Health impact assessment of folate biofortified rice in China.

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Abstract

Introduction: As folate deficiency is mainly caused by the dependency on folate-poor staple crops, such as rice, the implementation of rice with a high level of natural folate could be a successful pro-rural and pro-poor intervention strategy to reduce folate deficiencies in China, where about 260 million people are considered to be folate deficient. Consuming folate biofortified rice instead of conventional rice could prevent someone from negative health outcomes of folate deficiency, such as megaloblastic aneamia and neural-tube defects. Especially for poor Chinese women of childbearing age, folate biofortification could be important to prevent them from having a baby with a neural-tube defect, the main adverse health outcome. As Northern and Southern China differ significantly in terms of rice consumption and production, and folate intake, a regional comparison of the potential health benefits of folate biofortified rice could further underpin the introduction of this strategy in China.

Objective: The aim is to measure the potential regional health impact of folate biofortified rice (12 µg per 1 gram of rice) in China.

Method: Based on the Disability-Adjusted Life Years (DALY) approach, the health impact of folate enriched rice in China is evaluated as the numbers of DALYs lost that can be reduced. As there is only data available on contribution of folate deficiency to its main adverse health outcome of folate deficiency, i.e. neural-tube defects, the health impact refers to the neural-tube defects that are caused by folate deficiency. Furthermore, two coverage rate of the introduction of folate enriched rice are included based on previous research.

Results: Based on the efficacy of folate biofortified rice, the total daily folate intake for Chinese women of childbearing age after biofortification amounts to 1 120 µg, which is significantly higher than the required folate intake. The application of the DALY method shows that the implementation of folate biofortified rice could save 116 090 DALYs (low impact scenario) and 257 345 DALYs (high impact scenario) per year. Although rice consumption is significantly lower in Northern China, the folate intake after biofortication is still high enough to alleviate the burden of neural-tube defects caused by folate deficiency. Furthermore, a rough estimation of the costs of folate biofortification indicates that this policy intervention could be a cost-effective method as well.

Conclusions: Although these results underpin folate biofortification of rice as a valuable policy intervention to tackle folate deficiency in different regions of China, further research is required to compare the benefits and costs with other interventions or folate biofortified products.

Keywords: Folate biofortification, health impact, neural-tube defects, DALYs, China
JEL codes: I1; D6

1. Introduction

Folate deficiency is an important type of micronutrient malnutrition characterized by a low intake of folates (< 400 µg per day). Suboptimal folate intake leads to an increased risk of several diseases, like neural-tube defects (NTD), megaloblastic anaemia and aggravation of iron deficiency anaemia. (Molloy & Scott, 2001). Folate is a water-soluble vitamin (Vitamin B9) and is available in different kinds of foods, such as beans and strawberries. Recently, folate biofortified rice with a high natural folate content was developed by Storozhenko *et al.* (2007). This type of folate biofortification, i.e. the enhancement of the natural folate content of a staple crop, can be considered as an alternative strategy to increase folate intake levels. Especially in regions where folic acid fortification, i.e. increasing the synthetic folate content of staple crops, folic acid supplementation, i.e. distributing folic acid pills, or food diversification, i.e. increasing the intake of folate-rich food products, are less successful or practically less feasible, folate biofortification could offer a solution.

With 258.8 million or 19.6 % of the Chinese population being folate deficient, China is an interesting region to analyze the health impact of folate biofortified rice as a policy intervention to tackle folate deficiency (De Steur et al., 2010a). As a consequence, the prevalence of neural-tube defects, i.e. the most important health outcome of folate deficiency, in China is among the highest in the world. Especially Shanxi Province, where each year 60 NTDs per 10,000 births are born, folate deficiency is a major health problem (Dai et al., 2002; Gu et al., 2007; Li, Ren, Zhang, Guo, & Li, 2006). Furthermore, China is a key player in the production and consumption of rice and genetically modified rice (Jia, Jayaraman, & Louët, 2004; Wang & Johnston, 2007). The recently granted bio-safety certificates of biotech Bt rice and phytase maize by the Chinese Ministry of Agriculture (MOA) support this statement (Shuping & Miles, 2009).

In this paper the health benefits of a folate biofortified product are quantified, based on the Disability-Adjusted Life Years (DALY) framework (Murray & Lopez, 1996; Stein, Meenakshi, Quinlivan, Nestel, Sachdev, & Bhutta, 2005). Because of the regional differences in rice consumption and folate status between the northern and southern regions, the health impact is analyzed at regional (administrative regions) level. Folate biofortification is not yet available on the market, by which this study is considered as an ex-ante evaluation of the introduction of folate biofortified rice. While previous health impact studies measured the impact of different biofortified crops, such as Golden Rice (Stein, Sachdev, & Qaim, 2006; Zimmermann & Qaim, 2004), on the prevalence of main micronutrient deficiencies (e.g. vitamin A deficiency), the focus here lies on folate biofortified rice as a policy intervention to reduce folate deficiency.

As a recent study analyzed the health impact of folate biofortified rice in China (De Steur et al., 2010a), this paper builds further on their findings and includes the calculation of the potential costs and the cost-effectiveness.

First, the current burden of folate deficiency in China is calculated in terms of "healthy" life years (DALYs lost) that are lost due to the disease. The health impact focuses on one particular health outcome of folate deficiency, neural-tube defects, as it is the only outcome which has a clear contribution level of folate deficiency. Periconceptional folate intake reduces the risk of having a baby with an NTD, i.e. the most common congenital malformation in the world (Lumley, Watson, Watson, & Bower, 2001; MRC Vitamin Study Research Group, 1991; Pinar, Tatevosyants, & Singer, 1998; Stockley & Lund, 2008). Second, the potential impact of the introduction of folate biofortification in China on this burden is measured by comparing the number of DALYs lost before and after folate biofortification. Third, the costs of this introduction are briefly discussed to come up with a rudimentary analysis of the potential cost-effectiveness of folate biofortification in China.

2. The current burden of folate deficiency in China (DALYs lost)

The DALY formula

The Disability-Adjusted Life Years approach quantifies the burden of a disease, e.g. folate deficiency as the number of DALYs lost. The number is a combination of the “Years Lived with Disability” (YLD) and “Years of Life Lost” (YLL), which represent, respectively, disability-weighted morbidity and cause-specific mortality due to folate deficiency. The DALY formula (Stein et al., 2005; Zimmermann et al., 2004) is expressed as:

$$\mathrm{DALYs_{lost}} = \mathrm{Y_{ears}L_{ived}D_{isability}} + \mathrm{Y_{ears}L_{ife}L_{ost}} = \sum_j T_j I_{ij} D_{ij}\left(\frac{1-e^{-rd_{ij}}}{r}\right) + \sum_j T_j M_j\left(\frac{1-e^{-rL_j}}{r}\right)$$

The input parameters of the formula are:

- the total number of people in target group j (T_j)
- the mortality rate associated with the deficiency in target group j (M_j)
- the incidence rate of functional outcome i in target group j (I_{ij})
- the disability weight for functional outcome i in target group j, (D_{ij})
- the duration of functional outcome i in target group j (d_{ij})
- the average remaining life expectancy for target group j (L_j), and
- the discount rate for future life years (r)

Because there is only data available on the contribution of folate deficiency to NTDs as an adverse health outcome, the three main NTD types (i.e. spina bifida, anencephaly and encephalocele) determine the current burden of folate deficiency. Thus, only the NTDs that are attributable to folate deficiency are included as functional outcomes. These outcomes refer to fatal (e.g. abortions or stillbirths) and non-fatal NTD-births (live births suffering from spina bifida or encephalocele (Access Economics, 2006; Mathers, Vos, & Stevenson, 1999). The sections below describe the calculation method and the value(s) of the different input parameters.

Input parameters of the DALY formula: Neural-tube defects caused by folate deficiency in China

To calculate the number of NTDs caused by folate deficiency in China, the total number of (all) NTDs is measured, based on demographic and NTD-related statistics in China and its regions (Northeast, Northwest, Southeast and Southwest). Table 1 gives an overview of these data.

In 2007, about 14 million babies were born in China. The most recent life expectancy of these Chinese births is 71.24 years in 2000 (National Bureau of Statistics of China, 2008). The regional life expectancies at birth refer to the average remaining life expectancy (L_j) of stillbirths and abortions, one of the input parameters of the DALY formula.

Application of the regional NTD prevalence rates (Dai et al., 2002) to the regional number of births results in the total number of NTDs in China (see Table 1). The share of the different functional outcomes is based on the composition of NTDs in the Chinese study of Li *et al.* (2006), where 31 % of all NTDs are abortions, and for 40.09 % and 28.91 % of all NTDs are considered as live births and stillbirths, respectively. Similar findings are found in other Chinese NTD studies (Moore et al., 1997; U.S. Department of Health and Human Services & Centers for Disease Control, 1989). The composition of the two non-fatal categories is based on the Chinese study of Dai e*t al.* (2002). The total annual number of NTDs in China, i.e. NTDs caused by folate deficiency or other factors, such as genetic or environmental causes (Sever, 1995), accounts 18 020, of which nearly 60 % is assumed to be fatal. The number of NTDs in Northern China is significantly higher than in its Southern counterpart. Almost 70 % of NTDs in China occur in one of the Northern regions.

It is important to notice that the current burden of folate deficiency includes only the NTDs that are caused by folate deficiency, instead of taking all NTDs into account. Therefore, the contribution level of folate deficiency to NTDs has to be defined.

There is scientific evidence on the relationship between folate deficiency and neural-tube defects, its main adverse health outcome. Several authors explored the effect of achieving the recommended folate intake on the risk of delivering a baby with an NTD (Daly et al., 1997; De Wals et al., 2007; Lumley et al., 2001; Molloy et al., 2001; MRC Vitamin Study Research Group, 1991). As a consequence, the WHO (2006) defined a daily dose of 400 μg of folates per women of childbearing age as the minimum folate level required for the prevention of a neural-tube defect. An intake below this level is considered as folate deficiency.

In a Chinese study, Berry *et al.* (1999) found that if women achieve the daily folate recommendation of 400 μg, the number of NTDs can be reduced by 40 % and 85 % in Southern and Northern China, respectively. Thus, 40 % and 85% are considered as the contribution levels of folate deficiency (<400 μg) to NTDs in southern and northern regions, respectively. By applying these contribution levels to the total number of NTDs, the number of NTDs caused by folate deficiency can be measured for each region. Due to the high contribution level in Northern China, its number of NTDs attributable to folate deficiency is significantly higher than in Southern China. Especially in Northwest China the burden of folate related NTDs is high.

With respect to the different functional outcomes, spina bifida is the most common outcome of NTD live births, while abortions occur slightly more than stillbirths when the NTD results in a fatal outcome.

The non-fatal and fatal outcomes of NTDs caused by folate deficiency are considered as the combined input parameters T_jI_{ij} and T_jM_j of the DALY formula, respectively.

Table 1 Demographic statistics of China, total population and births, life expectancy at birth, and neural-tube defects in China (all versus caused by folate deficiency) per functional outcome, per region

		North			**South**			**China**
		Northeast	Northwest	Total	Southeast	Southwest	Total	
Births[a]		4 761 446	1 267 500	6 028 946	6 524 892	2 216 919	8 741 811	**14 770 757**
Life expectancy[b]		73.59	72.39	73.19	69.96	68.23	69.42	**71.24**
NTD prevalence rate		19.2	22.2	19.9	5.6	6.6	5.8	**12.9**
NTDs[c]	Non-Fatal	3 791	1 197	4 988	1 664	572	2 236	**7 224**
	Spina bifida	3 057	900	3 957	1 176	409	1 584	**5 541**
	Encephalocele	734	298	1 031	488	163	651	**1 683**
	Fatal	5 666	1 789	7 454	2 486	855	3 341	**10 796**
	Abortions	2 932	926	3 857	1 287	442	1 729	**5 586**
	Stillbirths	2 734	863	3 597	1 200	413	1 612	**5 210**
	All NTDs	**9 457**	**2 986**	**12 443**	**4 150**	**1 427**	**5 577**	**18 020**
NTDs caused by folate deficiency[d]	Non-Fatal	3 223	1 018	4 240	666	229	894	**5 134**
	Spina bifida	2 599	765	3 363	470	163	634	**3 997**
	Encephalocele	624	253	877	195	65	261	**1 137**
	Fatal	4 816	1 521	6 336	995	342	1 337	**7 673**
	Abortions	2 492	787	3 279	515	177	692	**3 970**
	Stillbirths	2 324	734	3 058	480	165	645	**3 703**
	All NTDs < folate deficiency	**8 038**	**2 538**	**10 576**	**1 660**	**571**	**2 231**	**12 807**

[a] Based on birth rates in 2007 (in the China Statistical Yearbook 2008 (National Bureau of Statistics of China, 2008) and population figures of 2007, in the China Statistical Yearbook 2008 (National Bureau of Statistics of China, 2008)

[b] Regional life expectancy at birth in 2000, in the China Statistical Yearbook 2008 (National Bureau of Statistics of China, 2008)

[c] Based on regional NTD prevalence rates between 1996 – 2000, in Dai *et al* (2002).

[d] Based on the total number of NTDs and the contribution level of folate deficiency to NTDs in Northern (85 %) and Southern China (40 %).

Other input parameters of the DALY formula

Besides the number of fatal and non-fatal NTDs caused by folate deficiency, the DALY formula requires additional input parameters. The disability weights of the functional outcomes (D_{ij}) of these NTDs refer to the level of disability, with a range between health (D=0) and death (D=1) (Murray et al., 1996). While the disability weight of abortions and stillbirths, including anencephaly as a fatal NTD type, is 1, spina bifida and encephalocele have a disability weight of 0.593 and 0.520, respectively (1999). The duration (d_{ij}) of the latter two types are assumed to be permanent, by which d_{ij} equals the remaining life expectancy (L_j) or the life expectancy at birth (see Table 1). In accordance with previous applications of the DALY method (Stein et al., 2005; Zimmermann et al., 2004), the discount rate for future life years (r) is 3 percent.

The current burden of folate deficiency in China (DALYs lost)

The current burden of folate deficiency in China and its main regions, i.e. number of DALYs lost per year due to the prevalence of NTDs caused by folate deficiency, can be measured by entering the input parameters into the DALY formula. If the current rice consumption patterns are maintained and folate biofortification is not implemented, the annual loss of folate deficiency in China amounts to 314,180 DALYs, of which 72 % and 28 % are attributable to fatal and non fatal outcomes, respectively. Due to a different NTD prevalence rate and a different contribution level of folate deficiency to NTDs, there is a higher burden of disease in Northern China and, in particular, in its northeast part. Most of the non-fatal DALYs are lost due to malformations of the back, also known as spina bifida.

Table 2 The current burden of folate deficiency in China (DALYs lost per year), per functional outcome, per region

	North			**South**			**China**
	Northeast	Northwest	Total	Southeast	Southwest	Total	
Non-Fatal (YLD)	55 242	17 327	72 569	11 137	3 794	14 931	**87 500**
Spina bifida	45 642	13 425	59 067	8 169	2 809	10 978	**70 044**
Encephalocele	9 600	3 902	13 502	2 968	985	3 954	**17 456**
Fatal (YLL)	142 608	45 046	187 654	29 115	9 911	39 026	**226 680**
Abortions	73 791	23 309	97 100	15 066	5 128	20 194	**117 294**
Stillbirths	68 816	21 737	90 554	14 050	4 783	18 832	**109 386**
Total	**197 849**	**62 374**	**260 223**	**40 252**	**13 705**	**53 957**	**314 180**

YLD, years lived in disability; YLL, years of life lost

4. The health impact of folate biofortified rice in China (DALYs saved)

Data and assumptions

Figure 1 presents the framework to measure the health benefits of folate biofortified rice in China, by means of the DALY approach. To be able to calculate this health impact, additional data on the characteristics of folate biofortified rice (efficacy) and market characteristics (coverage, current rice consumption and current folate intake) are needed. The calculation method of these different determinants is described below. In cases were data is not available, additional assumptions had to be made.

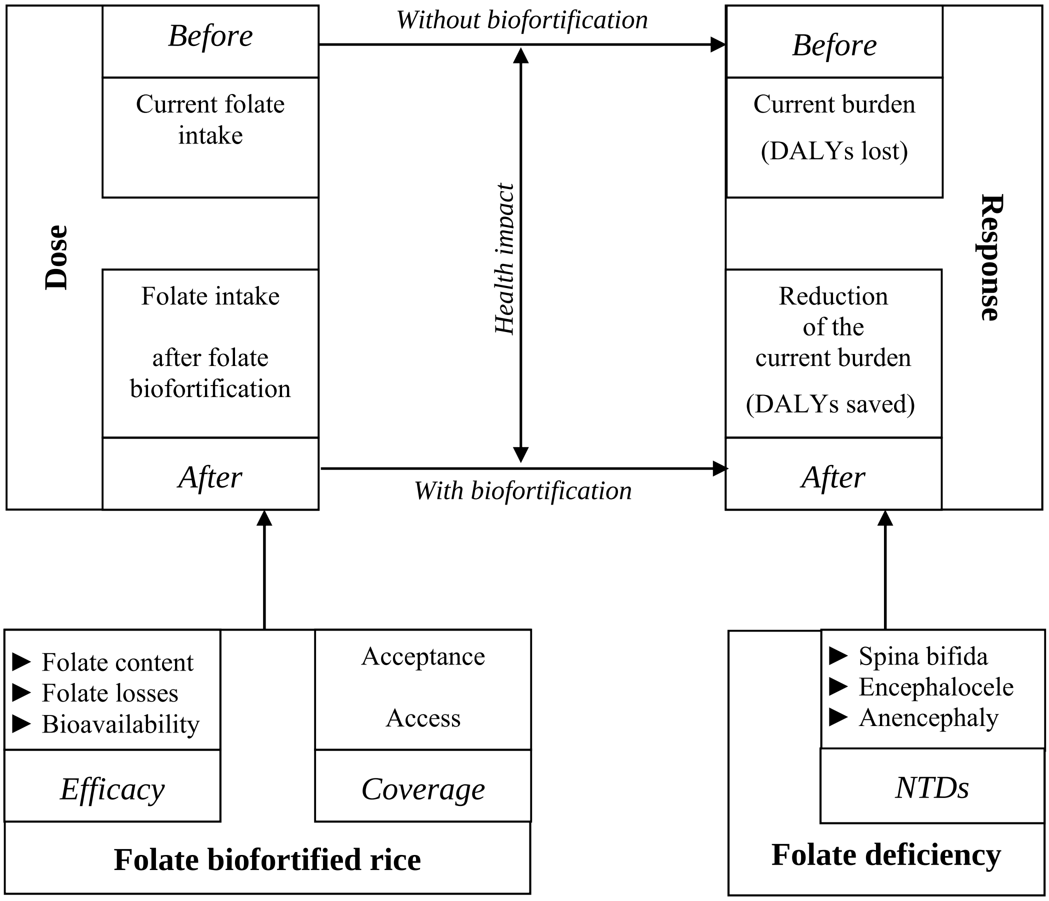

Figure 1 Health impact assessment of folate biofortified rice as a means to tackle folate deficiency. Application of the DALY method (based on Zimmerman & Qaim, 2004).

The efficacy of folate biofortified rice (product characteristics) determines the additional folate that will be consumed. It consists of three determinants: the (additional) folate content of folate biofortified rice, the folate losses after processing rice and the bioavailability of natural folate.

With respect to the folate content of folate biofortified rice, different transgenic lines were obtained by Storozhenko *et al.* (2007). Compared to the initial folate content of rice, 0.08 µg per g of raw polished grains, the transgenic lines are 20 to 100 times higher (US Department of Agriculture Agricultural Research Service, 2009). Instead of selecting one of the outliers, we decided to use 12 µg per g raw polished grains as the folate content of folate biofortified rice. However, due to cooking the rice (Storozhenko et al., 2007) and the bioavailibity of natural folate, 50 % (Bailey, 2004; FSAI, 2006), only 25 % of folate in the biofortified rice will be absorbed by the human body. This results in a total folate content of folate biofortified rice of 3 µg per g rice or an additional folate content of 2.92 µg per g when taking into account the initial folate content of rice.

The total folate intake after folate biofortification is further determined by the current rice consumption patterns and folate intake levels in China (see Table 3). In comparison with Northern China, rice consumption in Southern China is more than two times larger, with the highest rice consumption in the southeast (435 g per day per person) (CNGOIC, 2009a). Also the current folate intake of women of childbearing age is significantly higher in Southern China (213 µg per day) than in its northern counterpart (188 µg per day). Based on these current rice consumption patterns and folate intake levels, the regional folate intake of women of childbearing age after folate biofortification varies between 638 µg per day in Northwest China and 1 487 µg per day in Southeast China. The folate intake level after the introduction of folate biofortification exceeds the recommended nutrient intake level of folates.

Table 3 Current rice consumption and folate intake before/after folate biofortification in China, and % of RNI, per region

		North			South			China
		Northeast	Northwest	Total	Southeast	Southwest	Total	
Rice consumption[a]	g /day/person	186.5	156.1	181.1	435.5	348.8	412.9	**315.3**
Folate intake								
Before	µg /day/CBA[b]	190.9	182.7	188.0	215.1	210.4	212.9	**199.8**
	% of RNI[c]	47.7	45.7	47.0	53.8	52.6	53.2	49.9
After	µg /day/CBA	**735.4**	**638.4**	**716.9**	**1 486.8**	**1 228.9**	**1 418.6**	**1 120.4**
	% of RNI[c]	183.9	159.6	179.2	371.7	307.2	354.6	**280.1**

RNI, the recommended nutrient intake; CBA, woman of childbearing age

[a] The daily rice consumption per person is based on data from China's National Grain and Oils Information Center per person, in 2007 (CNGOIC, 2009b),

[b] The current, regional folate intake levels are based on to a study of Zhao *et al*(2009).

[c] Comparison of the total folate intake before/after biofortification with the recommended nutrient intake (RNI) of folate: 400 µg per day.

The coverage rate defines the market potential of folate enriched rice and refers to the acceptance of women and the accessibility to farmers in favor of folate biofortified rice.

A low and high coverage rate are defined, based on the acceptance rates of folate biofortified rice from a recent study in the Chinese Shanxi Province (De Steur et al., 2010b). The authors found that 55.4 % of all female rice consumers are willing to accept it, while 32.3 % react indifferent and 12.3 % are reluctant. The acceptance rate of farmers is 66.7 %, with 26.7 % of the farmers being indifferent. The low (36.95 %) coverage rate consists of female consumers in favor of folate biofortified rice, which have access to enthusiastic farmers. The high coverage rate (81.91 %) includes both females and farmers that are favorable of or indifferent to folate biofortified rice. By doing so, the coverage rate defines a market of women that can and will switch completely to folate biofortified rice.

Finally, the health impact of these folate intake levels after the introduction of folate biofortification (see Table 3) should be defined. Due to a lack of scientific evidence on the health effect of an increased folate intake, the dose-response function refers to the required folate intake level to prevent the risk of having a baby with an NTD, a daily folate intake of 400 µg. Therefore, folate intake levels above this threshold are assumed to result in the prevention of folate deficiency and its adverse health outcomes, such as neural-tube defects. Table three shows that all regional folate intake levels after biofortification exceeded the threshold of folate deficiency. In Southern China, for instance, the folate intake level after implementing the folate biofortified rice is 355 % of the required folate intake. In Northern China, the folate intake level is significantly lower than in Southern China, but still high enough to prevent women from having a baby with an NTD caused by folate deficiency.

Thus, introducing folate enriched rice with a folate content of approximately 12 µg per g rice prevents maternal folate deficiency and the risk of having a baby affected with an NTD caused by folate deficiency.

Health impact assessment of introducing folate biofortified rice in China (DALYs saved)

Due to the efficacy of folate enriched rice and the dose-response relationship, the introduction of folate biofortified rice in China is expected to lower the current burden of folate deficiency. Based on the low (36.95 %) and high (81.91 %) coverage rate of folate biofortified rice, the health impact of its introduction can be measured in terms of DALYs saved, which is:

Health impact = DALYs saved = DALYs lost (current burden of folate deficiency) – DALYs lost (reduced burden of folate deficiency)

The results are expressed as the number of DALYs saved through the implementation of folate enriched rice (see Table 4).

These scenarios start from the assumption that the total folate intake under biofortification in each administrative area in China is significantly higher than the threshold to prevent folate deficiency and the risk of delivering a baby affected with an NTD (see Table 6).

Each year, respectively 116 090 DALYs and 257 345 DALYs can be saved in the low and high impact scenario. In comparison with non-fatal outcomes of NTDs, the fatal outcomes gain more or less twice the number of DALYs. After biofortification, about 200 000 and 57 000 DALYs are still lost each year, due to folate deficiency (and its relationship with NTDs). While the lowest number of saved DALYs obtained in Southwest China, the benefits are the highest in Northeast China.

Table 4 Health impact assessment of folate biofortified rice in China, low and high impact scenario (DALYs saved per year, per functional outcome), per region

		North			**South**			**China**
		Northeast	Northwest	Total	Southeast	Southwest	Total	
Low impact[a]	Non-Fatal (YLD)	20 412	6 402	26 814	4,115	1 402	5 517	**32 331**
	Spina bifida	16 865	4 960	21 825	3 018	1 038	4 056	**25 881**
	Encephalocele	3 547	1 442	4 989	1 097	364	1 461	**6 450**
	Fatal (YLL)	52 694	16 645	69 338	10 758	3 662	14 420	**83 758**
	Abortions	27 266	8 613	35 879	5 567	1 895	7 462	**43 340**
	Stillbirths	25 428	8 032	33 460	5 191	1 767	6 959	**40 418**
	Total	**73 105**	**23 047**	**96 152**	**14 873**	**5 064**	**19 937**	**116 090**
High impact[b]	Non-Fatal (YLD)	45 248	14 193	59 441	9 122	3 108	12 230	**71 671**
	Spina bifida	37 385	10 996	48 382	6 691	2 301	8 992	**57 373**
	Encephalocele	7 863	3 197	11 060	2 431	807	3 238	**14 298**
	Fatal (YLL)	116 810	36 897	153 707	23 848	8 118	31 966	**185 674**
	Abortions	60 442	19 092	79 535	12 340	4 201	16 541	**96 076**
	Stillbirths	56 367	17 805	74 173	11 508	3 917	15 426	**89 598**
	Total	**162 058**	**51 090**	**213 149**	**32 971**	**11 226**	**44 197**	**257 345**

YLD, years lived in disability; YLL, years of life lost

[a] Based on a low coverage rate, i.e. 36.95 %.

[b] Based on a high coverage rate, i.e. 81.91 %.

Table 5 presents the relative health impact of folate biofortification in China, i.e. population weighted DALYs. These results show that the burden and health impact are relatively lower in Northern China, especially in the northwest. Although the absolute burden of folate deficiency is higher in the northeast, relatively more DALYs lost in Northwest China.

Table 5 Absolute and relative (DALYs per 10 000 persons) health impact assessment of folate biofortified rice in China, current burden, low and high impact scenario, per region

	North			South			China
	Northeast	Northwest	Total	Southeast	Southwest	Total	
DALYs lost (current)							
Absolute	197 849	62 374	260 223	40 252	13 705	53 957	**314 180**
Relative	4.31	6.39	4.68	0.71	0.69	0.71	**2.38**
DALYs saved (low)[a]							
Absolute	73 105	23 047	96 152	14 873	5 064	19 937	**116 090**
Relative	1.59	2.36	1.73	0.26	0.25	0.26	**0.88**
DALYs saved (high)[b]							
Absolute	162 058	51 090	213 149	32 971	11 226	44 197	**257 345**
Relative	3.53	5.23	3.83	0.58	0.56	0.58	**1.95**

[a] Based on a low coverage rate, i.e. 36.95 %.

[b] Based on a high coverage rate, i.e. 81.91 %.

5. Cost-effectiveness of folate biofortified rice

Building upon the investigated health impact, the cost-effectiveness of the introduction of folate biofortified rice in China can be assessed. This can be done by juxtaposing the costs of biofortification, research and social marketing costs, and the calculated health benefits. The time frame used in this study is 30 years, which is in correspondence with previous health impact studies, such as Stein et al. (2007; 2008). Table 6 gives an overview of the first rudimentary cost calculation of the introduction of folate biofortification in China. It is important to notice that the results are only an indication of the potential cost-effectiveness of folate biofortification in China. These findings should be interpreted very carefully and need to be verified and/or adjusted by additional experts in the field.

As the R&D of folate biofortified rice builds upon efforts to develop Golden Rice, the most advanced biofortified staple crop, the R&D costs of folate enriched rice are expected to be lower than for Golden Rice (ca 7.5 million US$ see Stein et al., 2006). The country-specific costs and, in particular, the regulatory process are important determinants of the cost-effectiveness of this policy intervention. As folate biofortification of rice does not alter the color of rice, the costs to disseminate and promote folate biofortified rice in China are assumed to be lower than in the case of the yellowish Golden Rice (between 15 and 30 million US$, see Stein et al., 2008) Nevertheless, as a consumer survey in Shanxi Province shows, it will be an important challenge to reach the high-risk groups, such as poor, low educated women from rural regions, as these are the ones that are least willing to accept folate biofortified rice (De Steur et al., 2010b).

As the coverage rate probably will not be reached in the first years of the implementation of folate biofortified rice in China, a growing share of the coverage rates is included in the time frame. It is assumed that after the release of folate biofortified rice, it will take about 8 years to reach the coverage rate, the maximum spread of folate enriched rice, based on its acceptance and accessibility. The coverage rates depend on the rice variety that has been selected. Crossing the folate trait with rice with successful agronomic traits, such as Bt Rice, is assumed to have a positive influence on the market share of folate enriched rice.

Table 6 Estimation of the duration, the costs and the coverage rate of introducing folate biofortified rice in China, low and high impact scenario

	Time frame	**Costs (US$)**		**Coverage rate (% reached)** [g]	
	(2002-2031)[d]	**Low**[e]	**High**[f]	**Low**	**High**
Costs					
Basic R&D[a]	2002-2010	6 mi.	3 mi.	NA	NA
Advanced R&D[b]	2010-2012	2 mi.	1 mi	NA	NA
Country-specific costs[c]	2012-2017	12 mi.	8 mi.	NA	NA
Social marketing	2017-2031	8 mi.	15 mi.	NA	NA
Maintenance breeding	2017-2031	3 mi.	2 mi.	NA	NA
Coverage rate					
Phase 1	2017-2018	NA	NA	25 %	25 %
Phase 2	2019-2021	NA	NA	50 %	50 %
Phase 3	2022-2024	NA	NA	75 %	75 %
Phase 4	2025-2031	NA	NA	100 %	100 %
Total	**2002-2031**	**32 mi.**	**29 mi.**	**36.95 %**	**81.91 %**

Remark: estimated release of folate enriched rice in 2017

Source: Expert meetings with Golden Rice Humanitarian Board & Department of Physiology of Ghent University; Stein et al. (2008)

NA, not applicable

[a] Development of rice with a high folate content

[b] Development of alternative antibiotic resistant markers instead of the antibiotic marker genes

[c] Chinese R&D costs include field trials (2012-2016), backcrossing costs (elite event selection in 2014), small and large scale feeding tests (2014-2017) and regulatory process (2014-2017)

[d] The costs and benefits of the introduction of folate biofortified rice in China are projected over 30 years.

[e] The costs in the low impact scenario consists of higher R&D and country-specific costs, but lower social marketing costs, which is based on the assumption of weak governmental support.

[f] The costs in the high impact scenario consists of lower R&D and country-specific costs, but the strong political support increases the efforts, and thus, costs of intensive country-wide social marketing activities.

[g] The percentages refer to the share of the coverage rate, the total number of women of childbearing age with a biofortified diet. As the total coverage rate is not reached in the first years, 4 different phases are included. Each phase refers to a specific percentage of the coverage rate and a defined period, starting in 2017 to 2025, where the total coverage rate is achieved.

Based on the health impact analysis (see Table 5) and the cost estimates (see Table 6), the cost per DALY saved can be assessed. This is done by comparing the Net Present Value (NPV) of the total costs and total DALYs saved, discounted at 3 %, similar to previous cost-effectiveness analyses of biofortified staple crops (Stein et al., 2007; Stein et al., 2008):

$$\frac{NPV_{costs}}{NPV_{DALYs\ saved}} = \frac{\sum_{t=1}^{30}[(C_t)(1+r)^{-1}]}{\sum_{t=1}^{30}[(DALYs\ saved_t)(1+r)^{-1}]}$$

The input parameters of the formula are year (t), ranging from 1 to 30, the total costs at year t (C_t), and the discount rate for future life years (r). The total cost per DALY saved is, respectively 31.17 US$ and 12.31 US$ in the low and high impact scenario. Compared with the World Bank (1994) threshold of cost-effective micronutrient policy interventions, US$ 50 per DALY saved in 1994, or 73.55 US$ in 2010 (BLS, 2010), the rudimentary estimate of the cost-benefit of folate biofortification seems to be promising.

Table 7 Estimation of the cost per DALY saved, based on the Net Present Value (NPV) of the total costs and total DALYs, in US$, low and high impact scenario

	Low	High
NPV costs	20.52 mi. US$	17.40 mi US$
NPV DALYs	0.64 mi. DALYs	1.41 mi. DALYs
Costs per DALY saved	32.17 US$	12.31 US$

6. Discussion

The results of the application of the DALY method to the potential introduction of folate enriched rice in China are highly dependent of the quality and appropriate use of the different parameters of the DALY framework (see also De Steur, et al, 2010). The use of a threshold of folate deficiency instead of a dose-response relationship is one of the most important limitations of the study. To analyze the response of the folate doses in the different regions (i.e. intake levels after biofortification), these doses are compared with the general threshold to prevent a mother of having a baby with a neural-tube defect caused by folate deficiency, i.e. 400 µg of folate per day, per person. Nevertheless, as there is no clear non-linear relationship between folate deficiency and neural-tube defects, the general recommended threshold is a valuable indicator to evaluate folate intake levels after folate biofortification.

Furthermore, only the main adverse health outcome of folate deficiency is included in the health impact analysis, i.e. neural-tube defects. Taking into account other negative health outcomes, such as aneamia, would definitely increase the burden of folate deficiency, and thus, the health impact of folate biofortified rice. Also the input parameters of the DALY framework have an important effect on the number of DALYs lost and saved. Using maternal instead of general rice consumption data, for instance, could have an influence on the results. Other input parameters refer to different years, such as the life expectancy rate in 2000 and the birth rate in 2007.

Although the health impact focuses on the reduction of neural-tube defects and, thus, newborns, it is important to notice that also women are directly influenced through their biofortified diet. Therefore, women should be the main target of social marketing to increase the coverage rate of folate biofortified rice. As poor, less educated women, for whom the need is greatest, are less willing to consume folate biofortified rice (De Steur et al., 2010b), specific groups and regions need to be tackled in communication programs.

Regarding the cost-effectiveness analysis, in-depth analysis and verification of the different costs of the introduction of folate biofortification in China is required. Furthermore, policy issues regarding the price of folate enriched rice, promotion campaigns, the selected variety, and so on, needs to be addressed. Nevertheless, a first glance at the costs of introducing folate biofortified rice in China reveals that this policy intervention could be a valuable, cost-effective method to reduce folate deficiency and the number of neural-tube defects. Given that the burden of folate deficiency will be larger when all negative health outcomes of folate deficiency would be included, the cost per DALY saved could be even lower.

Future research should further improve the quality of some of the input parameters of the DALY framework and the cost-calculation. With respect to folate deficiency, there is need for a well defined contribution level to each of its health outcomes. In this way, the total burden of folate deficiency could be measured, instead of the burden of neural-tube defects caused by folate deficiency. Furthermore, as our coverage rates are based on a regional consumer survey in Shanxi Province, the potential coverage rate of folate biofortified rice should be investigated in each region. To further evaluate the market potential of folate biofortified rice, it is important to compare the costs and benefits of different policy interventions to reduce (the impact of) folate deficiency in China, such as the distribution of folic acid supplementation or introducing grains fortified with folic acid.

7. Conclusions

By applying the DALY method, the potential health impact of folate biofortified rice in China is assessed in terms of the number of DALYs that can be saved through the biofortified diet. Compared with the current burden of folate deficiency, 314 180 DALYs, between 166 090 and 257 345 DALYs can be saved in low and high impact scenario. With respect to the Chinese regions, the burden and health impact are significantly lower in Southern China. Although folate deficiency rates are higher and rice consumption is lower in Northern China, the additional folate intake after biofortification of 2.92 µg per g rice is sufficient to prevent women from having a baby with a neural-tube defect caused by folate deficiency. The regional, average daily folate intake levels range between 545 µg and 1 941 µg per woman of childbearing age, which exceed the recommended threshold of folate deficiency (400 µg).

Although China is a valuable region to introduce folate biofortified rice as a means to tackle folate deficiency, given its world leading position in rice production and consumption and its favorable position towards genetically modified rice, increasing the coverage rate will be one of the main challenges to successfully implement folate biofortification in China. Especially in poor regions where other folate interventions are practically not feasible, the implementation of folate biofortified rice could be a valuable alternative. Nevertheless, a combined intervention will be probably the most effective way to alleviate folate deficiency.

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