

### RESEARCH ARTICLE

## Effect of Picture-based health education and counselling on knowledge and adherence to preconception Iron-folic acid supplementation among women planning to be pregnant in Eastern Ethiopia: a randomized controlled trial

Anteneh Berhane<sup>1,2\*</sup>  and Tefera Belachew<sup>2</sup>

<sup>1</sup>Department of Public Health, College of Medicine and Health Science, Dire Dawa University, Dire Dawa, Ethiopia

<sup>2</sup>Department of Nutrition and Dietetics, Faculty of Public Health, Institute of Health, Jimma University, Jimma, Ethiopia

(Received 10 May 2022 – Final revision received 7 June 2022 – Accepted 10 June 2022)

*Journal of Nutritional Science* (2022), vol. 11, e58, page 1 of 11

doi:10.1017/jns.2022.51

#### Abstract

The present study examined the effect of picture-based nutrition education on knowledge and adherence to pre-conception iron–folic acid supplement (IFAS) in Ethiopia, a country where there is a high burden of neural tube defects (NTDs) and anaemia. In eastern Ethiopia, a parallel randomised controlled trial design was employed among women planning to get pregnant. The interventional arm ( $n$  122) received a preconception picture-based nutrition education and counselling along with an IFAS and the control arm ( $n$  122) received only a preconception IFAS. The effects of the intervention between-group differences were assessed using a  $\chi^2$  and independent sample  $t$ -test. Bivariate and multivariable linear regression model was fitted to detect independent variables affecting the outcome. The outcome measures regarding the knowledge and adherence to the IFAS intake during the three months of the intervention period were determined. It was observed that large proportion of women in the intervention group (42.6 %) had an adherence to IFAS compared to the control group (3.3 %); ( $P < 0.0001$ ). Based on bivariate and multivariable linear regression analyses, among NTDs affecting pregnancy, the history of spontaneous abortion and knowledge were independently associated with adherence to the IFAS ( $P < 0.05$ ). Preconception nutrition education with regular follow-ups could be effective in improving knowledge and adherence to the IFAS intake. This intervention is very short, simple, cost-effective and has the potential for adaptation development to a large-scale implementation in the existing healthcare system in Ethiopia to prevent NTDs and adverse birth outcomes among women who plan to get pregnant. This clinical trial was registered on 6 April 2021 under the ClinicalTrials.gov with an identifier number PACTR202104543567379.

**Key words:** Adherence: Iron–folic acid: Knowledge: Nutrition education: RCT

#### Introduction

The adoption of modern contraception methods has significantly increased in sub-Saharan Africa<sup>(1–3)</sup>. In Ethiopia, the contraceptive prevalence rate (CPR) among currently married women is 41 %<sup>(4)</sup>; however, 35 % of modern contraception device (medical products including sub-dermal implants, intra-uterine devices (IUDs) or loops which are designed to prevent

pregnancy) users discontinued them before their removal date<sup>(5)</sup>. The desire for pregnancy is the second most common reason for early discontinuation and it accounts for almost 27.3 %<sup>(6–9)</sup>. Any woman who could get pregnant is at a risk of having a baby with neural tube defects (NTDs)<sup>(10)</sup>. The aetiology of NTDs is complex, multifactorial in origin, but mainly dietary factors play a major role<sup>(11–23)</sup>. An optimal intake of the

**Abbreviations:** ANC: antenatal care; IFAS: iron–folic acid supplement; NTD: neural tube defect.

\* **Corresponding author:** Anteneh Berhane, email [antishaction@gmail.com](mailto:antishaction@gmail.com)



iron–folic acid supplement (IFAS) is very crucial for increasing folate concentrations in red blood cells and could significantly reduce the risk of iron deficiency anaemia and congenital anomalies such as NTDs<sup>(24–27)</sup>. Iron can modulate folate availability via a cellular one-carbon pathway, and low iron status could alter folate utilisation despite an adequate folate intake and extracellular folate concentrations<sup>(28,29)</sup>. A sufficient amount of iron plays an important role in the development of the neural tube and for a successful neural tube closure; however, deficits in iron might cause some cases of NTDs<sup>(30–32)</sup>.

Ethiopia has one of the highest rates of micronutrient deficiencies, including iron deficiency, making it a significant public health concern<sup>(33–35)</sup>. In Ethiopia, 84 % of women of reproductive age (WRA) had low levels of red blood cell folate<sup>(33,36–39)</sup>. Because of WRA with low serum folate levels, the incidence of NTDs in Ethiopia has increased alarmingly recording the highest rate and emerged as a major public health concern<sup>(40,41)</sup>, so there is an urgent need to develop an effective intervention programme to address the above-mentioned problem. Despite the fact that the Ethiopian healthcare system has a fertile ground for the provision of the IFAS to reduce the risk of NTDs, there is no preconception care services to women who discontinue modern contraception methods for planned pregnancy, and thus the golden opportunity for instituting key NTD preventative interventions is lost.

In Ethiopia, providing IFASs to pregnant women is a primary strategy for preventing maternal and newborn morbidity and mortality due to anaemia<sup>(42)</sup>. However, knowledge and adherence to iron–folic acid remain relatively low, and various barriers to the programme's success have been identified<sup>(43–52)</sup>. Lessons are learnt from the current healthcare strategy for the provision of the IFAS, and alternative approaches are required to improve adherence to the preconception of the IFAS intake. Evidence from other studies indicates that health education intervention is an important tool to improve knowledge and adherence to micronutrient supplementation<sup>(49,53–60)</sup>. For effective intervention, it needs to be locally appropriate, simple and practically implemented through the existing healthcare system. We assumed that the preconception picture-based health education intervention package for women planning to get pregnant is the best approach to reduce the risk of NTDs and other adverse outcomes. Therefore, the aim of the present study was to evaluate the effect of picture-based health education and counselling intervention on knowledge and adherence to the IFAS intake among women planning to get pregnant.

## Materials and methods

### Study area and period

The present study was conducted in Dire Dawa city administration located 515 km in the eastern part of Ethiopia. It was subdivided into 9 urban and 38 rural kebeles. In 2022, the population of Dire Dawa city administration is 445 000, and has increased by 4.46 % from 2021. A number of Ethiopian languages are widely spoken in Dire Dawa city administration by the people from the various nations and nationalities living in Dire Dawa city administration. The study was conducted between May 2021 and October 2021.

**Trial design.** A double-blind parallel randomised controlled trial was conducted in gynecology and family planning clinic at a healthcare facility to determine the effect of pictured-based nutrition education and counselling on the importance of adherence to the IFAS intake during pregnancy.

**Participants.** Participants included women in the age group of 18–45 years who requested to interrupt contraception to become pregnant and women with spontaneous abortion who refused to adopt a contraceptive method with an intention to become pregnant.

The inclusion criteria included women currently living in the study area (women who are usual residents and live or intend to live in the area for six or more months) and have given consent to participate in the study. Women who took IFAS or any other microsupplements in the past two months and participants who are mentally/physically challenged to provide consent were excluded from the study. The study was carried out in accordance with the ethical principles of the Helsinki declaration and the requirement of good clinical practice<sup>(61)</sup>.

### Intervention and its procedure

The details of the study protocol were published elsewhere<sup>(62)</sup>. In accordance with the protocol, midwifery nurses who work in the gynecology ward and family planning clinics invited all eligible women to participate in the study and collected the baseline data. In addition, health extension workers were provided home-to-home picture-based nutrition education and counselling<sup>(63)</sup> for women who were assigned to the interventional arm.

Individual picture-based nutrition education and counselling including picture and text messages were delivered to the intervention group using conventional inter-personal communication intervention for 10–20 min by trained health extension workers on a monthly basis. Education includes warnings about lifestyle, dietary habits, risk factors for anaemia and NTDs, adverse effects of NTDs and IFAS guidelines. The IFAS guide includes information on how to take the IFAS, when to take it, how to absorb it more, side effects of the IFAS and foods rich in iron and folic acid. Educational brochures were also distributed at the end of the education session. The brochure contained key messages with images and text. After completing the education session, an opportunity was given to the participants to discuss the education content and clarify any confusion.

Each participant in the interventional arm received two educational health message reminders (on Mondays and Thursdays) in their local language, via mobile during the daytime to avoid disturbing them, every week to make sure they were taking the IFASs. Anyone at home or in the neighborhood who can read is encouraged to read the texts for women who cannot read.

The key messages included 'eat a diversified food', 'take one IFAS tablet per day for at least 90 days', 'contact your healthcare provider if you have any complaint related to IFA tablets', 'reach and maintain a healthy weight', 'visit health facility before and during pregnancy like antenatal care (ANC) and



**Table 1.** Intervention protocol for preconception picture-based education and counselling for women, who had an intention to be pregnant, of Dire Dawa city administration, Ethiopia

Key action (message)	Strategy of intervention	Responsibility	Frequency	Adherence to the IFAS
Preconception and prenatal healthcare service	Brochure with take-home key message (in local languages);Counselling and discussion on uptake of the IFAS and risk factors of NTDs and other adverse pregnant and birth outcome as well as methods of preventing them;Reminding SMS text messages via mobile phone	Trained healthcare providers, health extension workers and principal investigator	Once	Number of intervention participants who received the brochure
Visiting health facility before and during pregnancy like ANC and check your health frequently			Per month	Frequency
Take iron folic acid every day and consumption of diversified diet (the ten food groups)				
Lifestyle (stop drinking alcohol, smoking and using certain drugs, do not stay in smoking environment)				
Avoid toxic substances and environmental contaminants			Two messages per week	Frequency
If you don't follow this, then you may be at risk of giving birth to a child with NTDs and other negative birth outcomes like anaemia, low birth weight and preterm birth				

check your health frequently', 'avoid toxic substances and environmental contaminants', 'avoid living in a stressful or abusive environment; or working with or living around toxic substances' and 'Learn your and your partner's family history' (Table 1). The brochure with take-home messages was also distributed to help participants understand what they have learnt.

Every month there was an interaction with their partners and discussion on the issues. These interactions were also important in reducing drop out and assisting participants with any questions that may arise and to increase the involvement of partner in the reproductive health.

The IFAS (thirty iron capsules with 60 mg of ferrous sulphate and 0.5 mg of folic acid) was provided to all participants in the intervention and the control groups every month immediately after they removed modern contraception devices<sup>(64)</sup>.

While collecting the IFAS, all participants received a brief information for about 5–10 min regarding the proper usage of the IFAS from the health professional. The information session included the importance of the IFAS, duration of the IFAS to be consumed, the possible side effects of the supplement and ways of handling the side effects. Due to the absence of preconception services for women who plan to get pregnant, the midwifery nurse encouraged the control group to visit the healthcare facility every month to consume the IFAS pills and contacted them if they missed their appointment date. Health professionals did not interfere at any conditions with control arm practices, only the provision and count of the IFAS were done. After the end of the study, similar nutrition information was given to the control group.

### Intervention fidelity

The investigators developed criteria to assess the fidelity of the intervention based on the preconception care and dietary guidelines in accordance with WHO recommendations. The criteria included checklists to assess the intervention design,

training of counsellors, counselling process and receipt of intervention. Content validity for the education was assured by sending its content to two experts in nutrition and health educational and behavioural science from academic centre. In addition, two expert meetings were held with health professionals for the development of materials. To balance the variations, equal numbers of eligible participants were selected for the intervention and control groups. In addition, to minimise between-educators and counsellors variation, the same health extension workers made three repeated visits for each participant. The intervention process was pretested before the implementation of the trial. Besides, each woman received equal number and frequencies of counselling, and the lengths of contacts within an intervention group were similar to make the process standardised. Picture-based nutrition educator and counsellor's knowledge and skills were assessed by pre- and post-training tests and practical evaluation.

Counting of the remaining IFAS pills were used to measure the adherence of participants to the IFAS intake with the help of the interview about their understanding of the core content of the intervention during home-to-home visits in every month.

Study participants, data collectors (who work at gynecology and family planning service), educator and counsellors were blinded to the study hypotheses and group allocation. Additionally, the data entry clerk was blinded by labelling the groups with a non-identifiable unique number until the analysis was finalised.

**Outcomes.** The primary outcome of this trial was the adherence to the IFAS intake and knowledge about the IFAS and NTDs.

### Sample size

The sample size was calculated using Gpower based on the study considering 80 % power, 0.3 effect size and 95 %



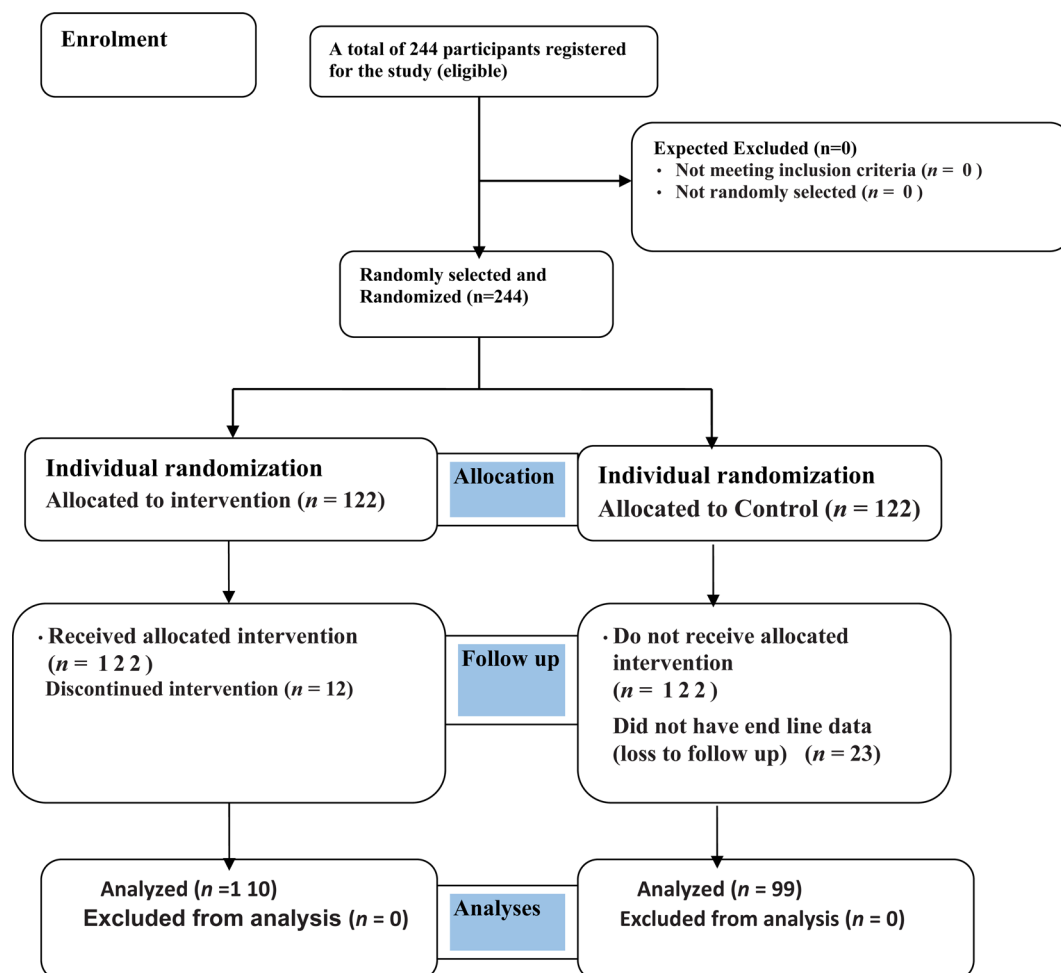
confidence interval with an intervention to control ratio of 1 and margin of error of 0.05. The calculated sample size is 111 and 10% loss to follow-up was added. The final sample size for a single arm was 122 in the intervention and control arms each. The total sample size was 244.

**Randomisation.** The study subjects were enrolled when they came to the health facility to remove their modern contraception device with an intention to get pregnant or after they had a spontaneous abortion and when they decide that they want to get pregnant immediately. All the necessary information including full address, mobile phone number and a unique ID number of the study participants were recorded. A list of the ID numbers was compiled and sent to the researcher on a weekly basis. Simple randomisation with 1:1 allocation ration was done using ENA for Smart Software. Women randomised to the intervention group only ( $n = 122$ ) received picture-based nutrition education and counselling, where participants in both groups would receive the IFAS and other services being given by the health facility. This study considered the Comprehensive Criteria for Reporting Trials (CONSORT) as a guide for study randomisation (Fig. 1).

#### Data collection tools and procedures

Data collection was started after receiving official permission to conduct the study and written informed consent from the participants, and before the intervention programme started. Midwifery nurses working in the gynecology and family planning section of health facilities interviewed all eligible participants using face-to-face structured questionnaire. The questionnaire included about the participants' age, education, occupation, family monthly income, obstetric history and knowledge. Before the formal data collection, the questionnaire was repeatedly pretested and revised based on the analysis of the results. Each interview took around 20–30 min, in a specified room in the gynecology and family planning section.

Twenty-six trained (six midwife nurses and twenty health extension workers) professionals participated in the study. Data collectors and nutrition educator were trained for three days using a training manual that included the following: how to enrol women to the study, how to take the IFAS and the necessary information including the baseline data. In addition, health extension workers received training on how to provide picture-based nutrition education and counselling.



**Fig. 1.** Consort flow diagram showing the effect of picture-based health education and counselling targeting knowledge and adherence to the preconception of iron-folic acid supplement among women who planned to be pregnant: a randomised controlled trial.





The supervisors and the principal investigator closely monitored the data collection process. Additionally, nutrition counsellors also have monthly meetings with supervisors to discuss any problems they are encountering while providing nutrition counselling. Feedback is provided to the counsellors in these meetings.

#### Operational definition of terms

**Intervention group.** Randomly selected women who were given preconception picture-based education and counselling along with 60 mg of elemental iron and 400 µg (0.4 mg) of folic acid supplementation for 3 months beginning with the date of contraceptive device removal and pregnancy termination.

**Control group.** Randomly selected adults taking 60 mg of elemental iron and 400 µg (0.4 mg) of folic acid but not given preconception picture-based education and counselling for 3 months beginning with the date of contraceptive device removal and pregnancy termination.

#### Adherence to the IFAS intake

During the three-month intervention period, the participants were expected to take ninety IFAS pills, on the assumption of one tablet of the IFAS is taken each day starting from the removal of modern contraception device. The participants were divided into two groups based on their adherence to the IFAS intake. If they were able to take at least seventy-two and more IFAS pills or 80 % from the total take period, they were considered an adherent to the IFAS intake, whereas those who were not able to take less than seventy-two IFAS tablets or less than 80 % from the total intake period were considered non-adherents to the IFAS intake<sup>(25,45)</sup>. Women who did not attend all counselling sessions were deemed non-adherent to the guidelines. Women who dropped out of the study, on the other hand, were labelled as lost to follow-up.

**Knowledge.** Subjects were graded by asking a series of ten questions about the IFAS and NTDs marking correct answers out of a hundred. 'Poor knowledge' was defined as an average knowledge score of 50 % or less.

**Intention to treat.** Intention to treat (ITT) was calculated by including all participants who were considered randomised in the statistical analysis and were analysed according to the group they were originally assigned.

**Duration of the intervention.** The time period of picture-based health education and counselling given to the intervention group was 3 months starting from the second half of May 2020 to October 2021.

**Modern contraception.** Defined as a medical product including sub-dermal implants, IUDs or loops which are designed to prevent pregnancy.

#### Statistical analysis

Data were presented in the form of descriptive statistics, such as frequency, percentages, mean and standard deviation. The Kolmogorov–Smirnov test was used to check the normality of the distribution. The effects of the intervention between-group differences were assessed using a  $\chi^2$  test for categorical variables and an independent *t*-test for continuous variables with normal distributions. Within-group changes were assessed using a paired *t*-test after 3 months. The Cohen's *d* statistic (effect size) was used to measure the significance of the intervention's effect. It was categorised as follows: <0.2 has no effect, 0.2 to <0.5 has a small effect, 0.5 to <0.8 has a moderate effect and >0.8 has a significant effect indicating a strong relationship between the two variables<sup>(65)</sup>. Adherence to the IFAS intake was conducted with the goal of considering the ITT concept.

Univariate and multivariable linear regression analyses modelling were performed to detect the most independent variables affecting adherence and knowledge to the IFAS by controlling the possible confounding variables. Analyses are based on valid data available for each (set) of variables analysed and no missing data are imputed. Variables with a *P*-value of <0.05 were considered statistically significant in univariate and multivariable analyses. IBM SPSS Statistics 25 was used for these analyses.

**Patient and public involvement.** In the present study, neither patient nor public was involved in study proposal development, design and analysis of the study.

#### Results

During the recruitment period (May 2021 and end of October 2021), a total of 244 eligible participants who were enrolled in the study (ITT population). A total of 35 (14.3 %) participants (*n* 12 from intervention and *n* 23 from control arm) were declined from the study due to different reasons. Overall, the mean (and SD) age of the participants was 28.1 ± 5.19 years, with 42 % of the participants being between the ages of 26 and 34 years. All participants were married. There were no statistically significant differences between the socio-demographic characteristics and pregnancy-related information of participants in the intervention group and those participated in the control group in terms of age, educational status of women, partner educational status and history of taking IFAS during pregnancy (*P* > 0.05). Additionally before the intervention programme, there were no significant differences between the two groups in terms of history of IFAS or FAS before pregnancy, knowledge on NTDs and preconception of IFAS (*P* > 0.05). However, there were statistically significant differences between two groups in terms of history of ANC visit during pregnancy, history of NTDs affecting pregnancy and history of spontaneous abortion (*P* < 0.05) (Table 2).

After 3 months of intervention, the proportion of adherence to the IFAS was 23 % (*n* 56). With regard to adherence within the groups, 42.6 % (*n* 52) in the intervention group and 3.3 % (*n* 4) in the control group and the intervention group were



**Table 2.** The socio-demographic characteristics and pregnancy-related information of the study participants (*n* 244)

Variables	Intervention arm ( <i>n</i> 122) <i>n</i> (%)	Control arm ( <i>n</i> 122) <i>N</i> (%)	<i>P</i>
Age (years)			
18–25	41 (33.6)	43 (35.2)	0.6
26–34	49 (40.2)	53 (43.4)	
>34	32 (26.2)	26 (21.3)	
Mean age (years)	28.1 ± 5.19		
Educational status			
Illiterate	22 (18)	24 (19.7)	0.74
Literate	100 (82)	98 (80.3)	
Partner educational status			
Illiterate	17 (13.9)	10 (8.2)	0.15
Literate	105 (86.1)	112 (91.8)	
History of IFAS or FAS before pregnancy			
No	11 (97.5)	121 (99.2)	0.32
Yes	3 (2.5)	1 (0.8)	
History of visited ANC during pregnancy			
No	46 (37.7)	65 (53.3)	0.015
Yes	76 (62.3)	57 (46.7)	
History of IFASs taken during pregnancy			
No	74 (60.7)	86 (70.5)	0.1
Yes	48 (39.3)	36 (29.5)	
History of NTDs affecting pregnancy			
No	110 (90.2)	118 (96.7)	0.03
Yes	12 (9.8)	4 (3.3)	
History of spontaneous abortion			
No	113 (92.8)	120 (98.4)	0.03
Yes	9 (7.4)	2 (1.6)	

FAS, folic acid supplement; IFAS, iron and folic acid supplement.  
Pearson correlation ( $\chi^2$  test), significant at  $P < 0.05$ .

significantly higher than in the control group. In the intervention group, the proportion of adherence to the IFAS intake among participants increased by 40.1 % and they were statistically different ( $P < 0.0001$ ). At the end of the study, the proportion of adherence to the IFAS increased slightly in the control group and it was increased by 2.5 % in the control group ( $P = 0.31$ ). The difference in difference between the two groups of adherence to the IFAS intake was 37.6 % and they were statistically significant ( $P < 0.0001$ ) (Table 3). The endline data of adherence between the groups did differ from the baseline data ( $P = 0.31$  *v.*  $P < 0.0001$ ).

Table 4 presents the changes in knowledge between and within group. Level of knowledge between the groups did differ before and after intervention ( $P = 0.87$  *v.*  $P < 0.0001$ ). The mean knowledge scores were 48 ( $\pm 26$  sd) at their highest and 13 ( $\pm 8.3$  sd) at their lowest. A comparison of the scores at the baseline and end of 3 months follow-up showed that the mean change in knowledge was 17.6 ( $\pm 28$  sd) points in the

intervention group and 18.5 ( $\pm 18.8$  sd) in the control group. The overall mean change in knowledge mean (and SE) between groups was 0.9 ( $\pm 3.04$  SE) and there were significant differences between two groups ( $P < 0.001$ ).

Univariate and multivariate linear regression analyses were conducted to identify the variables that could independently predict higher adherence rates among the participants of the intervention group following the programme. History of NTDs affecting pregnancy, history of spontaneous abortion and knowledge were independently associated with adherence to the IFAS intake ( $P < 0.05$ ). The most identified factors that affected the adherence to the IFAS intake were history of NTDs affecting pregnancy and knowledge levels ( $P < 0.001$ ) (Table 5).

## Discussion

Many research findings regarding the knowledge and adherence to the IFAS intake among pregnant women have been published. To our knowledge, no study has been conducted regarding the knowledge and adherence to the IFAS intake among women who plan to get pregnant. The present study is the first parallel randomised controlled trial to evaluate the effectiveness of nutrition education on the knowledge and adherence to the IFAS intake using an individual's knowledge through picture-based nutrition education and counselling approach. The major goal of this intervention was to encourage women who plan to get pregnant to have a thorough knowledge about and adherence to the IFAS intake to avert the risk of developing NTDs affecting pregnancy and other related negative impacts on women and neonates.

In the present study, the adherence to the IFAS intake was 2.2 and 42.6 % (before and after the intervention) within the intervention group ( $P < 0.0001$ ) compared with the 0.8 and 3.3 % (before and after intervention) within the control group ( $P = 0.31$ ) and the average number of supplements taken in the intervention group was significantly higher than in the control group.

This implies that the nutrition education intervention package has a significant positive impact in improving women's health adhered to preconception of the IFAS intake in the intervention group than the control group. Therefore, institutionalised along with link to home delivery nutrition education is one of the promising interventions that could improve the pregnancy and birth outcome and extend to future generation and community as whole<sup>(66)</sup>. Even though the study participants were different from our study, the present study was in agreement with the study conducted in Ethiopia<sup>(67)</sup> in

**Table 3.** Differences between baseline and endline adherence to the IFAS and difference in difference between intervention and control groups

Variable	Intervention group ( <i>n</i> 122)			<i>P</i> -value within group	Control group ( <i>n</i> 122)			<i>P</i> -value within group	Difference in difference	<i>P</i> -value between group
	Baseline	Endline	Difference (EL – BL)		Baseline	Endline	Difference (EL – BL)			
Adherence (%)	2.2	42.6	40.1	<0.0001	0.8	3.3	2.5	0.31	37.6	<0.0001

BL: baseline; EL: endline.  
Significant at  $P < 0.05$ .



**Table 4.** A comparison between participants' mean scores for knowledge of the IFAS

Parameter	Intervention			Control			P-value between groups (after intervention)	P-value between groups (before intervention)	Effect size Eta (Cohen's <i>d</i> statistic)	Label
	Baseline Mean (±SD)	Endline Mean (±SD)	Difference (BL – EL) <sup>1</sup>	Baseline Mean (±SD)	Endline Mean (±SD)	Difference (BL – EL) <sup>1</sup>				
	31 (±13.6)	48 (±26)	17.6 (±28)	13 (±8.3)	31.5 (±19.5)	18.5 (±18.8)				
Knowledge				0.9 (±3.04)	0.87	<0.0001	0.87	0.87	Significant effect	

DID: difference in difference.

Significant at  $P < 0.05$ .

<sup>1</sup> Intervention group (n=122) and Control group (n=122).

Bihar, India<sup>(68)</sup>, in Kenya<sup>(69)</sup>, from Jordan, Saudi Arabia, India and Indonesia<sup>(70–74)</sup>.

The nutrition knowledge scores were significantly higher at the endline and 3 months after the sessions compared with the baseline and there was a statistical significant difference between the intervention and control groups. However, the mean score of knowledge in the control group showed some improvement after intervention. The results of previous studies are in line with our own, as we found that the nutrition education has a significant impact in improving knowledge<sup>(75–78)</sup>. In addition, these studies reported a significant difference in the mean scores between two groups (intervention and control) after intervention only, whereas no significant mean difference was observed at the baseline concurrent with our findings. This may be due to the sensitisation that occurred during the initial exposure to the questionnaire and the recall of the answers from the baseline question<sup>(79,80)</sup>. The significant improvement in knowledge and adherence among the intervention group may also be related to the methods and repetition of the nutrition education intervention package for 3 months with a strict follow-up<sup>(64)</sup>. Similarly, home visits encourage participants to practice what they know to improve their health<sup>(81)</sup>. The repetition education remained longer in memory according to the information process theory<sup>(82)</sup>. However, the proportion of improvement in knowledge and adherence was reported different between studies<sup>(83)</sup>. These differences are related to the duration of the intervention and the method(s) used to deliver the intervention<sup>(76)</sup>.

The study setting could be the second possible justification. The present study was conducted on women in urban areas. Urban women were more exposed to different media about the importance of the iron folate intake compared with the rural counterparts. Their partners may also be more exposed to various sources of information and more easily understand what the healthcare workers advice.

Despite the fact that the biomarker test of the participants was not performed, and it is unknown whether the level of red blood cell folate is increased or the same as before the intake of the IFAS, various laboratory-based researches provided evidence that the intake of the IFAS over at least 12 weeks before the conception by women of child-bearing age increased the level of red blood cell folate, potentially lowering the risk of NTD-affected pregnancy and<sup>(26,27,36,81,84–90)</sup>. Based on this concrete evidence, we would expect women who adhere to the IFAS to be more protective against NTDs if they become pregnant, because folate sufficiency or optimal blood folate concentrations are directly linked to the risk of NTDs<sup>(24,25)</sup>.

In general, positive aspects of this intervention include a significant improvement in women's knowledge of nutrition to reduce the risk of NTDs, so the intervention should ideally have a positive impact on both the women themselves and their children. The positive effect will help mothers to form a basis for proper nutrition in subsequent years.

The present study has also a significant practical implication for improving the IFAS adherence, which will avert the risk of developing NTDs and improve maternal and child health in order to achieve the Sustainable Development Goals

**Table 5.** Bivariate and multivariable linear regression analyses for the factors affecting adherence to the IFAS

Parameters	Bivariate		Multivariable	
	Beta Coefficient (95 % CI)	P	Beta Coefficient (95 % CI)	P
Age	0.03 (−0.035–0.1)	0.35	0.03 (−0.03–0.1)	0.34
Educational status of participants	0.014 (−0.13–0.16)	0.85	0.015 (−0.12–0.14)	0.82
Partner educational status	0.04 (−0.15–0.28)	0.68	0.04 (−0.13–0.2)	0.63
History of visited ANC during pregnancy	−0.045 (−0.02–0.1)	0.5	−0.03 (−0.16–0.1)	0.62
History of taken IFAS during pregnancy	−0.034 (−0.17–0.1)	0.6	−0.04 (−0.18–0.1)	0.54
History of NTDs affecting pregnancy	0.5 (0.2–0.7)	0.001*	0.4 (0.21–0.6)	<0.0001*
History of spontaneous abortion	0.36 (0.06–0.65)	0.01*	0.32 (0.09–0.5)	0.007*
Knowledge	0.006 (0.004–0.008)	<0.0001*	0.006 (0.004–0.008)	<0.0001*

B, unstandardised coefficients; CI, confidence interval.

$R^2 = 0.19$ ;  $F = 14.7$ . All variables with  $P < 0.05$  were included in the multivariate analysis.

\* Statistically significant at  $P < 0.05$ .

(SDGs). The findings imply the importance of implementing community-level education through health extension as well as at family planning services and other appropriate departments within the health facility through health extension workers as well as by involving males. Furthermore, this approach has the potential to increase adherence and decrease dropout rates of the ANC programme in the country. Therefore, our intervention designed in a way that can be applicable anywhere in a healthcare system. So, the findings of the present study also highlight the importance and effectiveness of adapting preconception policy and national guidelines. Our intervention programmes have no interference and neither did the authors gave financial incentives for health counsellor of either arms. In conclusion, nutrition and health knowledge may not lead to actual behavioural changes, and other behavioural studies need to be done to reach general conclusions.

## Conclusion

In conclusion, the picture-based nutrition education intervention approach along with frequent follow-ups through household visits has a significant impact on knowledge and adherence to the preconception of the IFAS intake among women who plan to get pregnant. It helped to improve women's knowledge on anaemia and NTDs during pregnancy, to raise women's awareness on better dietary practices, and to reduce neonatal and maternal morbidity and mortality.

This intervention is very short, simple and cost-effective. We strongly recommend that this intervention should be widely implemented in the country because of the fertile ground of the health care system. We have the following recommendations for the health policy: the first recommendation is to emphasise that the preconception picture-based nutrition education package programme should be endorsed by policy-makers for women who have removed the modern contraception devices and planned to be pregnant and to focus on the behavioural intake of preconception of the IFAS intake on the existing healthcare system (linking to health facility with health extension programme). Additionally, this intervention package will be developed into a comprehensive national strategy to prevent adverse pregnancy and birth outcome during pregnancy. Also, to resolve the nauseating effect of the IFAS as this was the majority side effect reported by

participants in the study; so, the healthcare providers will provide a brief explanation with possible solution. Our third recommendation is for the Ethiopian government to support food fortification consumed by a larger proportion of the population. A large-scale community-based study with a larger sample size is required to determine whether this approach is cost-effective.

## Acknowledgements

The authors thank all of the study participants, data collectors and supervisors who participated in the study, as well as the kind and cooperative staff of the health facilities in eastern Ethiopia.

Development of the original idea, study concept, design, analysis, and preparation and writing of the original draft was done by A. B. Analysis, writing, review and editing of the whole document was done by T. B.

There was no fund granted for this work.

We declare here in that we have no conflict of interest. The funders had no role in the design of the study; in the collection, analyses or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

All data generated or analysed during this study are included in this published article.

The Institutional Review Board of Jimma University was granted the ethical clearance with the reference number IHR PGY/738/20. Written informed consent was obtained from a parent and/or legal guardian for study participation after providing detailed information on study objectives, benefits. The procedure used in this study was adhered to the principles of the Helsinki Declaration.

This clinical trial was registered on 6 April 2021 under the ClinicalTrials.gov with identifier number PACTR2021 04543567379.

The full trial study protocol was published elsewhere and can be accessed on Berhane, A. and Belachew, T., 2022. Effect of preconception pictured-based health education and counseling on adherence to iron–folic acid supplementation to improve maternal pregnancy and birth outcome among women who plan to pregnant: randomized control trial. *Clinical Nutrition Open Science*. <https://doi.org/10.1016/j.nutos.2021.12.002>





## References

1. Bearak J, Popinchalk A, Alkema L, *et al.* (2018) Global, regional, and subregional trends in unintended pregnancy and its outcomes from 1990 to 2014: estimates from a Bayesian hierarchical model. *Lancet Glob Health* **6**, e380–e389.
2. Sedgh G, Singh S & Hussain R (2014) Intended and unintended pregnancies worldwide in 2012 and recent trends. *Stud Fam Plan* **45**, 301–314.
3. United Nations. World Fertility and Family Planning Highlights 2020.
4. Central Statistical Agency (CSA) [Ethiopia] & ICF (2019) Ethiopia Mini Demographic and Health Survey 2019. Addis Ababa, Ethiopia, and Rockville, Maryland, USA.
5. Central Statistical Agency (CSA) [Ethiopia] & ICF (2016) Ethiopia Demographic and Health Survey 2016. Addis Ababa, Ethiopia, and Rockville, Maryland, USA.
6. Nega G, Abera M & Tadele A (2021) Discontinuation rate and associated factors among contraceptive implant users in Kersa district, southwestern Ethiopia. *Arch Public Health* **79**, 1–9.
7. Bekele T, Gebremariam A & Tura P (2015) Factors associated with contraceptive discontinuation in Agarfa district, Bale Zone, south east Ethiopia. *Epidemiology* **5**.
8. Burusie A (2015) Reasons for premature removal of Implanon among users in Arsi zone, Oromia region, Ethiopia, 2013. *Reprod Syst Sex Disord* **4**, 1–6.
9. Belete N, Zemene A, Hagos H, *et al.* (2018) Prevalence and factors associated with modern contraceptive discontinuation among reproductive age group women, a community based cross-sectional study in Humera town, northern Ethiopia. *BMC Women's Health* **18**, 1–8.
10. Bibbins-Domingo K, Grossman DC, Curry SJ, *et al.* (2017) Folic acid supplementation for the prevention of neural tube defects: US Preventive Services Task Force Recommendation statement. *JAMA* **317**, 183–189.
11. Berhane A, Fikadu T & Belachew T (2022) Dietary practice among cohort pregnant women who gave birth to neonates with and without neural tube defect: a comparative cross-sectional study. *J Nutr Sci* **11**.
12. Gupta R & Hanson A (2022) Fetal development and maternal diet. In *Pediatric Nutrition for Dietitians*, pp. 51–63. Boca Raton, Florida: CRC Press.
13. Crivellenti LC, Zuccolotto DCC & Sartorelli DS (2018) Development of a diet quality index adapted for pregnant women. *Rev Saúde Pública* **52**.
14. Biagi C, Di Nunzio M, Bordonì A, *et al.* (2019) Effect of adherence to Mediterranean diet during pregnancy on children's health: a systematic review. *Nutrients* **11**, 997.
15. Carmichael SL, Yang W & Shaw GM (2010) Periconceptional nutrient intakes and risks of neural tube defects in California. *Birth Defects Res Part A* **88**, 670–678.
16. Groenen PM, van Rooij IA, Peer PG, *et al.* (2004) Low maternal dietary intakes of iron, magnesium, and niacin are associated with Spina bifida in the offspring. *J Nutr* **134**, 1516–1522.
17. Safi J, Joyeux L & Chalouhi G (2012) Periconceptional folate deficiency and implications in neural tube defects. *J Pregnancy* **2012**.
18. Scott JM, Weir D & Kirke P (1995) Folate and neural tube defects. *Folate Health Dis* **1**, 329–360.
19. Laurence K (1989) Causes of neural tube malformation and their prevention by dietary improvement and preconceptional supplementation with folic acid and multivitamins. *Recent Vitam Res*, 178–195.
20. Schorah C, Smithells R & Scott J (1980) Vitamin B12 and anencephaly. *Lancet* **315**, 880.
21. Group MVS (1991) Prevention of neural tube defects: results of the medical research council vitamin study. *Lancet* **338**, 131–137.
22. Bhide P (2021) Neural tube defects and folate status in India. *Birth Defects India*, 235–249.
23. de la Fournière B, Dhombres F, Maurice P, *et al.* (2020) Prevention of neural tube defects by folic acid supplementation: a national population-based study. *Nutrients* **12**, 3170.
24. Stevens GA, Finucane MM, De-Regil LM, *et al.* (2013) Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. *Lancet Glob Health* **1**, e16–e25.
25. World Health Organization (WHO) (2012) *Guideline: Daily Iron and Folic Acid Supplementation in Pregnant Women*. Geneva, Switzerland: World Health Organization.
26. World Health Organization (WHO) (2015) *WHO Guideline Optimal Serum and Red Blood Cell Folate Concentrations in Women of Reproductive Age for Prevention of Neural Tube Defects*. Geneva, Switzerland: World Health Organization.
27. Cordero AM, Crider KS, Rogers LM, *et al.* (2015) Optimal serum and red blood cell folate concentrations in women of reproductive age for prevention of neural tube defects: World Health Organization guidelines. *MMWR Morb Mortal Wkly Rep* **64**, 421.
28. Oppenheim EW, Adelman C, Liu X, *et al.* (2001) Heavy chain ferritin enhances serine hydroxymethyltransferase expression and de novo thymidine biosynthesis. *J Biol Chem* **276**, 19855–19861.
29. Valberg L (1980) Plasma ferritin concentrations: their clinical significance and relevance to patient care. *Can Med Assoc J* **122**, 1240.
30. Mao J, McKean DM, Warriar S, *et al.* (2010) The iron exporter ferroportin 1 is essential for development of the mouse embryo, forebrain patterning and neural tube closure. *Development* **137**, 3079–3088.
31. Zohn IE, Anderson KV & Niswander L (2007) The Hectd1 ubiquitin ligase is required for development of the head mesenchyme and neural tube closure. *Dev Biol* **306**, 208–221.
32. Zohn IE, De Domenico I, Pollock A, *et al.* (2007) The flatiron mutation in mouse ferroportin acts as a dominant negative to cause ferroportin disease. *Blood* **109**, 4174–4180.
33. Haidar J, Melaku U & Pobocik R (2010) Folate deficiency in women of reproductive age in nine administrative regions of Ethiopia: an emerging public health problem. *S Afr J Clin Nutr* **23**, 132–137.
34. Ababiya T & Gabriel T (2014) Prevalence of anemia among pregnant women in Ethiopia and its management: a review. *Int Res J Pharmacy* **5**, 737–750.
35. Herrador Z, Sordo L, Gadisa E, *et al.* (2014) Micronutrient deficiencies and related factors in school-aged children in Ethiopia: a cross-sectional study in Libo Kemkem and Fogera districts, Amhara Regional State. *PLoS ONE* **9**.
36. Bationo F, Songré-Ouattara LT, Hama-Ba F, *et al.* (2019) Folate status of women and children in Africa – current situation and improvement strategies. *Food Rev Int* **36**, 1–14.
37. Ethiopian Public Health Institute (EPHI) (2017) *Ethiopian National Micronutrient Survey Report*. Ethiopian Public Health Institute.
38. Habte K, Adish A, Zerfu D, *et al.* (2015) Iron, folate and vitamin B12 status of Ethiopian professional runners. *Nutr Metab (Lond)* **12**, 62.
39. Haider BA, Olofin I, Wang M, *et al.* (2013) Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. *Br Med J* **346**.
40. Berihu BA, Welderufael AL, Berhe Y, *et al.* (2018) High burden of neural tube defects in Tigray, northern Ethiopia: hospital-based study. *PLoS ONE* **13**, e0206212.
41. Berhane A & Belachew T (2022) Trend and burden of neural tube defects among cohort of pregnant women in Ethiopia: where are we in the prevention and what is the way forward? *PLoS ONE* **17**, e0264005.
42. Fiedler J, D'Agostino A & Sununtnasuk C (2014) *Nutrition Technical Brief: A Simple Method for Making a Rapid, Initial Assessment of the Consumption and Distribution of Iron-Folic Acid Supplements among Pregnant Women in Developing Countries*. Arlington, VA: USAID/ Strengthening Partnerships, Results and Innovations in Nutrition Globally (SPRING) Project.
43. Boti N, Bekele T, Godana W, *et al.* (2018) Adherence to iron-folate supplementation and associated factors among Pastoralist's pregnant



- women in Burji districts, Segen area People's zone, southern Ethiopia: community-based cross-sectional study. *Int J Reprod Med* **2018**.
44. CSA & ICF (2017) International, Ethiopia Demographic and Health Survey 2011. Addis Ababa, Ethiopia and Calverton, Maryland, USA: Central Statistical Agency and ICF International.
  45. Sendeku FW, Azeze GG & Fenta SL (2020) Adherence to iron-folic acid supplementation among pregnant women in Ethiopia: a systematic review and meta-analysis. *BMC Pregnancy Childbirth* **20**, 1–9.
  46. Gebremichael TG & Welesamuel TG (2020) Adherence to iron-folic acid supplement and associated factors among antenatal care attending pregnant mothers in governmental health institutions of Adwa town, Tigray, Ethiopia: cross-sectional study. *PLoS ONE* **15**, e0227090.
  47. Galloway R, Dusch E, Elder L, *et al.* (2002) Women's perceptions of iron deficiency and anemia prevention and control in eight developing countries. *Soc Sci Med* **55**, 529–544.
  48. Aguayo VM, Koné D, Bamba SI, *et al.* (2005) Acceptability of multiple micronutrient supplements by pregnant and lactating women in Mali. *Public Health Nutr* **8**, 33–37.
  49. Taye B, Abeje G & Mekonen A (2015) Factors associated with compliance of prenatal iron folate supplementation among women in Mecha district, Western Amhara: a cross-sectional study. *Pan Afr Med J* **20**.
  50. Kulkarni B, Christian P, LeClerq SC, *et al.* (2010) Determinants of compliance to antenatal micronutrient supplementation and women's perceptions of supplement use in rural Nepal. *Public Health Nutr* **13**, 82–90.
  51. Zavaleta N, Caulfield LE, Figueroa A, *et al.* (2014) Patterns of compliance with prenatal iron supplementation among Peruvian women. *Mater Child Nutr* **10**, 198–205.
  52. Bali S, Joshi A, Tiwari S, *et al.* (2017) How non consumers differ from consumers: a qualitative approach to synthesize the attributes of iron folic acid end users. *J Clin Diagn Res* **11**, LC18.
  53. Girard AW & Olude O (2012) Nutrition education and counselling provided during pregnancy: effects on maternal, neonatal and child health outcomes. *Paediatr Perinat Epidemiol* **26**, 191–204.
  54. Nagata JM, Gatti LR & Barg FK (2012) Social determinants of iron supplementation among women of reproductive age: a systematic review of qualitative data. *Mater Child Nutr* **8**, 1–18.
  55. Martin SL, Seim GL, Wawire S, *et al.* (2017) Translating formative research findings into a behaviour change strategy to promote antenatal calcium and iron and folic acid supplementation in western Kenya. *Mater Child Nutr* **13**.
  56. World Health Organization (WHO) (2016) *WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience*. Geneva, Switzerland: World Health Organization.
  57. Cena ER, Joy AB, Heneman K, *et al.* (2008) Learner-centered nutrition education improves folate intake and food-related behaviors in nonpregnant, low-income women of childbearing age. *J Am Diet Assoc* **108**, 1627–1635.
  58. Temel S, van Voorst SF, Jack BW, *et al.* (2014) Evidence-based preconceptional lifestyle interventions. *Epidemiol Rev* **36**, 19–30.
  59. Stephenson J, Heslehurst N, Hall J, *et al.* (2018) Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. *Lancet* **391**, 1830–1841.
  60. Forrest JD (1994) Epidemiology of unintended pregnancy and contraceptive use. *Am J Obstet Gynecol* **170**, 1485–1489.
  61. Association WM (2001) World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *Bull WHO* **79**, 373.
  62. Berhane A & Belachew T (2022) Effect of preconception pictured-based health education and counseling on adherence to iron-folic acid supplementation to improve maternal pregnancy and birth outcome among women who plan to pregnant: randomized control trial. *Clin Nutr Open Sci* **41**.
  63. Bhutta ZA, Das JK, Rizvi A, *et al.* (2013) Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet* **382**, 452–477.
  64. World Health Organization (WHO) (2011) *Guideline Intermittent Iron and Folic Acid Supplementation in Menstruating Women*. Geneva, Switzerland: World Health Organization.
  65. Cohen J (2013) *Statistical Power Analysis for the Behavioral Sciences*. Milton Park, Abingdon-on-Thames, Oxfordshire, England, UK: Routledge.
  66. Mok WKH, Poh BK, Wee LH, *et al.* (2018) Juara Sihat: assessing the sustained impact of a school-based obesity intervention. *Med J Malaysia* **73**.
  67. Mengesha MB, Hidru HD, Welay FT, *et al.* (2021) Effect of maternal education on prenatal adherence of iron-folic acid supplementation in Ethiopia: a systematic review and meta-analysis. *Curr Rev Clin Exp Pharmacol* **16**, 247–255.
  68. Wendt A, Young M, Stephenson R, *et al.* (2014) Antenatal care and counseling measures increase iron and folic acid receipt among pregnant women in Bihar, India (256.3). *FASEB J* **28**, 256.3.
  69. Matri E, Pied E, Velez O, *et al.* (2015) Improving Iron-Folic Acid and Calcium Supplementation Compliance Through Counseling, Reminder Cards and Cell Phone Messages in Kenya. *Eur J Nutr Food Saf* **5** (Special issue 5), 1128–1129.
  70. Nahrishah P, Somrongthong R, Viriyautsahakul N, *et al.* (2020) Effect of integrated pictorial handbook education and counseling on improving anemia status, knowledge, food intake, and iron tablet compliance among anemic pregnant women in Indonesia: a quasi-experimental study. *J Multidiscip Healthc* **13**, 43.
  71. Elsharkawy NB, Abdelaziz EM, Ouda MM, *et al.* (2022) Effectiveness of health information package program on knowledge and compliance among pregnant women with anemia: a randomized controlled trial. *Int J Environ Res Public Health* **19**, 2724.
  72. Abujilban S, Hatamleh R & Al-Shuqerat S (2019) The impact of a planned health educational program on the compliance and knowledge of Jordanian pregnant women with anemia. *Women Health* **59**, 748–759.
  73. Noronha JA, Bhaduri A, Bhat HV, *et al.* (2013) Interventional study to strengthen the health promoting behaviours of pregnant women to prevent anaemia in southern India. *Midwifery* **29**, e35–e41.
  74. Permatasari TAE, Rizqiya F, Kusumaningati W, *et al.* (2021) The effect of nutrition and reproductive health education of pregnant women in Indonesia using quasi experimental study. *BMC Pregnancy Childbirth* **21**, 1–15.
  75. Sisay G & Tesfaye A (2021) Effects of nutrition education and counseling intervention on maternal weight and obstetric outcomes among pregnant women of Gedeo Zone, Southern, Ethiopia: a cluster randomized control trial. *Nutr Health*, 02601060211056745.
  76. Gitau GN, Kimiywe JO, Waudu JN, *et al.* (2013) Effects of nutrition education on nutrition knowledge and iron status in primary school pupils of Gatanga District, Muranga County, Kenya. *Curr Res Nutr Food Sci J* **1**, 115–123.
  77. Kostanjevec S, Jerman J & Koch V (2012) The influence of nutrition education on the food consumption and nutrition attitude of schoolchildren in Slovenia. *US-China Educ Rev A* **11**, 953–964.
  78. Ardanjani AE, Reisi M, Javadzade H, *et al.* (2015) The effect of nutrition education on knowledge, attitude, and performance about junk food consumption among students of female primary schools. *J Educ Health Promotion* **4**.
  79. Barthassat J (2014) Positive and negative effects of parental conflicts on children's condition and behaviour. *J Eur Psychol Stud* **5**.
  80. Prelock PA, Hutchins T & Glascoe FP (2008) Speech-language impairment: how to identify the most common and least diagnosed disability of childhood. *Medscape J Med* **10**, 136.
  81. Brämsswig S, Prinz-Langenohl R, Lamers Y, *et al.* (2009) Supplementation with a multivitamin containing 800 µg of folic acid shortens the time to reach the preventive red blood cell folate concentration in healthy women. *Int J Vitam Nutr Res* **79**, 61–70.
  82. Shiffrin RM & Schneider W (1977) Controlled and automatic human information processing: II. Perceptual learning, automatic attending and a general theory. *Psychol Rev* **84**, 127.
  83. Wang D, Stewart D, Chang C, *et al.* (2015) Effect of a school-based nutrition education program on adolescents' nutrition-related



- knowledge, attitudes and behaviour in rural areas of China. *Environ Health Prev Med* **20**, 271–278.
84. Hao L, Yang Q-H, Li Z, *et al.* (2008) Folate status and homocysteine response to folic acid doses and withdrawal among young Chinese women in a large-scale randomized double-blind trial. *Am J Clin Nutr* **88**, 448–457.
85. Crider KS, Devine O, Hao L, *et al.* (2014) Population red blood cell folate concentrations for prevention of neural tube defects: Bayesian model. *Br Med J* **349**.
86. Lamers Y, Prinz-Langenohl R, Brämwig S, *et al.* (2006) Red blood cell folate concentrations increase more after supplementation with [6 S]-5-methyltetrahydrofolate than with folic acid in women of childbearing age. *Am J Clin Nutr* **84**, 156–161.
87. World Health Organization (WHO) (2015) *Serum and Red Blood Cell Folate Concentrations for Assessing Folate Status in Populations*. Geneva, Switzerland: World Health Organization.
88. De Bruyn E, Gulbis B & Cotton F (2014) Serum and red blood cell folate testing for folate deficiency: new features? *Eur J Haematol* **92**, 354–359.
89. Norsworthy B, Skeaff CM, Adank C, *et al.* (2004) Effects of once-a-week or daily folic acid supplementation on red blood cell folate concentrations in women. *Eur J Clin Nutr* **58**, 548–554.
90. Samson KL, Loh SP, Lee SS, *et al.* (2020) Weekly iron–folic acid supplements containing 2.8 mg folic acid are associated with a lower risk of neural tube defects than the current practice of 0.4 mg: a randomised controlled trial in Malaysia. *BMJ Glob Health* **5**, e003897.