Ex-ante evaluation of the health impact of rice with a high folate content in Shanxi Province, China. The Disability-Adjusted Life Years Approach.

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Contributed paper prepared for presentation at the
IAMA 20th Annual World Forum and Symposium
Boston, MA, USA, June 19 - 22, 2010

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Abstract

This paper examines the potential health impact of genetically modified rice with a high folate content, i.e. folate biofortified rice, as an alternative tool to tackle folate deficiency in Shanxi Province. This poor Chinese region, with 33 million inhabitants, is currently characterized by suboptimal folate intake levels, partly due to the low intake of folic acid supplements. Furthermore, Shanxi Province has one of the world's highest reported prevalence rates of neural-tube defects (NTDs), which is the main adverse health outcome of folate deficiency. By using the Disability-Adjusted Life Years (DALY) approach, the introduction of folate biofortified rice in Shanxi Province is evaluated in terms of "healthy" years saved. Currently, NTDs attributable to folate deficiency in Shanxi Province are responsible for an annual loss between 67 195 and 114 232 years of "healthy" life. Under the assumption that folate biofortification in Shanxi Province results in an average daily folate intake of 637.4 µg, which protects women to have a baby with an NTD caused by folate deficiency, each year 24 830 and 93 569 DALYs can be saved in the low-low and high-high biofortification scenario, respectively. Our findings demonstrate that folate biofortification of rice can alleviate the burden of folate deficiency and the number of NTDs in Shanxi Province. Further studies are needed to assess and compare the cost-effectiveness of this and other interventions to reduce folate deficiency, such as folic acid fortification or supplementation.

Introduction

Together with the main micronutrient deficiencies (Vitamin A, iron and zinc), folate deficiency or the suboptimal intake of folates remains a serious threat to the health of populations worldwide, in particular for children and pregnant woman. The main adverse health outcomes of folate deficiency are neural-tube defects (NTDs), i.e. the most important birth defect in the world (Christianson et al., 2006). There is a clear relationship between maternal folate deficiency and the risk of having a baby with an NTD (Molloy and Scott, 2001; MRC Vitamin Study Research Group, 1991). Adequate periconceptional use of folic acid supplements significantly reduces this risk (Lumley et al., 2001). Because the use of folic acid pills is not well established in poor regions, folate biofortification, improving the micronutrient content of staple food crops, can be considered as a valuable alternative for pharmaceutical folic acid supplementation (Storozhenko et al., 2007).

Shanxi Province, a coal mining region in the North of China, has one of the highest reported prevalence rates of NTDs in the world, with more than 100 out of 10 000 births suffering from an NTD (Gu et al., 2007; Li et al., 2006). This high incidence is correlated with low awareness and use of folic acid pills (Li et al., 2007; Ren et al., 2006) and suboptimal dietary folate intake levels of women of childbearing age (Ren et al., 2007; Zhang et al., 2008). This makes Shanxi Province an excellent region to investigate the health impact of folate biofortification.

Although wheat is the main staple crop in Shanxi Province, this paper aims to evaluate the health impact of the introduction of folate biofortified rice in this region. So far, rice with a high folate content is the most advanced folate biofortified staple crop (Blancquaert et al., 2008; McIntosh et al., 2008). By metabolic engineering, Storozhenko et al. (2007) obtained different transgenic lines with a folate content ranging from 350 to 1 700 µg per 100 g of raw polished grains, which is 20 to 100 times higher than the initial folate level of rice. Due to this high folate content of conventional rice, biofortification of the world’s most widely consumed staple crop is expected to have a large impact on public health, even in regions where rice is less consumed, such as Shanxi Province.

By applying the Disability-Adjusted Life Years (DALY) approach (Murray and Lopez, 1996), the health benefits of folate biofortified rice in Shanxi Province are quantified in terms of the number of “healthy” life years saved. During the last decade a lot of efforts have been made to analyze the health impact of different biofortified crops on the burden of the main micronutrient deficiencies (Horton, 2006; Meenakshi et al., 2007; Stein et al., 2005). Recently, De Steur et al. (2010a) evaluated the introduction of folate biofortified rice in China. This paper builds further on their findings and focuses on the potential introduction of folate biofortified rice in Shanxi Province, i.e. the most problematic region in terms of NTD prevalence.

As folate enriched rice is not yet available on the market, this study should be considered as an ex-ante analysis of the potential health impact of the introduction of folate biofortified rice on the burden of folate deficiency in a particular high risk region of Northern China. While women of childbearing age are considered as the target group of folate biofortified rice consumption, newborns are the ones who will benefit from their mothers' biofortified diet.

Materials and methods

Mainly two analyses are inherent in the Disability-Adjusted Life Years framework as a means to calculate the health benefits of biofortified crops: the estimation of the current burden of the disease and the assessment of the potential reduction of this burden by biofortification. When applied to folate biofortified rice, the current burden of folate deficiency is estimated (1), which enables to assess the potential reduction of this burden resulting from folate biofortification of rice, i.e. the health impact (2).

In the following subsections the use of the DALY framework and the data collection are described for each of these analyses. With respect to the theoretical background of applying the DALY approach to micronutrient deficiency and folate deficiency, special reference is made to Stein et al. (2005) and De Steur et al. (2010a), respectively. Therefore, the focus here lies on the data collection to measure the impact of folate enriched rice on folate deficiency in Shanxi Province. Although folate deficiency also results in other functional outcomes, such as megaloblastic anemia, only NTDs are covered in this research. The main reason is the lack of evidence of the contribution of folate deficiency to its different health outcomes. Thus, the 'burden of folate deficiency' refers to the negative health outcomes of the disease, i.e. NTDs. The latter is split up into three types, according to the malformation of the NTD. While anencephaly and encephalocele result in a malformed skull and brain, spina bifida is characterized by malformations in the spine (Molloy and Scott, 2001).

Estimation of the burden of folate deficiency: the DALY formula

Based on the DALY formula (Stein et al., 2005; Zimmermann and Qaim, 2004), the burden of a disease can be calculated in terms of the number of DALYs lost due to the mortality ("Years of Life Lost", YLL) or morbidity ("Years Lived with Disability", YLD) caused by the disease. The general DALY formula is expressed as follows:

$$\mathrm{DALYs_{lost}} = \mathrm{YLL} + \mathrm{YLD} = \sum_j T_j M_j \left(\frac{1-e^{-rL_j}}{r}\right) + \sum_j T_j I_{ij} D_{ij} \left(\frac{1-e^{-rd_{ij}}}{r}\right)$$

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

With respect to the DALY approach to measure the burden of folate deficiency, the target groups of the DALY formula refer to fatal or non-fatal births, and the functional outcomes are the different NTD types, caused by folate deficiency. Mortality refers to abortions and stillbirths, while morbidity mainly consists of live births suffering from two NTD types, spina bifida or encephalocele. Because infants born with anencephaly always die before or shortly after birth, this type is covered in the mortality statistics (Access Economics, 2006; Mathers et al., 1999).

Table 1 summarizes the required data related to NTDs in Shanxi Province. The indicator definitions, calculation methods and sources on which these data rely are presented. Based on the population and the birth rate for Shanxi Province (Shanxi Province Statistical Bureau, 2007), it is possible to define the total births (live births and stillbirths) and the composition of NTDs according to morbidity and mortality. The data about NTD related figures and the input parameters of the DALY formula are further described below.

Table 1 All neural-tube defects in Shanxi Province, indicator definition, calculation method and source.

	Numbers for Shanxi	Indicator definition/ Calculation method	Source
Total population	34 379 272	persons in 2006	(Shanxi Province Statistical Bureau, 2007)
Birth rate	11.48	per 1000 population in 2006	(Shanxi Province Statistical Bureau, 2007)
Births	394 674	BR*Total population/1000	
NTD prevalence rate	138.70	per 10 000 births	(Li et al., 2006)
Total NTDs	5474	PR*Births/10 000	
1. NTD Live births	2194	40.09 % of NTDs	(Li et al., 2006)
a. Spina bifida	1605	73.14 % of NTD live births	(Berry et al., 1999; Gu et al., 2007; Li et al., 2006; Liu et al., 2007)
b. Encephalocele	589	26.86 % of NTD live births	(Berry et al., 1999; Gu et al., 2007; Li et al., 2006; Liu et al., 2007)
2. NTD Stillbirths	1583	28.91 % of NTDs	(Li et al., 2006)
3. NTD Abortions	1697	31.00 % of NTDs	(Li et al., 2006)
NTD Morbidity	2195	1a + 1b	
NTD Mortality	3280	2 + 3	

BR, birth rate; NTD, neural tube defects; PR, prevalence rate of neural-tube defects

First, the prevalence rate of NTDs in Shanxi Province is determined. Various authors examined the prevalence of NTDs in this region. Due to different data collection systems or different periods of analysis, the prevalence rates in these studies differ significantly. Expressed per 10 000 births, the following rates are found in order of appearance: 105.5 in 1987 (Xiao, 1989), 149.0 in 1997 (Moore C et al., 1997), 138.7 in 2003 (Li et al., 2006) and 199.38 in 2002-2004 (Gu et al., 2007). As the latter prevalence rate only refers to two rural counties in the Lvliang mountain area of Shanxi Province, which partly explains its high rate, the NTD rate of Li et al. (2006) is selected because it is the most recent and it is in line with previous findings. As this prevalence rate refers to the number of NTDs within a time period, this rate is used as an approximate incidence rate.

Second, the share of the three NTD types in the total number of NTD live births is based on findings from two country-wide Chinese (Berry et al., 1999; Liu et al., 2007) and two Shanxi studies (Gu et al., 2007; Li et al., 2006). As anencephaly is a part of NTD mortality, only the average prevalence of spina bifida and encephalocele are considered, based on a share between respectively 47.5-59.3 % and 7.5-34.4 % of all NTDs. These figures are in line with studies in the U.S. (Feuchtbaum et al., 1999), Canada (De Wals et al., 2007; Gucciardi et al., 2002) and Ireland (FSAI, 2006).

Third, the mortality findings of the Shanxi study of Li et al. (2006) are adopted to the total number of NTDs, with 31 % and 28.91 % of all NTDs considered as abortions and stillbirths, respectively. Together, live births and stillbirths account for 69 % of NTDs.

The NTD figures above refer to NTDs caused by folate deficiency as well as other causes, such as genetic and environmental factors (FSAI, 2006). Because this paper analyses the health impact of folate biofortification, only the NTDs that are attributable to folate deficiency are included in the DALY framework. To gather scientific evidence of the contribution of folate deficiency as a cause of NTDs, literature is reviewed on the relationship between maternal folic acid supplementation during the periconceptional period and the risk of having a baby with an NTD. While a few authors attempt to retrieve the non-linear association between folate intake and reduction of NTD incidence (Daly et al., 1997; Moore et al., 2003), most of the studies analyzed the effect of a daily folate intake of 400 µg (Lumley et al., 2001; Molloy and Scott, 2001). This dose is also advised by the WHO (2006) and the United States Public Health Service (USFDA, 1996).

If women consume this recommended amount of folates, between 50 to 70 % of all cases of NTDs in the world can be prevented (Daly et al., 1997; Lumley et al., 2001; Molloy and Scott, 2001). According to a study in Northern China (Berry et al., 1999), the number of NTDs caused by folate deficiency is even higher (85 %). Thus, under the assumption that folate deficiency refers to a daily folate intake below 400 µg, 50 % to 85 % of all NTDs are considered to be attributable to folate deficiency in Shanxi Province. The general contribution levels (50% and 70%) and the higher percentage (85 %) are chosen as the three reference points to define the number of NTDs attributable to folate deficiency.

Table 2 presents the total number of NTDs caused by folate deficiency, split up into two non-fatal (morbidity) and two fatal (mortality) functional outcomes. According to the highest contribution scenario, around 4653 NTDs are attributable to folate deficiency in Shanxi province. Almost 60 % of these NTDs are characterized by a fatal outcome.

Table 2 All NTDs and NTDs attributable to folate deficiency in Shanxi Province, low, medium and high contribution scenario

Functional outcome	All NTDs (see Table 1)	Contribution of folate deficiency to NTDs			% of total NTDs
		Low[a]	Medium[b]	High[c]	
Morbidity					
Spina bifida	1 605	802	1 124	1 364	29.3
Encephalocele	589	295	412	501	10.8
Total	2 194	1 097	1 536	1 865	40.1
Mortality					
Stillbirths	1 583	792	1 108	1 345	28.9
Abortions	1 697	848	1 188	1 443	31.0
Total	3 280	1 640	2 296	2 788	59.9
Total	5 474	2 737	3 832	4 653	100.00

[a] Low: 50 % of NTDs attributable to folate deficiency

[b] Medium: 70 % of NTDs attributable to folate deficiency

[c] High: 85 % of NTDs attributable to folate deficiency

With respect to the DALY formula, the number of NTDs for each non-fatal and fatal functional outcome is considered as the combined input parameter T_jI_{ij} and T_jM_j respectively. Besides these parameters, the DALY formula requires additional information to measure the current burden of folate deficiency, i.e. the number of DALYs lost under the status quo. Table 3 gives an overview of the main input parameters of the DALY formula.

Table 3 Input parameters of the DALY formula, related to Shanxi Province

Functional outcome	T_jI_{ij}			T_jM_j					
	Low[a]	Medium[b]	High[c]	Low[a]	Medium[b]	High[c]	$L_j = d_{ij}$	D_{ij}	r
Morbidity									
Spina bifida	802	1 124	1 364	NA	NA	NA	73.11 yrs	0.593	3 %
Encephalocele	295	412	501	NA	NA	NA	73.11 yrs	0.520	
Mortality									
Stillbirths	NA	NA	NA	792	1 108	1 345	73.11 yrs	1.0	3 %
Abortions	NA	NA	NA	848	1 188	1 443	73.11 yrs	1.0	

NA, not applicable

[a] Low: 50 % of NTDs attributable to folate deficiency

[b] Medium: 70 % of NTDs attributable to folate deficiency

[c] High: 85 % of NTDs attributable to folate deficiency

First, the input parameters regarding incidence (T_jI_{ij}) and mortality rates (T_jM_j) within each target group are based on the number of NTDs caused by folate deficiency, as shown in Table 2. Second, the average remaining life expectancy (L_j) refers to the average life expectancy at birth in Shanxi Province, 73.11 years (Shanxi Province Statistical Bureau, 2007). Third, disability weights (D_{ij}) for morbidity are described in the Global Burden of Disease (GBD) study (Murray and Lopez, 1996) and a more recent study in Australia (Mathers et al., 1999). Disability weights ranges from 0 (‘no disability’) to 1 (‘death’) according to the level of “severity” or “disability”. With respect to the non-fatal NTDs, the severity of encephalocele and spina bifida are more or less equal. The fourth input parameter, the duration of NTD morbidity (d_{ij}), is assumed to be permanent, by which d_{ij} equals the average life expectancy at birth. Fifth, the discount rate for future life years (r) amounts 3 percent, similar to previous health impact studies (Stein et al., 2005; Zimmermann and Qaim, 2004).

Factors influencing the health impact of folate biofortification

The framework to assess the NTD related health benefits of folate biofortified rice is based upon previous literature (Qaim et al., 2006; Zimmermann and Qaim, 2004) and consists of the parameters that influence the number of DALYs lost under the "with" hypothesis, i.e. when folate biofortified rice is consumed (Figure 1).

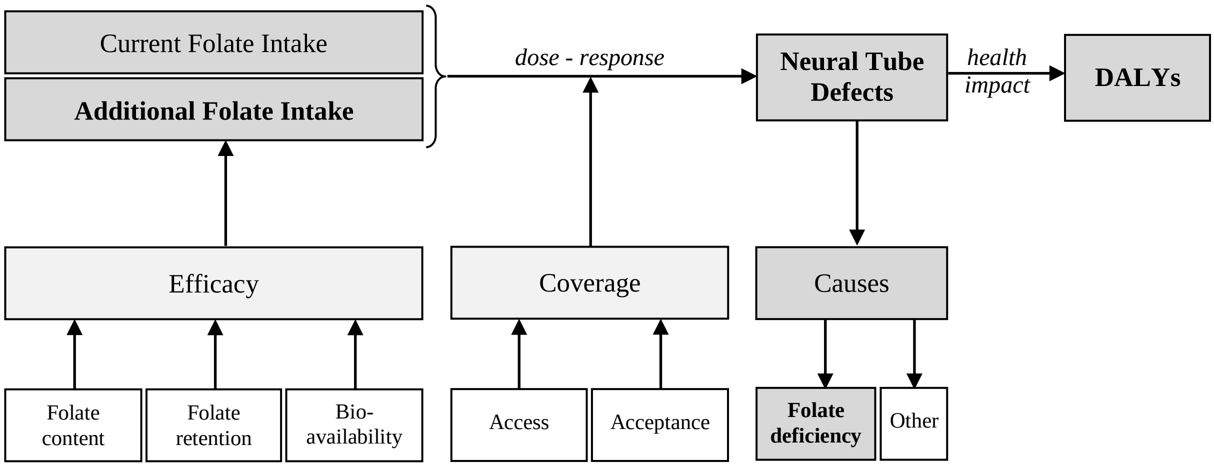

Figure 1 Framework to assess the health impact of introducing folate biofortified rice
Source: De Steur et al. (2010a)

As figure 1 illustrates, the health impact of folate biofortified rice depends primarily on biofortification characteristics (efficacy) and consumer characteristics (coverage).

Efficacy is determined by the level of enhancement of folates in rice, potential folate losses after rice processing and its bioavailability. Compared with the initial folate content of rice, 8 µg per 100 g (US Department of Agriculture Agricultural Research Service, 2009), folate biofortification of rice resulted in different transgenic lines with a folate content between 350 and 1700 µg per 100 g of raw polished grains (Storozhenko et al., 2007). The calculations in this study are based on a folate content of 1200 µg per 100g raw polished rice. Processing of rice, i.e. cooking, will retain approximately 50 % of the total folate content (Storozhenko et al., 2007). The degree of bioavailability depends on the source of folate. While folic acid in biofortified food is 85 % bioavailable and folic acid supplements are around 100 % bioavailable, natural folate in food has been shown to be only 50 % bioavailable (Bailey, 2004; FSAI, 2006). Although research is necessary to evaluate the exact bioavailability of folate biofortified rice, the theoretical bioavailability of natural folate (50 %) is taken into account. Based on the efficacy parameters, the folate intake of biofortified rice amounts 300 µg per 100 g rice.

The coverage rate refers to consumers' acceptance of and accessibility to farmers in favor of folate enriched rice. The acceptance rate of rice with high folate content in Shanxi Province is based on an earlier study (De Steur et al., 2010b) where 55.4 % of all female rice consumers are willing to accept folate biofortified rice, 32.3 % react indifferent and 12·3 % are reluctant. Regarding Shanxi farmers the acceptance rate is 66.7 %, while 26.7 % of the farmers are indifferent. Based on these figures, a low and high coverage rate are defined. The low coverage rate (36.95 %) consists of female consumers willing to accept folate biofortified rice and having access to farmers in favor of this product. The high coverage rate (81.91 %) also takes into account women that are indifferent to this product and access to farmers that are indifferent. The coverage rate is thus determined by the percentage of women that switch completely to folate biofortified rice, compared with a group of women that still consume traditional rice. The higher the coverage rate, the more NTDs that can be prevented by women's consumption of biofortified rice.

To determine the total folate intake after biofortification, additional knowledge of the current rice consumption pattern and folate intake is needed. According to China's National Grain and Oils Information Center (CNGOIC, 2009), Shanxi Province has an average rice consumption of 157.8 g per person, per day in 2008, which is remarkably lower than the Chinese average of 315.29 g. Given this current rice consumption pattern and the average folate intake of biofortified rice, biofortification results in an average added folate intake of 460.7 µg per person, per day. The current folate intake level of women of childbearing age in Shanxi Province amounts 167.7 µg per day (Zhang et al., 2008). Adding the additional folate intake to this current daily folate intake, gives a total folate intake under biofortification of 637.4 µg per women of childbearing age, per day.

Further, the "dose-response", the effect of additionally absorbed folates on folate attributable NTDs, has to be assessed. Due to the lack of individual dietary intake data, the "dose" is based on the average folate intake in Shanxi Province under the biofortification scenario, around 640 µg per person, per day. This folate intake level is almost four times higher than the current intake level and, more important, exceeds the general accepted threshold to prevent folate deficiency and its adverse health effects, 400 µg per person, per day. Therefore, the "response" to biofortified folate intake is understood as the prevention of all NTDs caused by folate deficiency. Although Shanxi Province is mainly a wheat consuming region, with an annual rice consumption of only 58 kg per person, introducing rice with a folate content of approximately 1200 µg per 100 g rice would contribute to achieve the recommended daily folate intake of 400 µg per person in Shanxi Province.

Results

The burden of folate deficiency in Shanxi Province, expressed in DALYs lost

Based on the input parameters from Table 3, the DALY formula is used to calculate the current burden of folate deficiency in Shanxi Province. Table 4 presents this burden in terms of lost DALYs, for each contribution scenario. Based on consumption of traditional rice (i.e. without folate biofortified rice), the number of DALYs lost due to folate deficiency varies between 67 195 DALYs in the low and 94 073 DALYs in the high contribution scenario. The contribution of morbidity and mortality to the current burden amounts to 27.73 % and 72.27 %, respectively. The number of years lived with disability is the highest for spina bifida, while the lost life years are more or less equally divided between the two fatal functional outcomes.

Table 4 Burden of folate deficiency in Shanxi Province, per functional outcome and contribution scenario, expressed in the number of DALYs lost

	Contribution of folate deficiency to NTDs		
Functional outcome	Low[a]	Medium[b]	High[c]
Morbidity			
Spina bifida	14 094	19 732	23 960
Encephalocele	4 539	6 354	7 716
Total (YLD)	18 633	26 086	31 676
Mortality			
Stillbirths	23 434	32 808	39 838
Abortions	25 128	35 179	42 718
Total (YLL)	48 562	67 987	82 555
Total (YLD + YLL)	67 195	94 073	114 232

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

[a] Low: 50 % of NTDs attributable to folate deficiency

[b] Medium: 70 % of NTDs attributable to folate deficiency

[c] High: 85 % of NTDs attributable to folate deficiency

The health impact of folate biofortification of rice, expressed in DALYs saved

The benefits of the introduction of folate biofortified rice in Shanxi Province is expressed as the number of DALYs gained through the intervention. This number is assessed by juxtaposing the number of DALYs lost under the current situation (“without”, see Table 4), and under a folate biofortification scenario (“with”, see Table 5).

Taking into account the coverage rate and contribution of folate deficiency to NTDs, six impact scenario’s can be distinguished (Table 5). The average maternal folate intake after biofortification in Shanxi Province saves between 24 830 DALYs in the "low-low" scenario and 93 569 DALYs in the "high-high" scenario (see Table 5). Due to a lower coverage rate and a diminished health effect, between 42 365 and 72 021 DALYs are still lost in the low impact scenario. These findings are based on the assumption that the average daily folate biofortified rice intake of 637.4 µg prevents women of having a baby with an NTD caused by folate deficiency.

Table 5 Folate biofortification of rice in Shanxi Province, per functional outcome and contribution scenario, expressed in the number of DALYs saved per impact scenario

	Low impact scenario			High impact scenario		
Functional outcome	Low[a]	Medium[b]	High[c]	Low[a]	Medium[b]	High[c]
Morbidity						
Spina bifida	5 208	7 291	8 854	11 545	16 163	19 626
Encephalocele	1 677	2 348	2 851	3 718	5 205	6 320
Total (YLD)	6 885	9 639	11 705	15 263	21 368	25 947
Mortality						
Stillbirths	8 659	12 123	14 721	19 195	26 873	32 632
Abortions	9 286	12 999	15 785	20 583	28 816	34 991
Total (YLL)	17 945	25 122	30 506	39 778	55 689	67 623
Total (YLD + YLL)	24 830	34 761	42 211	55 041	77 057	93 569

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

[a] Low contribution scenario: 50 % of NTDs attributable to folate deficiency

[b] Medium contribution scenario: 70 % of NTDs attributable to folate deficiency

[c] High contribution scenario: 85 % of NTDs attributable to folate deficiency

Discussion

The objective of this paper is to analyze ex-ante the health benefits of a folate biofortified rice intervention in a high NTD prevalence region. Although biofortified food products are still not produced, the commercialization of biofortified rice in China is more and more likely to happen. Recently, the Chinese Ministry of Agriculture (MOA) approved Bt rice as the first major biotech food crop, which is expected to be fully commercialized in two to three years (Shuping and Miles, 2009). This illustrates China's governmental support for research on biofortified rice using transgenic techniques (Fan et al., 2009; Pray and Huang, 2007). China's support for rice biofortification is not surprising. China is not only the largest producer of conventional rice, but also a key player of genetically modified rice production (Jia et al., 2004; Wang and Johnston, 2007). Therefore, China's - and the world's - most consumed staple crop, rice, will be probably preferred as the biofortified food product to tackle folate deficiency, which is not only a health problem in Shanxi Province (Zhang et al., 2008), but also in China as a whole (De Steur et al., 2010a; Zhao et al., 2009). Furthermore, folate biofortified rice is currently the most advanced folate biofortified staple crop (Blancquaert et al., 2008). Therefore, rather than using wheat, which is more consumed in Shanxi Province, our study on the health impact of folate biofortification focused on rice. Other folate biofortified products, such as lettuce (Nunes et al., 2009) and tomato (Diaz de la Garza et al., 2007) are less relevant to introduce in Shanxi Province, given the current dietary patterns.

Although the use of the DALY approach to evaluate the health impact of biofortified crops has become popular, this method was subject to criticism (Allotey et al., 2003; Anand and Hanson, 1998; Lyttkens, 2003). In this section the DALY framework as such is not discussed, but the data on which it is based.

This paper compares the current burden of NTDs caused by folate deficiency with six biofortification scenarios. These scenarios are determined by the coverage rate of the folate enriched rice intervention and the importance of folate deficiency as a cause of NTDs. With respect to the latter, 50 % ('low'), 70 % ('medium') and 80 % ('high') of the NTDs are assumed to be attributable to folate deficiency. If different contribution rates would be applied, such as the rate found in the Chinese study of Chen et al. (2008), 80 %, the size of the burden of folate deficiency will be directly influenced. Although our "high" contribution level is based on a study in Shanxi Province, we decided to include the general accepted range of contribution levels as alternative scenarios.

The choice of these percentages reveals a lack of data on the specific non-linear relationship between dose and response. Therefore, the average daily folate intake under biofortification is considered as the dose, by which Shanxi women of childbearing age are protected from having a baby with an NTD caused by folate deficiency. This assumption is based on the difference between the average daily folate intake before (176.4 µg) and after (637.4 µg) the intervention and the contribution of the latter to the folate intake requirements, i.e. 159.4 %. Connecting individual consumption data with a non-linear dose-response function of folate intake and neural-tube defects would have provided a more realistic view on the health benefits of folate biofortification. However, such a dose-response function is not yet determined.

Another limitation regarding the use of an average daily folate intake is the risk of extreme folic acid intake. A daily folic acid intake of 1 000 µg is set as an upper level which is safe for all populations. When exceeding this level, Vitamin B_{12} deficiency may be masked (Bailey, 2004; Bekaert et al., 2008). Although this is not traceable with the current data, this risk is less important in regions with a low intake of folic acid pills, such as Shanxi Province. Moreover, folate biofortified rice mainly contains 5-methyl-tetrahydrofolate, a folate species known to have a much lesser effect on masking B_{12} deficiency (Storozhenko et al., 2007).

Regarding the health impact of folate biofortification, the saved DALYs under the biofortification scenarios have to be understood as an estimated number. First, the health benefits only refer to the reduction of the number of NTDs as the main functional outcome of folate deficiency. If data on the contribution of folate deficiency to all its adverse health outcomes would be available, the total burden and the health benefits are expected to be much higher. Second, this health impact analysis would be more accurate if rice consumption data refers to women of childbearing age, instead of the total average in Shanxi Province. Therefore, primary data collection of female rice consumption patterns is required.

Because most of the parameters used in the DALY framework are based on secondary data, sometimes referring to different years (e.g. NTD prevalence rate in 2003 and life expectancy in 2006), additional research is needed to collect primary data. Furthermore, the impact of some of the efficacy parameters needs to be further explored, such as the bioavailability of folate biofortified rice. Another research topic is the cost-effectiveness of a folate biofortified intervention, which is assumed to be a pro-rural and pro-poor approach, and the comparison with other interventions to improve folate intake. On the one hand, increasing the consumption of folate rich products is less favorable in Shanxi Province, as it is hard to change dietary habits in a poor region. On the other hand, awareness and use of folic acid pills is still low in this province, with maternal intake levels of about 10 % (Li et al., 2007; Ren et al., 2006). Furthermore, because industrial folic acid fortification in grains requires appropriate infrastructure and quality control, it is less effective in poor Chinese regions (Campos-Bowers and Wittenmyer, 2007) as compared to developed countries (Cordero et al., 2008).

If China would approve folate enriched rice as in the future, several policy issues should be addressed, such as labeling, intellectual property rights and trade or price policy issues (Campos-Bowers and Wittenmyer, 2007). Furthermore, the implementation of folate biofortification programs should initially reach its target group, women of childbearing age from poor, rural areas. Also the procedures to commercialize the rice and distribute the seeds (through farmers or other channels; voluntary or mandatory) should be clarified and supported. And even if the Chinese policy would accept the production of biofortified staple crops, it should be taken into account that biofortification alone will only alleviate micronutrient malnutrition. A combination of interventions will be probably the most feasible and effective strategy to combat folate deficiency.

Conclusions

This paper is an attempt to investigate the health benefits of a folate biofortified product in a specific region. In particular, it is an ex-ante evaluation of the health impact of folate enriched rice on folate deficiency in Shanxi Province, China. This region is characterized by one of the highest NTD prevalence rates in the world, partly due to its inadequate average folate intake level of 176.4 µg per women, per day. While other interventions are less successful or practically less feasible in developing regions, like Shanxi Province, folate biofortified rice can be a valuable alternative to combat folate deficiency and its adverse health outcomes, such as NTDs. Application of Disability-Adjusted Life Years approach shows that the introduction of folate biofortified rice would save between 24 830 and 42 211 DALYs in the low impact scenario and between 55 041 and 93 569 DALYs in the high impact scenario. These findings are based on an estimated average folate intake after the introduction of biofortification, i.e. 637.4 µg per person, per day, which is significantly higher than the recommended intake of 400 µg to prevent the risk of having a baby with an NTD caused by folate deficiency.

Although the DALY approach is a useful method to quantify the impact of folate biofortification on public health, the results are highly dependent on the value and the reliability of the parameters, in particular with respect to Shanxi Province. Primary data collection of the required parameters in Shanxi Province would give a more up-to-date picture of the burden and the potential health benefits. Nevertheless, these findings indicate that folate biofortification of rice has the potential to reduce the number of NTDs in high risk regions and should be considered as a potential alternative policy measure to further combat folate deficiency.

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