Impact of Folate Biofortified Food Supplement on Rural Women Health and Willingness-to-pay: A Study Based on A Connected Randomized Controlled Trial- Becker–DeGroot–Marschak Experiment in China

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Research article

Keywords: biofortification, folate-fortified maize, health effect, randomized controlled trial, consumer valuation

Posted Date: September 9th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-853253/v1>

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Abstract

We examined whether folate-fortified maize (FFM) improves the health of rural women of childbearing age and whether the health intervention is associated with the formulation of consumer willingness-to-pay (WTP). A randomized single-blind folate-fortified maize intervention trial was conducted in rural childbearing-aged women. Participants consumed one stalk of either folate-fortified maize (FFM) (treatment group) or ordinary maize (control group) daily for 2 months ($n = 55$). Serum folate levels were assessed at baseline, mid stage (after 1 month), and final stage (after 2 months) to assess the effect of FFM. Results showed that the serum folate level in the treatment group (13.31 ng/mL) was 3.40 ng/mL higher than that in the control group (9.91 ng/mL) in the final stage of the study. We obtained suggestive evidence that regular dietary FFM intake significantly increased serum folate levels in rural Chinese women. We further recruited 181 local rural women with similar demographic characteristics to participate in a Becker–DeGroot–Marschak (BDM) bidding experiment to measure their WTP for FFM. Results showed that local consumers were willing to pay 2.82 CNY per FFM stalk, approximately 1.21 CNY higher than the price of ordinary maize. We provide evidence on the health improvement effect of biofortified foods and shed light on the associated consumer valuation and policy implementation.

1. Introduction

Malnutrition problems comprise two aspects: protein-energy malnutrition and micronutrient deficiencies. Specific micronutrient deficiencies, which are also referred to as "hidden hunger," are more common and affect a larger population in developing countries, where food varieties are lacking due to economic and political conditions [1]. With the development of technology, replenishment of protein-energy, and supplementation of certain micronutrients can be achieved simultaneously through biofortification of staple crops. Biofortification, that is, improving the micronutrient content of staple foods through crop breeding, could be a pro-poor, pro-rural, agriculture-based intervention to reduce the health burden of micronutrient malnutrition [2–3]. Therefore, biofortification is a feasible and effective way to improve malnutrition in developing countries [4]. When appropriately implemented, the biofortification crop program can positively affect long-term economic and social benefits in developing countries [5].

Folate deficiency is a common micronutrient deficiency that exists in both developed and developing countries. Due to limitations in economic development level, local food varieties, and culinary habits, developing countries are at a higher risk of folate deficiency and its adverse effects [6]. With increasing physiological folate need for procreation, folate deficiency often appears in women of childbearing age [7]. Folate deficiency could affect health, lead to severe consequences for future generations, and bring further substantial economic and social losses [8]. For instance, inadequate preconception and prenatal folate intake are associated with increased risks for spontaneous abortion and neonatal neural tube defects (NTD) [9], and the direct economic loss caused by NTD in China is more than 200 million CNY per year [10].

China has remarkably moved its large population out of poverty in the past four decades [11]. Poverty is considered the leading cause of malnutrition and hunger [12]; China's poverty alleviation reduces hunger [13]. However, micronutrient deficiencies remain a widespread issue in China [2]. It is estimated that approximately 258.8 million people in China suffer from folate deficiency; about 18,000 babies in China are born with NTD every year [6], which accounts for approximately 9% of the global prevalence figure. In areas with a high prevalence of NTD, the rates of plasma and red blood cell folate deficiencies in China were 43.8% and 35.0%, respectively [14]. The overall folate deficiency among Chinese women of childbearing age was 1–20% [15–16]. At the provincial level, the folate deficiency rate in the Henan province in our sample province is high, with its neonatal neural tube malformation rate reaching 19.8% [17–18]. Previous surveys have shown that only 37.9% of women of childbearing age regularly take folate

supplements [19]. Among those who have taken folate supplements, most take less than the recommended daily folate dose [20].

Folate supplementation during the preconception period is recommended in most countries [21–22]. Although recommended, many people in developing countries inadequately recognize the necessity of folate supplements during pregnancy, especially in rural areas [23]. Biofortification is one strategy that can increase the uptake of folate using staple food crops (rice, wheat, and maize). Therefore, an intervention for the current supplement program could be folate-fortified maize (FFM), as it has the potential to improve folate deficiency without changing the dietary habits of women of childbearing age.

Although promising, macro-level policy design and implementation still require more micro-level evidence to explicitly quantify the physiological and economic impacts, especially at the individual level [6]. This study aims to answer whether and how FFM could improve women's health at childbearing age and elicit the targeted consumers' valuation for FFM using a connected randomized controlled trial (RCT) and Becker-DeGroot-Marschak (BDM) experiment method.

2. Materials And Methods

This study relies on a connected RCT-BDM experiment to evaluate the health outcomes and consumer valuation of FFM. First, we implemented a three-stage randomized, single-blind, placebo-controlled, folate-fortified maize intervention experiment to examine whether and how biofortified food affects the blood folate concentrations of childbearing women. Second, to assess the consumer valuation of FFM, we adopted the BDM bidding experiment to elicit consumer values. By combining the two experiments, we evaluated the health effects and consumer valuations of the FFM.

2.1. Participants

2.1.1. RCT Participants

Recruitment of the RCT participants occurred between June 2018 and August 2018, with the cooperation of the local Center for Disease Control and Prevention (CDC) and local government. All recruitment and intervention visits occurred at the village clinic in the Xieying and Taqiao Villages in Nanyang City, Henan Province, China. Recruitment ended when proper sample size was achieved. The appropriate sample size calculation using published data [24–26] indicated that a total of 15–30 participants per group were needed to observe significant changes. Through the mobilization of the village head, 200 women of childbearing age were willing to participate in this study. Overall, 121 subjects met the screening criteria after the baseline survey.

The inclusion criteria were as follows: women of childbearing age who were 18 to 49 years of age, with a red blood cell folate concentration lower than 906 nmol/L, no genetic diseases, no pregnancy planning, no smoking habit, and no history of folate or vitamin supplementation in the past 3 months. Participants also had to be willing to commit to the study instructions from the baseline survey until the end of the intervention. The instruction was to eat one stalk daily of maize provided by the researchers. Participants were also asked to report on the use of new medications and avoid natural health product consumption or changes in lifestyle habits.

24 women refused to take part in the study and 52 were excluded due to not meeting the selection criteria. In addition, 3 women could not be contacted. A final sample of 121 participants was recruited to participate in the study; 60 were randomized to the treatment group and 61 to the control group following a single-blind randomization method.

Unfortunately, only 41 women in the treatment group and 45 in the control group, and 25 in the treatment group and 30 in the control group attended the mid and final stage intervention assessments, respectively. Although the sample size shrank to 86 and 55 in the mid stage and final stage examinations respectively, there were still more than 15 subjects in each group. According to previous studies [24–26], we could still observe significant changes. Figure 1 shows a flowchart of the recruitment process and RCT design.

2.1.2. BDM experiment Participants

Recruitment of the BDM experiment participants occurred in August 2018. The BDM experiment was performed after the first stage of the RCT. We recruited 181 women who participated in the RCT or were from nearby locations. Among them, 47 were those who participated in and finished the RCT (hereafter referred to as, the complete RCT sample), 39 were those who had dropped off during the intervention (hereafter referred to as, the not complete RCT sample), and 95 were from the neighboring village who did not attend the RCT (hereafter referred to as, the non RCT sample).

2.2. Experimental setting and design

2.2.1. RCT design

Randomization

This RCT was a randomized, single-blind, placebo-controlled, folate-fortified maize intervention. Women of childbearing age were randomly assigned to either the FFM group (treatment group) or the ordinary maize group (control group). Randomization was performed using sealed opaque envelopes [26].

Description of the Intervention

When eligibility was confirmed after the baseline survey, the participants were enrolled in the intervention. At the start of the intervention (1 week after baseline survey), the participants were randomized to consume either the FFM or the ordinary maize for 2 months. Maize was developed and provided by the Biotechnology Research Institute of the Chinese Academy of Agricultural Sciences (CAAS). The cultivar of FFM was Jingkenuo 928; the average weight of one stalk was 115 g, and its average folate content was 96.9 ug per stalk. The cultivar of ordinary maize was Jing 2000; the average weight of one stalk was also 115 g, but the average folate content was 35.6 ug per stalk. Both types of maize were packaged in labeled identical packets identified (for blinding) by the CAAS before sent to the study site (village clinic). Sufficient maize was provided to the participants for each stage of the survey. The participants had to eat 115 g (one stalk) of maize daily. Maize was distributed to the participants 1 week after the baseline survey. The participants were provided seven maize stalks once a week at the same location and time, which lasted for 2 months. The three-stage RCT was conducted from August 13, 2018, to October 19, 2018.

The baseline survey was conducted on August 13, 2018, including screening questionnaires, dietary intake surveys, basic information questionnaires, physical measurements, and fasting venous blood tests. We began the intervention 1 week after the baseline survey, that is, on August 20, 2018. We distributed seven maize stalks per person at the same location and time each week, according to their treatment assignment. Subsequently, we re-examined their serum folate content after 1 month (on September 19, 2018) and 2 months (on October 19, 2018) as the mid stage and final stage results. A similar dietary intake survey, physical measurement, and fasting venous blood tests were also performed in the mid and final stages.

Data Collection

Data were collected during a personal interview at the baseline survey, mid stage survey, and final stage survey. The following information was collected by a researchers through face-to-face interviews with the participants at the baseline survey. The participants completed a sociodemographic and screening questionnaire, including age, residence, education, marital status, number of children, health status, maize preference, height, and weight. The purpose of the screening questionnaire was to select the participants.

Dietary intake was assessed using a past-month food frequency questionnaire (FFQ) [27]. Briefly, the participants were asked to report their consumption of 142 items grouped into 11 categories, including cereals and grain products, beans, vegetables, edible fungi and algae, fruits, dairy products, meat, aquatic products, snacks, beverages, and "other foods". Using the FFQ, we calculated the participants' folate content in the diet during the experimental period. The specific method was to query the folate content of each food item per 100 g through the "China Food Composition" [28], and then combine it with the consumption amount and consumption frequency of each food item. The dietary folate intake of each food item were calculated, and all food items and dietary folate intake were added together to get the total dietary folate intake.

Weight and height were measured using an electronic scale, with participants wearing light indoor clothes and no shoes. The weight was measured to the nearest 0.1 kg; the height was measured to the nearest millimeter.

Fasting venous blood was used to test the folate content in the red blood cells and serum. The serum folate level was considered an indicator of recent folate intake, while red blood cell folate concentrations are useful for indicating long-term folate status. Red blood cell folate concentrations respond slowly to changes in folate intake, since the erythrocytes only accumulate folate during erythropoiesis in its 120-day lifespan. Thus, we used them as the screening criteria; participants were excluded from the study if their red blood cell folate content exceeded 906 nmol/L. Serum folate content was used as an indicator to evaluate the health effects of FFM. Folate content was detected using an improved microbiological assay method [29–30].

Ethical Considerations

This study was approved by the Ethics Committee of the Chinese Center for Disease Control and Prevention (NINH 2018-015). All participants provided written informed consent prior to the study. The reporting of this study adheres to the Consolidated Standards of Reporting Trials (CONSORT) guidelines [31](Schulz et al., 2010).

2.2.2. BDM experiment design

We conducted a basic information survey for all participants in BDM. The subjects were interviewed face-to-face and one-on-one by trained staff following the BDM experiment procedure, which was less prone to group effects [32]. Initially, the trained staff introduced an auction product (namely, one stalk of the FFM), funding (namely, 10 CNY), and the standard BDM experiment procedure. Each trained staff member had a paper bag with quotation notes; the quotation range was 1–10 yuan, with 0.1 yuan as the interval of 100 pieces of paper. First, the participants made bids by writing a random price on a blank paper according to the description of FFM. Then, the trained staff randomly extracted a quote from the folder. If the bid was higher than the quote, participants could buy the FFM at the bid; otherwise, they had no opportunity to buy it.

Moreover, we performed the same bidding procedure for three rounds, and the first two were to familiarize them with the experimental procedures. We also filtered those who could not understand the game by the end of the experiment. Finally, we obtained the actual WTP, which was equal to the bid in the third round of the BDM experiment.

In our BDM experiment, eliciting the WTP for FFM was the final objective. Participants were asked to give the maximum price they would agree to buy for the FFM they had just evaluated since it was in their best interest. If they underestimated it, they might lose an opportunity to buy at a price they would have been pleased to pay. If they overestimated it, they just took the risk to pay more than they would have liked to [33].

After the BDM experiment, the participants completed a questionnaire containing basic information, including age, location, education, job, household size, income, marital status, number of children, maize preference, and the cognition of folate and FFM. The questionnaire can directly reflect the participants' preferences and demands for FFM, which were essential for the follow-up analysis of WTP.

2.3. Statistical analysis

Statistical analyses were performed using SPSS 24.0. Statistics are presented as the mean $\pm$ standard deviation. In the RCT, a t-test was used to test for differences in dietary folate intake and individual characteristics, including age, residence, education, marital status, number of children, maize preference, height, and weight. Group differences in serum folate content were examined using an ANOVA approach. In the BDM experiment, t-test and Probit regression were used. First, a t-test was used to test for differences in the WTP and individual characteristics, including age, education, income, household size, number of children, maize preference, knowledge of FFM, and knowledge of folate among the complete RCT, not-complete RCT, and non-RCT samples. Second, a bivariate Probit model was used to explore the factors affecting the WTP for FFM. The dependent variable was defined as whether the subjects' WTP was higher than the average price of all participants. The factors were sociodemographic characteristics, folate and FFM knowledge, and RCT participation collected from the questionnaire. *P* values < 0.05 were considered significant.

3. Results

3.1. Participant characteristics

Table 1 shows the summary statistics of the sample that completed the three-stage RCT experiment. The average age of the participants was 40; they were in good health status. Their average height and weight were approximately 160 cm and 60 kg, respectively. There were no statistical differences between the treatment and the control groups in physical conditions, including age, height, weight, and health status, thereby ensuring the validity of the RCT. Nevertheless, demographic characteristics varied between the groups. The treatment group resided more in rural areas, were less educated, had more children, and had lower maize preferences.

Table 1
Summary statistics of variables in the RCT and comparison between treatment and control group.

Variable	Description	Treatment group	Control group	Difference (1)-(2) ^a
		(1)	(2)	(3)
Age	Age of the participants (years)	40.280 (5.311)	39.400 (6.196)	0.880 (0.578)
Residence	1=rural; 0=city	0.960 (0.200)	0.070 (0.254)	0.890** (0.001)
Education	1=below elementary; 2=elementary; 3=9-year circle; 4=high school; 5=college; 6= undergraduate; 7=postgraduate	2.680 (0.900)	5.340 (0.814)	-2.660** (0.001)
Marital status	1= married 0=unmarried	0.920 (0.277)	0.970 (0.183)	-0.050 (0.457)
Number of children	Number of children in a household	2.290 (0.690)	1.410 (0.568)	0.880*** (0.001)
Health status ^[1]	1=good 0=other	1.000 (0.000)	0.97 (0.183)	-0.030 (0.366)
Maize preference	1= extremely like; 2=like; 3= neither like nor dislike; 4=dislike	1.920 (0.702)	2.430 (0.774)	-2.660** (0.001)
Height	Height of participants (cm)	160.058 (5.884)	159.333 (5.965)	0.725 (0.702)
Weight	Weight of participants (kg)	59.335 (8.073)	62.142 (12.043)	-2.807 (0.409)
Number of observations	-	25	30	

Note: a) A difference represents the mean value difference between the treatment and control groups. b) Mean values are reported in the table with standard deviations in parentheses. c) *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$. d) P -values were calculated using the t-test.

[1] The health status was measured by a self-evaluation question “How do you evaluate your health status”. The summary statistics of the variables used in the BDM experiment are presented in Table 2. The ages of the connected BDM participants were identical, while the other demographic information varied between the three sample groups. Of the participants, the average education level was 9 years, and those who completed the RCT had significantly higher levels of education than the other two groups. The average BDM participant had an average annual household income of 32,633 CNY, with five family members, including three children. Regarding income, the

subjects who did not finish the RCT ranked the lowest, while those who completed the RCT ranked the highest. Their preference for maize is all above average-favored, especially the non-RCT sample, providing the grounds that the program's implementation could be possible once proven effective and feasible. All of the sample subjects knew little about FFM and folate, but the complete RCT sample had higher knowledge than the other two sample groups.

Table 2
Willingness-to-pay and sociodemographic variables across sample groups in the BDM experiment.

Variable	Description	Total sample	Complete RCT sample	Not complete RCT sample	Non RCT sample	Diff 1 ^a	Diff 2 ^b	Diff 3 ^c
		Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)			
WTP	Willingness-to-pay for FFM	2.817 (1.761)	3.028 (2.096)	2.251 (0.958)	2.945 (1.801)	0.776* (0.378)	0.082 (0.311)	-0.694* (0.332)
Age	Age of the participants (years)	42.807 (8.856)	41.234 (5.325)	43.641 (7.569)	43.342 (10.556)	-2.407 (1.918)	-2.008 (1.579)	0.399 (1.684)
Education	1 = below elementary; 2 = elementary; 3 = 9-year circle; 4 = high school; 5 = college	2.930 (1.123)	3.790 (1.250)	2.460 (0.822)	2.710 (0.933)	1.326*** (0.217)	1.082*** (0.179)	-0.244 (0.191)
Income	Total household income (1000 CNY)	32.633 (33.384)	54.128 (45.895)	18.205 (14.544)	27.921 (26.039)	35.923*** (6.668)	26.207*** (5.490)	-9.176 (5.854)
Household size	Total household members	4.720 (1.453)	4.320 (1.461)	4.670 (1.364)	4.950 (1.454)	-0.348 (0.311)	-0.628* (0.256)	-0.281 (0.273)
Children	Number of children in a household	2.900 (0.883)	2.660 (0.915)	3.100 (0.718)	2.940 (0.909)	-0.443* (0.189)	-0.277 (0.156)	0.166 (0.166)
Preference	1 = dislike extremely; 2 = dislike; 3 = neither like nor dislike; 4 = like; 5 = like extremely	4.220 (0.852)	4.040 (0.977)	4.130 (0.801)	4.340 (0.794)	-0.086 (1.183)	-0.294 (0.151)	-0.209 (0.161)
Knowledge of FFM	1 = none; 2 = low; 3 = common; 4 = sufficient; 5 = good	2.910 (1.048)	3.460 (0.877)	3.130 (1.060)	2.630 (1.025)	0.328 (0.381)	0.830* (0.323)	0.502 (0.307)

Note: a) The t-test results on the difference in the mean between the complete RCT sample and the not complete RCT sample. b) The former test results between the complete RCT sample and non-RCT samples. c) The former test results between the not complete RCT sample and non-RCT samples. d) Mean values are reported in the table with standard deviations in parentheses. e) *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$. f) P -values were calculated using the t-test.

Variable	Description	Total sample	Complete RCT sample	Not complete RCT sample	Non RCT sample	Diff 1 ^a	Diff 2 ^b	Diff 3 ^c
		Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)			
Knowledge of folate	1 = none; 2 = low; 3 = common; 4 = sufficient; 5 = good	2.820 (1.323)	3.300 (1.214)	2.180 (1.254)	2.840 (1.307)	1.118*** (0.276)	0.456* (0.227)	-0.663*** (0.242)
RCT	1 if participants complete RCT, 0 otherwise	0.260 (0.438)	1 (0)	0 (0)	0 (0)	-	-	-
Observations	-	181	47	39	95	-	-	-
Note: a) The t-test results on the difference in the mean between the complete RCT sample and the not complete RCT sample. b) The former test results between the complete RCT sample and non-RCT samples. c) The former test results between the not complete RCT sample and non-RCT samples. d) Mean values are reported in the table with standard deviations in parentheses. e) *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$. f) P -values were calculated using the t-test.								

3.2. Health improvement effects of FFM

3.2.1. Dietary folate intake

We applied ANOVA analysis on dietary folate intake to analyze the statistical differences. As presented in Table 3, in the baseline period, the difference in the dietary folate intake between the treatment group (207.04 μg) and the control group (278.15 μg) was statistically insignificant ($P > 0.05$). In the mid-stage survey, women in the treatment group (122.02 μg) took significantly ($P < 0.05$) less food-sourced folate than the control group (200.67 μg). In the final stage, the dietary folate intake difference between the treatment group (159.66 μg) and the control group (169.29 μg) was statistically insignificant ($P > 0.05$). Dietary folate intake in both the treatment and control groups decreased. The food folate intake of the treatment group was never significantly higher than that of the control group.

Table 3
Changes of dietary folate intake and serum folate content in three stages.

Variable	Timeline	Treatment group	Control group	Difference
Serum folate content (ng/mL)	Baseline	11.042	12.305	-1.263
		(4.077)	(6.365)	(0.396)
	Mid stage	12.720	12.124	0.596
		(4.486)	(5.385)	(0.662)
	Final stage	13.306	9.908	3.398*
		(8.297)	(3.423)	(0.046)
Dietary folate intake (ug)	Baseline	207.001	278.146	-71.145
		(192.089)	(249.094)	(0.258)
	Mid stage	121.980	200.667	-78.687*
		(78.331)	(164.100)	(0.034)
	Final stage	159.656	169.286	-9.630
		(96.939)	(98.900)	(0.720)
Note: a) Mean values are reported in the table with standard deviations in parentheses. b) *** p < 0.001, ** p < 0.01, * p < 0.05. c) P-values were calculated using the t-test. d) P-values were calculated using analysis of variance.				

3.2.2. Average effects on women health

The results of the repeated-measures ANOVA shows that the main effect of time was not significant ($F = 0.062$, $P > 0.05$), but the effect of treatment $\times$ time interaction was significant ($F = 5.391$, $P = 0.024 < 0.05$), which indicated that the serum folate content of the participants in the treatment and control groups was significantly different after eating FFM.

Post hoc comparisons were used to further explain the intervention effect of FFM. The results showed that in the baseline survey, the treatment group of women had an average serum folate level of 11.04 ng/mL (see Table 3), while that of the control group was 12.31 ng/mL. The two groups of folate content at baseline showed no statistically significant differences ($P > 0.05$). In the mid-stage survey, the women's average serum folate content in the treatment and control groups was 12.72 ng/mL and 12.12 ng/mL, respectively. Their difference remained statistically insignificant ($P > 0.05$). The treatment group's serum folate content increased to 13.31 ng/mL by the final-stage survey, which was significantly higher than that in the control group (9.91 ng/mL) at the 5 percent significance level ($P < 0.05$).

Based on the above analysis, we found that the treatment group's serum folate content in the final-stage was significantly higher than that in the control group ($P < 0.05$), provided the treatment and control groups' serum folate levels did not differ significantly ($P > 0.05$) in the baseline survey. This provides strong evidence that eating one stalk FFM per day can increase serum folate content in the treatment group by the end of the two-month experiment, suggesting that FFM had a significant effect on improving serum folate content.

Previous studies have shown that, due to dietary and other reasons, there were significant seasonal differences in serum folate levels among Chinese women in different seasons [34]. Serum folate levels were higher in summer than in autumn. In particular, the levels of serum folate in August and September were higher than those in October [34–35];

the analysis of dietary folate intake also confirmed this finding. The dietary folate intake in both the treatment and control groups decreased. Therefore, under normal circumstances, in the final stage of the RCT, the serum folate levels of the treatment and control groups should both decrease. However, the results of serum folate analysis showed that the serum folate level of the treatment group increased, which was due to the intervention of FFM. The serum folate level of the control group decreased due to the absence of FFM intervention. Therefore, our experimental results showed that FFM could significantly increase the treatment group's serum folate content in women of childbearing age, even when the dietary intake decreases. The findings provided micro-level evidence that FFM could improve women's health status and provide a practical basis for introducing FFM supplementation programs in rural areas in China.

3.3. Consumer valuation of FFM

3.3.1. WTP measurement results and heterogeneity

We recruited 181 participants in nearby villages where the RCT was implemented and assessed their valuation of the FFM. Based on the BDM mechanism, we further elicited the WTP of 181 local rural women of similar characteristics to be 2.82 CNY per maize stalk, with a standard deviation of 1.76 and a premium of approximately 1.21 CNY per stalk over ordinary maize (mean = 1.61). The experiment results indicate that rural women have a higher evaluation of FFM and have up to a 43% premium of the price on the folate attribute. The existence of a price premium indicates market opportunities and potential profits, which are likely to be shared with market participants along the supply chain.

Table 2 reports the WTP measurement results across the sample groups in the BDM experiment in detail. In the BDM experiment, there were significant differences in WTP between those who completed RCT and those who did not. The WTP for those who completed RCT was 3.03 CNY, while that for the RCT's non-completed participants was 2.25. We carried out the difference t-test for the experimental results between these two groups; the difference was significant at the 5% level (see Fig. 2). Women who completed the RCT also had a more extensive range and variation in FFM evaluation. There was no significant difference in the average WTP between subjects who completed the RCT and those who did not participate. Approximately 40.9% of the total sample would bid above or equal to the average.

In these groups, we further analyzed the differences in their knowledge of the folate and FFM of these groups and found significant differences between groups. Specifically, the non-RCT sample presented the highest knowledge of FFM, while the complete RCT sample ranked the lowest. The subjects who did not finish the RCT ranked the lowest in folate knowledge, while those who completed the RCT ranked the highest. Overall, all the sample subjects knew little about FFM and folate, but the complete RCT sample had higher knowledge than the other two sample groups.

3.3.2. Predictors of consumer's WTP

We continued to explore whether the consumer valuation is related to sociodemographic characteristics, folate and FFM knowledge, and RCT participation. We applied a Probit regression using whether subjects' WTP was higher than the average price as the dependent variable on the BDM auction participants.

Table 4 shows the Probit regression results for the BDM auction participants. First, regarding the influence of sociodemographic characteristics, we found that an increase in age and a decrease in income would significantly reduce FFM valuation. As they got older, the possibility of childbearing activity declined. People with higher incomes might care more about their health status and have a higher purchasing power, so they are also willing to pay higher FFM prices. However, without the market introduction of such an FFM, the income effect is minor in the experimental group. With an increase of 1000 CNY, the auction participants are 3% more likely to purchase with a higher price than average.

Table 4
Predictors of the willingness-to-pay of folate fortified maize.

Variables	Coefficients		Marginal effects	
Age	-0.036 ^{***}	(0.012)	-0.012	(0.004) ^{***}
Education	-0.017	(0.125)	-0.006	(0.041)
Income	0.008 ^{**}	(0.004)	0.003	(0.001) [*]
Household size	-0.141	(0.088)	-0.046	(0.028)
Children	-0.009	(0.130)	-0.003	(0.043)
Preference	0.111	(0.133)	0.036	(0.043)
Knowledge of FFM	-0.234 ^{**}	(0.096)	-0.077	(0.031) [*]
Knowledge of folate	-0.072	(0.268)	-0.024	(0.088)
RCT	-0.596 ^{***}	(0.216)	-0.196	(0.067) ^{***}
Constant	2.004 ^{**}	(0.956)		
Chi ²	33.89			
Prob > Chi ²	0.001			
Pseudo R2	0.142			
Observations	181			
Note: a) Robust standard errors are in parentheses. b) ^{***} p < 0.001, ^{**} p < 0.01, [*] p < 0.05.				

Second, the effect of FFM knowledge was evaluated. The knowledge of female subjects on folate and FFM was limited. To some extent, understanding FFM would enable people to remove their overestimation of FFM functions. Additionally, they might also have a lower valuation of the new technology being used in the staple crops, thus being 7.7% less likely to bid a price higher than average. Finally, we examined the influence of participation in RCTs. Among all the factors, participation in the RCT was the most influential factor in our estimation specification, as the participants were 19.6% less likely to have a higher than average WTP bid. It is possible that their anticipation of receiving the product reduced their psychological expectations of FFM.

4. Discussion

This randomized, single-blind, controlled trial investigated the health effects of a two-month FFM intervention. Compared to ordinary maize, FFM could significantly increase the serum folate content and thus improve the situation of folate deficiency in rural women of childbearing age. The study demonstrates that FFM may have potential health-related effects. To our knowledge, this is the first study to assess changes in serum folate content resulting from FFM supplementation. Other investigators found similar results using iron-biofortified rice, pearl, or bean [36–38]. Haas et al.'s study showed a 17% difference in the total iron consumed in the iron-biofortified rice group compared with the control group throughout the 9-month intervention period. Additionally, Finkelstein et al. also showed significant health improvements after 4 months of an iron-biofortified pearl millet intervention.

However, it should be noted that serum folate content in the control group showed a downward change; dietary folate intake in both groups showed downward changes. This may be due to the influence of seasonal diet, which indicated that season and diet had a certain impact on the changes in serum and dietary folate content. Similar results were observed in previous studies [34–35]. A study by Hao et al. found significant seasonal differences in serum folate levels. Additionally, the decline in dietary intake may be because the baseline survey was conducted during summer. Seasonal vegetables in summer, such as spinach, lentils, and tomatoes, contain high folate content [39]. On the contrary, the mid and final stages were conducted in autumn, when dietary folate intake declined. Our experimental results showed that FFM could significantly increase the treatment group's serum folate content in women of childbearing age, even when the dietary intake decreased.

Based on the BDM auction experiment and Probit model, we analyzed WTP for FFM and its influencing factors. The results showed that WTP for FFM was significantly higher than that for ordinary maize. Women of childbearing age were willing to pay a premium for FFM. This is consistent with previous research results, that is, nutrition information can enhance consumers' WTP [40]. The higher WTP for FFM can reflect the greater economic benefits of FFM; the greater economic benefits can further increase the income of the main body in the industrial chain, thus promoting the development of the biofortification industry. The results also showed that the individual characteristics of women of childbearing age had a significant impact on WTP for FFM. Similar results were reported by other investigators using biofortified yellow cassava [41]. Younger women are more likely to pay higher than the average price for FFM; their premium is also greater, that is, they are willing to pay more for FFM. Women with a larger family size are not willing to pay a higher price for FFM; their WTP is lower than the average price. Lastly, women with higher annual income were willing to pay a higher price for FFM; Additionally, their understanding of FFM also significantly and negatively affected their WTP.

Limitations

The present RCT-BDM study has several limitations. Despite randomization, due to the need for three blood tests and other reasons (for example, busy farming or out as a migrant worker), some participants did not complete the RCT experiment, resulting in a high dropout rate. Therefore, the two groups were not ideally balanced concerning the demographic variables. The treatment group resided more in rural areas, were less educated, had more children, and had lower maize preferences than the control group. We cannot exclude entirely the possibility that this might have accentuated the differences between the groups during treatment. However, we mainly focused on the health effects of FFM on serum folate content. At baseline, there was no significant difference in serum folate levels between the two groups. There was a significant difference in serum folate levels between the two groups in the final stage of the experiment. In addition, residence, education, number of children, and maize preference did not affect the serum folate level in a short period. The results could still explain the intervention effect of FFM.

Furthermore, due to the influence of season and diet, there were seasonal differences in serum folate levels, which led to a decrease in serum folate levels in the control group during the final stage of the experiment. The serum folate content of the treatment group should also decrease. Still, due to the intervention of FFM, the serum folate level increased, which could explain the effect of the intervention. However, we did not control the serum folate level in the control group, which may have reduced the effect of FFM intervention. Therefore, we could choose the appropriate time (the season with stable dietary folate intake) to carry out future experiments to ensure that serum folate levels don't change significantly during the experimental period.

Additionally, because of the limitations of objective conditions, funds, and time, this trial only lasted for 2 months, with a relatively short intervention time. However, ensuring the effectiveness of the experiment was made to be attained. In the future, the intervention time could be appropriately extended to explore the positive changes in serum and red

blood cell folate content, which could further improve the population's nutritional health. Finally, in the BDM experiment, we only explored the influence of demographic variables, subjective nutrition knowledge, and folate information on consumers' WTP. We can explore the influence of more factors, such as the different types of information on consumers' WTP in the future.

5. Conclusions

We conducted a connected RCT-BDM experiment to explore the effects of FFM on the population's nutritional health and consumer valuation. First, for the health effects, the two-month FFM nutrition intervention experiment found that the treatment group's serum folate levels were significantly higher than those in the control group, suggesting that FFM significantly increased folate levels in the blood, thereby showing a positive effect of improving folate deficiency in women of childbearing age. This result still holds even considering the impact of seasonal diet intake of folate.

Second, for consumer valuation, the BDM experiment based on 181 women of childbearing age shows that the average consumer WTP for FFM was 2.82 CNY, with a standard deviation of 1.76. Furthermore, a price premium of 1.21 was observed between the FFM and ordinary maize, which suggests a premium of up to 43% by the folate attribute. Therefore, consumer valuation is related to the participation of the intervention program, indicating the economic value of information on the acceptance of new food products. Regression analysis further showed that RCT participation, product and nutrition knowledge, and demographic factors (i.e., age and income) tend to play a role in the formation of consumer valuation. Our conjoint experiment provided useful information on the future commercialization of this product from the perspectives of micro efficacy and consumer pricing.

Declarations

Ethics approval and consent to participate: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Chinese Center for Disease Control and Prevention, and the ethical review number is NINH 2018-015. Informed consent was obtained from all participants.

Consent for publication: Not applicable.

Availability of data and materials: Data described in the manuscript will be made available by the corresponding author upon request pending application and approval.

Competing interests: There are no conflicts to declare. The funder was not involved in study design, collection, analysis or interpretation of data, or in preparation of the manuscript.

Funding: This research was funded by the National Natural Science Foundation of China, grant number 71561147001 and 71803058.

Author Contributions: Authors contributed the following: Conceptualization, P. Q. and Y. L.; methodology, P. Q., Y. L., J. H., A. W., J. S. and H. M.; formal analysis, P.Q., Y. L., F.L., J. H. and L. W.; writing—original draft preparation, P.Q., F. L., J. F., J. L., and J. H.; writing—review and editing, P.Q., J. L., T. C. and J. H. All authors have read and agreed to the published version of the manuscript.

Acknowledgments: The authors would like to acknowledge all the participants in the RCT and BDM experiments who made this study possible.

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Figures

Figure 1

CONSORT diagram describing study design and flow of participants.

Figure 2

Average WTP differences between target groups.