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# Zinc-enriched fertilisers as a potential public health intervention in Africa

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## Abstract

### *Background*

In this review, we examine the potential of Zn-enriched fertilisers to alleviate human dietary Zn deficiency. The focus is on 10 African countries where dietary Zn supply is low and where fertiliser subsidies are routinely deployed on cereal crops.

### *Scope*

Dietary Zn supply and deficiency prevalence were quantified from food supply and composition data. Typical effects of soil (granular) and foliar Zn applications on Zn concentrations in maize (*Zea mays* L.), rice (*Oryza sativa* L.) and wheat (*Triticum aestivum* L.) grains were based on a systematic literature review. Reductions in disease burdens attributable to Zn deficiency and cost-effectiveness were estimated using a disability-adjusted life years (DALYs) approach.

### *Conclusions*

Baseline Zn supply in 2009 ranged from 7.1 (Zambia) to 11.9 (Mali) mg *capita*<sup>-1</sup> d<sup>-1</sup>; prevalence of Zn deficiency ranged from 24 (Nigeria) to 66 % (Zambia). In reviewed studies, soil Zn application led to an increase in median Zn concentration in maize, rice and wheat grains of 23, 7 and 19 %; foliar application led to increases of 30, 25 and 63 %. Enriching granular fertilisers within current subsidy schemes would be most effective in Malawi, reducing DALYs lost due to Zn deficiency by 10 %. The cost per DALY saved ranged from US\$ 624 to 5,893 via granular fertilisers and from US\$ 46 to 347 via foliar fertilisers. Foliar applications are likely to be more cost effective than soil applications due to fixation of Zn in the soil but may be more difficult to deploy. Zinc fertilisation is likely to be less cost-effective than breeding in the longer term although other micronutrients such as selenium could be incorporated.

## Keywords

Agronomic biofortification; Fertiliser; HarvestPlus; Micronutrient deficiency; Phytic Acid; Zinc

## Introduction

Zinc (Zn) is an integral component of thousands of proteins for all organisms. Adult human bodies contain 1.5-2.5 g of Zn with a daily intake requirement of 10-14 mg (WHO and FAO 2004). The estimated prevalence of inadequate dietary Zn intake is >25 % in sub-Saharan Africa (Wessells and Brown 2012; Wessells et al. 2012; Joy et al. 2014). Dietary Zn deficiency can have a range of health impacts including increased risk of child mortality due to diarrhoeal disease and stunting (Salgueiro et al. 2002) and imposes considerable individual suffering as well as social and economic costs (Stein 2010, 2014). An estimated 0.7 % of the global disease burden is attributable to Zn deficiency, rising to 1.5 % in low income countries (WHO 2009). Factors contributing to Zn deficiency in humans include low consumption of animal products, high phytate intakes that inhibit Zn absorption and low concentrations of Zn in crops grown on Zn deficient soils (Cakmak et al. 1999; Sandstead 2000; Gibson 2012). Phytate refers to mixed salts of phytic acid (PA), the principal form of phosphorus (P) in cereal grains, and is a potent inhibitor of Zn absorption in the human gut. A PA:Zn molar ratio of >15 is commonly used to classify diets having low levels of bioavailable Zn.

In crop plants, a leaf Zn concentration of 15-20 mg Zn kg<sup>-1</sup> dry weight (DW) is typically required for adequate growth (Broadley et al. 2007). However, Zn deficiency in crops is widespread globally, in particular, due to low phytoavailability of Zn in soils. Such soils are commonly defined as having a Zn concentration extractable by ethylene diamine tetra-acetic acid (EDTA) or diethyl triamine penta-acetic acid (DTPA) less than 1.5 and 1.0 mg kg<sup>-1</sup> DW of soil, respectively (Trierweiler and Lindsay 1969; Lindsay and Norvell 1978). Low phytoavailability of Zn can result from low soil Zn concentrations or the influence of soil characteristics that limit Zn solubility such as high pH values or large concentrations of available phosphate or CaCO<sub>3</sub> (Brümmer et al. 1983; Graham et al. 1992; White and Zasoski 1999; Cakmak 2002, 2004; Alloway 2008; Lu et al. 2011). Deficiency of Zn on cultivated soils is widespread, affecting >50 % of soils in India, Pakistan and Turkey, >30 % of soils in China and most soils in Western Australia and Africa (Alloway 2008).

Zinc fertilisers are widely used to improve crop yields where soil Zn phytoavailability is low (Ahmad et al. 2012). The first reports of using Zn fertilisers to ameliorate crop Zn deficiency were in peach, pecan and pineapple orchards (Hoagland 1948). However, major increases in arable crop production due to Zn fertiliser use are now well-established. For example, wheat grain yield increases of >600 % were reported in Central Anatolia in Turkey from the mid-1990s which returned economic benefits of ca. US\$ 100 million annually in the following decade (Cakmak 2004). More recently, there has been research exploring the use of Zn fertilisers to increase Zn concentrations beyond that which is needed for maximum yield, to enrich the edible portions of crops for human health benefits (Rengel et al. 1999; Genc et al. 2005; Ortiz-Monasterio et al. 2007; Broadley et al. 2007; Cakmak 2008; White and Broadley 2009, 2011). However, the cost-effectiveness of this approach has not previously been determined.

Several Zn forms have been used in fertilisers, including Zn-sulphate (ZnSO<sub>4</sub>) and Zn-oxide. Such forms can be delivered either in combination with granular nitrogen (N) fertilisers or as a foliar spray. An advantage of enriching granular fertilisers is that farmers already using fertilisers can be reached with no extra labour or machinery required at the farm level, nor additional distribution infrastructure. However, plant uptake of soil-applied Zn is limited by a low availability or diffusion of Zn in certain soils, particularly those with high pH, organic matter or CaCO<sub>3</sub> contents (Tye et al. 2003; Zhao et al. 2014). For example, recovery of soil-applied Zn may be <1 % in calcareous soils (Lu et al. 2012). Thus, a more effective strategy for increasing grain Zn concentrations might be *via* foliar sprays. With foliar application, Zn is absorbed by the leaf epidermis, remobilized and transferred to the grain through the phloem (Fernández and Eichert 2009; White and Broadley 2011).

Common soil fertility management practices can also affect soil Zn status and concentrations of Zn in the grain. For example, N application can increase Zn uptake, xylem transport and remobilization *via* the phloem, and hence the concentration of Zn in the grain (Erenoglu et al. 2002, 2011; Kutman et al. 2010, 2011; Xue et al. 2012), while excessive P fertilisation can reduce availability of Zn in the soil

100 (Marschner 1993; Lu et al. 2011). Manzeke et al. (2012) reported that farmer fields in Zimbabwe  
101 receiving cattle manure or leaf litter in combination with NPK had greater concentrations of EDTA-  
102 extractable Zn in soils and greater concentrations of Zn in maize grain compared to unfertilised fields  
103 or those receiving only NPK, while rotation with legumes was also reported to increase concentration  
104 of Zn in maize grain.

105  
106 The use of Zn-containing fertilisers to increase dietary Zn supply is one of several strategies to  
107 address dietary Zn deficiency. These include dietary diversification, provision of supplements and  
108 addition of Zn during food processing (Gibson et al. 2000; Shrimpton et al. 2005). Other agricultural  
109 strategies to increase the concentration of Zn in harvested grain include crop breeding for high-Zn  
110 varieties (Cakmak 2008; White and Broadley 2009, 2011; Bouis and Welch 2010), while soaking or  
111 ‘priming’ of seeds in ZnSO<sub>4</sub> solution might be more efficient than soil applications and confer yield  
112 benefits (Slaton et al. 2001; Harris et al. 2007; Harris et al. 2008) although increased Zn concentration  
113 in progeny grain is not consistently reported (Johnson et al. 2005). It may also be possible to breed  
114 lower PA concentrations into the grains of staple crops and the benefits of even marginal reductions in  
115 grain PA concentration on Zn bioavailability could be large at population scales (Joy et al. 2014).  
116 Interestingly, it has been reported that Zn-enriched fertilisers can decrease concentrations of PA in  
117 cereal grains while Zn deficiency may lead to increased P uptake and accumulation in plants  
118 (Loneragan et al. 1982; Erdal et al. 2002).

119  
120 The impact of public health interventions can be measured using a disability-adjusted life-years  
121 (DALYs) approach. A DALY is equivalent to a lost year of ‘healthy life’ and is the sum of years of  
122 life lost due to premature mortality and years of life lost due to a disability (YLD; Murray 1994). The  
123 YLD is the product of the number of incident cases, average duration of the disease and a disability  
124 weight to reflect the severity of the disease, which ranges between 0 (i.e. full health) and 1 (i.e. death).  
125 As there are limited resources available to invest in public health, a DALY approach allows direct  
126 comparison between different public health interventions to guide policy making and to increase the  
127 efficient use of scarce funds. Previously, Stein et al. (2006) estimated that biofortification *via* breeding  
128 for high-Zn rice and wheat varieties could save up to 55 % of the 2.8 million DALYs lost annually  
129 due to Zn deficiency in India at a cost of US\$ 0.68 and 8.80 *per* DALY saved, for optimistic and  
130 pessimistic scenarios respectively. Fielder et al. (2013) estimated that fortifying maize meal with a  
131 premix containing vitamin A, iron and Zn at large-scale mills in Zambia could save 5,657 DALYs  
132 annually of which 1,757 were due to Zn deficiency, at a cost of US\$ 401 *per* DALY saved. Similar  
133 studies have not yet been conducted for fertilisers and so the aim of this review is to assess the cost-  
134 effectiveness of Zn fertilisers in reducing disease burdens due to dietary Zn deficiency.

135  
136 The focus of the review is sub-Saharan Africa because of the high incidence of Zn deficiency relative  
137 to other regions of the World (Lim et al. 2012; Wessells and Brown 2012). Specifically, we have  
138 focussed on 10 countries which routinely deploy fertiliser subsidy schemes (Burkina Faso, Kenya,  
139 Ghana, Mali, Malawi, Nigeria, Senegal, Tanzania and Zambia) or which have government control of  
140 imports (Ethiopia) as this offers a mechanism for mandating Zn-enrichment of fertilisers (Jayne and  
141 Rashid 2013; Wanzala-Mlobela et al. 2013).

142  
143 The first aspect of this review quantifies dietary Zn supply and deficiency prevalence for the 10 focus  
144 countries using food supply and food composition data, the latter adjusted according to cereal  
145 processing methods. The second aspect is a meta-analysis of published field experiments that  
146 investigate the effect of soil- and foliar-applied Zn fertilisers on Zn and PA concentrations in the grain  
147 of three staple crops: maize (*Zea mays* L.), rice (*Oryza sativa* L.) and wheat (*Triticum aestivum* L.).  
148 The third aspect of this study models the effect of enriching fertilisers with Zn on dietary Zn supplies,  
149 deficiency and associated disease burdens using a DALY framework. We model the effect of  
150 enriching subsidised fertiliser with Zn and compare it to a scenario in which subsidised and non-  
151 subsidised fertilisers are enriched.

## 152 153 **Materials and methods**

155 *Baseline dietary Zn supplies and deficiency prevalence*

156  
157 Baseline national dietary Zn supplies and deficiencies were estimated for 10 countries on the basis of  
158 food supply and composition data: Burkina Faso, Ethiopia, Ghana, Kenya, Malawi, Mali, Nigeria,  
159 Senegal, Tanzania and Zambia. Food supply and population data were downloaded from United  
160 Nations datasets (UNDSEA 2013; FAO 2014a). Food Balance Sheets (FBSs) compiled by the FAO  
161 record estimates of food supply for up to 92 edible items at a national level, representing net *per*  
162 *capita* food supply calculated from national production, trade, transport losses, storage, non-food uses,  
163 livestock feed *etc.*, but with no adjustment for household waste or inter- and intra-household variation  
164 in access to food (FAO 2001). Data are now available for 2011, but 2009 was chosen as the reference  
165 year to match with available fertiliser usage statistics (Supplementary Table 1). The Institute for  
166 Health Metrics and Evaluation's (IHME) estimates of DALYs lost due to Zn deficiency are based on  
167 the study of Wessells and Brown (2012) (Lim et al. 2012). Thus food composition data compiled by  
168 Wessells and Brown (2012) are used in the present study, including adjustments made due to  
169 processing of staple foods, such as milling and fermentation of cereals and cassava (*Manihot*  
170 *esculenta* Crantz; Supplementary Table 2). Food supply and composition data were combined in order  
171 to generate estimates of dietary Zn and PA supplies by food item (Wessells and Brown 2012;  
172 Supplementary Tables 2 and 3). National mean supplies of Zn and PA were estimated and the amount  
173 of absorbable Zn in the diet was calculated using the Miller equation (Miller et al. 2007;  
174 Supplementary Table 4). As assumed previously (Wessells and Brown 2012; Wessells et al. 2012),  
175 variation in individual intakes was captured through a coefficient of variation in absorbable Zn intake  
176 of 25 %. We adopted the approach employed in the Estimated Average Requirement (EAR) cut-point  
177 method, in that the proportion of the population below the mean national physiological requirement  
178 for Zn was assumed to be deficient.

179  
180 *Effect of Zn-enriched fertilisers on concentrations of Zn and PA in the grains of maize, rice and wheat*

181  
182 A systematic literature review was conducted in order to assess the impact of Zn fertilisers on Zn  
183 concentrations in major grains. The terms 'zinc OR Zn AND biofortification', 'zinc OR Zn AND  
184 fertili\*', 'zinc OR Zn AND application', 'zinc OR Zn AND concentration', 'zinc OR Zn AND  
185 response', 'zinc OR Zn AND uptake', 'zinc OR Zn AND soil' and 'zinc OR Zn AND foliar' were  
186 queried in the search engines Web of Science (Thomson Reuters, New York, U.S.A.), Science Direct  
187 (Elsevier, Philadelphia, U.S.A.) and Google Scholar (Google Inc., California, U.S.A.). Further studies  
188 were identified by searching reference sections of review and research papers found using the search  
189 terms stated. Criteria for inclusion were that studies were published in a peer-reviewed journal, that  
190 Zn was added *via* either soil or foliar applications under field conditions, and that concentrations of  
191 Zn in the grain were reported for treatments and controls. Both rainfed and irrigated plots were  
192 included. A number of studies assessed Zn applications in combination with varying N or P  
193 application rates. In such instances, the treatment closest to 100 kg ha<sup>-1</sup> yr<sup>-1</sup> of N and 25 kg ha<sup>-1</sup> yr<sup>-1</sup> of  
194 P was included for consistency. The effect of Zn fertiliser was determined for maize, wheat and rice;  
195 insufficient studies were identified to allow a similar systematic analysis of data on other crops. The  
196 most commonly used form of Zn in both granular and foliar fertilisers is ZnSO<sub>4</sub>.7H<sub>2</sub>O. Other forms of  
197 Zn including Zn-bonded amino acids may be more effective at increasing grain Zn concentrations  
198 (Ghasemi et al. 2013), however insufficient studies were identified to include alternatives to ZnSO<sub>4</sub> in  
199 this review.

200  
201 The effect of Zn fertiliser was quantified as concentration of Zn in the grain at harvest as a percent of  
202 control and the median effect was used across studies by taking study site, crop type, cultivar,  
203 application method (soil or foliar) and application rate (kg Zn ha<sup>-1</sup>) as factors. Mean effect over  
204 seasons was taken for multi-season trials. Some studies examined the residual effect of Zn fertilisers  
205 but these data were not included; this is revisited in the Discussion. Studies examining the effect of  
206 different application timings of foliar sprays with later applications (i.e. post-flowering) appeared to  
207 have a greater impact on grain Zn concentration but possibly a lower impact on grain yield (Cakmak  
208 et al. 2010; Mabesa et al. 2013); in such instances, the treatment when Zn was applied at flowering or  
209 heading stages was taken for consistency.

210  
211 Results from 26 journal articles were included in the literature review: four studies of maize, six of  
212 rice, 15 of wheat and one of maize and wheat (Table 1). Fourteen and four studies, respectively,  
213 reported effects of soil and foliar applications while eight reported effects of both soil and foliar  
214 applications. No studies were identified that reported the effect of Zn application *via* soil on PA  
215 concentration in the grain of rice, nor *via* foliar spray in maize. Preliminary analysis of results from all  
216 studies revealed that Zn application *via* soil and foliar routes tended to increase concentrations of Zn  
217 in the grain. However, larger application rates did not appear to increase concentrations more than  
218 smaller rates when comparing trials. This is likely to be due to the variety of soil characteristics  
219 encountered. The majority of studies did not report variance of Zn or PA concentration in the grain so  
220 it was not possible to perform a standard meta-analysis in which variance is used to weight the  
221 contribution of effect size (Field and Gillett 2010). For these reasons, results were pooled by crop and  
222 application method (soil or foliar) with the median effect on crop Zn and PA concentrations taken.  
223

224 Milling of maize, rice and wheat grains is common practice. It was assumed that the relative increase  
225 in Zn concentration in the whole grain and the endosperm fraction were equivalent (the assumption is  
226 revisited in the Discussion). Thus, studies that reported whole grain data were assumed to give a good  
227 prediction of the effect of Zn fertilisation on the Zn concentration of edible portions. Rice is most  
228 commonly eaten in its polished form; data for polished rice were used where available, otherwise,  
229 brown rice data were used.  
230

### 231 *Effect of Zn fertilisers on Zn deficiency prevalence*

232

233 Four scenarios were modelled to quantify the impacts of agronomic biofortification with Zn on  
234 dietary Zn and PA supplies at national levels in the 10 focus countries:  
235

- 236 • the first scenario modelled a policy to enrich *subsidised* fertiliser, which would be easiest to  
237 implement given the pre-existing government involvement;
  - 238 • the second scenario modelled a policy to enrich *subsidised and non-subsidised* fertiliser;
  - 239 • the third scenario modelled a policy to introduce foliar fertilisation of cereals with a target of  
240 50 % coverage; and
  - 241 • the fourth scenario modelled a policy to introduce foliar fertilisation of cereals with a target of  
242 75 % coverage.
- 243

244 All scenarios assumed that maize, rice and wheat crops were targeted. In Ethiopia, teff (*Eragrostis tef*  
245 (Zucc.) Trotter) was also included as this grain accounts for almost one-fifth of national energy  
246 consumption from cereals and *ca.* 40 % of national inorganic fertiliser consumption (CSA 2011; FAO  
247 2014a). Demand for fertiliser was also assumed to arise from millet (*Eleusine coracana* L. and  
248 *Pennisetum glaucum* L.), sorghum (various spp.), cocoa (*Theobroma cacao* L.), coffee (*Coffea* spp.),  
249 cotton (*Gossypium* spp.), palm oil (*Elaeis guineensis* Jacq.), sugarcane (*Saccharum officinarum* L.)  
250 and tobacco (*Nicotiana* spp.). Scenarios one and two assumed that fertiliser used as basal dressing was  
251 enriched using  $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$  to give a N:Zn mass ratio of 2:1. Assuming recommended application  
252 rates of N (see below) this would provide 23, 12, 20 and 12  $\text{kg ha}^{-1} \text{ yr}^{-1}$  of Zn for hybrid maize, local  
253 maize, rice and wheat, respectively. A compliance of 90 % was used to account for enforcement  
254 problems. Scenarios three and four assumed that 600  $\text{L ha}^{-1}$  of 0.5 % (w/v) aqueous  $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$   
255 solution was sprayed twice annually on maize, rice and wheat crops, supplying 1.36  $\text{kg ha}^{-1}$  of Zn.  
256

257 The efficacy and costs of scenarios one and two are partly determined by the quantity of fertiliser  
258 enriched and the proportion of maize, rice, wheat and teff covered by this fertiliser. Fertiliser usage  
259 data were derived from the International Fertilizer Development Center (IFDC) for subsidised  
260 fertiliser consumption (IFDC 2013a) and total national fertiliser consumption (IFDC 2011, 2012a-f,  
261 2013 b,c; Supplementary Table 5) from which the supply of N was calculated. Fertiliser was assumed  
262 to contain 23 % N by mass where product information was not available. ‘Demand’ for N was  
263 calculated as the product of crop-specific fertiliser requirements and cropping areas of maize, rice,

264 wheat and cash crops (Supplementary Table 5). Cropping areas were derived from FAO production  
 265 data (FAO 2014b; Supplementary Table 5)<sup>1</sup>. Half of maize production area was assumed to be hybrid  
 266 varieties and half local varieties in all countries. Crop-specific recommended fertiliser application  
 267 rates were identified only for Malawi, (Malawi Government Ministry of Agriculture and Food  
 268 Security, date unknown, accessed 2014; Supplementary Table 5) and were applied to all countries for  
 269 most crops. Teff was assumed to require the same N rate as wheat. Requirements for tea, coffee, palm  
 270 oil and cocoa were identified through a literature search (FAO 1984; Grice 1990; Makono and  
 271 Chanika 2008).

272  
 273 Thus, the proportion of crops receiving Zn-enriched fertiliser in scenarios one and two was calculated  
 274 as supply of N divided by demand for N (equation 1).

$$275 \quad P_{Zn} = F_{s,w} \times q / \sum (C_{a-l} \times A_{a-l}) \quad (1)$$

276  
 277  
 278 Where:

279  $P_{Zn}$  = proportion of crop receiving Zn-enriched fertiliser;

280  $F_{s,w}$  = national N usage (metric tonnes, t) *via* subsidised fertiliser (s) or subsidised and non-subsidised  
 281 fertiliser (w);

282  $C_{a-j}$  = Cropping area of maize (a), rice (b), wheat (c), teff (d), millet (e), sorghum (f), cocoa (g), coffee  
 283 (h), cotton (i), palm oil (j), sugarcane (k) and tobacco (l);

284  $A_{a-j}$  = Recommended N application rate ( $t \text{ ha}^{-1} \text{ yr}^{-1}$ ) for maize (a), rice (b), wheat (c), teff (d), millet  
 285 (e), sorghum (f), cocoa (g), coffee (h), cotton (i), palm oil (j), sugarcane (k) and tobacco (l); and

286 q = compliance factor (0 to 1).

287  
 288 The effect of Zn fertilisers was modelled through changes to the concentrations of Zn and PA in the  
 289 grains of maize, rice and wheat. The proportion of each crop receiving fertiliser was multiplied by the  
 290 median effects of applied Zn on grain Zn and PA concentrations to generate new composition data for  
 291 maize, rice, wheat and teff. Teff grain was assumed to have the same response to Zn-enriched  
 292 fertiliser as wheat grain. National dietary Zn and PA supplies, quantity of absorbable Zn in the diet  
 293 and estimated prevalence of Zn deficiency were re-calculated using the new composition data,  
 294 assuming that composition of all other food items and quantity of food supply had not changed. The  
 295 proportion of DALYs saved was assumed to equal the reduction in proportion of deficiency  
 296 prevalence.

297  
 298 *Estimating the cost-effectiveness of an agronomic biofortification approach to addressing Zn*  
 299 *deficiency in sub-Saharan Africa*

300  
 301 Baseline disease burdens attributable to Zn deficiency for the 10 focus countries were derived from  
 302 the Global Burden of Disease Study in which a proportion of ‘diarrheal diseases’, ‘typhoid and  
 303 paratyphoid fevers’ and ‘lower respiratory infections’ are attributed to Zn deficiency and assigned a  
 304 ‘disability weight’ (Lim et al. 2012; IHME 2014).

305  
 306 The cost of enriching fertilisers with Zn was estimated assuming a wholesale retail price of  
 307  $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$  of US\$ 500  $\text{t}^{-1}$ . Only the fertiliser used by maize, rice, wheat and teff was assumed to be  
 308 enriched and, for soil applications, only the proportion applied as a basal dressing (Supplementary  
 309 Table 6). The proportion of crops receiving basal fertiliser was assumed to equal the proportion of  
 310 crops receiving fertiliser (equation 1). The cost of supplying knapsack sprayers was estimated for the  
 311 foliar scenarios by assuming that knapsack sprayer sets cost US\$ 150 *per* unit and that each would last  
 312 10 years and cover 20 ha of cropland annually through sharing among farmers (Supplementary Table

---

<sup>1</sup> Total cereal production area in Ethiopia in 2009 was  $9.2 * 10^6$  ha and teff appears to be included in the production sub-category ‘Cereals, nes’ (production area  $2.6 * 10^6$  ha) rather than the sub-category ‘Millet’ (production area  $0.4 * 10^6$  ha), contrary to the FAO’s own production definitions (FAO 2014c). ‘Cereals, nes’ production area was assumed to be solely teff.

6). Other implementation costs including agricultural extension services and the distribution of equipment and fertiliser were not considered.

## Results

### *Baseline dietary Zn supplies and deficiency prevalence*

Dietary Zn deficiency is likely to be widespread in sub-Saharan Africa. Using national-level food supply and food composition data adjusted by common processing methods, we estimate a high prevalence of Zn deficiency in the 10 focus countries, ranging from 24 % in Nigeria to 66 % in Zambia (Table 2; Supplementary Table 4). The estimated large disease burden attributable to Zn deficiency is consistent with previous work. For example, IHME (2014) estimated that the burden of Zn deficiency in the 10 focus countries ranged from 161 to 1,219 DALYs lost 100 k population<sup>-1</sup> in Ghana and Burkina Faso, respectively. This is two orders of magnitude greater than in the UK where it is estimated that <4 DALYs 100 k population<sup>-1</sup> are lost due to Zn deficiency (IHME 2014).

### *Effect of Zn-enriched fertilisers on concentrations of Zn and PA in the grains of maize, rice and wheat*

A summary of the studies included in the literature review is presented in Table 1. The trials combined a range of soil types and cultivars (Table 3; Supplementary Tables 7 and 8). In control plots (i.e. without application of Zn), concentration of Zn in maize grain ranged from 14.9 mg kg<sup>-1</sup> DW on calcareous, Zn-deficient silty-clay-loam soils in Pakistan (Harris et al. 2007) to 22.5 mg kg<sup>-1</sup> DW on Zn-deficient sandy-loam in Pakistan (Kanwal et al. 2010); concentration of Zn in brown rice (i.e. husk removed but grain unpolished) ranged from 9.9 mg kg<sup>-1</sup> DW in Thailand (Phattarakul et al. 2012) to 41.6 mg kg<sup>-1</sup> DW in 'high-Zn', upland soil in the Philippines (Wissuwa et al. 2008); concentration of Zn in polished rice grain ranged from 12.3 mg kg<sup>-1</sup> DW in pH 7.7 soils in Turkey (Phattarakul et al. 2012) to 28.0 mg kg<sup>-1</sup> DW in Zn-adequate soils in China (Wei et al. 2012); and concentration of Zn in wheat grain ranged from 6.6 mg kg<sup>-1</sup> DW in borderline Zn-deficient soils with pH 7.8 in Iran (Khoshgoftarmanesh et al. 2012) to 40.2 mg kg<sup>-1</sup> DW in Zn-adequate soils in India (Zou et al. 2012).

The median increases in Zn concentration in the grains of maize, rice and wheat were, respectively, 28, 11 and 18 % for soil application and 30, 24 and 63 % for foliar application (Table 4; Figure 1; Supplementary Tables 7 and 8). The result for maize with foliar-applied Zn is based on only one data point (Wang et al. 2012). Application of Zn-enriched fertilisers *via* the soil decreased PA concentration in the grain of wheat by 11 % while foliar application decreased concentration in the grain of rice and wheat by 1 and 13 %, respectively. No studies were identified that reported the effect of Zn application *via* soil on PA concentration in the grain of rice, nor *via* foliar spray in maize.

Yield data are important to rule out the 'concentration effect' whereby lower yields may lead to greater Zn concentrations in the grain as the Zn taken up by the plant is distributed to fewer or smaller grains. This is particularly so for foliar applications as high concentrations of Zn in the spray solution could damage leaf cuticles (Eichert and Fernández 2012). Yield was reported for only 122 out of 273 plots included in the systematic review so a consistent approach to excluding plots with low yield relative to control was not possible, although this is re-visited in the Discussion. Of the studies that reported yield data, soil application led to a median 10-11 % increase in grain yield for maize, rice and wheat, whereas foliar application had no obvious effect (Table 4; Supplementary Table 7). In addition, of the studies that did not report yield data by plot, Mabesa et al. (2013) found no significant difference in yield of rice due to foliar application of Zn, but also reported a significant negative correlation among different varieties between grain yield and grain Zn concentration, a relationship also reported by Wissuwa et al. (2008). Very high yield responses of >150 % of control were found in 10 and four wheat data points for soil and foliar-applied Zn, respectively (Supplementary Table 7). All of these data points also exhibited high Zn concentrations in grains relative to controls, with Q1, median and Q3 of 170, 189 and 257 % for the soil-applied treatments and 252, 295 and 316 % for the foliar-applied treatments.



368 *Effect of Zn fertilisers on Zn deficiency prevalence*

369

370 The effectiveness of the biofortification approach is greatly dependent on the coverage of fertilisers,  
371 i.e. the proportion of crops that would receive fertilisers enriched with Zn. Scenario one modelled the  
372 potential impact of Zn-enrichment of granular fertiliser currently distributed under national subsidy  
373 schemes. The Ethiopian Government control fertiliser imports so all fertiliser usage was considered  
374 under the ‘subsidised’ bracket. The percentage of cereal production receiving subsidised fertiliser  
375 was: Burkina Faso (2), Ethiopia (18), Ghana (6), Kenya (8), Malawi (24), Nigeria (10), Senegal (9),  
376 Tanzania (6) and Zambia (20) (Supplementary Table 5). Data for Mali were not available. The  
377 estimated reduction in DALYs lost due to Zn deficiency was lowest in Burkina Faso (<1 %) and  
378 greatest in Malawi (10 %) where there would be a 3 % increase in the mean amount of absorbable Zn  
379 in the diet (Table 5; Supplementary Tables 9 and 10).

380

381 Scenario two modelled the potential impact of Zn-enrichment of all fertiliser currently used. The  
382 percentage of cereal production receiving both subsidised and non-subsidised fertiliser was: Ghana  
383 (24), Kenya (39), Malawi (39), Mali (14), Nigeria (22), Senegal (21), Tanzania (13) and Zambia (33)  
384 (Supplementary Table 5). Data for Burkina Faso were not available. The estimated reduction in  
385 DALYs lost due to Zn deficiency was lowest in Mali (3 %) and greatest in Malawi (15 %) where there  
386 would be a 5 % increase in the national mean amount of absorbable Zn in the diet (Table 5;  
387 Supplementary Tables 9 and 10).

388

389 Scenarios three and four modelled the potential impact of foliar Zn application, covering 50 and 75 %,  
390 respectively, of maize, rice and wheat production. The response of grain Zn concentration to foliar Zn  
391 application was greater in wheat than in maize or rice and it was assumed that Zn concentration in teff  
392 grain responded as in wheat. Wheat and teff consumption combined was greatest in Ethiopia, (161 g  
393 *capita*<sup>-1</sup> d<sup>-1</sup>; Supplementary Table 1), where the increase in mean amount of absorbable Zn in the diet  
394 for scenarios three and four, respectively, was 13 and 19 % and the estimate of DALYs lost due to Zn  
395 deficiency decreased by 41 and 54 %, respectively (Table 5; Supplementary Tables 9 and 10).  
396 Response of grain PA concentration to foliar Zn application was greatest for rice, and dietary PA  
397 supply in scenario four decreased by 2.8, 1.5 and 1.4 % in Senegal, Ghana and Mali where rice  
398 consumption was 188, 157 and 72 g *capita*<sup>-1</sup> d<sup>-1</sup>, respectively (Table 5; Supplementary Tables 1 and  
399 9).

400

401 *Estimating the cost-effectiveness of an agronomic biofortification approach to addressing Zn*  
402 *deficiency in sub-Saharan Africa*

403

404 The cost effectiveness of agronomic biofortification of crops using soil or foliar-applied ZnSO<sub>4</sub>.7H<sub>2</sub>O  
405 was estimated. Where the outcomes of public health interventions are not measured in monetary  
406 terms, decision-makers cannot rely on conventional tools of economic evaluation, such as internal  
407 rates of return or benefit-cost ratios, to determine whether the ‘investment’ in an intervention  
408 represents a good use of scarce resources. Instead, their relative cost-effectiveness can be assessed by  
409 comparing the average cost of saving one DALY across interventions, or against benchmarks.

410

411 Scenario one modelled a policy to enrich granular fertilisers currently distributed under government  
412 subsidy schemes with Zn. The cost *per* DALY saved ranged from US\$ 624 to 5,747 in Burkina Faso  
413 and Ghana, respectively (Table 5; Figure 2; Supplementary Table 11). Scenario two modelled a policy  
414 to enrich subsidised and non-subsidised granular fertilisers used as basal dressings and cost *per*  
415 DALY saved ranged from US\$ 977 to 5,893 in Senegal and Ghana, respectively (Table 5; Figure 2;  
416 Supplementary Table 11). Variation in cost effectiveness between countries was partly a function of  
417 the baseline disease burden attributable to Zn deficiency with higher burdens leading to lower costs  
418 *per* DALY saved. Foliar application is likely to be a more efficient use of Zn by avoiding fixation of  
419 Zn in the soil. Costs *per* DALY saved in scenario three, in which 50 % of cereal production received  
420 foliar Zn fertiliser, ranged from US\$ 46 to 332 in Senegal and Ghana, respectively, while in scenario  
421 four, in which 75 % of cereal production received foliar Zn fertiliser, the cost ranged from US\$ 49 to  
422 347, also in Senegal and Ghana, respectively (Table 5; Figure 2; Supplementary Table 11).

423  
424 The World Health Organization (WHO 2001) and the World Bank (World Bank 1993) have provided  
425 benchmarks to assess the cost-effectiveness of health interventions; if the cost of saving a DALY is  
426 below the benchmark then it is considered a good investment. The WHO benchmark is calculated in  
427 relative terms as 300 % of a country's *per-capita* Gross Domestic Product (GDP), hence in 2009, from  
428 US\$ 678 to 5,550 *capita*<sup>-1</sup> in Malawi and Ghana, respectively (World Bank 2014; Supplementary  
429 Table 11). The World Bank benchmark is in absolute terms, taking a value of US\$ 150 *per* DALY in  
430 1990 as a base year which is equivalent to US\$ 246 in 2009 after adjusting for inflation. Thus, even in  
431 the poorest country, the World Bank benchmark is lower and harder to meet than that of WHO.  
432 According to the WHO benchmark, pursuing Zn enrichment of soil-applied granular fertilisers  
433 appears to be cost-effective in Burkina Faso, Ethiopia, Kenya, Senegal and Zambia, but not other  
434 countries, while foliar application of Zn appears to be cost-effective in all countries. According to the  
435 World Bank benchmark, the only cost-effective scenarios are foliar application of Zn in Burkina Faso,  
436 Ethiopia, Kenya, Malawi, Mali, Nigeria, Senegal and Zambia (Table 5; Figure 2; Supplementary  
437 Table 11).

438

## 439 **Discussion**

440

### 441 *Baseline dietary Zn supplies and deficiency prevalence*

442

443 Robust estimates of dietary Zn supplies and risk of deficiency underpin the evaluation of approaches  
444 to address Zn deficiency. There are potential weaknesses in using FBS food supply data including  
445 underestimating food supply as some subsistence production is not captured, or overestimating supply  
446 by failing to account for household-level food waste (FAO 2001). These weaknesses have been  
447 discussed extensively elsewhere (de Haen et al. 2011; Wessells et al. 2012; Joy et al. 2014). A further  
448 source of error may arise from composition data derived from sources that will not capture local  
449 variation in elemental composition of crops and there is a lack of spatially-resolved food composition  
450 data in sub-Saharan Africa (Joy et al. 2014; Joy et al. 2015). However, in the absence of wide-scale  
451 analysis of biomarkers of nutrient status, e.g. blood serum, estimating national dietary supplies of  
452 bioavailable Zn remains a valuable method of estimating the prevalence of Zn deficiency at a national  
453 level (Gibson et al. 2008).

454

455 An alternative to FBSs is to use food consumption data captured in nationally-representative  
456 household surveys (Fielder et al. 2008). These data are available for eight of the 10 focus countries in  
457 this study (Ethiopia, Ghana, Kenya, Malawi, Mali, Nigeria, Tanzania and Zambia). For example,  
458 Fielder et al. (2013) estimate mean and median intakes of Zn in Zambia of 5.8 and 4.4 mg *capita*<sup>-1</sup> d<sup>-1</sup>  
459 and a 73.1 % prevalence of inadequate Zn intakes, compared to US Institute of Medicine dietary  
460 requirements of Zn. An advantage of household surveys is that they allow sub-national resolution of  
461 dietary estimates and shed light on distributional issues. One drawback is that they rely on household  
462 member recall, which is subject to misreporting, both intentional and unintentional (Archer et al.  
463 2013; Moltedo et al. 2014). Zinc intakes and status can also be measured directly through analysis of  
464 dietary composites or concentration of Zn in blood plasma or serum samples. Through such methods,  
465 high prevalence of Zn deficiency have been reported previously in sub-populations in Burkina Faso  
466 (e.g. Müller et al. 2003), Ethiopia (e.g. Abebe et al. 2007; Kasso et al. 2008; Stoecker et al. 2009),  
467 Kenya (e.g. Siekmann et al. 2003), Malawi (e.g. Siyame et al. 2013), Nigeria (e.g. Gegios et al. 2010),  
468 Tanzania (e.g. Veenemans et al. 2011) and Zambia (e.g. Duggan et al. 2005).

469

470 New baseline Zn deficiency estimates correlated well with the IHME estimates of DALYs lost due to  
471 Zn deficiency (Spearman's Rank,  $r = 0.588$ ,  $p = 0.018$ , d.f. = 9). This is expected as both the present  
472 study and the IHME DALY estimates were derived from the underlying data and methodology  
473 developed by Wessells et al. (2012) (Wessells and Brown 2012; Lim et al. 2012). However, there is  
474 no correlation between the results of Joy et al. (2014) and Wessells and Brown (2012) which is  
475 surprising given the similar underlying methodologies. This may have arisen because the studies used  
476 different reference years and food composition tables and prevalence of deficiency in the Wessells  
477 and Brown (2012) study are based on estimated dietary supplies of 'bioavailable' Zn. Also, Wessells

478 and Brown (2012) assumed certain milling and fermentation practices of cereals and other crops and  
479 adjusted the concentrations of Zn and PA accordingly. For example, estimated dietary PA supplies in  
480 Ethiopia are 2,802 mg *capita*<sup>-1</sup> d<sup>-1</sup> in the Joy et al. (2014) study, but 1,724 mg *capita*<sup>-1</sup> d<sup>-1</sup> in the  
481 Wessells and Brown (2012) study in which 59 % of wheat, 90 % of maize, millet and sorghum and  
482 100 % of other cereals (i.e. teff) are assumed to be fermented (Supplementary Table 2).  
483

484 Zinc deficiency confers increased risk of diarrhoea and is a potential underlying cause of stunting  
485 which is defined as having a height-for-age more than two standard deviations below the median of  
486 the WHO growth reference (WHO 1995). Although deficiency estimates in the current study, which  
487 are based on dietary intakes of Zn and PA, show a general positive relationship with the WHO  
488 estimates of childhood stunting prevalence, the relationship is not statistically significant ( $P > 0.1$ ) for  
489 both the absolute and log-transformed values. Other potential underlying causes of stunting include  
490 caloric deficiency (Stein et al. 2003), mother's body mass index (Mamiro et al. 2005) access to clean  
491 drinking water (Esrey et al. 1988) and sanitation and hygiene practices (Fink et al. 2011; Spears et al.  
492 2013).  
493

494 *Effect of Zn-enriched fertilisers on concentrations of Zn and PA in the grains of maize, rice and wheat*  
495

496 The efficacy of applied Zn in increasing grain Zn concentration depends in part on the crop species  
497 and cultivar. Across studies, the effect of soil-applied Zn on grain Zn concentrations was greater in  
498 maize and wheat than in rice (Table 4; Figure 1). This may be due to abiotic factors such as the  
499 reducing conditions and high organic matter content typically found in anaerobic flooded paddy soil  
500 (Alloway 2008), or biotic factors such as root morphology or root exudates (Widodo et al. 2010).  
501 Cereal crops can respond to Zn deficiency stress by releasing compounds capable of chelating soil-  
502 bound Zn including low-molecular-weight organic acids and a class of non-protein amino acids  
503 known as phytosiderophores (Kochian 1993; Hoffland et al. 2006; Suzuki et al. 2006, 2008; Widodo  
504 et al. 2010). Alternatively, the lower efficacy in rice may have been due to the higher soil pH values  
505 and lower baseline DTPA-extractable Zn concentrations in maize and wheat trials than rice trials,  
506 possibly leading to lower concentrations of Zn in grains from control plots and a greater response to  
507 Zn application (Table 3). In addition, average Zn application rates were greater in maize and wheat  
508 trials than rice (Table 3).  
509

510 The effect of foliar-applied Zn was greater in wheat than in rice (Table 4; Figure 1). Biotic factors  
511 including the ability to remobilize Zn from ageing leaves to the grain may be responsible, while the  
512 rate at which remobilization occurs may be dependent on the Zn nutritional status of the plant which  
513 will, in turn, be affected by soil properties. Also, a portion of the foliar-applied Zn may run down the  
514 stem and reach the rhizosphere where availability to the plant root will depend on soil properties.  
515

516 Several studies reported significant differences in the Zn concentration of grains and the efficacy of  
517 soil or foliar Zn application between cultivars of rice and wheat (Yilmaz et al. 1997; Ekiz et al. 1998;  
518 Erdal et al. 2002; Wissuwa et al. 2008; Yang et al. 2011a; Khoshgoftarmanesh et al. 2012; Phattarakul  
519 et al. 2012; Wei et al. 2012; Ghasemi et al. 2013; Mabesa et al. 2013), suggesting that agronomic and  
520 crop breeding biofortification efforts should be aligned. Only one study investigated different  
521 cultivars of maize, finding no significant difference between two cultivars (Kanwal et al. 2010).  
522

523 The majority of trials reviewed here were conducted in Western, Central and Eastern Asia where Zn-  
524 deficiency in crops commonly arises in calcareous soils with pH >7.5 (Table 1; Alloway 2008). In  
525 highly-weathered tropical soils, Zn deficiency may be a product of leaching and low total Zn content  
526 (Alloway 2008). Only two of the studies reviewed here included trials located in Africa, both of soil-  
527 applied Zn, reporting an 18 % increase in the concentration of Zn in the grain of maize on borderline  
528 Zn-deficient soils in Zimbabwe (Manzeke et al. 2014) and a 4 % increase in the concentration of Zn in  
529 the grain of wheat grown on Zn-deficient soils in Zambia (Zou et al. 2012). Clearly, more studies are  
530 required across the varied environmental conditions found in sub-Saharan Africa to verify the  
531 estimates of the effects of applied Zn on grain Zn concentration.  
532

533 Although soil-application of Zn is likely to improve yields of crops grown on Zn-deficient soils, it  
534 could inhibit the absorption of other nutrients such as copper, while foliar sprays with high Zn  
535 concentration could damage leaf cuticles. Reduced yields could lead to a ‘concentration effect’, where  
536 Zn in the leaves or shoot is distributed to fewer or smaller grains. Although this may increase  
537 concentrations of Zn in the edible portion, it would clearly be undesirable. Yield data were reported  
538 for 122 treatment plots in total with soil applications appearing to generally improve yields while  
539 foliar applications had no obvious effect (Table 4). The yields of just six of the treatment plots were  
540 <90 % of the relevant control plot and all of these plots also exhibited increased concentration of Zn  
541 in the grain relative to the control plot (Supplementary Table 7). However, removing these data points  
542 from the study had minimal impact on the estimated efficacy and cost-effectiveness of the four Zn-  
543 fertilisation scenarios: median effects across studies of soil applied Zn would remain unchanged for  
544 maize, rice and wheat and median effect of foliar-applied Zn would be unchanged for maize and  
545 would be 124 and 160 % for rice and wheat, compared to 125 and 163 %.

547 Zinc is distributed unevenly across cereal grain fractions, with higher concentrations in the bran and  
548 embryo than the endosperm. Thus, milling and processing generally reduce the concentration of Zn in  
549 the edible product (Bityutskii et al. 2002; Ozturk et al. 2006; Liang et al. 2008; Cakmak et al. 2010;  
550 Joy et al. 2015). Many of the studies included in the meta-analysis only reported Zn concentrations in  
551 whole grain, with and without application of Zn. It is possible that greater concentration of Zn in the  
552 whole grain with Zn fertilisation is a result of increased concentrations in the bran and embryo and not  
553 the endosperm. However, Cakmak et al. (2010) examined Zn concentrations across the different  
554 fractions of wheat grain and reported that the greatest relative increase in Zn concentrations with Zn  
555 fertilisation is likely to be in the endosperm. In addition, those studies that reported milled or polished  
556 grain Zn concentrations generally found positive effects of Zn fertilisation. For example, Wei et al.  
557 (2012) found that foliar application increased Zn concentration in the polished grains of three rice  
558 cultivars by 18-28 % and Zhang et al. (2012) found significantly greater Zn concentrations in 60-65 %  
559 extraction wheat flour (i.e. bran and germ removed) with soil ( $P < 0.05$ ) and foliar ( $P < 0.001$ )  
560 applications of Zn. Despite these findings, when looking across the studies reviewed here, application  
561 of Zn *via* the soil increased concentrations of Zn in brown rice (median = 110, Q1 = 102, Q3 = 120 %  
562 of control, n = 27) but not white rice (median = 99, Q1 = 98, Q3 = 104 % of control, n = 3) and foliar  
563 application increased concentrations more in brown (median = 130, Q1 = 114, Q3 = 147 % of control,  
564 n = 28) than white (median = 117, Q1 = 112, Q3 = 122 % of control, n = 6) rice. Thus, agronomic  
565 biofortification of rice may be less effective at increasing Zn in the diet than assumed and future  
566 studies could confirm or allay this concern by reporting data for both whole grain and polished rice.

567  
568 No studies were identified that reported the effect of Zn application *via* soil on PA concentration in  
569 the grain of rice, nor *via* foliar spray in maize. Were such data available, it is likely that estimates of  
570 efficacy and cost-effectiveness of the agronomic biofortification strategies would improve. In  
571 addition, this review excluded data reporting the effects of residual soil-applied Zn in subsequent  
572 crops. Thus, applied Zn that is not taken up by the crop or permanently ‘fixed’ within mineral phases  
573 is potentially available for subsequent crop uptake and some studies show a cumulative increase in  
574 grain Zn concentrations in successive seasons following Zn application (Srivastava et al. 2009; Wang  
575 et al. 2012; Abid et al. 2013; Manzeke et al. 2014), although positive residual effects are not always  
576 found (Lu et al. 2012; Yang et al. 2011a). Therefore, the efficacy of Zn fertilisation might be under-  
577 estimated here by excluding residual effects, especially in lower-pH soils. Conversely, meta-analyses  
578 are subject to systematic bias due to preferential reporting and publishing of ‘positive’ findings  
579 (Dickerson et al. 1992). This may lead to an over-estimate of the efficacy of Zn-enrichment on  
580 concentrations of Zn in grains.

581  
582 Cereals contribute *ca.* 50 % or more of energy intake across 46 countries in Africa, but root and tuber  
583 crops contribute >30 % of energy supplies in 10 countries (Joy et al. 2014). Concentration of Zn in the  
584 tuber of potato (*Solanum tuberosum* L.) is generally low (i.e. 10-20 mg kg<sup>-1</sup>) due to limited  
585 translocation of Zn from shoots to tubers *via* the phloem, although there is significant variation  
586 between genotypes and concentrations up to *ca.* 30 mg kg<sup>-1</sup> are achievable with foliar Zn application  
587 (White and Broadley 2011; White et al. 2012). Hence, Zn biofortification of potatoes appears to be

588 feasible, in principle. The prospect for supplying Zn *via* granular fertilisers to cassava and sweet  
589 potato (*Ipomoea batatas* L.) is likely to be more limited as these crops are generally grown with few  
590 external inputs (Kelly 2006), while a foliar fertilisation programme must consider that the leaves of  
591 these crops are consumed in some cultures in sub-Saharan Africa. Leafy vegetables contribute little to  
592 dietary energy, but substantially to dietary Zn, intakes due to greater concentrations of Zn in leaves  
593 than grains, tubers or fruits (Broadley et al. 2007). For example, Joy et al. (2015) report  
594 concentrations of Zn in edible leaves from Malawi of *ca.* 40-70 mg kg<sup>-1</sup> DW. The concentration of Zn  
595 in edible leaves is dependent on both environmental factors, such as the concentration of extractable  
596 Zn in the soil, and genetic factors which show high heritability in some, but not all, species (Wu et al.  
597 2007, 2008; Broadley et al. 2010); thus there is scope for biofortification of edible leaves through  
598 agronomic or breeding approaches.

#### 600 *Effect of Zn fertilisers on Zn deficiency prevalence*

601  
602 Assumptions were made regarding the coverage of fertilisers and hence the proportion of crops that  
603 could receive fertiliser enriched with Zn. The proportion of maize, rice, wheat and teff receiving  
604 fertiliser was derived from the ratio of national N demand and usage. Demand may be underestimated  
605 (thus coverage overestimated) as some crops were not included (e.g. horticultural and oil crops), or  
606 may be over-estimated (thus coverage underestimated) as some non-target crops such as millet and  
607 sorghum are grown extensively in sub-Saharan Africa with little fertiliser applied (Ahmed et al.  
608 2000). In addition, fertiliser usage data were generally derived from national government statistics  
609 (IFDC 2011, 2012a-f, 2013 b,c) and are likely to vary in accuracy. Fertiliser usage data for 2009 were  
610 used due to the availability of IFDC reports. However, usage, and thus the potential reach of a  
611 programme to enrich granular fertilisers with Zn, is likely to vary annually depending on prices,  
612 farmer purchasing power and government subsidy programmes. For example, estimated N  
613 consumption in Zambia in 2009 was 39,400 t based on total fertiliser consumption of 171,000 t in  
614 2007/08 (IFDC 2013c). By 2012/13, estimated fertiliser consumption had increased to 250,000-  
615 300,000 t (IFDC 2013c).

616  
617 A further limitation of the study is that average changes in the composition of maize, rice and wheat  
618 (a product of the average effect of Zn-enriched fertilisers on crop composition and coverage of  
619 fertiliser usage) were applied to all of the national supply of these food items provided in the Food  
620 Balance Sheets. However, a national programme to introduce Zn enrichment *via* soil or foliar applied  
621 fertilisers will only alter the composition of crops produced in-country. Thus, the effect on average Zn  
622 concentration may be over-estimated as imported crops are not enriched while some of the benefits of  
623 the fortification may not be captured as exported crops are enriched.

#### 625 *Estimating the cost-effectiveness of an agronomic biofortification approach to address Zn deficiency* 626 *in sub-Saharan Africa*

627  
628 In the current study, costs of Zn and knapsack sprayers were considered whereas other costs,  
629 including for agricultural extension, intra-national distribution of consumables and quality control,  
630 were not. This is likely to underestimate the cost of the modelled strategies. Estimating full costs  
631 would require detailed study of national agricultural extension services, laboratory capacities *etc.*

632  
633 The EAR cut-point approach might underestimate the cost-effectiveness of a population-level  
634 fortification programme to alleviate Zn deficiency as only the reduction in deficiency prevalence is  
635 considered. In this study, 'deficient' status was defined as dietary Zn supply below the mean national  
636 EAR. Increasing Zn concentration in staple foods and in the national diet moves a proportion of the  
637 population from below to above the EAR cut point. However, those who remain below the EAR may  
638 still have derived health benefits from increased Zn intake, (e.g. individuals who move from 'severe'  
639 to 'mild' Zn deficiency), and this benefit is not captured. Moreover, a non-linear relationship between  
640 the level of dietary micronutrient deficiencies and the severity of related health outcomes is normally  
641 assumed (Stein et al. 2005). Hence, even if an intervention does not completely eliminate a

642 deficiency, it will have a relatively larger impact when alleviating the more severe levels of the  
643 deficiency.

644  
645 Several studies have demonstrated that Zn-enrichment of granular fertilisers can be a cost-effective  
646 strategy due to improvements in crop yield (e.g. van Asten et al. 2004; Harris et al. 2007; Cakmak  
647 2009). From the limited yield data available in the studies reviewed here, it appears that soil-applied  
648 Zn has a small (*ca.* 10 %) positive impact on yield of maize, rice and wheat while foliar application  
649 has minimal effect. The lack of yield response with foliar sprays may be because post-flowering  
650 applications were preferred as these late applications have a greater impact on grain Zn concentration  
651 with a smaller impact on grain yield (Cakmak et al. 2010; Mabesa et al. 2013). The very high yield  
652 responses (i.e. >150 % greater than control) found in a few cases are likely to be due to severe crop  
653 deficiency of Zn and these plots also exhibited great response in grain Zn concentration. Thus, an  
654 economic argument for the use of Zn fertilisers due to yield improvements will be highly dependent  
655 on the soil characteristics.

656  
657 The feasibilities of the different scenarios require consideration. Previously, it has been suggested that  
658 the yield of crop varieties bred for high-Zn concentration must be maintained or improved if farmer  
659 acceptance is to be encouraged (Welch and Graham 2004) and yield improvements have been an  
660 important driver of the uptake of Zn-enriched fertilisers in Turkey in areas of Zn-deficient soils  
661 (Cakmak 2009). Further studies are required to test whether potential yield improvements due to  
662 granular or foliar Zn application are sufficient to drive their uptake among resource-poor smallholder  
663 farmers in sub-Saharan Africa. Governments or international donors might be persuaded to subsidise  
664 or mandate Zn-enrichment of fertilisers due to the potential public health benefits, possibly  
665 implemented through existing fertiliser subsidy schemes. To the authors' knowledge, acceptance of  
666 micronutrient sprays by smallholder farmers in sub-Saharan Africa has not been studied and is likely  
667 to depend on observable benefits such as yield improvements. In addition, it is questionable whether  
668 knapsack sprayers are suitable for foliar application of Zn to maize, which might be *ca.* 2 m in height  
669 at tasselling, compared to *ca.* 1 m for mature stands of rice, wheat and teff.

670  
671 *Comparison of agronomic biofortification with other strategies to alleviate Zn deficiency*

672  
673 A fertiliser approach can be compared directly against other Zn interventions. Crop breeding is  
674 another strategy to potentially decrease the prevalence and disease burden of Zn deficiency. The  
675 HarvestPlus (H+) programme is developing nutrient-rich staple crops through exploitation of existing  
676 genotypic variation including in wild relatives, setting target Zn concentrations of 38, 28 and 38 mg  
677 kg<sup>-1</sup> DW in whole maize grain, polished rice grain and whole wheat grain, respectively (Bouis and  
678 Welch 2010; Velu et al. 2014). Stein et al. (2006) estimated that biofortification of crops by breeding  
679 for high Zn concentration would be one-to-three orders of magnitude more cost effective than the  
680 fertiliser approaches modelled here. However, the potential of new varieties to deliver greater  
681 concentrations of Zn in the grain depends on there being plant-accessible Zn stores in the soil, thus  
682 breeding and agronomic biofortification strategies are likely to be complementary.

683  
684 Fielder et al. (2013) estimated that fortifying maize meal with a premix containing Zn at large-scale  
685 mills in Zambia could save 5,657 DALYs annually of which 1,757 were due to Zn deficiency, at a  
686 cost of US\$ 401 *per* DALY saved. The cost *per* DALY saved is favourable compared to application  
687 of Zn *via* the soil and equivalent or slightly more expensive than *via* foliar spray, although it should be  
688 noted that this is not a direct comparison as the premix also contained iron and vitamin A. Flour  
689 fortification during milling currently has limited reach in Zambia as few households purchase maize  
690 flour from large, centralised milling factories and those that do are generally wealthier with greater  
691 baseline Zn intakes (Fielder et al. 2013). Thus, while application of Zn to crops *via* the soil is  
692 approximately 10-fold more expensive than *via* foliar sprays or fortification of flour at centralised  
693 mills, it has the potential to reach more households and consequently be more equitable in outcome.

694  
695 In the studies reviewed here, median Zn concentrations in grain from control plots were 19.0 (Q1 =  
696 15.4, Q3 = 22.0, n = 7) and 15.8 (Q1 = 9.8, Q3 = 25.2, n = 141) mg kg<sup>-1</sup> for whole maize and wheat

697 grains, respectively, and 18.8 (Q1 = 15.2, Q3 = 23.9, n = 6) and 18.8 (Q1 = 13.4, Q3 = 27.6, n = 44)  
698 mg kg<sup>-1</sup> for polished and brown rice, respectively. That there was no difference in median Zn  
699 concentration between polished and brown rice samples across studies is surprising and cannot be  
700 explained with the available data. If brown and polished rice are considered together and median  
701 increases found in reviewed studies are applied, Zn concentrations of 23.4, 16.9 and 22.4 mg kg<sup>-1</sup> in  
702 maize, rice and wheat appear achievable using soil-applied Zn, and 24.7, 19.8 and 30.6 mg kg<sup>-1</sup> using  
703 foliar-applied Zn. Even with 100 % coverage of soil or foliar-applied Zn, these concentrations are  
704 well below the H+ breeding targets (Figure 1; White and Broadley 2009; Bouis and Welch 2010).  
705 Thus, while agronomic biofortification of staple grains with Zn may be a useful strategy to mitigate  
706 inadequate dietary Zn supplies, the elimination of Zn deficiency will require complementary  
707 approaches including crop breeding, dietary diversification and possibly fortification during  
708 processing. If synergies can be exploited when pursuing such a combined approach, the cost-  
709 effectiveness of these interventions might also improve.

710  
711 Zinc is just one of a number of micronutrients with widespread risk of deficiency in sub-Saharan  
712 Africa. For example, in Malawi, approximately 80 % of the population is at risk of selenium (Se)  
713 deficiency due to low concentrations of Se in edible portions of crops grown on low-pH soils  
714 (Chilimba et al. 2011; Hurst et al. 2013; Joy et al. 2015). Adding Se to the staple crop maize *via*  
715 subsidised fertiliser could supply adequate amounts of Se in the diets of the *ca.* 1.5 million households  
716 who benefit from the Malawi government Fertiliser Input Subsidy Scheme, at a total cost of 250-550  
717 US\$ k yr<sup>-1</sup> (Chilimba et al. 2012). This is approximately 50-fold cheaper than scenario one in the  
718 present study, at US\$ 0.016-0.035 *capita*<sup>-1</sup> yr<sup>-1</sup> compared to US\$ 1.08 *capita*<sup>-1</sup> yr<sup>-1</sup>, assuming that costs  
719 are spread equally across the national population. However, unlike for Zn, the disease burden of Se  
720 deficiency has not yet been quantified so cost *per* DALY saved cannot be estimated using the same  
721 frameworks. Agronomic fortification *via* soil-applied fertiliser requires only 5 g ha<sup>-1</sup> yr<sup>-1</sup> of Se  
722 compared to *ca.* 10-25 and 1-4 kg ha<sup>-1</sup> yr<sup>-1</sup> of Zn *via* soil and foliar application methods, respectively.  
723 Thus, although the unit cost of Se is greater than that of Zn, fortification with Zn is more expensive.  
724 However, combining multiple elements such as Zn and Se in granular or foliar fertilisers could deliver  
725 wider health benefits and improve the cost-effectiveness of agronomic biofortification strategies.

## 726 727 **Conclusions**

728  
729 Agronomic biofortification of crops with elements important for human health has been advocated as  
730 a public health strategy to address mineral element deficiencies in humans that can have severe  
731 consequences for the well-being of individuals and the welfare of affected societies. We  
732 systematically reviewed the literature for studies of the impact of Zn fertiliser on Zn and PA  
733 concentrations in the grains of maize, rice and wheat. In a simplified meta-analysis, the median effects  
734 of soil-applied Zn on the concentration of Zn in the grains of maize, rice and wheat were 23, 7 and 19  
735 % increases above the control, respectively, while the corresponding figures for foliar applied Zn  
736 were 30, 25 and 63 %.

737  
738 We focused on 10 countries in sub-Saharan Africa that currently implement fertiliser subsidy schemes  
739 or have strong governmental control over fertiliser imports and therefore have the necessary leverage  
740 to implement and enforce Zn enrichment of granular fertiliser. For the nine countries with the  
741 necessary data available, enriching subsidised fertiliser with Zn could save a total of 63 k DALYs yr<sup>-1</sup>  
742 lost due to Zn deficiency with cost effectiveness ranging from US\$ 624 to 5,747 DALY<sup>-1</sup> saved.  
743 Enriching subsidised and non-subsidised fertilisers in the eight countries with necessary data could  
744 save a total of 83 k DALYs yr<sup>-1</sup> with cost effectiveness ranging from US\$ 977 to 5,893 DALY<sup>-1</sup>.  
745 Foliar sprays may be a more cost-effective approach, saving 375 k and 523 k DALYs yr<sup>-1</sup> for 50 and  
746 75 % coverage of cereals, respectively, at a cost of US\$ 46 to 347 DALY<sup>-1</sup> although it is likely that  
747 there would be significant administrative costs in implementing such a programme and these costs  
748 were not considered here.

749  
750 Cost-effectiveness of the fertiliser approach varies and, if compared against international cost-  
751 effectiveness benchmarks, these results indicate that adoption of a fertiliser approach needs to be

752 assessed on a case-by-case basis to allow decision-makers to optimise the allocation of scarce  
753 resources to alternative and complementary public health interventions. Generally, the cost-  
754 effectiveness of foliar-applied Zn appears to be equivalent to fortification of staple flours at  
755 centralised milling facilities. Soil-applied Zn appears to be more expensive but has the potential  
756 advantage of reaching more households. Moreover, synergies might be realised if agronomic  
757 (fertilisation) and genetic (breeding) biofortification efforts are combined, potentially improving both  
758 impact and cost-effectiveness of these interventions.



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766

767 **References**

768

769 Abebe Y, Bogale A, Hambidge KM, Stoecker BJ, Arbide I, Teshome A, Krebs NF, Westcott JE,  
770 Bailey KB, Gibson RS (2007) Inadequate intakes of dietary zinc among pregnant women from  
771 subsistence households in Sidama, Southern Ethiopia. *Public Health Nutr* 11:379–386. doi:  
772 10.1017/S1368980007000389

773

774 Abid M, Ahmed N, Qayyum MF, Shaaban M, Rashid A (2013) Residual and cumulative effect of  
775 fertilizer zinc applied in wheat-cotton production system in an irrigated aridisol. *Plant Soil Environ*  
776 59:505-510

777

778 Ahmad W, Watts MJ, Imtiaz M, Ahmed I, Zia MH (2012) Zinc deficiency in soils, crops and humans:  
779 A review. *Agrochimica* 56:65–97

780

781 Ahmed MM, Sanders JH, Nell WT (2000) New sorghum and millet cultivar introduction in Sub-  
782 Saharan Africa: impacts and research agenda. *Agr Syst* 64:55–65. doi: 10.1016/S0308-  
783 521X(00)00013-5

784

785 Alloway BJ (2008) Zinc in soils and crop nutrition. Second Edition. International Zinc Association  
786 and International Fertilizer Industry Association, Brussels, Belgium and Paris, France

787

788 Archer E, Hand GA, Blair SN (2013) Validity of U.S. nutritional surveillance: National Health and  
789 Nutrition Examination Survey caloric energy intake data, 1971–2010. *PLoS ONE* 8:e76632. doi:  
790 10.1371/journal.pone.0076632

791

792 Bityutskii NP, Magnitkskiy SV, Korobeynikova LP, Lukina EI, Soloviova AN, Patsevitch VG,  
793 Lapshina IN, Matveeva GV (2002) Distribution of iron, manganese, and zinc in mature grain and their  
794 mobilization during germination and early seedling development in maize. *J Plant Nutr* 25:635–653.  
795 doi: 10.1081/PLN-120003387

796

797 Bouis HE, Welch RM (2010) Biofortification – A sustainable agricultural strategy for reducing  
798 micronutrient malnutrition in the global south. *Crop Sci* 50:S20–S32. doi:  
799 10.2135/cropsci2009.09.0531

800

801 Broadley MR, White PJ, Hammond JP, Zelko I, Lux A (2007) Zinc in plants. *New Phytol* 173:677–  
802 702. doi: 10.1111/j.1469-8137.2007.01996.x

803

804 Broadley MR, Ó Lochlainn S, Hammond JP, Bowen HC, Cakmak I, Eker S, Erdem H, King GJ,  
805 White PJ (2010) Shoot zinc (Zn) concentration varies widely within *Brassica oleracea* L. and is  
806 affected by soil Zn and phosphorus (P) levels. *J Hortic Sci Biotechnol* 85:375-380.

807

808 Brümmer G, Tiller KG, Herms U, Clayton PM (1983) Adsorption-desorption and/or precipitation-  
809 dissolution processes of zinc in soils. *Geoderma* 31:337–354. doi: 10.1016/0016-7061(83)90045-9

810

811 Cakmak I (2002) Plant nutrition research: priorities to meet human needs for food in sustainable  
812 ways. *Plant Soil* 247:3–24. doi: 10.1023/a:1021194511492

813  
814 Cakmak I (2004) Identification and correction of widespread zinc deficiency in Turkey – a success  
815 story (a NATO-Science for Stability Project). Proceedings of the International Fertiliser Society 552.  
816 International Fertiliser Society, York  
817  
818 Cakmak I (2008) Enrichment of cereal grains with zinc: Agronomic or genetic biofortification? *Plant*  
819 *Soil* 302:1–17. doi:10.1007/s11104-007-9466-3  
820  
821 Cakmak I (2009) Enrichment of fertilizers with zinc: An excellent investment for humanity and crop  
822 production in India. *J Trace Elem Med Bio* 23:281–289. doi: 10.1016/j.jtemb.2009.05.002  
823  
824 Cakmak I, Kalayci M, Ekiz H, Braun HJ, Kilingç Y, Yilmaz A (1999) Zinc deficiency as a practical  
825 problem in plant and human nutrition in Turkey: A NATO-science for stability project. *Field Crop*  
826 *Res* 60:175–188. doi: 10.1016/S0378-4290(98)00139-7  
827  
828 Cakmak I, Kalayci M, Kaya Y, Torun AA, Aydin N, Wang Y, Arisoy Z, Erdem H, Yazici A, Gokmen  
829 O, Ozturk L, Horst WJ (2010) Biofortification and localization of zinc in wheat grain. *J Agric Food*  
830 *Chem* 58:9092–9102. doi: 10.1021/jf101197h  
831  
832 Central Statistics Agency (CSA 2011) Agriculture in figures: Key findings of the 2008/09-2010/11  
833 agricultural sample surveys for all sectors and seasons. Country summary. Comprehensive Africa  
834 Agriculture Development Program (CAADP) Ethiopia Study, Final Report, Volume 1, 2009. Cited in  
835 IFDC (2012a).  
836  
837 Chilimba ADC, Young SD, Black CR, Meacham MC, Lammel J, Broadley MR (2012) Agronomic  
838 biofortification of maize with selenium (Se) in Malawi. *Field Crop Res* 125:118–128. doi:  
839 10.1016/j.fcr.2011.08.014  
840  
841 Chilimba ADC, Young SD, Black CR, Rogerson KB, Ander EL, Watts MJ, Lammel J, Boradley MR  
842 (2011) Maize grain and soil surveys reveal suboptimal dietary selenium intake is widespread in  
843 Malawi. *Sci Rep* 1. doi: 10.1038/srep00072  
844  
845 de Haen H, Klasen S, Qaim M (2011) What do we really know? Metrics for food insecurity and  
846 undernutrition. *Food Policy* 36:760-769. doi: 10.1016/j.foodpol.2011.08.003  
847  
848 Dickersin K, Min YI, Meinert CL (1992) Factors influencing publication of research results: Follow-  
849 up of applications submitted to two institutional review boards. *J Amer Med Assoc* 267:374–378.  
850 doi:10.1001/jama.267.3.374  
851  
852 Duggan C, MacLeod WB, Krebs NF, Westcott JL, Fawzi WW, Premji ZG, Mwanakasale V, Simon  
853 JL, Yeboah-Antwi K, Hamer DH (2005) Plasma zinc concentrations are depressed during acute phase  
854 response in children with falciparum malaria. *J Nutr* 135:802–807  
855  
856 Ekiz H, Bagci SA, Kiral AS, Eker S, Gültekin I, Alkan A, Cakmak I (1998) Effects of zinc  
857 fertilization and irrigation on grain yield and zinc concentration of various cereals grown in zinc-  
858 deficient calcareous soils. *J Plant Nutr* 21:2245–2256. doi: 10.1080/01904169809365558  
859  
860 Erdal I, Yilmaz A, Taban S, Eker S, Cakmak I (2002) Phytic acid and phosphorus concentrations in  
861 seeds of wheat cultivars grown with and without zinc fertilization. *J Plant Nutr* 25:113–127. doi:  
862 10.1081/PLN-100108784  
863  
864 Erenoglu EB, Kutman UB, Ceylan Y, Yildiz B, Cakmak I (2011) Improved nitrogen nutrition  
865 enhances root uptake, root-to-shoot translocation and remobilization of zinc (<sup>65</sup>Zn) in wheat. *New*  
866 *Phytol* 189:438–448. doi:10.1111/j.1469-8137.2010.03488.x  
867

868 Erenoglu B, Nikolic M, Romheld V, Cakmak I (2002) Uptake and transport of foliar applied zinc  
869 (<sup>65</sup>Zn) in bread and durum wheat cultivars differing in zinc efficiency. *Plant Soil* 241:251–257. doi:  
870 10.1023/A:1016148925918  
871

872 Esrey SA, Habicht J-P, Latham MC, Sisler DG, Casella G (1988) Drinking water source, diarrheal  
873 morbidity, and child growth in villages with both traditional and improved water supplies in rural  
874 Lesotho, southern Africa. *Am J Public Health* 78:1451–1455. doi: 10.2105/AJPH.78.11.1451  
875

876 Fernández V, Eichert T (2009) Uptake of hydrophilic solutes through plant leaves: current state of  
877 knowledge and perspectives of foliar fertilization. *CRC Cr Rev Plant Sci* 28:36–68. doi:  
878 10.1080/07352680902743069  
879

880 Field AP, Gillett R (2010) How to do a meta-analysis. *Brit J Math Stat Psy* 63:665–694. doi:  
881 10.1348/000711010X502733  
882

883 Fielder JL, Smitz MF, Dupriez O, Friedman J (2008) Household income and expenditure surveys: A  
884 tool for accelerating the development of evidence-based fortification programs. *Food Nutr Bull*  
885 29:306–319  
886

887 Fielder JL, Lividini K, Kabaghe G, Zulu R, Tehinse J, Bermudez OI, Jallier V, Guyonnet C (2013)  
888 Assessing Zambia’s industrial fortification options: Getting beyond changes in prevalence and cost-  
889 effectiveness. *Food Nutr Bull* 34:501–519. doi: 00000034/00000004/art00013  
890

891 Fink G, Günther I, Hill K (2011) The effect of water and sanitation on child health: evidence from the  
892 demographic and health surveys 1986–2007. *Int J Epidemiol* 40:1196–1204. doi: 10.1093/ije/dyr102  
893

894 Food and Agriculture Organization of the United Nations (FAO 1984) Better Farming Series.  
895 Chapters 22 and 24. Available online: <http://www.fao.org/docrep/006/t0309e/t0309e00.HTM>  
896 [accessed September 2014]  
897

898 Food and Agriculture Organization of the United Nations (FAO 2001) Food balance sheets: a  
899 handbook. FAO, Rome, Italy  
900

901 Food and Agriculture Organization of the United Nations (FAO 2014a) Food Balance Sheets.  
902 Available online: [http://faostat3.fao.org/faostat-gateway/go/to/download/FB/\\*/E](http://faostat3.fao.org/faostat-gateway/go/to/download/FB/*/E) [accessed July 2014]  
903

904 Food and Agriculture Organization of the United Nations (FAO 2014b) Crop production data.  
905 Available online: [http://faostat3.fao.org/faostat-gateway/go/to/download/Q/\\*/E](http://faostat3.fao.org/faostat-gateway/go/to/download/Q/*/E) [accessed July 2014]  
906

907 Food and Agriculture Organization of the United Nations (FAO 2014c) Crop production definitions.  
908 Available online: <http://faostat.fao.org/site/384/default.aspx> [accessed July 2014]  
909

910 Gegios A, Amthor R, Maziya-Dixon B, Egesi C, Mallowa S, Nungo R, Gichuki S, Mbanaso A,  
911 Manary MJ (2010) Children consuming cassava as a staple food are at risk for inadequate zinc, iron,  
912 and vitamin A intake. *Plant Foods Hum Nutr* 65:64–70  
913

914 Genc Y, Humphries JM, Lyons GH, Graham RD (2005) Exploiting genotypic variation in plant  
915 nutrient accumulation to alleviate micronutrient deficiency in populations. *J Trace Elem Med Bio*  
916 18:319–324. doi: 10.1016/j.jtemb.2005.02.005  
917

918 Ghasemi S, Khoshgofarmanesh AH, Afyuni M, Hadadzadeh H (2013) The effectiveness of foliar  
919 applications of synthesized zinc-amino acid chelates in comparison with zinc sulfate to increase yield  
920 and grain nutritional quality of wheat. *Europ J Agronomy* 45:68–74. doi: 10.1016/j.eja.2012.10.012  
921

922 Gibson RS (2012) Zinc deficiency and human health: etiology, health consequences, and future  
923 solutions. *Plant Soil* 361:291–299. doi: 10.1007/s11104-012-1209-4  
924

925 Gibson RS, Hess SY, Hotz C, Brown KH (2008) Indicators of zinc status at the population level: a  
926 review of the evidence. *Brit J Nutr* 99:S14–S23. doi: 10.1017/S0007114508006818  
927

928 Gibson RS, Hotz C, Temple L, Yeudall F, Mtitimuni B, Ferguson E (2000) Dietary strategies to  
929 combat deficiencies of iron, zinc, and vitamin A in developing countries: development,  
930 implementation, monitoring, and evaluation. *Food Nutr Bull* 21:219–231  
931

932 Graham RD, Ascher JS, Hynes SC (1992) Selecting zinc-efficient cereal genotypes for soils of low  
933 zinc status. *Plant Soil* 146:241–250. doi: 10.1007/BF00012018  
934

935 Grice WJ (1990) *Tea Planter's Handbook*. Tea Research Foundation of Central Africa, Malawi.  
936

937 Harris D, Rashid A, Miraj G, Arif M, Shah H (2007) 'On-farm' seed priming with zinc sulphate  
938 solution - A cost-effective way to increase the maize yields of resource-poor farmers. *Field Crop Res*  
939 102:119–127. doi: 10.1016/j.fcr.2007.03.005  
940

941 Harris D, Rashid A, Miraj G, Arif M, Yunas M (2008) 'On-farm' seed priming with zinc in chickpea  
942 and wheat in Pakistan. *Plant Soil* 306:3–10. doi: 10.1007/s11104-007-9465-4  
943

944 Hoagland DR (1948) *Lectures on the inorganic nutrition of plants*, Second edition. Chronica Botanica  
945 Company, Waltham, MA, U.S.A.  
946

947 Hoffland E, Wei C, Wissuwa M (2006) Organic anion exudation by lowland rice (*Oryza sativa* L.) at  
948 zinc and phosphorus deficiency. *Plant Soil* 283:155–162. doi: 10.1007/s11104-005-3937-1  
949

950 Hurst R, Siyame EWP, Young SD, Chilimba ADC, Joy EJM, Black CR, Ander EL, Watts MJ,  
951 Chilima B, Gondwe J, Kang'ombe D, Stein AJ, Fairweather-Tait SJ, Gibson RS, Kalimbira AA,  
952 Broadley MR (2013) Soil-type influences human selenium status and underlies widespread selenium  
953 deficiency risks in Malawi. *Sci Rep* 3:1–6. doi:10.1038/srep01425  
954

955 Institute of Health Metrics and Evaluation (IHME 2014) Global Health Data Exchange, country-level  
956 Global Burden of Disease data. Available online: <http://ghdx.healthdata.org/> [accessed July 2014]  
957

958 International Fertilizer Development Center (2011) Improving fertilizer markets in West Africa: The  
959 fertilizer supply chain in Mali. IFDC, Alabama, U.S.A.. Available online: [www.ifdc.org/R-  
960 D/Research/Mali\\_tech\\_Final111913/](http://www.ifdc.org/R-D/Research/Mali_tech_Final111913/) [accessed June 2014]  
961

962 International Fertilizer Development Center (2012a) Ethiopia fertilizer assessment. IFDC, Alabama,  
963 U.S.A.. Available online: [www.ifdc.org/R-D/Research/Ethiopia-Fertilizer-Assessment/](http://www.ifdc.org/R-D/Research/Ethiopia-Fertilizer-Assessment/) [accessed  
964 June 2014]  
965

966 International Fertilizer Development Center (2012b) Ghana fertilizer assessment. IFDC, Alabama,  
967 U.S.A.. Available online: [www.ifdc.org/R-D/Research/Ghana-Fertilizer-Assessment/](http://www.ifdc.org/R-D/Research/Ghana-Fertilizer-Assessment/) [accessed June  
968 2014]  
969

970 International Fertilizer Development Center (2012c) Kenya fertilizer assessment. IFDC, Alabama,  
971 U.S.A.. Available online: [www.ifdc.org/R-D/Research/Kenya-Fertilizer-Assessment/](http://www.ifdc.org/R-D/Research/Kenya-Fertilizer-Assessment/) [accessed June  
972 2014]  
973

974 International Fertilizer Development Center (2012d) Improving fertilizer markets in West Africa: The  
975 fertilizer supply chain in Nigeria. IFDC, Alabama, U.S.A.. Available online: [www.ifdc.org/R-  
976 D/Research/Nigeria\\_tech\\_Final111913/](http://www.ifdc.org/R-D/Research/Nigeria_tech_Final111913/) [accessed June 2014]

977  
978 International Fertilizer Development Center (2012e) Improving fertilizer markets in West Africa: The  
979 fertilizer supply chain in Senegal. IFDC, Alabama, U.S.A.. Available online: [www.ifdc.org/R-](http://www.ifdc.org/R-D/Research/Senegal_tech_rev111913.pdf/)  
980 [D/Research/Senegal\\_tech\\_rev111913.pdf/](http://www.ifdc.org/R-D/Research/Senegal_tech_rev111913.pdf/) [accessed June 2014]  
981  
982 International Fertilizer Development Center (2012f) Tanzania fertilizer assessment. IFDC, Alabama,  
983 U.S.A.. Available online: [www.ifdc.org/R-D/Research/Tanzania-Fertilizer-Assessment/](http://www.ifdc.org/R-D/Research/Tanzania-Fertilizer-Assessment/) [accessed  
984 June 2014]  
985  
986 International Fertilizer Development Center (2013a) NEPAD Policy Study: Practices and policy  
987 options for the improved design and implementation of fertilizer subsidy programs in sub-Saharan  
988 Africa. IFDC, Alabama, U.S.A.. Available online: [http://www.ifdc.org/Documents/NEPAD-fertilizer-](http://www.ifdc.org/Documents/NEPAD-fertilizer-study-EN-web/)  
989 [study-EN-web/](http://www.ifdc.org/Documents/NEPAD-fertilizer-study-EN-web/) [accessed June 2014]  
990  
991 International Fertilizer Development Center (2013b) Malawi fertilizer assessment. IFDC, Alabama,  
992 U.S.A.. Available online: [www.ifdc.org/R-D/Research/Malawi-Fertilizer-Assessment/](http://www.ifdc.org/R-D/Research/Malawi-Fertilizer-Assessment/) [accessed June  
993 2014]  
994  
995 International Fertilizer Development Center (2013c) Zambia fertilizer assessment. IFDC, Alabama,  
996 U.S.A.. Available online: [www.ifdc.org/R-D/Research/Zambia-Fertilizer-Assessment/](http://www.ifdc.org/R-D/Research/Zambia-Fertilizer-Assessment/) [accessed June  
997 2014]  
998  
999 Jayne TS, Rashid S (2013) Input subsidy programs in sub-Saharan Africa: a synthesis of recent  
1000 evidence. *Agr Econ* 44:1–16. doi: 10.1111/agec.12073  
1001  
1002 Johnson SE, Lauren JG, Welch RM, Duxbury JM (2005) A comparison of the effects of micronutrient  
1003 seed priming and soil fertilization on the mineral nutrition of chickpea (*Cicer arietinum*), lentil (*Lens*  
1004 *culinaris*), rice (*Oryza sativa*) and wheat (*Triticum aestivum*) in Nepal. *Exp Agr* 41:427-448.  
1005 doi:10.1017/S0014479705002851  
1006  
1007 Joy EJM, Ander EL, Young SD, Black CR, Watts MJ, Chilimba ADC, Chilima B, Siyame EWP,  
1008 Kalimbara AA, Hurst R, Fairweather-Tait SJ, Stein AJ, Gibson RS, White PJ, Broadley MR (2014)  
1009 Dietary mineral supplies in Africa. *Physiol Plantarum* 151:208–229. doi: 10.1111/ppl.12144  
1010  
1011 Joy EJM, Broadley MR Young SD, Black CR, Chilimba ADC, Ander EL, Barlow TS, Watts MJ  
1012 (2015) Soil type influences crop mineral composition in Malawi. *Sci Total Environ* 505:587–595. doi:  
1013 10.1016/j.scitotenv.2014.10.038  
1014  
1015 Kanwal S, Rahmatullah A, Ranjha AM, Ahmed R (2010) Zinc partitioning in maize grain after soil  
1016 fertilization with zinc sulphate. *Int J Agric Biol* 12:299–302. doi: 10.13140/2.1.1484.3845  
1017  
1018 Kassu A, Yabutani T, Mulu A, Tessema B, Ota F (2008) Serum zinc, copper, selenium, calcium, and  
1019 magnesium levels in pregnant and non-pregnant women in Gondar, northwest Ethiopia. *Biol Trace*  
1020 *Elem Res* 122:97–106. doi: 10.1007/s12011-007-8067-6  
1021  
1022 Kelly VA (2006) Factors affecting demand for fertilizer in sub-Saharan Africa. *Agriculture and Rural*  
1023 *Development Discussion Paper 23*. The World Bank, Washington DC, U.S.A.  
1024  
1025 Khoshgoftarmanesh AH, Sharifi HR, Afiuni D, Schulin R (2012) Classification of wheat genotypes  
1026 by yield and densities of grain zinc and iron using cluster analysis. *J Geochem Explor* 121:49–54. doi:  
1027 10.1016/j.gexplo.2012.06.002  
1028  
1029 Kochian LV (1993) Zinc absorption from hydroponic solution by plant roots. Chap 4 in Robson AD  
1030 (ed.) *Zinc in Soils and Plants*, Kluwer Academic Publishers, Dordrecht. pp 45-58  
1031

- 1032 Kutman UB, Yildiz B, Cakmak I (2011) Improved nitrogen status enhances zinc and iron  
1033 concentrations both in the whole grain and the endosperm fraction of wheat. *J Cereal Sci* 53:118–125.  
1034 doi: 10.1016/j.jcs.2010.10.006  
1035
- 1036 Kutman UB, Yildiz B, Ozturk L, Cakmak I (2010) Biofortification of durum wheat with zinc through  
1037 soil and foliar applications of nitrogen. *Cereal Chem* 87:1–9. doi: 10.1094/CCHEM-87-1-0001  
1038
- 1039 Liang J, Li Z, Tsuji K, Nakano K, Robert Nout MJ, Hamer RJ (2008) Milling characteristics and  
1040 distribution of phytic acid and zinc in long-, medium- and short-grain rice. *J Cereal Sci* 48:83–91. doi:  
1041 10.1016/j.jcs.2007.08.003  
1042
- 1043 Lim SS, Vos T, Flaxman AD et al. (2012) A comparative risk assessment of burden of disease and  
1044 injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic  
1045 analysis for the Global Burden of Disease Study 2010. *Lancet* 380:2224–2260. doi: 10.1016/S0140-  
1046 6736(12)61766-8  
1047
- 1048 Lindsay WL, Norvell WA (1978) Development of a DTPA soil test for zinc, iron, manganese, and  
1049 copper. *Soil Sci Soc Am J* 42:421–428. doi: 10.2136/sssaj1978.03615995004200030009x  
1050
- 1051 Loneragan JF, Grunes DL, Welch RM, Aduayi EA, Tengah A, Lazar VA, Cary EE (1982)  
1052 Phosphorus accumulation and toxicity in leaves in relation to zinc supply. *Soil Sci Soc Amer J*  
1053 46:345–352. doi: 10.2136/sssaj1982.03615995004600020027x  
1054
- 1055 Lu XC, Cui J, Tian XH, Oggunniyi JE, Gale WJ, Zhao AQ (2012) Effects of zinc fertilization on zinc  
1056 dynamics in potentially zinc-deficient calcareous soil. *Agron J* 104:963–969. doi:  
1057 10.2134/agronj2011.0417  
1058
- 1059 Lu XC, Tian XH, Cui J, Zhao AQ, Yang XW, Mai W (2011) Effects of combined phosphorus-zinc  
1060 fertilization on grain zinc nutritional quality of wheat grown on potentially zinc-deficient calcareous  
1061 soil. *Soil Sci* 176:684–690. doi: 10.1097/SS.0b013e3182331635  
1062
- 1063 Mabesa RL, Impa SM, Grewal D, Johnson-Beebout SE (2013) Contrasting grain-Zn response of  
1064 biofortification rice (*Oryza sativa* L.) breeding lines to foliar Zn application. *Field Crop Res* 149:223–  
1065 233. doi: 10.1016/j.fcr.2013.05.012  
1066
- 1067 Makono RCJ, Chanika CM (2008) Density and fertiliser requirement of Catimor coffee in smallholder  
1068 coffee farmers' fields in Malawi. Horticulture Commodity Group Annual Report. Malawi Government  
1069 Ministry of Agriculture and Food Security. Available online:  
1070 [www.cabi.org/gara/FullTextPDF/2008/20083323841.pdf](http://www.cabi.org/gara/FullTextPDF/2008/20083323841.pdf) [accessed September 2014]  
1071
- 1072 Mamiro PS, Kolsteren P, Roberfroid D, Tatala S, Opsomer AS, Van Camp JH (2005) Feeding  
1073 practices and factors contributing to wasting, stunting, and Iron-deficiency anaemia among 3-23  
1074 month old children in Kilosa District, rural Tanzania. *J Health Popul Nutr* 23:222–230  
1075
- 1076 Manzeke GM, Mapfumo P, Mtambanengwe F, Chikowo R, Tendayi T, Cakmak I (2012) Soil fertility  
1077 management effects on maize productivity and grain zinc content in smallholder farming systems of  
1078 Zimbabwe. *Plant Soil* 361:57–69. doi: 10.1007/s11104-012-1332-2  
1079
- 1080 Manzeke GM, Mtambanengwe F, Nezomba H, Mapfumo P (2014) Zinc fertilization influence on  
1081 maize productivity and grain nutritional quality under integrated soil fertility management in  
1082 Zimbabwe. *Field Crop Res* 166:128–136. doi: 10.1016/j.fcr.2014.05.019  
1083
- 1084 Marschner H (1993) Zinc uptake from soils, Chapter 5 in Robson AD (ed.) *Zinc in soils and plants*,  
1085 Kluwer Academic Publishers, Dordrecht  
1086

1087 Eichert T, Fernández V (2012) Uptake and release of elements by leaves and other aerial plant parts,  
1088 Chapter 4 in Marschner P (ed.) Marschner's Mineral Nutrition of Higher Plants, Third Edition.  
1089 Academic Press, London. doi:10.1016/B978-0-12-384905-2.00004-2  
1090  
1091 Martín-Ortiz D, Hernández-Apaolaza L, Gárate A (2009) Efficiency of a NPK fertilizer with adhered  
1092 zinc lignosulfonate as a zinc source for maize (*Zea mays* L.). J Agric Food Chem 57:9071–9078. doi:  
1093 10.1021/jf9017965  
1094 Miller LV, Krebs NF, Hambidge KM (2007) A mathematical model of zinc absorption in humans as a  
1095 function of dietary zinc and phytate. J Nutr 137:135–141. doi: 10.1017/S000711451200195X  
1096  
1097 Ministry of Agriculture and Food Security, date unknown. National Fertiliser Strategy. Ministry of  
1098 Agriculture and Food Security, Lilongwe, Malawi. Available online:  
1099 [http://fsg.afre.msu.edu/mgt/caadp/format\\_for\\_national\\_fertilizer\\_strategy9.pdf](http://fsg.afre.msu.edu/mgt/caadp/format_for_national_fertilizer_strategy9.pdf) [accessed September  
1100 2014]  
1101  
1102 Molteldo A, Troubat N, Lokshin M, Sajaia Z (2014) Analyzing food security using household survey  
1103 data: streamlined analysis with ADePT software. World Bank, Washington, DC, U.S.A.  
1104  
1105 Müller O, Garenne M, Reitmaier P, van Zweeden AB, Kouyate B, Becher H (2003) Effect of zinc  
1106 supplementation on growth in West African children: a randomized double-blind placebo-controlled  
1107 trial in rural Burkina Faso. Int J Epidemiol 32:1098–1102 doi: 10.1093/ije/dyg190  
1108  
1109 Murray CJ (1994) Quantifying the burden of disease: the technical basis for disability-adjusted life  
1110 years. Bull World Health Organ 72:429–445  
1111  
1112 Ortiz-Monasterio JI, Palacios-Rojas N, Meng E, Pixley K, Trethowan R, Peña RJ (2007) Enhancing  
1113 the mineral and vitamin content of wheat and maize through plant breeding. J Cereal Sci 46:293–307.  
1114 doi: 10.1016/j.jcs.2007.06.005  
1115  
1116 Ozturk L, Yazici MA, Yucel C, Torun A, Cekic C, Bagci A, Ozkan H, Braun H-J, Sayers Z, Cakmak  
1117 I (2006) Concentration and localization of zinc during seed development and germination in wheat.  
1118 Physiol Plant 128:144–152. doi: 10.1111/j.1399-3054.2006.00737.x  
1119  
1120 Phattarakul N, Rerkasem B, Li LJ, Wu LH, Zou CQ, Ram H, Sohu VS, Kang BS, Surek H, Kalayci  
1121 M, Yazici A, Zhang FS, Cakmak I (2012) Biofortification of rice grain with zinc through zinc  
1122 fertilization in different countries. Plant Soil 361:131–141. doi: 10.1007/s11104-012-1211-x  
1123  
1124 Rengel Z, Batten GD, Crowley DE (1999) Agronomic approaches for improving the micronutrient  
1125 density in edible portions of field crops. Field Crop Res 60:27–40. doi: 10.1016/S0378-  
1126 4290(98)00131-2  
1127  
1128 Salgueiro MJ, Zubillaga MB, Lysionek AE, Caro RA, Weill R, Boccio JR (2002) The role of zinc in  
1129 the growth and development of children. Nutrition 18:510–519  
1130  
1131 Sandstead HH (2000) Causes of iron and zinc deficiencies and their effects on brain. J Nutr  
1132 130:S347–S349  
1133  
1134 Shivay YS, Kumar D, Prasad R, Ahlawat IPS (2008) Relative yield and zinc uptake by rice from zinc  
1135 sulphate and zinc oxide coatings onto urea. Nutr Cycl Agroecosyst 80:181–188. doi: 10.1007/s10705-  
1136 007-9131-5  
1137  
1138 Shrimpton R, Gross R, Darnton-Hill I, Young M (2005) Zinc deficiency: what are the most  
1139 appropriate interventions? BMJ 330:347–349. doi: 10.1136/bmj.330.7487.347  
1140

1141 Siekmann, JH, Allen LH, Bwibo NO, Demment MW, Murphy SP, Neumann CG (2003) Kenyan  
1142 school children have multiple micronutrient deficiencies, but increased plasma vitamin B-12 is the  
1143 only detectable micronutrient response to meat or milk supplementation. *J Nutr* 133:S3972–S3980  
1144

1145 Siyame EWP, Hurst R, Wawer AA, Young SD, Broadley MR, Chilimba ADC, Ander EL, Watts MJ,  
1146 Chilima B, Gondwe J, Kang'ombe D, Kalimbira A, Fairweather-Tait SJ, Bailey KB, Gibson RS  
1147 (2013) A high prevalence of zinc- but not iron-deficiency among women in rural Malawi: a cross-  
1148 sectional study. *Int J Vitam Nutr Res* 83:176–187. doi: 10.1024/0300-9831/a000158  
1149

1150 Slaton NA, Wilson CE, Ntamatungiro S, Norman RJ, Boothe DL (2001) Evaluation of zinc seed  
1151 treatments for rice. *Agron J* 93:152-157. doi:10.2134/agronj2001.931152x  
1152

1153 Spears D, Ghosh A, Cumming O (2013) Open defecation and childhood stunting in India: An  
1154 ecological analysis of new data from 112 districts. *PLoS ONE* 8:e73784. doi:  
1155 10.1371/journal.pone.0073784  
1156

1157 Srivastava PC, Singh AP, Kumar S, Ramachandran V, Shrivastava M, D'souza SF (2009)  
1158 Comparative study of a Zn-enriched post-methanation bio-sludge and Zn sulfate as Zn sources for a  
1159 rice–wheat crop rotation. *Nutr Cycl Agroecosyst* 85:195–202. doi: 10.1007/s10705-009-9258-7  
1160

1161 Stein AD, Barnhart HX, Hickey M, Ramakrishnan U, Schroeder DG, Martorell R (2003) Prospective  
1162 study of protein-energy supplementation early in life and of growth in the subsequent generation in  
1163 Guatemala. *Am J Clin Nutr* 78:162–167. doi: 10.1016/S0140-6736(08)60205-6  
1164

1165 Stein AJ (2010) Global impacts of human mineral malnutrition. *Plant Soil* 335:133–154. doi:  
1166 10.1007/s11104-009-0228-2  
1167

1168 Stein AJ (2014) Rethinking the measurement of undernutrition in a broader health context: Should we  
1169 look at possible causes or actual effects? *Global Food Secur* 3:193–199.  
1170 doi:10.1016/j.gfs.2014.09.003  
1171

1172 Stein AJ, Meenakshi JV, Qaim M, Nestel P, Sachdev HPS, Bhutta ZA (2005) Analyzing the health  
1173 benefits of biofortified staple crops by means of the Disability-Adjusted Life Years approach: a  
1174 handbook focusing on iron, zinc and vitamin A. *HarvestPlus Technical Monograph 4*, International  
1175 Food Policy Research Institute, Washington and International Center for Tropical Agriculture, Cali.  
1176 Available online: [http://www.harvestplus.org/content/analyzing-health-benefits-biofortified-staple-  
1177 crops-means-disability-adjusted-life-years-app](http://www.harvestplus.org/content/analyzing-health-benefits-biofortified-staple-crops-means-disability-adjusted-life-years-app) [accessed July 2014]  
1178

1179 Stein AJ, Nestel P, Meenakshi JV, Qaim M, Sachdev HPS, Bhutta ZA (2006) Plant breeding to  
1180 control zinc deficiency in India: how cost-effective is biofortification? *Pub Health Nutr* 10:492–501.  
1181 doi:10.1017/S1368980007223857  
1182

1183 Stoecker BJ, Abebe Y, Hubbs-Tait L, Kennedy TS, Gibson RS, Arbide I, Teshome A, Westcott J,  
1184 Krebs NF, Hambidge KM (2009) Zinc status and cognitive function of pregnant women in Southern  
1185 Ethiopia. *Eur J Clin Nutr* 63:916-918. doi: 10.1038/ejcn.2008.77  
1186

1187 Suzuki M, Takahashi M, Tsukamoto T, Watanabe S, Matsushashi S, Yazaki J, Kishimoto N, Kikuchi  
1188 S, Nakanishi H, Mori S, Nishizawa NK (2006) Biosynthesis and secretion of mugineic acid family  
1189 phytosiderophores in zinc-deficient barley. *Plant J* 48:85–97. doi: 10.1111/j.1365-313X.2006.02853.x  
1190

1191 Suzuki M, Tsukamoto T, Inoue H, Watanabe S, Matsushashi S, Takahashi M, Nakanishi H, Mori S,  
1192 Nishizawa N (2008) Deoxymugineic acid increases Zn translocation in Zn-deficient rice plants. *Plant*  
1193 *Mol Biol* 66:609–617. doi: 10.1007/s11103-008-9292-x  
1194



1195 Trierweiler JF, Lindsay WL (1969) EDTA-ammonium carbonate soil test for zinc. *Soil Sci Soc Am J*  
1196 33:49–54. doi: 10.2136/sssaj1969.03615995003300010017x  
1197  
1198 Tye AM, Young SD, Crout NMJ, Zhang H, Preston S, Barbosa-Jefferson VL, Davison W, McGrath  
1199 SP, Paton GI, Kilham K, Resende L (2003) Predicting the activity of Cd<sup>2+</sup> and Zn<sup>2+</sup> in soil pore water  
1200 from the radio-labile metal fraction. *Geochim Cosmochim Ac* 67:375–385. doi: 10.1016/S0016-  
1201 7037(02)01138-9  
1202  
1203 United Nations Department of Social and Economic Affairs, Population Division (UNDSEA 2013)  
1204 World population prospects: the 2012 revision. United Nations, New York, U.S.A.  
1205  
1206 Van Asten PJA, Barro SE, Wopereis MCS, Defoer T (2004) Using farmer knowledge to combat low  
1207 productive spots in rice fields of a Sahelian irrigation scheme. *Land Degrad Develop* 15:383–396. doi:  
1208 10.1002/ldr.619  
1209  
1210 Veenemans J, Milligan P, Prentice AM, Schouten LRA, Inja N, van der Heijden AC, de Boer LCC,  
1211 Jansen EJS, Koopmans AE, Enthoven WTM, Kraaijenhagen RJ, Demir AY, Uges DRA, Mbugi EV,  
1212 Savelkoul HFJ, Verhoef H (2011) Effect of supplementation with zinc and other micronutrients on  
1213 malaria in Tanzanian children: A randomised trial. *PLoS Med* 8:e1001125. doi:  
1214 10.1371/journal.pmed.1001125  
1215  
1216 Velu G, Ortiz-Monasterio I, Cakmak I, Hao Y, Singh RP (2014) Biofortification strategies to increase  
1217 grain zinc and iron concentrations in wheat. *J Cereal Sci* 59:365–372. doi: 10.1016/j.jcs.2013.09.001  
1218  
1219 Wang JW, Mao H, Zhao HB, Huang DL, Wang ZH (2012) Different increases in maize and wheat  
1220 grain zinc concentrations caused by soil and foliar applications of zinc in Loess Plateau, China. *Field*  
1221 *Crop Res* 135:89–96. doi: 10.1016/j.fcr.2012.07.010  
1222  
1223 Wanzala-Mlobela M, Fuentes P, Mkumbwa S (2013) Practices and policy options for the improved  
1224 design and implementation of fertilizer subsidy programs in sub-Saharan Africa. NEPAD policy  
1225 document. IFDC, Alabama, U.S.A.  
1226  
1227 Wei Y, Shohag MJ, Yang X (2012) Biofortification and bioavailability of rice grain zinc as affected  
1228 by different forms of foliar zinc fertilization. *PLoS ONE* 7: e45428. doi:  
1229 10.1371/journal.pone.0045428  
1230  
1231 Welch RM, Graham RD (2004) Breeding for micronutrients in staple food crops from a human  
1232 nutrition perspective. *J Exp Bot* 55:353–364. doi: 10.1093/jxb/erh064  
1233  
1234 Wessells KR, Brown KH (2012) Estimating the global prevalence of zinc deficiency: Results based  
1235 on zinc availability in national food supplies and the prevalence of stunting. *PLoS ONE* 7: e50568.  
1236 doi: 10.1371/journal.pone.0050568  
1237  
1238 Wessells KR, Singh GM, Brown KH (2012) Estimating the global prevalence of inadequate zinc  
1239 intake from national Food Balance Sheets: Effects of methodological assumptions. *PLoS ONE* 7:  
1240 e50565. doi: 10.1371/journal.pone.0050565  
1241  
1242 White JG, Zasoski RJ (1999) Mapping soil micronutrients. *Field Crop Res* 60:11–26. doi:  
1243 10.1016/S0378-4290(98)00130-0  
1244  
1245 White PJ, Broadley MR (2009) Biofortification of crops with seven mineral elements often lacking in  
1246 human diets – iron, zinc, copper, calcium, magnesium, selenium and iodine. *New Phytol* 182:49–84.  
1247 doi: 10.1111/j.1469-8137.2008.02738.x  
1248

- 1249 White PJ, Broadley MR (2011) Physiological limits to zinc biofortification of edible crops. *Front*  
1250 *Plant Sci* 2:1–11. doi: 10.3389/fpls.2011.00080
- 1251
- 1252 White PJ, Broadley MR, Hammond JP, Ramsay G, Subramanian NK, Thompson J, Wright G (2012)  
1253 Bio-fortification of potato tubers using foliar zinc-fertiliser. *J Hortic Sci Biotech* 87:123–129
- 1254
- 1255 Widodo, Broadley MR, Rose T, Frei M, Pariaska-Tanaka J, Yoshihashi T, Thomson M, Hammond  
1256 JP, Aprile A, Close TJ, Ismail AM, Wissuwa M (2010) Response to zinc deficiency of two rice lines  
1257 with contrasting tolerance is determined by root growth maintenance and organic acid exudation rates,  
1258 and not by zinc-transporter activity. *New Phytol* 186:400–414. doi: 10.1111/j.1469-  
1259 8137.2009.03177.x
- 1260
- 1261 Wissuwa M, Ismail AM, Graham RD (2008) Rice grain zinc concentrations as affected by genotype,  
1262 native soil-zinc availability, and zinc fertilization. *Plant Soil* 306:37–48. doi: 10.1007/s11104-007-  
1263 9368-4
- 1264
- 1265 World Bank (1993) World Development Report. World Bank, Washington D.C.
- 1266
- 1267 World Bank (2014) National Gross Domestic Product *per capita*. Available online:  
1268 <http://data.worldbank.org/indicator/NY.GDP.PCAP.CD> [accessed October 2014]
- 1269
- 1270 World Health Organization of the United Nations (WHO 1995) Expert Committee Report: Physical  
1271 status: the use and interpretation of anthropometry. Technical Report Series 854. WHO, Geneva
- 1272
- 1273 World Health Organization of the United Nations (WHO 2001) Macroeconomics and Health:  
1274 Investing in Health for Economic Development. Report of the Commission on Macroeconomics and  
1275 Health. WHO, Geneva
- 1276
- 1277 World Health Organization of the United Nations (WHO 2009) Global Health Risks: Mortality and  
1278 burden of disease attributable to selected major risks. WHO, Geneva
- 1279
- 1280 World Health Organization and Food and Agriculture Organization of the United Nations (WHO and  
1281 FAO 2004) Vitamin and mineral requirements in human nutrition. Second Edition. WHO, Geneva  
1282 and FAO, Rome
- 1283
- 1284 Wu J, Schat H, Sun R, Koornneef M, Wang XW, Aarts MGM (2007) Characterization of natural  
1285 variation for zinc, iron and manganese accumulation and zinc exposure response in *Brassica rapa* L.  
1286 *Plant Soil* 291:167–180. doi: 10.1007/s11104-006-9184-2
- 1287
- 1288 Wu J, Yuan YX, Zhang XW, Zhao J, Song X, Li Y, Li X, Sun R, Koornneef M, Aarts MGM, Wang  
1289 XW (2008) Mapping QTLs for mineral accumulation and shoot dry biomass under different Zn  
1290 nutritional conditions in Chinese cabbage (*Brassica rapa* L. ssp. *pekinensis*). *Plant Soil* 310:25–40.  
1291 doi: 10.1007/s11104-008-9625-1
- 1292
- 1293 Xue YF, Yue SC, Zhang YQ, Cui ZL, Chen XP, Yang FC, Cakmak I, McGrath SP, Zhang FS, Zou CQ  
1294 (2012) Grain and shoot zinc accumulation in winter wheat affected by nitrogen management. *Plant*  
1295 *Soil* 361:153–163. doi: 10.1007/s11104-012-1510-2
- 1296
- 1297 Yang XW, Tian XH, Gale WJ, Cao YX, Lu XC, Zhao AQ (2011a) Effect of soil and foliar zinc  
1298 application on zinc concentration and bioavailability in wheat grain grown on potentially zinc-  
1299 deficient soil. *Cereal Res Commun* 39:535–543
- 1300
- 1301 Yang XW, Tian XH, Lu XC, Gale WJ, Cao YX (2011b) Foliar zinc fertilization improves the zinc  
1302 nutritional value of wheat (*Triticum aestivum* L.) grain. *Afr J Biotechnol* 10:14778–14785. doi:  
1303 10.5897/AJB11.780

1304  
1305 Yilmaz A, Ekiz H, Torun B, Gültekin I, Karanlik S, Bagci SA, Cakmak I (1997) Effect of different  
1306 zinc application methods on grain yield and zinc concentration in wheat cultivars grown on zinc-  
1307 deficient calcareous soils. *J Plant Nutr* 20:461–471. doi: 10.1080/01904169709365267  
1308  
1309 Zhang YQ, Sun YX, Ye YL, Karim MR, Xue YF, Yan P, Meng QF, Cui ZL, Cakmak I, Zhang FS,  
1310 Zou CQ (2012) Zinc biofortification of wheat through fertilizer applications in different locations of  
1311 China. *Field Crop Res* 125:1–7. doi: 10.1016/j.fcr.2011.08.003  
1312  
1313 Zhao AQ, Tian XH, Cao YX, Lu XC, Liu T (2014) Comparison of soil and foliar zinc application for  
1314 enhancing grain zinc content of wheat when grown on potentially zinc-deficient calcareous soils. *J Sci*  
1315 *Food Agric*, 94:2016–2022. doi: 10.1002/jsfa.6518  
1316  
1317 Zhao AQ, Xinchun L, Chen Z, Tian X, Yang X (2011) Zinc fertilization methods on zinc absorption  
1318 and translocation in wheat. *J Agr Sci* 3:28–35. doi: 10.5539/jas.v3n1p28  
1319  
1320 Zou CQ, Zhang YQ, Rashid A, Ram H, Savasli E, Arisoy RZ, Ortiz-Monasterio I, Simunji S, Wang  
1321 ZH, Sohu V, Hassan M, Kaya Y, Onder O, Lungu O, Yaqub Mujahid M, Joshi AK, Zelenskiy Y,  
1322 Zhang FS, Cakmak I (2012) Biofortification of wheat with zinc through zinc fertilization in seven  
1323 countries. *Plant Soil* 361:119–130. doi: 10.1007/s11104-012-1369-2

**Table 1** Summary of studies included in the meta-analysis. Application methods of zinc (Zn) are soil (S) or foliar (F). ‘n’ is the number of data points contributing to the meta-analysis in which individual studies were stratified by crop, cultivar, location and Zn application rate and pooled by application method

<b>Crop</b>	<b>Varieties</b>	<b>Application via (n)</b>	<b>Country</b>	<b>Reference</b>
Wheat		S (4)	Pakistan	Abid et al. 2013
Wheat	Bread and durum	S (1), F (3)	Turkey	Cakmak et al. 2010
Wheat		S (12)	Turkey	Ekiz et al. 1998
Wheat	20 cultivars	S (20)	Turkey	Erdal et al. 2002
Wheat	2 Zn-deficiency tolerant cultivars	F (2)	Iran	Ghasemi et al. 2013
Maize		S (2)	Pakistan	Harris et al. 2007
Maize	2 cultivars	S (6)	Pakistan	Kanwal et al. 2010
Wheat	30 cultivars	S (60)	Iran	Khoshgoftarmansh et al. 2012
Wheat		S (1)	China	Lu et al. 2011
Wheat	2 winter wheat cultivars	S (8)	China	Lu et al. 2012
Rice	10 biofortification breeding line genotypes	F (19)	Philippines	Mabesa et al. 2013
Maize		S (1)	Zambia	Manzeke et al. 2014
Maize		S (2)	Spain	Martín-Ortiz et al. 2009
Rice	Cultivars commonly used	S (10), F (10)	China, India, Lao PDR, Thailand, Turkey	Phattarakul et al. 2012
Rice		S (4)	India	Shivay et al. 2008
Rice		S (1)	India	Srivastava et al. 2009
Maize, wheat		S (1,1), F (1,1)	China	Wang et al. 2012
Rice	3 cultivars	F (3)	China	Wei et al. 2012
Rice	5 ‘high-’;5 ‘low-’ Zn genotypes	S (15)	Philippines	Wissuwa et al. 2008
Wheat	10 cultivars	S (15), F (6)	China	Yang et al. 2011a
Wheat		F (1)	China	Yang et al. 2011b
Wheat	3 bread, 1 durum	S (4), F (4)	Turkey	Yilmaz et al. 1997
Wheat	Common cultivars	S (1), F (7)	China	Zhang et al. 2012
Wheat		S (4)	China	Zhao et al. 2011
Wheat	5 cultivars. (Results not presented by cultivar)	S (1), F (1)	China	Zhao et al. 2014
Wheat	11 cultivars	S (14), F (13)	China, India, Kazakhstan, Mexico, Pakistan, Turkey, Zambia	Zou et al. 2012

1 **Table 2** Baseline national-level estimates of zinc (Zn) deficiency and associated disease burden in  
 2 comparison to published studies for the 10 focus countries of this review  
 3

Country	Estimated risk of inadequate Zn supply		Stunting	DALYs lost due to Zn deficiency	
	% total population		% children 0-59 months	100 k population <sup>-1</sup>	
	Rank of country for each study in (brackets)				
	Present study	Wessells & Brown (2012)	Joy et al. (2014)	UNICEF (2013)	IHME (2014)
Reference year	2009	2003-7	2009	2007-11	2012
Burkina Faso	49.6 (3)	39.4 (3)	5.5 (9)	35 (7)	1,219 (1)
Ethiopia	31.6 (6)	11.0 (10)	81.5 (1)	44 (3)	344 (7)
Ghana	27.1 (7)	21.6 (8)	36.4 (5)	28 (9)	161 (10)
Kenya	27.0 (8)	25.3 (5)	60.6 (4)	35 (7)	281 (9)
Malawi	54.8 (2)	40.6 (2)	32.8 (6)	47 (1)	769 (2)
Mali	25.5 (9)	22.3 (7)	5.2 (10)	38 (6)	448 (5)
Nigeria	24.1 (10)	20.6 (9)	8.7 (8)	41 (5)	408 (6)
Senegal	36.0 (5)	24.6 (6)	11.7 (7)	27 (10)	489 (4)
Tanzania	41.1 (4)	34.1 (4)	64.4 (3)	42 (4)	341 (8)
Zambia	65.7 (1)	44.9 (1)	72.4 (2)	45 (2)	665 (3)



**Table 3** Summary of baseline soil properties and zinc (Zn) application rates in maize, rice and wheat crops . ‘n’ is the number of data points contributing to the meta-analysis in which individual studies were stratified by crop, cultivar, location and Zn application rate and pooled by application method. Q1 and Q3 are first and third quartiles, respectively

Crop	Method	Baseline soil properties										Zn application rate							
		DTPA-extractable Zn					pH (H <sub>2</sub> O)												
		n	Mean	SD	Q1	Median	Q3	n	Mean	SD	Q1	Median	Q3	n	Mean	SD	Q1	Median	Q3
			mg kg <sup>-1</sup>												kg ha <sup>-1</sup>				
Maize <sup>†</sup>	Soil	11	0.69	0.12	0.68	0.72	0.72	11	8.05	0.11	7.98	7.98	8.20	12	15.72	18.75	3.44	8.50	18.00
Rice		29	1.75	1.52	0.79	0.97	2.70	30	6.89	1.13	5.70	6.85	7.80	30	11.77	4.18	11.00	13.00	15.00
Wheat		158	0.82	0.79	0.10	0.67	1.00	137	7.73	0.32	7.55	7.80	7.98	158	25.36	13.55	11.00	23.00	50.00
Maize	Foliar	1	0.56	*	*	0.56	*	1	8.24	*	*	8.24	*	1	0.91	*	*	0.91	*
Rice		33	1.30	1.74	0.28	0.36	2.10	34	6.59	0.76	6.35	6.40	6.95	34	3.18	1.51	1.25	4.00	4.00
Wheat		38	0.80	1.13	0.32	0.52	0.71	37	7.69	0.50	7.53	7.80	7.98	38	1.62	0.73	1.29	1.59	1.63

<sup>†</sup> Manzeke et al. (2014) measured pH in CaCl<sub>2</sub> and extractable Zn using EDTA so these data were excluded

1 **Table 4** Summary of the effects of zinc (Zn)-enriched fertiliser on Zn and PA concentration in the  
 2 grain of maize, rice and wheat. ‘n’ is the number of data points contributing to the meta-analysis in  
 3 which individual studies were stratified by crop, cultivar, location and Zn application rate and pooled  
 4 by application method. Q1 and Q3 = first and third quartiles, respectively  
 5

Crop	Application <i>via</i>	n	Mean	SD	Min	Q1	Median	Q3	Max
Zn concentration in the grain, % of control									
Maize	Soil	12	128	18	106	114	123	139	173
Rice		30	111	15	84	102	107	119	157
Wheat		158	143	57	51	105	119	174	373
Maize	Foliar	1	130	*	130	-	130	-	130
Rice		34	127	19	107	114	125	140	172
Wheat		38	178	55	112	143	163	203	333
PA concentration in the grain, % of control									
Maize	Soil	3	96	7	7	92	93	104	104
Wheat		26	91	15	65	83	89	98	121
Rice	Foliar	3	86	1	85	85	87	87	87
Wheat		15	97	10	82	89	99	102	121
Yield, % of control									
Maize	Soil	12	110	10	95	100	111	120	125
Rice		15	111	8	102	103	111	117	129
Wheat		47	188	246	90	99	110	129	1,607
Maize	Foliar	1	98	*	98	*	98	*	98
Rice		15	100	7	84	98	102	104	109
Wheat		32	142	173	77	99	102	111	1,071

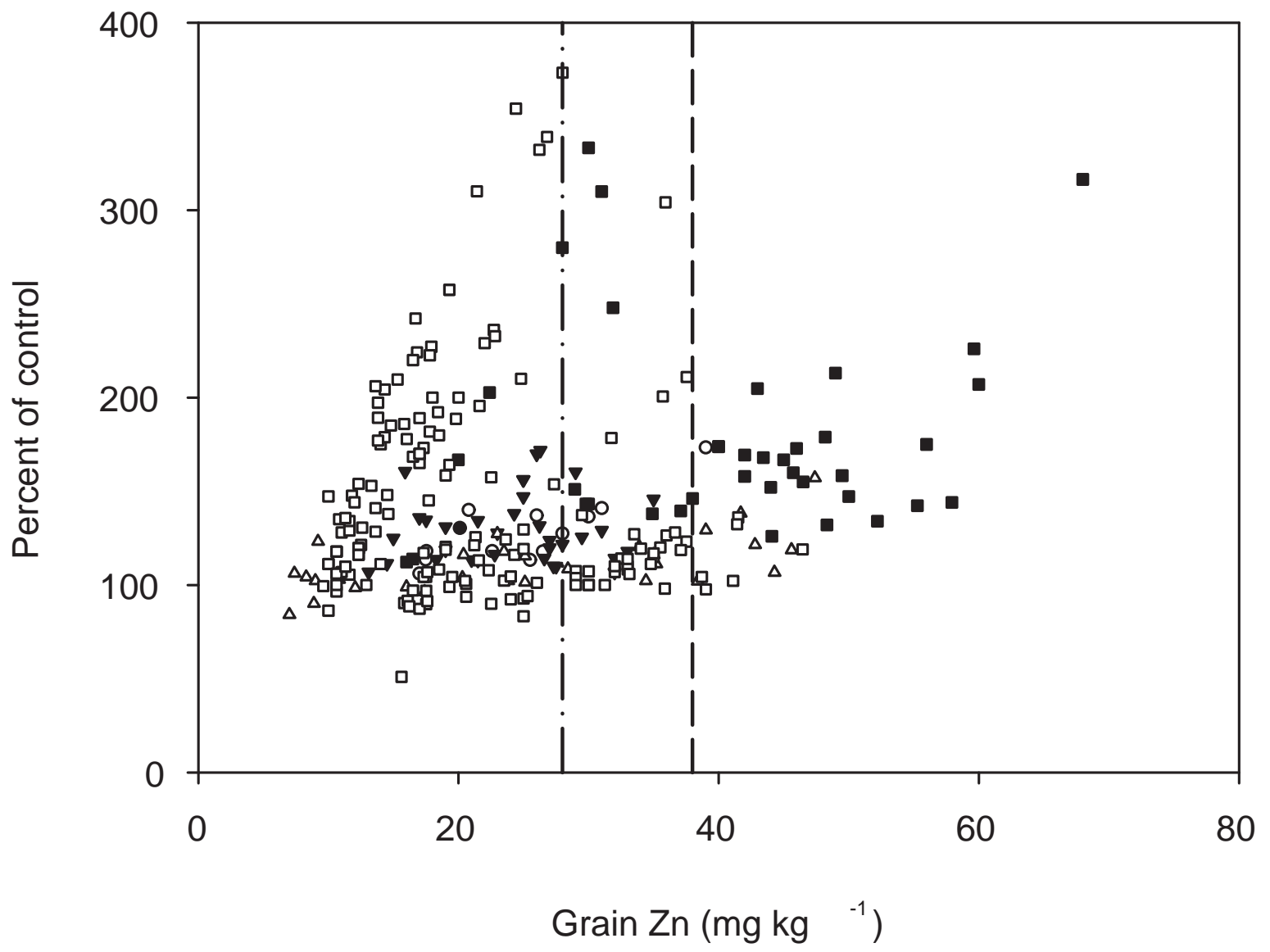


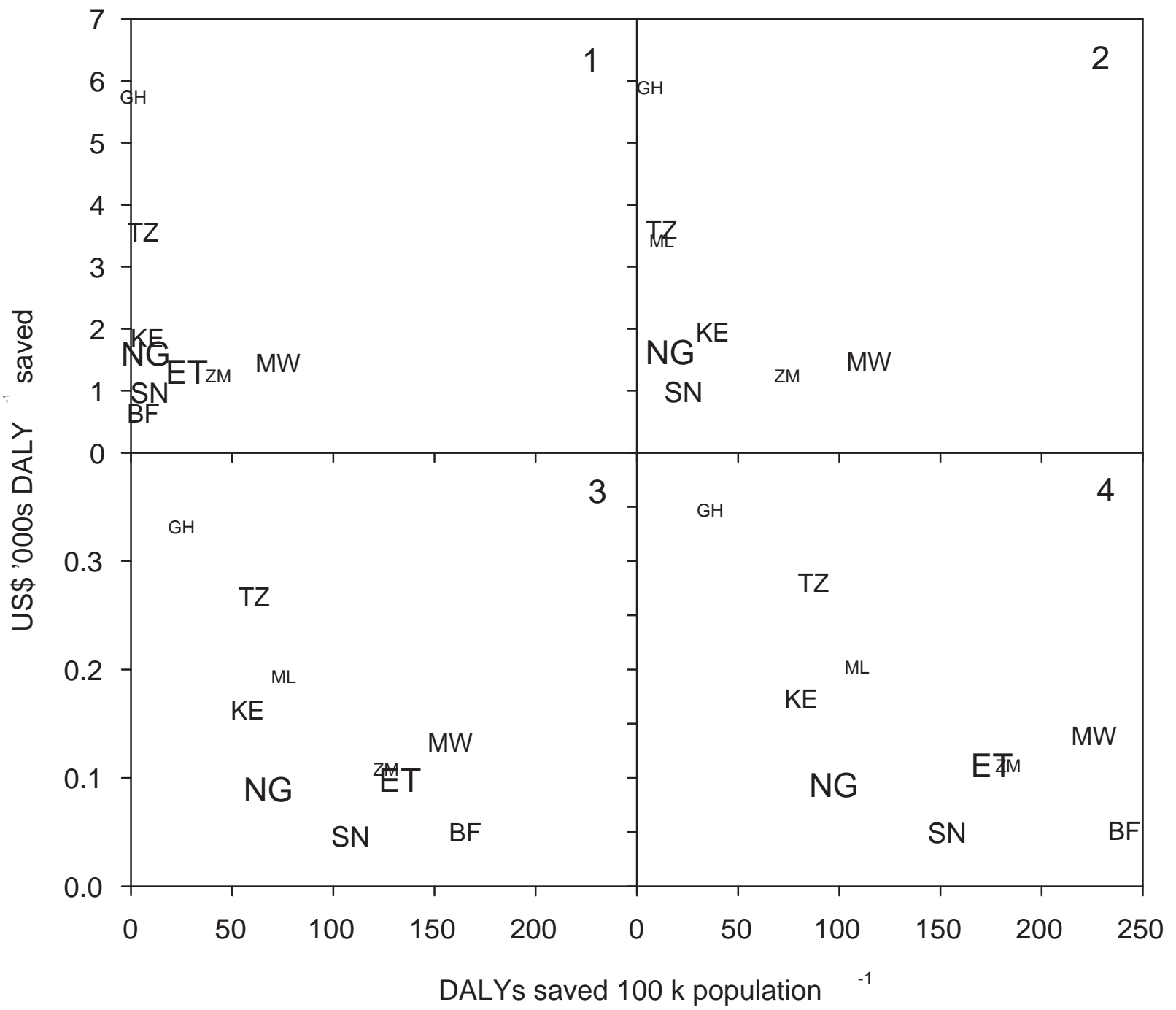


**Table 5** Effect of different zinc (Zn) fertilisation scenarios on dietary Zn and phytate supplies and estimated risk of Zn deficiency in 10 example countries in sub-Saharan Africa. Scenario '0' is baseline; 1 and 2 model enrichment of granular fertilisers, either subsidised or subsidised and non-subsidised; 3 and 4 model application of foliar Zn sprays to 50 and 75 % of target crops. Scenarios that are cost-effective in comparison to WHO (\*) or World Bank and WHO (\*\*) benchmarks are highlighted

Country	Scenario	Dietary Zn supply	Dietary phytate supply	Zn deficiency risk	DALYs lost due to Zn deficiency	Programme cost	Cost per DALY saved
		mg <i>capita</i> <sup>-1</sup> d <sup>-1</sup>		%	100 k population <sup>-1</sup>	US\$ '000s yr <sup>-1</sup>	US\$ yr <sup>-1</sup>
Burkina Faso	0	11.2	3,617	49.6	1288		
	1	11.2	3,615	49.4	1282	584	624*
	2	-	-	-	-	-	-
	3	11.7	3,606	43.3	1123	1,267	49**
	4	12.0	3,601	40.4	1048	1,900	51**
Ethiopia	0	8.2	1,830	31.6	329		
	1	8.4	1,818	28.9	300	31,983	1,302*
	2	-	-	-	-	-	-
	3	9.5	1,821	18.7	195	11,392	98**
	4	10.2	1,816	14.6	152	17,089	111**
Ghana	0	8.0	1,371	27.1	162		
	1	8.0	1,370	26.7	160	2,791	5,747
	2	8.1	1,366	25.8	155	10,640	5,893
	3	8.4	1,358	22.7	136	2,088	332*
	4	8.6	1,351	20.9	125	3,133	347*
Kenya	0	8.9	1,858	27.0	280		
	1	8.9	1,851	26.2	272	6,021	1,830*
	2	9.2	1,822	23.4	242	29,583	1,932*
	3	9.5	1,851	21.4	222	3,811	162**
	4	9.8	1,847	19.2	199	5,716	172**
Malawi	0	8.9	2,700	54.8	768		
	1	9.2	2,663	49.6	695	15,675	1,431
	2	9.3	2,641	46.6	653	25,115	1,456
	3	9.7	2,696	43.5	610	3,132	132**
	4	10.1	2,694	38.7	542	4,698	138**
Mali	0	11.9	2,795	25.5	495		
	1	-	-	-	-	-	-
	2	12.0	2,787	24.8	482	6,324	3,428
	3	12.4	2,769	21.5	419	2,072	194**
	4	12.7	2,756	19.8	385	3,108	203**

Nigeria	0	8.6	1,751	24.1	406		
	1	8.7	1,749	23.6	397	20,791	1,593
	2	8.7	1,745	23.0	388	45,002	1,613
	3	9.1	1,737	20.0	337	9,790	89**
	4	9.3	1,729	18.2	307	14,685	94**
Senegal	0	8.4	1,820	36.0	471		
	1	8.4	1,816	35.2	461	1,261	964*
	2	8.5	1,810	34.2	447	3,027	977*
	3	9.0	1,786	27.6	362	656	46**
	4	9.3	1,769	24.2	317	984	49**
Tanzania	0	8.0	2,037	41.1	341		
	1	8.4	2,033	40.4	335	9,630	3,547
	2	8.5	2,028	39.6	328	19,813	3,573
	3	9.0	2,026	33.8	280	7,323	267*
	4	8.8	2,021	30.6	253	10,985	279*
Zambia	0	7.1	2,100	65.7	664		
	1	7.3	2,076	61.3	620	7,222	1,237*
	2	7.4	2,059	58.2	589	12,358	1,244*
	3	7.8	2,097	53.1	537	1,817	108**
	4	8.1	2,095	47.4	480	2,726	112**





- 1 **Fig 1** Concentration of zinc (Zn) in the grains of maize (circles), rice (triangles) and wheat (squares)
- 2 following Zn application *via* soil (open) or foliage (filled). Y-axis represents the concentration as a
- 3 percentage of control. Vertical lines mark Harvest Plus breeding targets for maize and wheat (dashed)
- 4 and rice (dash-dot)

5 **Fig 2** Impact and cost-effectiveness of four zinc (Zn) fertilisation scenarios in 10 countries in sub-  
6 Saharan Africa: Burkina Faso (BF), Ethiopia (ET), Ghana (GH), Kenya (KE), Malawi (MW), Mali  
7 (ML), Nigeria (NG), Senegal (SN), Tanzania (TZ) and Zambia (ZM). Impact is defined as the  
8 reduction in disease burden attributable to Zn deficiency and is quantified in disability-adjusted life-  
9 years (DALYs; Supplementary Table 10). Cost-effectiveness is quantified in US\$ *per* DALY saved  
10 (Supplementary Table 11). Scenario 1 models enrichment of subsidised granular fertilisers; Scenario 2  
11 models enrichment of subsidised and non-subsidised granular fertilisers; Scenarios 3 and 4 model  
12 foliar application of Zn to 50 and 75 % of cereals, respectively. Not all countries are represented in  
13 Scenarios 1 and 2 due to lack of data. The text size represents the absolute number of DALYs saved  
14 annually (highly dependent on the country's population size): from smallest to largest, <25,000, 25-  
15 50,000, 50-75,000 and 75,000+





Electronic supplementary material

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