Effect of In-home Fortification of Complementary Feeding on Intellectual Development of Chinese Children[1]

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Objective To explore the effect of in-home fortification of complementary feeding on intellectual development of Chinese children aged below 24 months. **Methods** One thousand and four hundred seventy eight children aged 4-12 months were recruited and divided into study groups (formula 1 group and formula 2 group) and control group. In two study groups, in addition to the usual complementary food, children were fed with a sachet of fortified food supplement each day. Protein and micronutrients were provided in formula 1 group. Formula 2 group had the same energy intake as the formula 1 group . In addition to measurement of physical growth and detection of hemoglobin level, Development Quotient (DQ) or Intelligence Quotient (IQ) was assessed. **Results** The DQ of children aged below 24 months was 97.2, 95.5, and 93.8 in formula 1 group, formula 2 group and control group, respectively, and the differences were statistically significant (P<0.05). The DQ of children in formula 1 group, formula 2 group, and control group was 92.7, 90.4, and 88.3 respectively in the first follow up showing statistically significant differences (P<0.05). And, DQ of children in formula 1 group, formula 2 group and control group were 96.7, 94.5, and 93.7 respectively in the second follow up, showing statistically significant differences (P<0.05). Full-IQ of children in the formula 1 group was 3.1 and 4.5 points higher than that in formula 2 group and in control group respectively. Verbal IQ of children in the formula 1 group was 2.1 and 5 points higher than that in formula 2 group and control group respectively. Performance IQ was 2.5 and 3.1 points higher than that in formula 2 group and control group respectively. All above mentioned comparisons were statistically significant. **Conclusion** Fortification of complementary feeding showed persistent effect on intelligence development of young children which could persist to 6 years of age. The critical time for correction of anemia could be under 18 months.

Key words: Complementary feeding; Supplement; Development; Anemia; Infant

INTRODUCTION

Nutritional status in children aged under 24 months is extremely important because it is critical to physical growth with high velocity and the development of cognitive ability, movement and linguistic competence. Due to the long-term effect of malnutrition at this stage on intellectual development in later childhood and on productivity and disease risk in adulthood, it is urgently needed to explore effective measures to reduce malnutrition of children in this age group.

In rural China, the prevalence of underweight in children under 5 years was 13.8%, and the prevalence of stunting was 20.3 % in 2000[1]. The figures were even higher in poor rural areas: 21.0% of children under 5 years were underweight and 30.7% were stunted. Moreover, the prevalence of underweight and stunting in Western China were doubled in comparison with that in Eastern China[2]. According to the data from the Food and Nutrition Surveillance in China in 1998 and in 2000, the peak age for undernutrition among children under 5 years was 6-24 months. Failure to timely complementary feeding and inadequate complementary food were the major contributing factors to undernutrition in this age group[3]. Therefore, exploration of effective and affordable approaches to the solution of undernutrition problem among children in China's poor rural areas is imperative.

The authors carried out a study between 2001 and 2003. This study was to test effectiveness of in-home fortification using a nutrient-dense food supplement for complementary feeding to reduce undernutrition in poor rural areas in Gansu Province of China. In-home fortification to children in the first two years of their life was found to have improved growth and iron status and have reduced the

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incidence of diarrhea and respiratory infection[4-5]. Between 2004 and 2007, a follow-up study was conducted to assess the long-term effect of the above mentioned in-home fortification. This paper reports the results of the follow up study in terms of the effect of early complementary feeding supplements on intellectual development .

METHODS

Intervention Trial and Follow-up Study

In 2001, 1 478 children aged between 4 and 12 months were selected in five poor counties (Dingxi, Qingshui, Jingtai, Tianzhu, and Jingning) in Gansu province in Northwestern China. All selected children received breast feeding (In 2001, promotion of exclusive breastfeeding before 6 months of age was not yet formally implemented in China, thus children aged 4-5 months who were receiving complementary feeding were included in this study). In each county, two or three townships were selected based on birth rate, and then villages were randomly sampled within selected townships. In each selected village, children aged between 4 and 12 months were recruited into the formula 1 intervention group until 200 children had been enrolled in the county. Additional 100 children in the same age group were recruited into the formula 2 group from a nearby township with similar socioeconomic status. The overall situation in the counties selected for the study was similar to that of other poor rural counties in Gansu province with an annual per capita income lower than 1 500 Yuan (about $180 in 2001).

All the enrolled 1 478 children received sachets of an in-home fortification to be added daily to their normal complementary food. Caregivers were instructed to give complementary foods as usual but to add the supplement to these foods once a day. The intervention continued from the every day of the enrollment until the children reached 24 months of age.

The food supplement given to children in the formula 1 group included whole fat soybean flour fortified with five micronutrients. The food supplement given to children in the formula 2 group contained 10 g of rice flour with added vegetable oil to match the total energy contained in formula 1. Formula 2 was not fortified with micronutrients and contained only 0.7 g of protein (Table 1). In addition, during the intervention period, children in both groups were given age-appropriate doses of vitamin A every 6 months (100 000 IU for children 6-12 months of age and 200 000 IU for children older than 12 months of age, as per international recommendations).

TABLE1

The Composition of Formula 1 and Formula 2 in the Intervention Trial

	Formula 1	Formula 2
Total Weight (g)	10	10
Iron (NaFeEDTA) (mg)	6.0	-
Zinc ($ZnSO_4$) (mg)	4.1	-
Calcium ($CaCO_3$) (mg)	385	-
Vitamin B_2 (mg)	0. 2	-
Vitamin D(μg)	7.0	-
Protein (g)	3.8	0.7
Energy (kj)	167	167

Measurement of outcomes during the intervention trial lasted from enrollment until the children reached 24 months of age. Weight and height measurements were taken every 3 months and hemoglobin level was determined on finger blood specimens using the cyanmethemoglobin method with model 721 spectrophotometer every 6 months. According to the altitude of the study area (1 800 meters above the sea level), the cutoff point of anemia for the children was adjusted to 115 g/L[6]. Weight-for-age and height-for-age z-scores were calculated using the NCHS/WHO reference population. At age of 24 months, about 30% of the children from each group were randomly selected for developmental testing.

In addition to the formula 1 and formula 2 groups, 127 children aged 23.0-24.9 months were recruited from households of similar socioeconomic status in Dingxi County to serve as a community control group in April 2004. These children had not received either formula 1 or formula 2 or vitamin A supplementation. Identical anthropometric measurements and development tests were carried out for comparison with the formula 1 and formula 2 groups.

Between year 2004 and 2006, children from the formula 1 group and the formula 2 group were followed up with annual weight and height measurement, hemoglobin measurement and developmental testing. In September 2004, about 40 children in the same age from nearby villages with similar socioeconomic status in each county were recruited as new community controls. These children did not receive either formula 1 or formula 2 or vitamin A supplementation and were followed up in the subsequent periods (age 4-6 y), and identical development tests were carried out for comparison with the formula 1 and formula 2 groups.

Development Testing

A development diagnostic scale was used to assess children at 2, 3.5 to 4, and 4.5 to 5 years of age during the follow-up study with higher level of reliability and validity. The correlation coefficient with Gesell Development Scale was 0.9537[7-8]. This scale was meant for assessment of children aged 0-6 years. The development quotient (DQ), including indicators of gross and fine motor skills, adaptation, language skills, and social behavior, was also assessed. At the end of the follow-up study, the children aged 5.5 to 6 years were tested with the revised Wechsler Preschool and Primary Scale of Intelligence (WPPSI) and, full-scale intelligence quotient (FIQ), verbal IQ, and performance IQ were calculated[9].

Data Analysis

Statistical analyses were carried out using SAS statistical software package version 9.13 (SAS Institute Inc., Cary NC, USA). Baseline characteristics in the formula 1 and formula 2 groups were compared using the *t* test for continuous variables and the Chi square test for categorical variables. In comparing the formula 1 and, formula 2 groups with the community control groups, the statistical significance of differences was measured using a General Linear Model for analysis of variance. *P* value, 0.05 was considered statistically significant.

Quality Control

Interviewers were trained by experts from the national research team, and the same instruments for weight and height measurement were provided. Personnel who carried out the assessment of development were trained by the experts from the Capital Institute of Pediatrics and Beijing Normal University, and measurements were carried out by this authorized team in a quiet environment. They were blinded about the difference between formula 1 and formula 2. DQ and IQ were calculated by an independent group at the Department of Psychology of Beijing Normal University, and no information about the differences between formula 1 and 2 was provided.

Interviews and anthropometric measurement were carried out in village health stations or township health centers Data collected were checked by field supervisors. Data were input into EPIDATA 3.02 with logistic check, and converted to SAS datasets for cleaning.

The study was approved by the Ethics Review Committee of the Chinese Academy of Preventive Medicine (Now the Chinese Center for Disease Control and Prevention), and written consent forms were obtained from parents of children recruited for the study.

RESULTS

Characteristics of Study Participants

Table 2 shows the number of participants at age of 24 months and the results of DQ or IQ measurement in each group of the follow-up study. The first DQ and IQ testing showed that there was no statistically significant differences in male/female ratio, age, mother's educational level, the use of a safe source of household drinking water, the rate of exclusive breastfeeding , the prevalence of anemia, and the mean height-for-age and weight-for-age z-scores (Table 3). In addition, there was no statistically significant difference between the formula 1 and formula 2 groups in the duration of participation in the intervention trial before enrollment in the follow-up study. At the time of subsequent rounds of data collection and in the three groups, no statistically significant differences were shown in male/female ratio, mother’s educational level, or identity of the major caregiver. Moving out of the village and traveling were the major causes of loss to follow-up during the study. Those children showing no statistically significant differences from children whose data were successfully collected in male/female ratio, age, mother’s educational level, anemia prevalence, and mean height-for-age and weight-for-age z-scores at the time of enrollment.

TABLE 2

Number of Children in the Intervention Trial and Follow-up Study of Development and Intelligence Quotients at Various Points of Data Collection

	Formula 1 Group	Formula 2 Group	Community Control Group
Intervention Trial			
Baseline (2001)	978	500	None
DQ Assessment at 24 Months*	232	116	127
Follow-up Study			

(to be continued)

(continued)

	Formula 1 Group	Formula 2 Group	Community Control Group
Second Data Collection (2004)			
Sample Size	323	172	151
Average Age (in months)	47.1	46.9	46.0
Third Data Collection (2005)			
Sample Size	464	249	176
Average Age (in months)	57.4	56.9	57.5
Fourth Data Collection (2006)			
Sample Size	427	168	84
Average Age (in months)	70.1	70.0	69.2

Notes. At age of 24 months, about 30% of the children from each group were randomly selected for developmental testing. Between 2004 and 2006, the children from the formula 1 group and the formula 2 group who could be located were followed with developmental testing, so the sample size was different. *All children were aged 24 month (23.0-<25.0 months).

TABLE 3

Characteristics of Children Tested for Development and Intelligence Quotients at Age of 24 Months upon Enrollment in Follow-up Study, by Study Group

	Formula 1 Group N=232	Formula 2 Group N=116	Community Control Group N=127
Male/female Ratio*	56:44	53:47	58:42
Age in Months (Mean)	24.0	24.0	24.0
Education of Mother			
Below Middle-school (%)	44	45	35
Middle-school & above (%)*	56	55	65
Major Caregiver is Mother (%)*	64.6	68.3	65.5
Exclusive Breastfeeding in the First 4 Months (%)	61.3	61.7‡	N/A
Nutritional Status			
Anemia Prevalence (%)‡	5.6	11.2	N/A
Height-for-age Z-score (Mean)*	-1.01	-1.11	-0.95
Weight-for-age Z-score (Mean)*	-0.96	-0.90	-0.83
Duration of Participation in Intervention Trial (Month)‡	16.0	15.6	N/A

Note. *No significant difference between formula1, formula 2 and community control (P>0.05). ‡No significant difference between formula1 and formula 2 (P>0.05).

Developmental Testing at Age of 24 Months at the End of the Intervention Trial

In all the three groups, 475 children were tested for DQ at the first round of data collection during in the follow-up study when they were 24 months of age. At that time, the average DQ was 97.2, 95.5, and 93.8 in the formula 1, formula 2, and community control groups, respectively (Table 4). All paired differences were highly statistically significant (P<0.001). The individual components of the DQ showed mixed differences. The gross motor skills score of children in the formula 1 group was significantly higher than those in the formula 2 and community control groups, but the difference between the formula 2 group and the community control group was not statistically significant. The fine motor skills scores of children in the formula 1 and formula 2 groups were statistically significantly higher than the score for children in the community control group, but the difference between the formula 1 and formula 2 groups was not significant. Differences among the formula 1, formula 2, and community control groups in adaptation, language, and social behavior were minimal and not statistically significant.

TABLE 4

The Development Quotient and Component Scores for Children at 24 Months of Age (the First Round of Data Collection at the Beginning of the Follow-up Study), by Study Group

	Formula 1 Group (a)		Formula 2 Group (b)		Community Control Group (c)	
	Mean	*Sd*	Mean	*Sd*	Mean	*Sd*
Development Quotient	97.2[*ab,ac]	6.2	95.5[*bc]	6.3	93.8	6.1
Gross Motor	99.5[*ab,ac]	13.3	96.1	12.7	94.7	10.5
Fine Motor	103.3[*ac]	10.1	102.9[*bc]	12.2	96.1	11.2
Adaptation	95.8	10.2	93.6	10.5	94.0	9.3
Language	90.6	9.0	88.8	9.5	89.9	9.2
Social Behavior	96.9	10.2	96.2	11.1	94.1	9.0

Note. [*]Significant difference between mentioned groups, $P<0.05$.

Further study on children who were anemic at the baseline survey and were non-anemic at age of 24 months in formula 1 and 2 groups showed that the DQ of 68 children in formula 1 group was 97.1 which was significantly higher than DQ of 42 children in formula 2 group (97.1 *vs* 94.3, $P=0.034$). There was also a similar difference in gross motor score (101.4 *vs* 94.3, $P=0.007$).

Developmental Testing at Age of 3.5 to 4 Years (1.5 to 2 Years after the Completion of the Intervention Trial)

At the second round of data collection of the follow-up study, carried out 1.5 to 2 years after the enrollment, the average DQ in children in the formula 1, the formula 2, and the community control groups were 92.7, 90.4, and 88.3, respectively. (Table 5) As at the time of enrollment in the follow-up study, these average DQ scores were statistically significantly different from each other ($P<0.005$). On the other hand, the differences in gross and fine motor skills scores measured at the beginning of the follow-up study decreased and became statistically insignificant. Children in both formula 1 and formula 2 groups had statistically significantly higher average scores in adaptation and social behavior than children in the community control group. Moreover, children in the formula 1 group had a statistically significantly higher average score for adaptation than children in the formula 2 group ($P<0.005$).

TABLE 5

The Development Quotient and Component Scores for Children Aged 3.5 to 4 Years (the Second Round of Data Collection), by Study Group

	Formula 1 Group (a)		Formula 2 Group (b)		Community Control Group (c)	
	Mean	*Sd*	Mean	*Sd*	Mean	*Sd*
Development Quotient	92.7[*ab,ac]	8.5	90.4[*bc]	8.8	88.3	9.2
Gross Motor	98.8	11.4	97.8	11.9	98.0	12.8
Fine Motor	90.1	10.9	88.7	12.5	89.5	12.3
Adaptation	86.5[*ab,ac]	12.6	83.5[*bc]	10.8	79.1	9.9
Language	95.9	13.2	91.2	14.0	87.4	15.3
Social Behavior	92.0[*ac]	12.6	90.7[*bc]	13.4	87.4	14.1

Note. [*]Significant difference between mentioned groups, $P<0.05$.

Developmental Testing at Age of 4.5 to 5 Years (2.5-3 Years after the Completion of the Intervention Trial)

At the third round of data collection, carried out 2.5 to 3 years after the enrollment, the average DQ in children in the formula 1, formula 2, and the community control groups were 96.7, 94.5, and 93.7 respectively (Table 6) . In contrast to prior rounds of data collection, the difference between the average DQ score in the formula 2 group and the community control group was no longer statistically significant. For the average scores for fine motor skills and adaptation, the average score in the formula 1 group was significantly higher than the scores in both the formula 2 and the community control groups.

TABLE 6

The Development Quotient and Component Scores for Children Aged 4.5 to 5 Years (the Third Round of Data Collection), by Study Group

	Formula 1 Group (a)		Formula 2 Group (b)		Community Control Group (c)	
	Mean	*Sd*	Mean	*Sd*	Mean	*Sd*
Development Quotient	96.7[*ab,ac]	9.9	94.5	10.7	93.7	9.5
Gross Motor	100.8	9.0	99.7	10.7	99.1	10.5
Fine Motor	98.3[*ab,ac]	11.8	96.4	11.7	95.2	11.0
Adaptation	94.5[*ab,ac]	11.1	89.6	12.7	88.9	11.4
Language	96.2	14.5	95.6	14.3	93.7	13.3
Social Behavior	93.7[*ac]	11.6	91.1	13.8	91.3	12.1

Note. [*]Significant difference between mention groups, $P<0.05$.

Intelligence Testing at Age of 5.5 to 6 Years (3.5 to 4 Years after the Completion of the Intervention Trial)

The full intelligence quotient (FIQ) of children in the formula 1 group was shown 3.1 and 4.5 points higher than that in the formula 2 and community control groups respectively. The verbal IQ (VIQ) was 2.1 and 5 points higher than that in the formula 2 and community control groups, respectively. The performance IQ (PIQ) was 2.5 and 3.1 points higher than that in the formula 2 and community control groups, respectively (Table 7). All paired differences between the formula 1 group and the other two groups were statistically significant. In contrast, there were no statistically significant differences between the children in the formula 2 group and the community control group in the FIQ or any of its components. Adjustment of the analysis for gender, hemoglobin and mother's educational status did not substantially alter the results (103.2 *vs*. 101.0 *vs*. 99.1, $P<0.005$).

TABLE 7

The Intelligence Quotient and Component Scores for Children Aged 5.5 to 6 Years (the Fourth Round of Data Collection), by Study Group

	Formula 1 Group (a)		Formula 2 Group (b)		Community Control Group (c)	
	Mean	*Sd*	Mean	*Sd*	Mean	*Sd*
Full-IQ	101.1[*ab,ac]	11.0	98.0	11.5	96.6	13.4
Verbal IQ	98.3[*ab,ac]	11.4	95.2	11.6	93.3	14.2
Performance IQ	103.9[*ab,ac]	11.7	101.4	11.2	100.8	11.7

Note. [*]Significant difference between mention groups, $P<0.05$.

Further analyses of data from the formula 1 and formula 2 groups were carried out to explore the association between anemia and IQ. When children in these two groups were combined, the hemoglobin level at the age of 5.5 to 6 years was positively correlated with PIQ ($r=0.20$, $P<0.001$). In addition, an analysis was carried out for children who were enrolled in the intervention trial and were placed into the formula 1 group and who had anemia at that time. The average FIQ and PIQ in children whose anemia was corrected in 6 months of supplementation was statistically significantly higher than that in children whose anemia was only corrected after 6 to 12 months of supplementation (Table 8). Children whose

TABLE 8

Average IQ Levels for Children Aged 5.5 to 6 Years in the Formula 1 Group Who were Anemic at the Intervention Trial Enrollment Aged 4 to 12 Months, by the Time Required to Correct Anemia

	Anemia Corrected at 6 Month Visit (a)	Anemia Corrected within 6-12 Months (b)	Anemia not Corrected after 12 Months (c)
Number of Subjects	55	33	17
Full IQ	100.5[*ab,ac]	98.5	91.7
Verbal IQ	98.0	96.3	89.8
Performance IQ	103.1[*ab,ac]	99.6	95.2

Note. [*]Significant difference between mentioned groups, $P<0.05$.

anemia was not corrected after 12 months of supplementation had even lower average FIQ and PIQ than this group, albeit without statistical significanc. VIQ showed a similar association, but without statistical significance.

DISCUSSION

Studies on long-term effect of early childhood nutrition interventions are sparse but valuable. The most influential study carried out in Guatemala[10] provided evidence that early supplementary feeding had effects on intellectual performance much later in life. However, these studies, as well as other studies of the effect of food supplementation at an early age such as a study of children aged 6 to 20 months in Indonesia[11], were focused on the effect of energy and protein supplementation. In contrast, because iron deficiency anemia is such an important public health issue in China, long-term study of increasing iron consumption in early childhood is necessary. Such studies can not only demonstrate that iron fortification of complementary food prevents anemia, but also illustrate the consequences of iron deficiency on the subsequent development of young children. Retarded development of children is an important determinant of human capital growth and economic development of a nation.

This study aims at testing the effectiveness of a strategy for reducing micronutrient deficiency in a poor rural population. It is the first large-scale nutrition intervention using an in-home fortification to improve complementary feeding among children less than 2 years of age in rural China. Although intensive education on complementary feeding practice is currently taking place, it will take time to achieve substantial behavioral changes of mothers and will involve income problem. This study has tested an approach to prevent micronutrient deficiency, especially anemia, without requiring a change in the usual home-made complementary feeding so that the prevalence of micronutrient deficiency could be reduced as early as possible. To minimize the cost of the in-home fortification, only iron, zinc, calcium, vitamin D, and vitamin B_2 are added, which are the nutrients most commonly inadequate in the Chinese diet[12]. Zlotkin and his colleagues showed that home-fortification using micronutrient sprinkles was very successful in treating anemia, but this intervention alone was insufficient to improve zinc status or promote catch-up growth in stunted and wasted population[13], and only products containing fat, protein and micronutrients showed increases in growth and improved motor development approaching that of well-nourished children[14]. This is the reason why formula 1 also contains some protein.

After demonstration of the positive effects on anemia and stunting of in-home micronutrient fortification for children less than 2 years of age[4-5], a 3-year persistent effect on intelligence and development was further demonstrated by our follow-up study. The differences in development and intelligence of children in the formula 1 group and the community control group illustrated that mental development of children given additional micronutrients between 6 and 24 months of age was greater than in children not given additional micronutrients and the differences were gradually enlarged along with the advance of age. The differences in adaptation and social behavior were also consistent in the earlier follow up, and such differences may be as functionally important as lower IQ scores. Anemia correction results of different stage in formula 1 group suggested the importance of early anemia treatment. Lozoff's recent research in an African-American sample showed the dose-response relationship between severity of iron deficiency and infant social-emotional behavior[15]. Hemoglobin was the only measure of iron status in our study and anemia was presumed to be due to iron deficiency. Recent large, randomized trials of iron supplementation in developing countries consistently revealed benefits of iron, especially on motor development and social-emotional behavior[16]. Vitamin A administration to children in formula 2 group may explain the reduction in anemia[17]. However, the effect of vitamin A in reducing anemia was much smaller than iron contained in formula 1. The positive effect of formula 2 on intelligence development gradually diminished after age of 4 years. Applying a micronutrient-fortified food supplement to home-made complementary food beginning at 6 month of age in the first two years of life could substantially lead to improved development and intelligence which persisted to 6 years of age.

Several papers reported an association between iron status during early childhood and mental development later in childhood. A survey in Israel by Palti demonstrated that an iron intervention to the moderately anemic infants at 9 months of age had lower cognitive development score at age of 2, 3, and 5 years compared with those in the non-anemic children of the same age[18]. Observations in both France and Yugoslavia proved the relationship of hemoglobin level with IQ at age of 4[19-20]. From research in Costa Rica, Lozoff provided evidence of lower cognitive scores up to 19 years and motor scores to 11 to 14 years among individuals who had chronic, severe iron deficiency during infancy[21-22].

Our findings showed the introduction of nutrient-dense home-fortified soybean powder, as a supplement to the regular home-made complementary food to children at 6-12 months until 24 months of age in rural China had effectively improved the intellectual development at age of 24 months and 6 years onward. It demonstrated the extreme importance of nutrition status in early life and the social and economic development of a country, as described in the Lancet series in 2008[23]. Iron status certainly played a critical role in such consequences since the anemia prevalence in the formula 1 and formula 2 groups significantly reduced: from 34.9% to 18.5% and 34.5% to 27.7% after 6 months of intervention , respectively, and further reduction to 5.6% and 11.2% was seen after the completion of intervention at 24 months of age[4]. If such approach could be applied in a large scale, the nation could be economically benefited from anemia reduction in children. Ross estimated that the economic losses due to anemia in children accounted for 2.9% of China's Gross Domestic Products in 2001[24].

There are some limitation in the design and implementation of this study. Firstly, the study was quasi-experimental with townships not chosen randomly in each county due to the large sample size required, and children in the community control group for development and intelligence quotient study were recruited from nearby villages with similar socioeconomic status in the five counties, even though the community control group was matched in age with the formula 1 and formula 2 groups in every follow up survey. Secondly, due to resource limitation, the assessment of Hb was the only biological measurement and indicator for iron deficiency based on the assumption that the anemia in children is predominantly caused by iron deficiency. Thirdly, children development testers were not blinded to which children received formula and to which did not, and the lack of blindness might lead to bias, although testers were unaware themselves. Not all children were assessed with development scale at each follow-up survey and, there were potentials of bias due to loss to follow-up, even there was no significant difference in baseline characteristics of the dropouts and the participants. This might suggest that the results were applicable to the study population.

In summary, this kind of in home fortification intervention is feasible in rural China and could reduce the prevalence of anemia and improve the intellectual development of children in their first 2 years of life and possibly longer. However, how can such fortified food be translated from scientific studies into practical application is a major challenge faced by all of us. Furthermore, standardized and low cost products supported by an appropriate supply chain to make them accessible to rural villages are critical in achieving the goal of food fortification. The involvement and participation by food producers and retailers in close collaboration with academic experts are urgently needed. It was a good news that a national standard for nutrient-dense food supplements for complementary feeding (GB/T22570-2008) was promulgated by the Government[25] and efforts have been made toward its early implementation in China. We believe that further follow up study into adolescence should be carried out to provide more evidences for the long-term benefit of such food fortification approach in the context of China's specific conditions[21, 26].

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