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Burden of selenium deficiency and cost-effectiveness of selenium agronomic biofortification of staple cereals in Ethiopia

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Abstract

Selenium (Se) deficiency among populations in Ethiopia is consistent with low concentrations of Se in soil and crops that could be addressed partly by Se-enriched fertilisers. This study examines the disease burden of Se deficiency in Ethiopia and evaluates the cost-effectiveness of Se agronomic biofortification. A disability-adjusted life years (DALY) framework was used, considering goiter, anaemia, and cognitive dysfunction among children and women. The potential efficiency of Se agronomic biofortification was calculated from baseline crop composition and response to Se fertilisers based on an application of 10 g/ha Se fertiliser under optimistic and pessimistic scenarios. The calculated cost per DALY was compared against gross domestic product (GDP; below 1–3 times national GDP) to consider as a cost-effective intervention. The existing national food basket supplies a total of 28·2 µg of Se for adults and 11·3 µg of Se for children, where the risk of inadequate dietary Se reaches 99·1 %–100 %. Cereals account for 61 % of the dietary Se supply. Human Se deficiency contributes to 0·164 million DALYs among children and women. Hence, 52 %, 43 %, and 5 % of the DALYs lost are attributed to anaemia, goiter, and cognitive dysfunction, respectively. Application of Se fertilisers to soils could avert an estimated 21·2–67·1 %, 26·6–67·5 % and 19·9–66·1 % of DALY via maize, teff and wheat at a cost of US$129·6–226·0, US$149·6–209·1 and US$99·3–181·6, respectively. Soil Se fertilisation of cereals could therefore be a cost-effective strategy to help alleviate Se deficiency in Ethiopia, with precedents in Finland.

Keywords: Cost-effectiveness: DALY: Selenium: Selenium agronomic biofortification: Ethiopia

Selenium (Se) is one of the essential trace minerals for humans and plays a crucial role in maintaining the proper functioning of the immune system, the thyroid gland, the oxidation defense system, the nervous system and enzymes[1]. Low Se concentrations in soil and crops are widespread, resulting in widespread human Se deficiency[2,3]. Selenium bioavailability in cereals varies by chemical form of Se, cereal type, and soil factors, where organic forms of Se (selenomethionine and selenocysteine) have better bioavailability[4–6]. For instance, Se bioavailability in rice reaches 62·3 %[7] and has a better bioavailability in wheat than maize[4]. Globally, an estimated 0·5–1 billion people (15 %) are Se deficient. In Africa, more than 230 million people are estimated to be affected by Se deficiency[8]. In Ethiopia, Se deficiency is a public health concern, affecting 35·5 % of the population based on human biomarker data[9]. However, the distribution shows significant spatial variability, such that in some areas, Se deficiency is nonexistent, while in other areas as many as 91 % of humans have Se deficiency[10]. Our recent district-level estimates also showed that cereal grains supply only 25 µg of Se/day[11], in the context of a recommended intake of 55 µg/day from all food sources, but with most Ethiopian diets dominated by cereal grains.

Existing micronutrient interventions like food fortification and supplementation have limited coverage[12]. Agronomic biofortification is a promising complementary intervention for rural populations practicing subsistence agriculture, provided that they have access to fertilisers[13]. Soil application of granulated or blended Se, with the Se being incorporated at

Abbreviations: DALY, disability adjusted life year; BI, biofortified intake; CI, current intake; CEA, cost effectiveness analysis; e, efficiency; FAO, Food and Agricultural Organization of the United Nation; ha, Hectare; GDP, gross domestic product; Hb, hemoglobin; IFDC, International Fertilizer Development Center; IHME, Institute for Health Metrics and Evaluation; OR, odds ratio; Se, selenium; PSA, preschool-age children; RDA, recommended dietary allowance; SAC, school-age children; WRA, women of reproductive age; YLD, years lived with disability; YLL, years lives lost; Zn, zinc.

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source, is safer than applying Se as a foliar spray to crops, although the latter approach has been used in experimental settings[14–16]. The Se biofortification program in Finland, which has been operational since 1983, uses Se in the form of soil-applied selenate, which is well suited for crop Se uptake and accumulation in edible parts of the grains[17,18]. Normal Se concentration in crops varies by crop and geographic factors, typically ranging from 0·01 to 2 mg/kg of dry weight, with most concentrations below 1 mg/kg[7]. Selenium fertilisers are effective at increasing grain Se levels, even in soils with low Se content[17], for example, a 0·1 mg/kg increase in grain Se concentration was observed for a 10 g/ha foliar application of Se fertiliser[16]. The Se agronomic biofortification program in Finland increased the national dietary Se intake four times and doubled human plasma Se concentration[17], bringing these levels in line with recommended levels.

Selenium deficiency is negatively associated with many functional outcomes in the body that can be quantified using the disability-adjusted life year (DALY) framework[1,19]. The DALY metric is a composite indicator of morbidity and mortality due to a particular health condition[20]. It is used to quantify the burden of diseases, including those due to micronutrient deficiencies[21,22]. In the present study, we used DALY metrics to quantify the existing health burden attributable to Se deficiency among the Ethiopian population. A cost-effectiveness analysis is a type of economic analysis that compares the health benefits of a specific intervention with the cost of saving one DALY associated with Se deficiency[22]. It can also be mathematically associated with the total program cost of agronomic biofortification to quantify the cost per DALY that can potentially be prevented, which allows for evaluating the cost-effectiveness of public health interventions[23].

To our knowledge, there is scarce evidence on the burden of Se deficiency and the potential cost-effectiveness of Se agronomic biofortification to prevent or reserve the existing burden. The recent GeoNutrition project reported the prevalence and spatial distribution of Se deficiency in Ethiopia[9]. This project produced evidence on Se concentrations across the soil, crop, food and human pathways[9,10,24–26] and explored the use of Se-enriched fertiliser[10,27] to reduce Se deficiencies. However, a robust social and economic feasibility evaluation is needed before the adoption of agronomic biofortification strategies[12,28]. Moreover, the potential advantages of Se biofortification over other interventions (e.g. dietary diversification, supplements and food fortification) need to be evaluated to better inform agricultural and health policies in resource-limited settings. Such evidence would be critical for decision-makers in allocating scarce resources to the most cost-effective intervention. Therefore, this paper aimed to (a) quantify the existing burden of Se deficiency and (b) evaluate the potential cost-effectiveness of Se agronomic biofortification of staple cereals in Ethiopia.

Materials and methods

Overview of the study

This *ex ante* impact assessment study was conducted to estimate the risk of dietary Se deficiency, the burden of Se deficiency and the cost-effectiveness of Se agronomic biofortification of staple cereals in Ethiopia. In Ethiopia, staple cereals (maize, teff and wheat) comprise the largest share of cropping area (87 %) and crop production (93 %)[29] and are the largest (65 %) contributor to daily energy consumption[30]. To achieve the objectives of the study, we used a series of sequential approaches and statistical procedures (Fig. 1). The risk of inadequate dietary Se intake was quantified from the Food and Agricultural Organization of the United Nations (FAO) food balance sheet and McCance and Widdowson food composition data for Se[31] and from the GeoNutrition national crop survey[24,32]. Then, the burden of Se deficiency was quantified using the standard DALY metrics, incorporating the relevant information and assumptions. Finally, using the baseline crop Se concentration, crop response to Se fertilisers and other relevant empirical evidence, we estimated the cost-effectiveness of Se agronomic biofortification in Ethiopia.

Dietary selenium supply estimates and risks of dietary selenium deficiency

The FAO food balance sheet for 2019 was used to provide an estimate of per capita food consumption in Ethiopia. These data contain the amount of food available for human consumption at the national level for ninety-six food items (online Supplementary Table 1)[33]. The per capita cereal consumption of children aged 4–6 years was considered 40–50 % of the consumption by adults[34]; hence, the dietary Se supply was also estimated accordingly. The Se concentrations of staple cereals (barley, maize, sorghum, wheat, teff and other cereals) were derived from a recent grain survey conducted across multiple regions of Ethiopia in the GeoNutrition project[24,32], supplemented by the Se composition data from relevant literature. Due to the skewed nature of the baseline crop Se concentration, we used the median Se concentration for maize (0·53 µg/kg), teff (0·7 µg/kg) and wheat (0·49 µg/kg). In addition, due to the lack of Se food composition data for other food items in Ethiopia, we used McCance and Widdowson food composition data[31]. The risk of dietary Se inadequacy was calculated using the estimated average requirement cut-point for Se, assuming a normal distribution of intake with a coefficient of variation of 25 %–30 %[35–38]. The estimated average requirement for Se was 25 µg/capita per day for preschool-age children (PSA), 35 µg/capita per day for school-age children (SAC)[39] and 45 µg/capita per day for adults[40]. The increased dietary Se intake with the use of Se fertilisers was estimated considering the coverage and crop response under different scenarios. The dietary Se intakes were weighted by the potential coverage of 20 % under a pessimistic scenario and 50 % under an optimistic scenario, along with the corresponding crop response (543–900 %) (online Supplementary Table 1).

Estimating the disease burden due to selenium deficiency

The burden of disease due to Se deficiency was estimated using a DALY framework, considering the most at-risk population groups and relevant outcomes associated with Se deficiency. DALY in the present study were calculated as follows:

$$\text{DALY lost} = \text{YLD} + \text{YLL} \quad (1)$$

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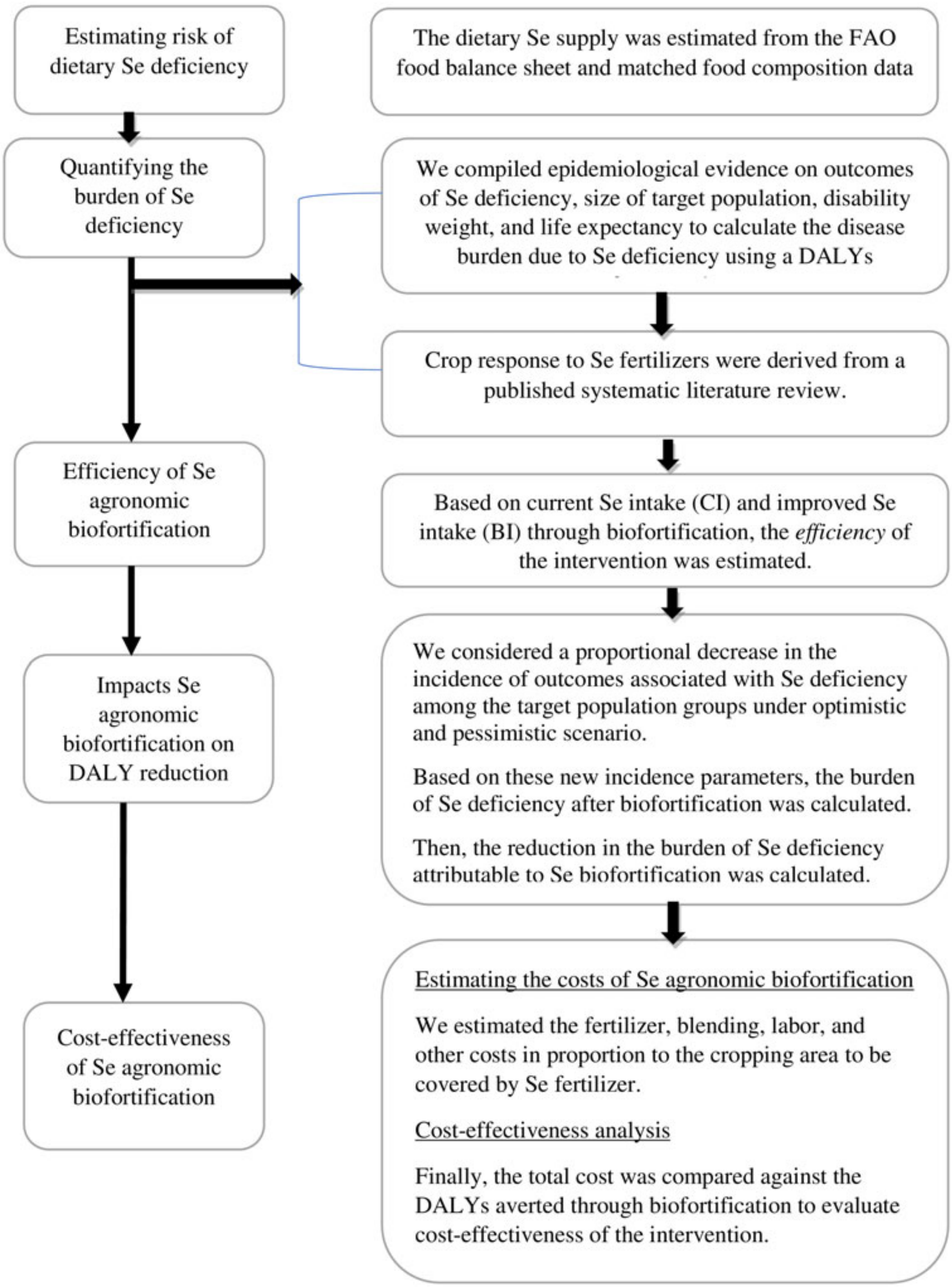

Fig. 1. Summary of the method to estimate risk of dietary Se deficiency, its disease burden and cost-effectiveness of Se agronomic biofortification of staple crops in Ethiopia.

$$\text{DALY lost} = \sum_{i=1}^{n} iT_i\, M_i \left(\frac{1-e^{-rLi}}{r}\right) + \sum_{i=1}^{n} T_i\, I_{ih}\, D_{hi} \left(\frac{1-e^{-rdhi}}{r}\right) \quad (2)$$

where[41]

YLD = years lived with disability; YLL = years of life lost; Ti = total number of people in target group i; Mi = mortality rate associated with the deficiency in target group i; r = discount rate for future life years; Li = average remaining life expectancy for target group i; I_{ih} = incidence rate of functional outcome h in target group i; D_{hi} = disability weight for functional outcome h in target group I and dhi = duration of functional outcome h in target group i.

Based on the risk of vulnerability for Se deficiency in preschool-age children, SAC (6–12 years), and women of reproductive age (WRA)[8–10,42], we considered in the present study quantifying the burden of Se deficiency. In Ethiopia, 52·3 % of young children, 40·6 % of school-aged children, and 26 % of

WRA were Se deficient[9]. The functional outcomes of Se deficiency have been linked to an increased risk of goiter and cognitive dysfunction among children[43].

A study from Uganda shows that higher Se concentrations in blood serum were significantly associated with lower odds of goiter (AOR = 0·3; 95 % CI: 0·13, 0·69)[44]. Similarly, in a literature review, Rayman *et al.*[45] reported that Se deficiency is linked to thyroid disorders, including goiter. Furthermore, there was a positive relationship between serum Se and T3 levels ($\beta = 0{\cdot}16$) in Ethiopian children (*n* 628)[43]. Although the cardiovascular and skeletal complications of Se deficiency are well documented in areas of extreme Se deficiency[46], there is no reported evidence of this situation in Ethiopia. As a result, we assumed that goiter and cognitive dysfunction were common functional consequences of Se deficiency in Ethiopia. We have taken the prevalence of goiter in Ethiopia among children (40·5 %)[47], SAC (42·9 %)[48] and WRA (35·8 %)[49]. We identified only a single, small-scale study reporting an 18·6 % prevalence of cognitive dysfunction in Ethiopia[50]. However, due to the persisting nature of cognitive dysfunction among PSA, SAC and late life, we have limited our estimate to PSA only. Relatedly, previous studies showed increased odds of goiter by 17·4 %[43] and cognitive dysfunction by 48 %[27] indicating the potential role of Se deficiency. For goiter and anaemia, we estimated the population attributable risk percent for each demographic group. Due to the lack of studies reporting relative risk for cognitive dysfunction, we estimated the relative risk and calculated the corresponding population attributable risk percent (online Supplementary File 1).

A recent estimate showed that 37 % of anaemia in low- and middle-income countries is attributable to Fe deficiency[51]. However, only about half of anaemia cases are responsive to Fe supplementation, where other micronutrient deficiencies, including Se, might have a potential role[52]. Many animal and human studies have also implicated Se deficiency in the increased occurrence of anaemia and haematologic parameters[53–55]. These associations are mainly explained by the antioxidant role of Se in erythrocytes and the mediation effects of Se on Zn for Hb synthesis[56,57]. A study among humans also indicated that higher serum Se concentrations could significantly reduce the risk of anaemia (OR = 0·75; 0·58–0·97)[58]. In Ethiopia, a positive correlation was obtained between serum Se and Hb concentration. In the present study, the prevalence of anaemia was obtained from the national micronutrient survey[59]; 22·9 % for PSA, 25·1 % for SAC and 11·3 % for WRA. The population attributable risk percent for each functional outcome was estimated considering empirical evidence from previous literature. For instance, Se deficiency might contribute to 14 %, 11 % and 12 % of anaemia among PSA, SAC and WRA, respectively (online Supplementary File 1).

Baseline data sources

Population data for the different demographic groups were obtained from the Uniited Nation estimates[60]. The age-specific life expectancy data were extracted from the Global Burden of Disease study[61], along with the disability weights for each outcome of Se deficiency found from the Institute for Health and Metrics[62].

Hence, we compiled the relevant disability weights for goiter, cognitive dysfunction and nutritional anaemia. Although the disability weight for each functional outcome attributable to Se deficiency is lacking, we took the disability weight that could best represent our scenario considering the existing alternative data sources. For instance, the disability weight for anaemia and cognitive dysfunction was taken from 'vitamin A deficiency with moderate anaemia' and 'mild motor plus cognitive impairments,' where the assigned disability weights under different causes were similar (0·052 and 0·031, respectively). We considered the weight of goiter as 'visible goiter without symptom'[61], assuming less profound effects of Se deficiency. Furthermore, we assumed anaemia and goiter to be temporary health conditions, while cognitive dysfunction was considered a permanent condition that could last for the rest of one's life expectancy. Thus, we considered a reasonable duration of goiter (2 years) where goiter might resolve after correcting iodine nutrition. Moreover, considering the average lifespan of red blood cells and the potential treatment response of anaemia, we considered the duration of anaemia to be 4 months[63].

With these data, the baseline burden of Se deficiency was calculated from Equation (1). The absorption efficiency of Se is generally high. Dietary Se from cereals also has a good bioavailability of above 80 %[39]. The major forms of Se in cereals, however, are organic forms, mainly selenomethionine, with better bioavailability[64]. Hence, in our calculations, we considered the bioavailability of Se to be 80 % under the pessimistic scenario and 90 % under the optimistic scenario.

A daily intake of 20 µg/capita per day is adequate to prevent severe deficiency, but a higher intake level of 45 µg/capita per day is required for optimal health and enzyme activity for an average adult[40,65]. The Institute of Medicine recommendation for dietary Se intake for optimal enzymatic activity: 25 µg/day for children under five, 35 µg/d for PSA children (6 to 12 years) and 55 µg/day for WRA was considered in the present study[37].

Cost-Effectiveness of selenium agronomic biofortification

Selenium fertiliser treatments and grain response. Selenium fertilisers in the form of selenate and selenite are used in many biofortification trials. Among these, selenate in the form of sodium selenate (Na_2SeO_4) is thirty-three times more bioavailable and efficient in improving grain Se concentration than selenite[16]. A selenate application rate of 10–20 g of Se ha^{-1} was found to be effective in increasing Se levels in edible parts in several biofortification studies[16,66,67]. Furthermore, research in Finland found that a fertiliser blending rate of 15–25 mg/kg was effective in increasing grain Se levels. With the current application of fertilisers and Se blending rate of 25 mg/kg, we found 10 g of Se ha^{-1} to be an adequate and safe application rate which was hence considered in the present modelling work.

In principle, Se can be applied to soil in granulated or blended forms, or to foliage as a foliar spray in the form of selenate only, and/or with other macronutrients[66,68]. The use of Se fertilisers in conjunction with other macronutrients may improve crop Se uptake[16]. Comparable crop responses can be achieved through foliar and soil fertilisation methods[15,16]. However, to our knowledge, foliar application of Se to cereals

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has only ever been conducted under experimental conditions, and it is not considered a realistic strategy for on-farm use, at least at the moment. Although foliar Se application can be more effective than soil application in experimental settings, its applicability on farmers' fields is likely limited by the potential risk of toxicity during application. These would further complicate the logistic demand and ensure safety during foliar application. Except for the costs of fertiliser blending or direct incorporation of Se during granulation, soil Se applications infer a much lower risk of toxicity to the applicator and could be applied along with the recommended macronutrient fertilisers(69) without additional personal protective equipment. Therefore, we considered soil application of Se fertilisers as a more practical and efficient way of addressing Se deficiency(70). The crop response (%) to Se fertilisation was derived from a meta-analysis of agronomic trials conducted globally(16), and we assumed the crop grain Se concentration response through soil Se fertilisation was increased by 543 % for pessimistic scenarios and 900 % for optimistic scenarios.

Scenarios for selenium fertilisation of crops. We built a pessimistic and optimistic scenario where granular/blended Se fertilisers could be scaled up in Ethiopia. Introducing Se fertilisers to large crop areas might incur several challenges related to fertiliser value chains, farmer acceptance, foreign exchange and the cost of fertilisers. Hence, we assumed a scenario whereby Se is included in granular/blended soil fertiliser products containing 10 g of Se ha^{-1} at a coverage of 20–50 % of maize, teff and wheat cropland area(71). Hence, we assumed scaling up Se fertilisers to 20–50 % of the cropping area based on the pessimistic and optimistic scenarios, respectively, which could be more feasible and realistic to introduce a new fertiliser in resource-limited settings. We have also assumed that Se fertiliser could either be blended with or incorporated directly into existing granular fertilisers during their manufacture to address application challenges and reduce logistical requirements, and we refer to both options as 'soil application'(72).

Efficiency of selenium agronomic biofortification of staple crops

The efficiency of Se biofortification to reduce the burden of Se deficiency is calculated from the current (baseline) and improved grain Se concentration, the consumption of these crops and the recommended dietary allowance for each target group, as follows (Equation 3)(19,73):

$$e = \frac{\ln\left(\frac{BI}{CI}\right) - \ln\left(\frac{BI-CI}{BI}\right)}{\ln\left(\frac{RDA}{CI}\right) - \ln\left(\frac{RDA-CI}{RDA}\right)} \quad (3)$$

where

e: efficiency of Se biofortification.

BI: dietary Se intake (μg/capita per day) following Se agronomic biofortification of maize, teff or wheat; CI: current dietary Se intake (μg/capita per day) without Se agronomic biofortification of maize, teff or wheat.

The per capita cereal consumption for each target group was calculated from the World Bank's 2018 socioeconomic survey(74). The details for estimating the per capita cereal consumption are described elsewhere(75). The recommended dietary allowance refers to the level of habitual daily Se intake that meets the requirements of almost all (97·5 %) of the population of a specific sex and age group(39,40).

Potential effects of selenium agronomic biofortification. The reduction in the burden of Se deficiency was calculated considering the baseline incidence of functional outcomes and the efficiency (*e*) (Equation 3) of Se fertilisers. With the efficiency rate *e*, a proportional decrease in the incidence of Se deficiency-associated functional outcomes was estimated and taken as the new incidence after the introduction of Se biofortification (Table 4). Based on the new incidence and prevalence estimates, we calculated the new burden of Se deficiency (the new DALY estimates) under the Se biofortification scenario. The impact of Se agronomic biofortification is then estimated as a percentage reduction in the burden of Se deficiency by comparing the baseline and new DALY estimates.

Estimated costs of selenium agronomic biofortification. The costs for soil Se fertilisation include the cost of the fertiliser, blending costs, and application labor. Since 42 % of sodium selenate is elemental Se(76), the optimal application rate of sodium selenate could be 24 g/ha sodium selenate to achieve a 10 g Se ha^{-1} application rate. We calculated the total estimated costs for each of the three cereal crops considered for agronomic biofortification and expressed it as a cost ha^{-1}.

We took the unit price for a kilogram of sodium selenate fertiliser at US$305 (https://www.retorte.com/Sodium-Selenate/07610-1000), including transport costs of 22 % from the International Fertilizer Development Center (IFDC) and other processing costs. Thus, the average cost of Se fertiliser ha^{-1} would be US$7·32 at an application rate of 10 g of Se ha^{-1} under an optimistic scenario. Under a pessimistic scenario, the unit cost of sodium selenate for one hectare would be US$10·32 for a 500-g package (https://www.retorte.com/Sodium-Selenate/07610-500). Based on the potential area covered by Se fertiliser, optimal application rate (10 g of Se ha^{-1}), and unit price of Se fertiliser, the total cost was estimated under pessimistic and optimistic scenarios as indicated in Tables 2, 3, and 5. Similarly, we considered a labor cost of US$5·3 ha^{-1}/day^{-1} for pessimistic scenarios and US$4 for optimistic scenarios, considering one person could cover an average of one ha/day(75).

Data processing and statistical analysis

Empirical data on population, functional outcomes, size of the target population, disability weight, life expectancy, bioavailability, grain Se content and grain response to Se fertiliser were compiled in a prespecified DALY Excel spreadsheet prepared by AJ Stein(77). The statistical analysis was done in Microsoft Excel (version 2016) and STATA (version 14·0). We prepared a separate Excel spreadsheet for assessing the burden of Se deficiency and the cost-effectiveness of such strategies (online Supplementary File 2). The necessary data were compiled on population size, life expectancy, cereal consumption and epidemiological information. The estimated burden of Se deficiency was also calculated in the DALY spreadsheet of AJ Stein(77) using Equation 1. In addition,

Table 1. Basic parameters and estimates of the burden of Se deficiency (in terms of DALYs lost) among children and WRA in Ethiopia

Functional outcomes	Targets	Population size	Incidence of disease/ ailment	Contribution of Se deficiency to disease *	Disability weight †	Duration of disease in years	DALY lost	% of the disease burden
Goiter	PSA	20,921,766	0·050 625	0·25	0·011	2	22 616	13·7 %
	SAC	21,284,896	0·045 045	0·21	0·011	2	20 473	12·4 %
	WRA	29,797,572	0·04296	0·24	0·011	2	27 334	16·6 %
Cognitive dysfunction	PSA	20,921,766	0·000423	0·16	0·031	70·30	8042	4·9 %
Anaemia ‡	PSA	20,921,766	0·09618	0·14	0·052	0·33	34 705	21·1 %
	SAC	21,284,896	0·08283	0·11	0·052	0·33	30 407	18·5 %
	WRA	29,797,572	0·04068	0·12	0·052	0·33	20 906	12·7 %
				Total DALYs lost due to Se deficiency			164 483	

DALY, disability-adjusted life years; PSA, preschool age children; SAC, school age children; WRA, women of reproductive age.
* The population attributable fractions were calculated after estimated the Relative risks from the odds and taking the prevalence of exposure from Belay *et al.*[9].
† The disability weight of each disease entity was compiled from the 2019 Institute for Health Metrics and Evaluation (IHME); https://ghdx.healthdata.org/record/ihme-data/gbd-2019-disability-weights), disease burden study.
‡ In addition, the prevalence estimates disaggregated by age group were taken from the same paper based on a nationally representative data.

Table 2. Estimated crop Se composition, cereal consumption per capita (g/capita per day) and baseline Se intake levels from the three staple crops calculated using data from the 2019 world bank socioeconomic survey in Ethiopia on household food consumption

Crops	Median grain Se composition in µg/g	Per capita cereal consumption (g/capita per day)			Baseline Se supply from each cereal in µg/capita per day		
		PSA	SAC	WRA	PSA	SAC	WRA
Maize	0·053	50	60	137·6	2·65	3·18	7·29
Teff	0·07	72	86·4	107·6	5·04	6·05	7·53
Wheat	0·049	26·1	31·32	98·8	1·28	1·54	4·84
Total	–	148·1	177·7	344	8·97	10·77	19·66

Table 3. Total cropping area (in hectares), potential area to be covered by Se fertiliser and crop response (%) to Se agronomic biofortification through the application of 10 g of Se ha^{-1} in the form of Na_2SeO_4 in Ethiopia

Crops	Total area covered	Se fertiliser coverage		Potential cropping area for Se fertiliser application		Increase in grain Se concentration (%)	
		Pessimistic scenario	Optimistic scenarios	Pessimistic scenario	Optimistic scenario	Pessimistic scenario	Optimistic scenario
Maize	2 526 212	20 %	50 %	505 242	1 263 106	543	900
Teff	2 928 206	20 %	50 %	585 641	1 464 103	543	900
Wheat	1 897 405	20 %	50 %	379 481	948 703	543	900
Total	7 351 823			1 470 364	3 675 912		

the cost-effectiveness of the intervention was estimated by comparing the total cost of the program with the total DALY averted following Se agronomic biofortification. This cost per DALY saved was compared against WHO and World Bank standards. Intervention with a value below 1–3 times times national GDP is considered cost effective[78].

Results

Dietary selenium supplies and prevalence of inadequate selenium intakes

Based on the national food balance sheet data, 109 g/capita per day of maize, 137 g/capita per day of teff and 99 g/capita per day of wheat are available for consumption in Ethiopia. We estimated consumption among children of 60 g of maize, 86 g of teff and 31 g of wheat/capita per day at the national level. The concentration of Se in food items was highly variable, and teff (70 µg/kg) had higher Se concentrations compared with wheat (49 µg/kg) and maize (53 µg/kg) (online Supplementary Table 1).

Baseline dietary Se supply was 28·2 (±1·07) µg/capita per day for adults and 11·3 (±0·43) µg/capita per day for children. Wheat and other cereal products comprise a large part of the daily Se intake (35·1 %), followed by maize (20·7 %), roots and tubers (3·1 %), barley (3·2 %) and sorghum (2·6 %), which contribute a lot to the daily Se intake. Thus, cereals, roots and tubers contribute to more than 64 % of the daily Se intakes. Almost all of WRA (99·1 %) and children (100 %) could have inadequate dietary Se intakes based on the national per capita food supply. Potential application of Se fertilisers on maize, teff and wheat

Table 4. The basic assumptions for the calculation of the efficiency (e) and cost-effectiveness of Se agronomic biofortification of staple crops by age group in Ethiopia

Crops	Targets	RDA in µg/capita per day	Baseline Se intake in µg/day*	Se intake with biofortification µg/capita per day (BI)		Efficiency (*e*)	
				Pessimistic scenario	Optimistic scenario	Pessimistic scenario	Optimistic scenario
Maize	PSA	25	8·97	11·70	22·2	0·407	0·983
	SAC	35	10·77	14·04	25·1	0·353	0·897
	WRA	55	19·7	23	52	0·245	0·997
Teff	PSA	25	8·97	13	26·5	0·504	0·996
	SAC	35	10·77	15	29·7	0·440	0·973
	WRA	55	19·7	24	63·0	0·311	0·975
Wheat	PSA	25	8·97	11·5	21·2	0·383	0·967
	SAC	35	10·77	13·8	24·0	0·331	0·870
	WRA	55	19·7	22·7	50·0	0·228	0·989

BI, biofortified Se intake; PSA, preschool age children; SAC, school age children; WRA, women of reproductive age.
* The dietary Se intakes from maize, teff and wheat were estimated from the Se composition and each cereal's consumption in a socioeconomic survey. The current intake (CI) is calculated from the average per capita cereal consumption and crop Se composition. The BI indicates the daily Se intake through Se agronomic biofortification of staple crops, considering the improved cereal Se composition and average cereal consumption data.

Table 5. The cost components and total cost of Se agronomic biofortification of staple crops with 10 g of Se per ha proportional to the cropping area under pessimistic and optimistic scenario in Ethiopia

Parameters	Scenarios	Maize	Teff	Wheat	Total
Area covered in ha	Pessimistic	505 242	585 641	379 481	1 470 364
	Optimistic	1 263 106	1 464 103	948 703	3 675 912
Fertiliser cost (US$ ha^{-1})	Pessimistic	10·32	10·32	10·32	
	Optimistic	7·32	7·32	7·32	
Total Fertiliser cost in US$	Pessimistic	5 214 097	6 043 815	3 916 244	15,174,156
	Optimistic	9 245 936	10,717,234	6 944 506	26,907,676
Labor cost (US$ ha^{-1})	Pessimistic	5·3	5·3	5·3	
	Optimistic	4·0	4·0	4·0	
Total labor cost US$	Pessimistic	2 677 783	3 103 897	2 011 249	7 792 929
	Optimistic	5 052 424	5 856 412	3 794 812	14,703,648
Total cost in US$	Pessimistic	7 891 880	9 147 712	5 927 493	22,967,086
	Optimistic	14,298,360	16,573,646	10,739,318	41,611,324

could increase the dietary Se intakes from 28·2 to 32·7–91·1 µg/capita per day for WRA and from 11·3 to 13·1–36·5 µg/capita per day for children under a pessimistic scenario and under an optimistic scenario, respectively. Hence, Se fertiliser could reduce the risk of inadequate Se intake among WRA from 99·1 % to 93·3 % under a pessimistic scenario and 2·1 % under an optimistic scenario. Similarly, this can reduce the risk of inadequate Se intake to 10·4 % among children under optimistic scenario (online Supplementary Table 1).

Burden of selenium deficiency

Overall, an estimated 0·164 million DALYs are lost attributable to Se deficiency in Ethiopia among PSA, SAC and WRA. According to our calculations, an estimated 65, 363 DALYs and 50, 880 DALY are lost among children and SAC accounting for 40 % and 31 % of the disease burden due to Se deficiency in Ethiopia. These was mainly due to Se-associated anaemia and goiter. Moreover, an estimated 48, 240 DALYs loss due to Se deficiency was among WRA contributing to 29 % of the disease burden. These differences are mainly a result of the differences in the prevalence of functional outcomes, the potential contribution of Se deficiency to the disease outcome (population attributable risk percent) and population size for different target groups. Disaggregated by each functional outcome, the DALYs lost due to Se deficiency were mainly due to Se-associated anaemia (86, 018 DALYs lost; 52 %), goiter (70, 423 DALYs lost; 43 %) and cognitive dysfunction (8042 DALYs lost; 5 %). Hence, disease burden due to Se deficiency could be attributed mainly to the role of Se in the prevention of anaemia (52 %), followed by goiter (43 %) and cognitive dysfunction (5 %) (Table 1).

Effectiveness of selenium agronomic biofortification in reducing selenium deficiency

Based on the fertiliser response, potential coverage and bioavailability of Se, we estimated the total DALY saved and the effectiveness of Se agronomic biofortification in reducing Se deficiency through soil application under pessimistic and optimistic scenarios.

The average cereal Se composition data were compiled by crop estimated from the recent GeoNutrition crop survey, and the daily per capita cereal consumption estimated from the 2019 socio-economic survey is presented in Table 2. These amounts were used to calculate the daily Se intake level from each crop without Se agronomic biofortification. Overall, maize, teff and wheat could contribute to 8·97, 10·77 and 19·7 µg/capita per day for PSA, SAC and WRA, respectively.

The cropping areas for maize, teff, and wheat were obtained for the 2021 main cropping season from the Ethiopian Agricultural Sample Survey Report. In our analysis, we considered 2·9, 2·5 and 1·9 million hectares of land is covered by teff, maize and wheat, respectively. The potential area to be covered by Se fertilisers was assumed to be 20 % under pessimistic scenario and 50 % under the optimistic scenario. In our analysis, we considered that 0·59–1·46 million hectares of land could be fertilised with Se for teff, 0·51–1·26 million hectares for maize and 0·38–0·95 million hectares for wheat. This cropping area was used to calculate the fertiliser and labour costs as shown in Table 3. The crop response to optimal Se fertilisation was obtained from a meta-analysis of agronomic biofortification trials, where the crop response might vary from 543 % to 900 % under pessimistic and optimistic scenarios. Based on the improved grain Se concentration with Se agronomic biofortification, efficiency (e) was calculated for maize, teff, and wheat biofortification separately under different scenarios, and a proportional decrease in the burden of Se deficiency was estimated.

The efficiency of Se agronomic biofortification was calculated using Equation (1) using the current Se intake (CI), biofortified Se intake and the age-specific recommended dietary allowance. The baseline dietary Se intake (CI) without biofortification was calculated from the average cereal consumption and mean Se composition without biofortification. The biofortified Se intake was calculated considering the improved Se composition of staple crops grown with agronomic biofortification. The efficiency of Se fertiliser for increasing Se intake varies between 0·245 and 0·997 for maize, between 0·311 and 0·996 for teff and between 0·228 and 0·989 for wheat crops under both pessimistic and optimistic scenarios (Table 4).

Table 5 shows the fertiliser and labor costs ha^{-1} of cropped land for Se fertiliser application. For the calculation of the total cost, fertiliser and labor costs were considered, while extension, public health and monitoring costs were not mentioned in this study. The unit cost per hectare was multiplied by the total area to be covered by each crop under pessimistic and optimistic scenarios. Therefore, the total costs for Se fertiliser application were estimated to be in the range of 7·89–14·3 million US$ for maize, 9·2–16·6 for teff and 5·93–10·7 for wheat crops under both optimistic and pessimistic scenarios (Table 5). The total costs were compared against the DALYs saved to evaluate the potential for reducing Se deficiency in a cost-effective manner under different scenarios, as presented in Table 6.

We have built scenarios, pessimistic and optimistic, where Se fertilisers could be scaled. The DALYs saved and cost-effectiveness of this intervention are presented in Table 6. Across demographic groups, soil application of Se fertiliser to maize could avert an estimated 34, 892 DALYs (21.2 %) under pessimistic scenarios and 110, 360 DALYs (67.1 %) under optimistic scenarios, respectively. Similarly, an estimated 43, 753 DALYs (26.6 %) and 110, 953 DALYs (67.5 %) of Se deficiency burden could be averted through Se fertilisation of teff

Table 6. Basic assumptions, DALY saved, percent of Se deficiency avoided and cost effectiveness analysis (CEA) of Se agronomic biofortification of staple crops (maize, teff and wheat) through granular Se fertilisation at rate of 10 g of Se ha^{-1} at coverage of 20–50 % of cropping area in the form of $NaSeO_4$ in Ethiopia

Parameters	Soil Se application		
Costs (US$ ha^{-1})	Maize	Teff	Wheat
Se fertiliser *	20 20		20
Labor †	4–5·3 4–5·3		4–5·3
Research and monitoring cost	–	–	–
Pessimistic scenario			
Coverage rate (%)	15	15	15
Costs (US$ million)	7·89	9·15	5·93
DALYs saved	34 892	43 753	32 664
% DALY averted	21·2 %	26·6 %	19·9 %
CEA (US$ per DALY saved)	226	209·1	181·6
Optimistic scenario			
Coverage rate (%)	50	50	50
Costs (US$ million)	14·3	16·6	10·8
DALYs saved	110 360	110 953	108 788
% DALY averted	67·1 %	67·5 %	66·1 %
CEA (US$ per DALY saved)	129·6	149·6	99·3

DALY, disability-adjusted life years; IFDC, International Fertilizer Development Center.

* Fertiliser cost ha^{-1} at 10 g of Se ha^{-1} (equivalent to 24 g of sodium selenate) was estimated from (https://www.retorte.com/Sodium-Selenate/07510–1000) where the price for 1 kg is US$250 and US$175 for 500g packages, excluding transport and other costs. Thus, the estimated cost of Se fertiliser per ha under an optimistic scenario would be US$7.32 and US$10.32 under a pessimistic scenario, including an estimated 22 % transport cost for Sub-Saharan Africa from IFDC.

† The labor cost is estimated to be US$4–5.3, where one daily laborer would cover an average of 1 ha.

crops under pessimistic and pessimistic scenarios, respectively. While Se fertilisation of the wheat crop could prevent 32, 684–108, 788 DALYs, reducing the burden of Se deficiency by 19.9–66.1 %. The corresponding cost per DALY saved was soil fertilisation: US$129.6–226.0 for maize, US$149.6–209.1 for teff, and US$99.3–181.6 for wheat. Overall, Se agronomic biofortification could be more cost effective in teff and wheat as compared with maize, mainly due to the low baseline Se concentrations in maize. Overall, Se fertilisation of maize, teff and wheat with 10 g of Se ha^{-1} could be a very cost-effective intervention at a cost of US$126.3–206.4 to save one DALYs lost due to Se deficiency in the country under pessimistic and optimistic scenarios, respectively (Table 6).

Discussion

In this study, we estimated the dietary Se supplies from all food sources in Ethiopia and calculated the risk of inadequate dietary Se intakes. The current diet provides 28·2 (±1·07) µg of Se for adults and 11·3 (±0·43) µg of Se for children aged 4–6 years. This was similar to the previous estimate of 25 µg of Se per day from staple cereals only[11]. The previous estimate was averaged at the district level based on each cereal's production statistics, which may overestimate the average Se supply. The Se composition of non-cereal foods used in the current estimate is taken from external sources. Still, the dietary supply of Se from the whole diet is clearly far below the average daily requirement of 45–55 µg of Se/day[37]. As a result, the risk of inadequate Se

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intake was also found to be high (100 % among children and 99·1 % in WRA), which is comparable with studies in the region based on socio-economic surveys[42,79]. A study from Malawi also indicated that 56 % of the households had inadequate Se supplies, where the risk is raised to above 80 % among the poorest households[80]. The estimated average requirement cut-off point method tends to overestimate the prevalence of inadequate intakes when the usual intake is below the estimated average requirement[81], which might be the case for Se.

This intake level is adequate to meet the daily requirement for the majority of children (25–35 µg/capita per day) and adults (55 µg/capita per day). It is also close to the tolerable upper intake levels of Se for children (90 µg/capita per day) yet below the tolerable upper intake levels for WRA (400 µg/capita per day) but could significantly reduce the burden of inadequate Se intake. However, it may be appropriate to consider optimal Se application rates, especially in areas with marginal or higher Se levels in the soil or crop.

Despite there being declining trends in the burdens of other micronutrient deficiencies[82], there is a lack of reliable evidence on Se deficiency. We believe that the current analysis is the first to quantify the burden of Se deficiency using robust and reliable context-specific information, based on Se-deficiency-associated relevant public health outcomes. The burden of disease from Se deficiency associated functional outcomes was estimated at 0·164 million DALYs, including anaemia, goiter, and cognitive dysfunction associated with Se deficiency[27,43]. For other micronutrient deficiencies, 0·45, 0·40 and 0·089 million DALYs could be lost due to Fe, vitamin A, and iodine deficiency in Ethiopia, respectively[82]. An estimated half million DALYs could be lost due to Zn deficiency[75]. However, these estimates consider only visible functional outcomes, excluding the other extreme forms of Se deficiency, which are not common in Ethiopia. For instance, a recent national estimate also showed that 20–52 % of children and women had Se deficiency, indicating prevailing Se deficiency in the country[9]. Although overt Se deficiency is associated with Keshan and Kashin-Beck disease in its severe form[1], evidence of its existence in Ethiopia is lacking; hence, these conditions are not considered in the current estimate. Considering the existing burden of Se deficiency, it should be considered a micronutrient deficiency of public health importance and included in potential policy responses.

Although Se is recognised as one of the essential minerals for human health, the understanding of Se deficiency has recently gained attention in sub-Saharan Africa, especially in Ethiopia, where soil, crop and human Se nutrition are suboptimal[9,10,25,42]. Hence, staple cereals, being a major source of energy and micronutrients, could be a target for increasing the dietary Se intake through Se agronomic biofortification[12,83] through the use of Se-enriched fertilisers applied to soils in granular/blended form.

The application of Se fertilisers to soils, in conjunction with nitrogen-containing fertilisers, could potentially improve crop responses to Se fertilisers[16]. Field application of soil Se fertiliser is more feasible when it is in the form of granulated Se fertiliser combined with other fertilisers, such as nitrogen-containing common fertiliser commodities. Hence, the potential advantage of this approach is that it can significantly reduce duplicate labour costs and thereby enhance productivity. Hence, an agronomic approach can be a feasible and effective way of increasing the Se content of staple crops and alleviating human Se deficiency[84]. Staple crops, namely wheat, maize, rice and barley, were found to be an effective route for better human Se intakes through Se-enriched fertilisers[85]. In addition, soil fertiliser application could significantly reduce labour and equipment costs related to foliar application.

In field experiments in Malawi, it was reported that Se fertilisation could significantly improve the Se content of maize by 15–21 µg/kg (following the application of 5 g of Se ha^{-1}) and the dietary Se supply by 26–37 µg/person per day[15]. A randomised control trial in Malawi showed that Se-fertilised maize flour consumption improved human Se status, suggesting a possible means for better human Se consumption and health[86]. Further experimental studies on these crops under typical Ethiopian cropping systems will help calibrate potential Se agronomic biofortification strategies and their relative efficiency for different cereal crops.

Beyond agronomic strategies, dietary diversification, micronutrient supplementation and dietary modification are common strategies to address micronutrient deficiencies[87]. However, such strategies are limited in reaching the majority of the rural poor, where diets are inherently poor in micronutrients and micronutrient deficiencies are more prevalent[88]. For instance, more than 70 % of the costs related to supplementation strategies are related to personnel and material costs, where their cost-effectiveness is very limited. Therefore, Se agronomic biofortification could be a more sustainable strategy to improve the Se content of the crops for human consumption[16,89], which could be integrated into the existing fertiliser subsidy program[90].

Given the low dose needed to achieve optimum crop Se content and the scarce nature of the element, it would be very cost effective to use a low dose (about 10 g of Se ha^{-1}) to achieve a better Se status in humans with minimal health risks.

In Finland, a national policy was introduced in 1984 to add Se to multi-nutrient fertilisers, having 15 mg Se/kg, leading to significant increases in dietary Se intakes and in average blood plasma Se concentrations into an 'optimal' range[70]. There has been no evidence of excessive intakes risking toxicity. However, the soil Se level has remained low over the past 37 years in Finland, mainly due to small application rates and the transformation of Se into insoluble (fixed) forms, which warrant the application of Se fertilisers each cropping cycle. A review study highlighted that Se recovery is low (14 %), which might lead to the waste of this element[91], although more work on the wider sustainability of the approach would be needed[92].

Our analysis indicated that granular Se fertilisation is likely to be a cost-effective strategy at a cost of US$126·3–206·4 per DALY saved. This shows a cost-effective public health intervention compared with the WHO value of gross per capita income. Agronomic biofortification using Zn may also be effective in addressing dietary Zn deficiency. For instance, Zn agronomic biofortification of staple cereals has been estimated to be cost effective in addressing Zn deficiency in Ethiopia, through soil and/or foliar zinc fertiliser at a cost of US$226 to 505 per DALY averted[75], which is broadly similar to ante-natal dietary supplementation interventions to address Fe and folic acid deficiencies (US$58–405 per DALY averted)[93] and multiple micronutrient supplementation programs (US$4–112 per DALY averted)[94]. Thus, agronomic biofortification could be developed to include multiple micronutrients and also become part of a suite of interventions to minimise the global burden of micronutrient deficiencies.

Although the risk of Se toxicity might be low at low doses[16], a strong monitoring and evaluation system is crucial to accompany an Se agronomic biofortification policy. The recommended fertiliser application rate and blending amount may vary from year to year depending on the dietary Se sufficiency level for human consumption. The Finnish experience has also shown that research and monitoring costs comprise a significant investment, yet they are crucial[92]. However, due to the complex nature of monitoring and evaluation costs and the potential to integrate monitoring and evaluation into existing micronutrient surveillance programs, we did not include a precise cost estimate for monitoring and evaluation of Se biofortification. Although these costs might be complex, a collaborative system involving leading organisations from health, agriculture and relevant academia is needed for effective and efficient implementation of Se fertilisation.

Limitations of the study

Although this study is a novel piece of evidence on dietary Se supplies, providing estimates of the burden of Se deficiency, and the cost-effectiveness of Se agronomic biofortification in Ethiopia based on multiple relevant assumptions, the findings of this study should be viewed in light of some limitations. The estimate of dietary Se supply used a Se composition database from multiple data sources[31] due to the lack of a specific database for Se in Ethiopia and the wider region. The use of this nutrient database might bias the nutrient composition of food items grown in the country. The fertiliser response estimates from the agronomic field trials might be affected by the spatially varying soil properties and crop varieties that will affect the crop's response to Se fertilisers, which were not considered in the current paper. It is also evident that Se deficiency is associated with more fatal skeletal and cardiovascular disorders, namely Kashin-Beck and Keshan diseases, respectively[1,46]. However, due to the lack of clear epidemiological evidence linking Se deficiency and such outcomes in Ethiopia, we could not consider such outcomes in our DALY estimate model. Furthermore, such outcomes are common in areas with extremely low soil and crop Se concentrations, where evidence of such extreme Se deficiency is not documented in Ethiopia. Our assumption did not consider future fertiliser prices, where we may not be able to predict such rises. Thus, considering the rising prices of Se fertilisers, it could affect the cost-effectiveness of Se agronomic biofortification in the country, yet it will still be very cost effective. Furthermore, our estimate of goiter prevalence and the relative contribution of Se deficiency were based on a localised study, due to a lack of more representative estimates, and this may have overestimated the burden of Se deficiency. Similarly, use of a local study report on the burden of cognitive impairment might not be representative at the national level and might have underestimated or overestimated cost-effectiveness. The contribution of Se deficiency to anaemia was based on a previous study[59] on SAC, and the association was not statistically significant, which might overestimate the DALY burden due to anaemia. Due to a lack of intervention trials or risk predictions for anaemia, we have used the odds ratio to derive the attributable fraction, which could further bias the DALY estimates. Hence, such inherent problems related to the incidence of goiter and cognitive impairment could overestimate or underestimate the DALY calculations.

Biofortification of cereals with Se is likely to increase Se intakes and the status of livestock, as was the case in Finland, leading to increases in the Se content of animal-sourced foods and with potential benefits for livestock health and productivity[70]. We did not capture these effects in the current study, but doing so would further improve the cost–benefit ratio.

Conclusion and recommendations

In Ethiopia, inadequate dietary Se intakes are widespread. The introduction of crops grown under Se agronomic biofortification (maize, teff and wheat) could significantly reduce the burden of Se deficiency in a cost-effective manner. The use of lower-dose Se fertiliser via soil-applied Se could be a more practical and feasible option to address Se deficiency in Ethiopia. Furthermore, Se fertilisers could be integrated into existing fertiliser use to alleviate Se deficiency in humans. In the presence of existing fertiliser subsidy programs and fertiliser use packages, the use of blended or granulated Se fertiliser could strongly supplement current strategies to alleviate micronutrient deficiency in the country. Strong monitoring and evaluation platforms should also be in place parallel to the implementation of Se biofortification, which helps adjust the optimal application rates in a safe manner. These could be managed by organising a multisectoral and collaborative national team of experts for a very efficient and effective implementation of Se agronomic biofortification.

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The authors declare that no conflicts of interest exist.

All relevant data are within the manuscript and its Supporting Information Files.

The study was ethically approved Addis Ababa University, College of Natural and Computational Sciences, Institutional Review Board Committee (CNCSDO/187/14/2021). Since we used secondary data sources and crop data under ethical approval, informed consent was not applicable.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114524001235

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