 (34) | 108 (44) |
| Hays et al. (2018) BE's, <i>n</i> (%)* | | | | |
| EAR cut-off ($60 \mu\text{g L}^{-1}$) | 11 (4) | 2 (1) | 9 (4) | 11 (4) |
| RDA ($100 \mu\text{g L}^{-1}$) | 30 (12) | 6 (2) | 23 (10) | 30 (12) |
| UL ($730 \mu\text{g L}^{-1}$) | 11 (4) | 6 (2) | 17 (7) | 11 (4) |
| MRL ($450 \mu\text{g L}^{-1}$) | 51 (21) | 32 (13) | 37 (16) | 51 (21) |

232 * Estimated Average Requirement (EAR), Recommended Dietary Allowance (RDA) and for
 233 toxicity, Tolerable Upper Intake Level (UL) and Minimal Risk Level (MRL)

234 Hays et al. (2018) recently proposed new boundaries for determining iodine deficiency,
 235 sufficiency and excess according to UIC by deriving Biomonitoring Equivalents (BEs).
 236 Established exposure and guidance criteria were used, such as the Estimated Average
 237 Requirement (EAR), Recommended Dietary Allowance (RDA) and for toxicity, Tolerable
 238 Upper Intake Level (UL) and Minimal Risk Level (MRL). For UIC, BE's were derived for
 239 adults as follows; 60,100, 730 and 450 $\mu\text{g L}^{-1}$, respectively. Zimmerman et al. (2016) also
 240 employed EAR and UL cutoff points to improve spot UIC to adjust I-intake distributions from
 241 UIC surveys where single sample per subject is collected. Whilst these approaches have
 242 not yet appeared in abundance for other studies in the literature, they are likely to gain
 243 greater interest to improve the validity of UIC spot measurements as cost effective survey
 244 tools. When considering Hays et al. (2018) BE's, for this study, using uncorrected UICs the
 245 proportion of volunteers $<$ EAR, $<$ RDA, $>$ UL and $>$ MRL, were 4, 12, 4 and 21%, respectively.
 246 Little difference in the proportion of UIC deficiencies results from these BE's, but excess is
 247 reduced from 44% for both the UL and MRL criteria.

248

249 **Influence of urinary dilution corrections**

250 For UICs with dilution correction, creatinine is the most commonly reported correction
 251 method, although has fallen out of favour (Cockell 2015). In this paper, creatinine corrected
 252 UIC ($\mu\text{g g}^{-1}$) provided a median of 232 $\mu\text{g L}^{-1}$, which was significantly higher than 203 $\mu\text{g L}^{-1}$
 253 reported in Malawi (Watts et al. 2015), but presented a higher proportion of individuals with a

254 UIC in a range of sufficiency. Meanwhile, the number of volunteers exhibiting excess UIC
255 reduced to 34 with creatinine adjustment from 44% (uncorrected) in this study.

256 Table 1 summarises the UIC data and influence of correction methods on the proportion of
257 volunteers considered to have excess I-intake ranging between 31 to 44%, with 44% of
258 volunteers in excess when using uncorrected UICs. No clear pattern can be discerned as to
259 the influence of each method of correction on changes to numbers of individuals within each
260 boundary for UICs for a study group of this size. Therefore, further analyses were
261 undertaken to evaluate the validity of each correction method, in comparison to a UIC
262 uncorrected for dilution.

263 Figure 2 shows each of the three dilution measurements in relation to one another.
264 Expectedly, a strong positive correlation ($R=0.82$) was observed between osmolality and SG
265 (Figure 2A), albeit a number of possible outliers - interferences on SG measurement by
266 refractometry are possible in the presence of large urinary solutes (i.e. proteinuria) (Imran et
267 al. 2010). Conversely, a weaker correlation was observed for creatinine in relation to both
268 osmolality (Figure 2B, $R=0.47$) and SG (Figure 2C, $R=0.48$). If, as is widely cited (Imran et
269 al. 2010), it is assumed that osmolality is the most robust measure of urinary dilution,
270 creatinine was a poor marker of urinary dilution in the present dataset, with only 22% of
271 variation explained by osmolality. This finding was markedly different when compared with
272 two western populations: 48% variation in creatinine was explained by osmolality in a set of
273 2151 samples from the US NHANES survey (CDC, 2018) and 67 % in a UK survey of 202
274 adults (Middleton et al. 2016a). This may indicate the particularly poor utility of creatinine in
275 an African population.

276 Figure 3 shows the correlations between both uncorrected (A-C) and corrected (D-F) UICs
277 and each dilution metric. Uncorrected concentrations showed positive correlations with each
278 metric, demonstrating the necessity of correcting to remove hydration-driven dilution
279 variation. As evident in Figure 3B, almost a quarter of variation in UICs was attributable to
280 sample dilution alone. This was less evident for creatinine (Figure 3A) reiterating its poor
281 reflection of urinary dilution. Figure 3 D-E show the efficacy (no correlation desired) of each
282 correction method in removing dilution variation from the sample set. No significant
283 correlation remained following correction by osmolality (Figure 3E) and SG (Figure 3F) – an
284 indication of their good performance. However, creatinine (Figure 3D) resulted in an
285 apparent over-correction, of a magnitude consistent with previous findings in relation to this
286 performance criterion (Middleton et al. 2016). It is possible to compensate for this over-
287 correction by modifying correction equations with a coefficient reflecting the disparity in
288 excretion slopes between creatinine and the analyte under investigation (Vij & Howell, 1998).
289 However, the apparent variation in creatinine concentrations is not explained by dilution in
290 the present dataset and would make any such improvements misleading indicators of
291 performance.

292 Finally, given the relative paucity of studies utilising alternative correction methods to
293 creatinine, there is a lack of consistency as to the reference values (D_{ref} in Equation 1) used
294 to normalise/scale datasets. This has profound implications when comparing between
295 populations and to published referenced values. Firstly, comparing distributions of
296 uncorrected values between populations assumes that they do not differ by hydration status.
297 However, the median osmolality of the present study group was 581 mOsm kg^{-1} ; compared
298 to 730 mOsm kg^{-1} in the US NHANES data (Centers for Disease Control and Prevention,
299 2015). Secondly, using the median osmolality of the present study group as D_{ref} yielded a
300 median UIC of $285 \mu\text{g L}^{-1}$, whereas using the NHANES median yielded a median UIC of 358
301 $\mu\text{g L}^{-1}$ – an increase of 25%. To ensure that studies are comparing like-for-like, standardised

302 guidelines on the proper use of dilution corrections, and the appropriate dilution reference
303 values, are urgently needed.

304

305 **Drinking water and comparison to UIC**

306 Drinking water concentrations for 268 samples provided a median of 3.2 $\mu\text{g L}^{-1}$ (0.2-304.1 μg
307 L^{-1}) and mean of $12.3 \pm 33.3 \mu\text{g L}^{-1}$. Whilst the median water-I concentration was not high
308 compared to other studies, the range was comparable, for example, in Denmark <1.0 to 139
309 $\mu\text{g L}^{-1}$ (Pedersen et al. 1999) and 55 to 545 $\mu\text{g L}^{-1}$ in Algeria (Barikmo et al. 2011). Almost no
310 correlation of UIC (uncorrected) with drinking water was observed ($R = 0.11$), unlike other
311 studies that observed a much stronger correlation (Hussein et al. 2012; Aakre et al. 2015).
312 Kassim et al. (2014) reported variations in Somalian UICs according to the source of drinking
313 water, with a greater association with borehole water, although the concentration of I in
314 water was not measured. In contrast to these studies, the maximum water-I concentration
315 reported in the USA was only 18 $\mu\text{g L}^{-1}$ (WHO, 2003). Given a typical water consumption of
316 1.8 L day^{-1} (Beal et al. 2017), drinking water could assist in preventing I-deficiency, but may
317 also contribute to I-excess intake above upper tolerable limits of 1100 $\mu\text{g day}^{-1}$ (Leung et al.
318 2015) where water-I is high. For example, in this study the mean water-I concentration would
319 contribute an intake of 22 $\mu\text{g day}^{-1}$ and at the maximum water-I range, 547 $\mu\text{g day}^{-1}$. There is
320 currently no defined guideline for iodine in drinking water (WHO, 2003).

321

322 **Conclusion**

323 Whilst 24 hour urinary collection is cited as 'ideal' for UIC measurements, UIC single spot
324 analyses are generally used in studies for practical reasons in the field. Often the sample
325 size of 300 or 500 subjects is referred to for smoothing out differences in hydration
326 (Andersen et al. 2008; Konig et al. 2011; Rohner et al. 2013). Creatinine correction for
327 hydration status has been repeatedly reported as unsuitable for UIC in a developing country
328 scenario where malnutrition may be a problem, although there appears to be a lack of
329 published quantitative evidence to reinforce this widely held view in the literature. Correction
330 for hydration status should be reconsidered, especially given the robustness, simplicity and
331 low cost of specific gravity measurements, which are comparable to the gold
332 standard/osmolality (Middleton et al. 2015). Use of specific gravity adjustments for spot urine
333 samples to account for urinary dilution presents an opportunity for studies with limited
334 budgets and studies that are most commonly reported to have less than the 300+
335 recommended number of subjects and for practical reasons where repeat sampling of
336 individuals may not be possible.

337 This study adds to the growing awareness of excess I-intake according to UIC since
338 Anderson et al. (2012) reported an increase from 5 to 11 countries between 2003 and 2011
339 in which the national median UIC was $>300 \mu\text{g L}^{-1}$. Whilst no correlation with drinking water
340 was observed in this study, further research to establish the association between water-I
341 concentration, physical and chemical parameters, alongside depth of boreholes, lithology
342 and extraction rates from aquifers is required. In combination with UIC, dietary and
343 physiological studies, a guideline value for water-I should be established to inform national
344 programmes for monitoring and alleviating iodine deficiency and preventing any adverse
345 health effects secondary to chronic excessive iodine intakes.

346

347 **Figure legends**

348 **Figure 1** Map illustrating location of household collection points in western Kenya.

349 **Figure 2** Scatterplots showing the relationship between urinary osmolality and creatinine (A),
350 urinary osmolality and specific gravity (B) and urinary specific gravity and creatinine (C).
351 Pearson correlation coefficients are significant to $P < 0.001$.

352 **Figure 3** Scatterplots of urinary iodine against dilution measurements both pre- (A-C) and
353 post- (D-F) correction by each method investigated. ** and * denote statistical significance to
354 $P < 0.001$ and < 0.05 , respectively.

355

356 **Acknowledgements**

357 The team would like to thank the BGS Global, BGS ODA and BGS Centre for Environmental
358 Geochemistry for financial support. We would like to thank the many people who assisted in
359 the collection of samples, including the Public Health Officers from each county and in
360 particular the field and lab staff from the University of Eldoret (UoE), Moi University (Moi) and
361 BGS. David Samoie, Doreen Meso, Charles Owano (UoE), Esilaba Anabwani Amimo
362 Anabwani (Moi), Nicholas Porter, Sophia Dowell (BGS). Thanks also to David Gardner at
363 the University of Nottingham School of Veterinary Sciences for creatinine and osmolality
364 measurements. This manuscript is published with the permission of the Executive Director
365 of the British Geological Survey.

366

367

368 **References**

369

370 Aakre, I., Bjoro, T., Norheim, I., Dtrand, T. A. & Barikmo, I. (2015). Excessive intake and thyroid
371 dysfunction among lactating Saharawi women, *Journal of Trace Elements in Medicine and Biology*,
372 31, 279-284.

373

374 Abizari, A-R., Dold, S., Kupka, R. & Zimmermann, M. B. (2017). More than two-thirds of dietary iodine
375 in children in northern Ghana is obtained from bouillon cubes containing iodised salt, *Public Health*
376 *Nutrition*, 20(6), 1107-1113.

377

378 Abu, B. A. Z., Oldewage-Theron, W. & Aryeetey, R. N. O. (2018). Risks of excess iodine intake in
379 Ghana: current situation, challenges and lessons for the future, *Annals of the New York Academy of*
380 *Sciences*, 1-22.

381

382 Andersen, S., Pedersen, K. M., Iversen, F., Terpling, S., Gustenhoff, P., Petersen, S. B. & Laurberg,
383 P. (2008). Naturally occurring iodine in humic substances in drinking water in Denmark is bioavailable
384 and determines population iodine intake, *British Journal Nutrition*, 99, 319-325.

385

386 Andersen, S., Guan, H. X., Teng, W. P. & Laurberg, P. (2009). Speciation of iodine in high iodine
387 groundwater in China associated with goitre and hypothyroidism, *Biological Trace Element*
388 *Research*, 128, 95-103.

389

390 Andersson, M., Karumbunathan, V. & Zimmerman, M. B. (2012). Global iodine status in 2011 and
391 trends over the past decade, *Journal Nutrition*, 142, 744-750.

392

393 Araki, S., Murata, K., Aono, H., Yanagihara, S., Niinuma, Y., Yamamoto, R. & Ishihara, N. (1986).
394 Comparison of the effects of urinary flow on adjusted and non-adjusted excretion of heavy metals and
395 organic substances in 'healthy' men, *Journal Applied Toxicology*, 6(4), 245-251.

396

397 Barikmo, L., Henjum, S., Dahl, I., Oshuag, A. & Torheim, L. E. (2011). Environmental implication of
398 iodine in water, milk and other foods in Saharawi refugee camps in Tindouf, Algeria, *Journal of Food*
399 *Composition and Analysis*, 24, 637-641.

400

401 Bath, S.C., Steer, C.D., Golding, J., Emmett, P. & Rayman, M. (2013). Effect of Inadequate iodine
402 Status in UK Pregnant Women on Cognitive Outcomes in Their Children: Results from the Avon
403 Longitudinal Study of Parents and Children (ALSPAC), *The Lancet*, 9889, 331-337.

404

405 Beal, T., Massiot, E., Arsenault, J. E., Smith, M. R. & Hijmans, R. J. (2017). Global trends in dietary
406 micronutrient supplies and estimated prevalence of inadequate intakes, *PLOSOne*, 12(4), 1-20.

407

408 Burgi, H. (2010). Iodine excess, *Best Practice and Research Clinical Endocrinology Metabolism*, 24,
409 107-115.

410

411 [Centers for Disease Control and Prevention \(CDC\). \(2018\) National Center for Health Statistics](https://www.cdc.gov/nchs/nhanes/index.htm)
412 [\(NCHS\). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of](https://www.cdc.gov/nchs/nhanes/index.htm)
413 [Health and Human Services, Centers for Disease Control and Prevention, accessed 2018,](https://www.cdc.gov/nchs/nhanes/index.htm)
414 <https://www.cdc.gov/nchs/nhanes/index.htm>.

415 [Accessed: 07/01/19]

416

417 Cockell, K. A. (2015). Measured iodine status in diverse populations, *British Journal of Nutrition*, 114,
418 499-500.

419

420 Farebrother, J., Zimmerman, M. B., Abdallah, F., Assey, V., Fingerhut, R., Gichohi-Wainaina, W. N.,
421 Hussein, I., Makokha, A., Sagno, K., Untoro, J., Watts, M. J. & Andersson, M. (2018). The effect of
422 excess iodine intake from iodised salt and/or groundwater iodine on thyroid function in non-pregnant
423 and pregnant women, infants and children: a multicenter study in East Africa, *Thyroid*, 28(9), 1-13.

424

425 Hays, S. M., Poddalgoda, D., Macey, K., Aylward, L. & Nong, A. (2018). Biomonitoring Equivalents for
426 interpretation of urinary iodine, *Regulatory Toxicology and Pharmacology*, 94, 40-46.

427

428 Henjum, S., Barikmo, I., Gjerlaug, A. K., Mohamed-Lehabib, A., Oshaug, A., Strand, T. A. & Torheim,
429 L. E. (2010). Endemic goitre and excessive iodine in urine and drinking water among Saharawi refugee
430 children, *Public Health Nutrition*, 13, 1472-1477.

431

432 Hussein, I. S., Min, Y., Ghebreskel, K. & Gaffar, A. M. (2012). Iodine status and fish intake of
433 Sudanese schoolchildren living in the Red Sea and White Nile regions, *Public Health Nutrition*, 15,
434 2265-2271.

435

436 Imran, S., Eva, G., Christopher, S., Flynn, E. & Henner, D. (2010). Is specific gravity a good estimate
437 of urine osmolality? *Journal Clinical Laboratory Analysis*, 24(6), 426-430.

438

439

440 Iodine Global Network (IGN; 2017). estimates state that 19 countries remain at risk of ID and 10 of
441 iodine excess (SAC data), but that certain population groups e.g. pregnant women, are more at risk.
442 Thirty-nine countries report inadequate intakes in PW.
443 (http://www.ign.org/cm_data/IGN_2017_Annual_Report.pdf)

444

445 Jooste, P. L. & Strydom, E. S. (2010). Methods for determination of iodine in urine and salt, *Best*
446 *Practice Research Clinical Endocrinology Metabolism*, 24, 77-88.

447

448 Kassim, I. A. R., Moloney, G., Busili, A., Nur, A. Y., Paron, P., Jooste, P., Gadain, H. & Seal, A. J.
449 (2014). Iodine intake in Somalia is excessive and associated with the source of household drinking
450 water, *Journal Nutrition*, 144, 375-281.

451

452 Katagiri, R., Yuan, X., Kobayashi, S. & Sasaki, S. (2017). Effect of excess iodine intake on thyroid
453 diseases in different populations: a systematic review and meta-analyses including observational
454 studies, *PLoS One*, 12:e0173722.

455
456 Kenya Ministry of Health (2011). Kenya National Micronutrient Survey 2011, Nutrition and Dietetics
457 Unit, Ministry of Health, Kenya.
458
459 Knudsen, N., Christansen, E., Brandt-Christiansen, M., Nygaard, B. & Perrild, H. (2000). Age- and
460 sex-adjusted iodine/creatinine ratio. A new standard in comparison to 24 h values, *European Journal*
461 *of Clinical Nutrition*, 54, 361-363.
462
463 Konig, F., Andersson, M., Hotz, K., Aeberli, I. & Zimmerman, M. B. (2011). Ten repeat collections for
464 urinary iodine from spot samples or 24-hour samples are needed to reliably estimate individual iodine
465 status in women, *Journal Nutrition*, 141, 2049-2054.
466
467 Leung, A. M. & Braverman, E. L. (2014). Consequences of excess iodine, *Natural Review*
468 *Endocrinology*, 10, 136-142.
469
470 Leung, A. M., Avram, A. M., Brenner, A. V., Duntas, L. H., Ehrenkranz, J., Hennessey, J. V., Lee, S.
471 L., Pearce, E. N., Roman, S. A., Stagnaro-Green, A., Sturgis, E. M., Sundaram, K., Thomas, M. J &
472 wexler, J. A. (2015). Potential risks of excess iodine ingestion and exposure: statement by the
473 American Thyroid Association Public Health Committee, *Thyroid*, 25, 145-146.
474
475 Medani, A. M. M. H., Elnour, A. A. & Saeed, A. M. (2012). Excessive iodine intake, water chemicals
476 and endemic goitre in a Sudanese coastal area, *Public Health Nutrition*, 16(9), 1586-1592.
477
478 Middleton, D. R. S, Watts, M. J., Hamilton, E. M., Ander, E. L., Close, R. M., Exley, K. S., Leonardi, G.
479 S., Fletcher, T. & Polya, D. A. (2016a). Urinary arsenic profiles reveal exposures to inorganic arsenic
480 from private drinking water supplies in Cornwall, UK, *Scientific Reports*, 9, 25656.
481
482 Middleton, D. R. S., Watts, M. J., Lark, R. M., Milne, C. J. & Polya, D. A. (2016b). Assessing urinary
483 flow rate, creatinine, osmolality and other hydration adjustment methods for urinary biomonitoring
484 using NHANES arsenic, iodine, lead and cadmium data, *Environmental Health*, 15(6)8, 1-13.
485
486 Nermell, B. et al. (2008). Urinary arsenic concentration adjustment factors and malnutrition,
487 *Environmental Research*, 106, 212-218.
488
489 NSO (National Statistics Office of the Republic of Malawi) (2012). Republic of Malawi Integrated
490 Household Survey 2010-2011. NSO, Zomba, Malawi. Available online:
491 [http://siteresources.worldbank.org/INTLSMS/Resources/3358986-1233781970982/5800988-](http://siteresources.worldbank.org/INTLSMS/Resources/3358986-1233781970982/5800988-1271185595871/IHS3_Report.pdf)
492 [1271185595871/IHS3_Report.pdf](http://siteresources.worldbank.org/INTLSMS/Resources/3358986-1233781970982/5800988-1271185595871/IHS3_Report.pdf) [accessed April 2019].
493
494 Obican, S. G., Jahnke, G. D., Soldin, O. P. & Scialli, A. R. (2012). Teratology Public Affairs Committee
495 Position Paper: Iodine Deficiency in Pregnancy, *Birth Defects Research (Part A)*, 94, 677-682.
496
497 Pedersen, K. M., Laurberg, P., Nohr, S., Jorgensen, A. & Andersen, S. (1999). Iodine in drinking
498 water varies by more than 100-fold in Denmark: importance for iodine content in infant formulas,
499 *European Journal of Endocrinology*, 140, 400-403.
500
501 Rana, R. & Raghuvanshi, R. S. (2013). Effect of different cooking methods on iodine losses, *Journal*
502 *Food Science Technology*, 50, 1212-1216.
503
504 Reimann, C., Bjorvatn, K., Frengstad, B., Melaku, Z., Tekle-Haimanot, R. & Siewers, U. (2003).
505 Drinking water quality in Ethiopian section of East African Rift Valley I – data and health aspects,
506 *Science of Total Environment*, 311, 65-80.
507
508 Rohner, F., Zimmerman, M. B., Jooste, P., Pandav, C., Caldwell, K., Raghavan, R. & Raiten, D. J.
509 (2013). Biomarkers of nutrition for development –iodine review, *Journal Nutrition*, 144, 1322S-1342S.
510
511 Sebotsa, M. L. D., Dannhauser, A., Jooste, P. L. & Joubert, G. (2005). Iodine status as determined by
512 urinary iodine excretion in Lesotho two years after introducing legislation on universal salt iodisation,
513 *Nutrition*, 21, 20-24.
514

515 Simpong, D. L., Adu, P., Bashiru, R., Morna, M. T., Yeboah, F. A., Akakpo, H & Ephraim, R. K. D.
516 (2016). Assessment of iodine status among pregnant women in a rural community in Ghana – a cross
517 sectional study, *Archives of Public Health*, 74(8), 1-5.
518

519 Vejbjerg, P., Knudsen, N., Perrild, H., Laurberg, P., Andersen, S., Rasmussen, L. B., Ovesen, L. &
520 Jorgensen, T. (2009). "Estimation of iodine intake from various urinary iodine measurements in
521 population studies." *Thyroid*, 19(11): 1281-1286.
522

523 Vij, H. S. & Howell, S. (1998). Improving the specific gravity adjustment method for assessing urinary
524 concentrations of toxic substances, *American Industrial Hygiene Association Journal*, 59(6), 375-380.
525

526 Watts, M. J., O'Reilly, J., Maricelli, A., Coleman, A., Ander E. L. & Ward, N. I. (2009). A snapshot of
527 environmental iodine and selenium in La Pampa and San Juan provinces of Argentina, *Journal*
528 *Geochemical Exploration*, 107, 87-93.
529

530 Watts, M. J., Joy, E. J. M., Young, S. D., Broadley, M. R., Chilimba, A. D. C., Gibson, R. S., Siyame,
531 E. W. P., Kalimbira, A. A., Chilima, B. & Ander, E. L. (2015). Iodine source apportionment in the
532 Malawian diet, *Scientific Reports*, 5, 15251.
533

534 Watts, M.J., Middleton, D.R.S., Marriott, A.L., Humphrey, O.S., Hamilton, E.M., Gardner, A., Smith,
535 M., McCormack, V.A., Menya, D., Munishi, M.O., Mmbaga, B.T., and Osano, O. (2019) Source
536 apportionment of micronutrients in the diets of Kilimanjaro-Tanzania and Western Kenya, *Scientific*
537 *Reports* (in press).
538

539 UNICEF (2007). Guidance and Monitoring of Salt Iodization Programmes and Determination of
540 Population Iodine Status, <https://www.unicef.org/nutrition/files/Monitoring-of-Salt-Iodization.pdf>
541 [Accessed April 2019].
542

543 WHO/UNICEF/ICCIDD (World Health Organisation/United Nations Children's Fund/International
544 Council for Control of Iodine Deficiencies Disorders). (2007). Assessment of the iodine deficiency
545 disorders and monitoring their elimination: A guide for programme managers, 3rd ed. Geneva: World
546 Health Organisation, WHO/NDH/01.1.
547

548 WHO (World Health Organisation) (2004). Iodine status worldwide, World Health Organisation Global
549 Database on Iodine Deficiency, Geneva.
550

551 WHO (World Health Organisation) (2013). Urinary iodine concentrations for determining iodine status
552 in populations, WHO/NMH/NHD/EPG/13.1.
553

554 Yeh, H-C., Lin, Y-S., Kuo, C-C, Weidemann, D., Weaver, V., Fadrowski, J., Neu, A. & Navas-Acien, A.
555 (2015). Urine osmolality in the US population: implications for environmental biomonitoring,
556 *Environmental Research*, 136, 482-490.
557

558 Zimmerman, M. B., Jooste, P. L. & Pandav, P. S. (2008). Iodine deficiency disorders, *Lancet*, 372,
559 1251-1262.

560 Zimmermann, M. B. & Andersson, M. (2012). "Assessment of iodine nutrition in populations: past,
561 present, and future." *Nutr Rev* 70(10): 553-570.

562 Zimmerman, M. B., Hussein, I., Ghannami, S. A., Badawi, S. E., Hamad, N. M. A., Hajj, B. A., Al-Thani,
563 M., Al-Thani, A. A., Winichagoon, P., Pongcharoen, T., Van der Haar, F., Qing-Zhen, J., Dold, S.,
564 Andersson, M. & Carriquiry, A. L. (2016). Estimation of the prevalence of inadequate and excessive
565 iodine intakes in school-age children from the adjusted distribution of urinary iodine concentrations
566 from population surveys, *The Journal of Nutrition*, 1204-1211.





