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Multivitamin supplements are not superior to nutrition Education in improving fat-soluble vitamin levels: A double-blind randomized controlled trial

doi: 10.6133/apjcn.202510/PP.0007

Published online: October 2025

Running title: Nutrition education vs. supplements for vitamins

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ABSTRACT

Background and Objectives: Vitamin deficiencies are closely associated with the development of chronic diseases. Therefore, effective and safe intervention strategies are critical to improving vitamin nutritional status. This study aimed to assess the effectiveness and differential impacts of nutrition education and multivitamin supplementation, providing a basis for selecting safer intervention strategies. **Methods and Study Design:** A 4-week, double-blind, randomized controlled trial was conducted among 155 adults (aged 18–65 years) with confirmed deficiencies in fat-soluble vitamins (A, D, or E). Participants were randomly assigned to receive either nutrition education with a multivitamin supplement or nutrition education with placebo. The concentrations of fat-soluble vitamins (A, D, or E), as well as their deficiency rates, were compared before and after the intervention. **Results:** A total of 155 participants completed the study. There were no significant differences in demographic characteristics between the two groups. In both groups, the concentration of vitamins (A, D, or E) significantly increased (all $p < 0.001$), and the deficiency rates for all three vitamins significantly decreased (all $p < 0.001$). However, there were no significant differences in the concentrations or deficiency rates of vitamins (A, D, or E) between the two groups after the intervention (all $p > 0.05$). **Conclusions:** Multivitamin supplements are not superior to nutrition education. Nutrition education alone may be a safer and effective approach to addressing deficiencies in vitamins A, D, and E, while reducing the risks associated with unnecessary vitamin supplementation in the general population.

Key Words: fat soluble vitamins, nutrition education, multivitamin supplements, randomized controlled trial, vitamin deficiency

INTRODUCTION

Vitamins are essential nutrients that the body requires in small amounts, playing a crucial role in the proper functioning of organisms.¹ Among them, fat-soluble vitamins, including vitamins A, D, and E, are particularly significant. Vitamin A is involved in cell differentiation and proliferation, offering potential anti-cancer effects and acting as an antioxidant.² It is also vital for various physiological activities, including immune function,³ vision,⁴ and reproduction.⁵ Vitamin D is essential for promoting bone health and strengthening the immune system.⁶ Vitamin E, a key antioxidant, is widely present in cell membranes and lipoproteins, regulating the body's redox balance.⁷ Current studies have demonstrated that fat-soluble vitamins play an indisputable role in various physiological processes, such as immune

regulation, vision, bone health, and mental health,⁸ all of which are crucial for maintaining overall health.

Recent research indicates that nearly one-third of elderly Chinese suffer from vitamin D deficiency or insufficiency.⁹ A survey on vitamin D status in mainland China shows that vitamin D deficiency among people aged 80 and above can reach as high as 70% to 90%.¹⁰ One study highlights that inadequate vitamin A intake is a critical public health concern among Chinese adults, affecting 78.9% of men and 74.6% of women.¹¹ Research also indicates that vitamin A deficiency among the elderly in China reached 360.43 per 100,000 persons in 2019.¹² Additionally, vitamin E deficiency is widespread. A review published in 2011 found that vitamin E deficiency ranged from 6% to 70% in children, 27% to 55% among the elderly, and 4% to 70% in mixed age groups in low- to middle-income countries between 1992 and 2009.¹³ Furthermore, numerous studies have shown that vitamin deficiencies are linked to the development of various diseases, such as anaemia, preeclampsia, dental caries, periodontitis, autoimmune diseases, infectious diseases, cardiovascular diseases, fatal cancers, type 2 diabetes, and neurological disorders.¹⁴ In conclusion, fat-soluble vitamins are essential for numerous physiological functions and the maintenance of overall health. Therefore, it is crucial to implement effective nutritional interventions to improve vitamin status and prevent the development of chronic diseases.

Currently, the primary approach to addressing vitamin deficiencies focuses on multivitamin supplements.¹⁵ It is believed that multivitamin supplements significantly increase blood concentrations and improve overall vitamin status.¹⁶ However, studies have revealed that as more individuals consume multivitamins to improve or maintain their health, concerns about the potential harmful effects of multivitamins are rising, with researchers paying close attention to the questions about their long-term safety.¹⁷ Recent epidemiological studies have indicated that taking multivitamins is associated with a higher risk of death.¹⁶ An experimental study reported that while the use of multivitamin supplements alleviated vitamin malnutrition, it is also important to consider the tolerable upper intake levels for populations.¹⁸ Moreover, due to the lack of proper guidance for therapeutic supplementation or public education, people often consume excess vitamins, leading to frequent incidents of vitamin toxicity, such as vitamin D poisoning.¹⁹ Similarly, improper use of vitamin supplements has been shown to result in vitamin A toxicity, as detailed in a recent study.²⁰ Even some adult studies suggest that the use of high doses (> 400 IU/d) of vitamin E supplements may increase all-cause mortality and should be avoided.²¹ Additionally, nutritional education is currently one of the key methods used to address vitamin deficiencies.

Recent evidence indicates that nutrition education on dietary supplements can enhance overall nutritional status, maintain health, increase longevity, and decrease the impact of chronic illness.²² Given these considerations, it is crucial to assess and compare the effectiveness and safety of nutritional education with multivitamin supplements. Therefore, our study hypothesizes that there are differential effects between the use of vitamin supplements and the implementation of health nutrition education.

MATERIALS AND METHODS

Study design and participants

This was a single-center, two-armed, parallel, randomized, double-blind study designed to assess the effectiveness and differential effects of using vitamin supplements compared to implementing health nutrition education on fat-soluble vitamin levels among adults after 4 weeks of nutritional intervention. The study protocol was approved by the Ethics Review Committee of Zhuhai People's Hospital (<https://www.chictr.org.cn> identifier: ChiCTR2100047303). All procedures involving human participants were conducted in accordance with the ethical standards of the institutional research committee and the Helsinki Declaration and its later amendments or comparable ethical standards.

Participants were recruited from Zhuhai People's Hospital between May and August 2021. All participants were free-living individuals residing in the same geographic area to minimize environmental and regional dietary differences. The enrolled volunteers participated in fasting venous blood sampling from May 22 to 25, 2021, for an initial screening assessment of their vitamin nutritional status, with a total of 326 individuals completing the fasting blood sampling and initial screening.

Individuals were excluded if they smoked or consumed alcohol regularly, suffered from any acute or chronic gastrointestinal disorders such as gastric ulcers, gastritis, or esophagitis, or were diagnosed with chronic conditions like diabetes, hypertension, cardiovascular or cerebrovascular diseases. Individuals who had taken medications affecting metabolism, such as drugs for blood pressure, blood sugar, or cholesterol, or who had consumed vitamin dietary supplements within the past month, were also excluded. Additionally, participants who had experienced significant weight changes (over 5 kg) or major alterations in their diet or lifestyle within the previous three months, along with pregnant women, were excluded from the study. Finally, 155 individuals were invited to participate in this randomized controlled trial. These individuals were aged between 18 and 65 years, had a Body Mass Index (BMI) below 28 kg/m², and demonstrated deficiencies in fat-soluble vitamins: blood concentrations

of vitamin A below 297.8 ng/mL, vitamin D below 16.5 ng/mL for males or 17.7 ng/mL for females, and vitamin E below 3.42 µg/mL.

Study procedures

Intervention and sample collection

Participants were randomly assigned to either the nutritional education + multivitamin supplement group (Group 1) or the nutritional education + placebo group (Group 2) in a 1:1 ratio using a computer-generated sequence. Allocation concealment was ensured using opaque, sealed envelopes prepared by an independent coordinator. The allocation sequence remained concealed from both participants and researchers until the completion of baseline data collection and the intervention. The study was designed as a four-week intervention trial, preceded by a one-week lead-in period during which baseline data were collected and participants received health nutrition education. During this phase, researchers distributed nutritional brochures and conducted standardized educational sessions to all participants. These sessions were designed to provide practical guidance on improving participants' intake of vitamin rich foods, such as fatty fish, fortified dairy products, and egg yolks. Participants were encouraged to incorporate these foods into their daily meals with meal planning suggestions and recipe ideas. The sessions also included both theoretical knowledge and actionable advice on making sustainable dietary changes, as detailed in Supplementary Table 1. After obtaining written informed consent, participants were allocated into two groups: the nutritional education + multivitamin supplement group received systematic health nutrition education and a daily multivitamin supplement, while the nutritional education + placebo group received the same health nutrition education but a placebo visually matching the multivitamin supplement. The multivitamin supplement primarily contained 900 µg of vitamin A, 800 IU of vitamin D3, and 15 mg of vitamin E (Supplementary Table 2), with excipients including lactose, microcrystalline cellulose, silicon dioxide, and magnesium stearate. The placebo only contained the excipients (lactose, microcrystalline cellulose, silicon dioxide, and magnesium stearate) without the active vitamins. The composition of the multivitamin supplement used in this study has been clearly stated, and both the safety and efficacy of the supplement have been thoroughly considered during the intervention process to ensure its suitability. Both groups adhered to the double-blind design, ensuring that neither participants nor researchers knew the group assignments. Blinding was maintained by using identical supplements and placebos, with the allocation concealed until after baseline data collection. Throughout the trial, participants were instructed to maintain their usual dietary

habits and avoid other dietary supplements. To monitor compliance, participants were required to log their daily intake and were asked to return any remaining supplements or placebo at the end of the intervention. Compliance was assessed based on the proportion of prescribed supplements taken and daily intake record table for participants. The study drugs, including multivitamins and placebos, were pre-coded and packaged by an independent entity to ensure identical appearance and maintain blinding. Biological sample collection involved drawing approximately 3 mL of peripheral venous blood from fasting participants, which was processed using automated dried blood spot extraction technology for high-throughput analysis. This minimally invasive method allowed for accurate detection of multiple vitamins, such as A, D, and E, thus facilitating a thorough assessment of the intervention's impact. A summary of the study design is shown in Figure 1.

Outcome

The primary outcome of the study was the difference in blood concentrations of fat-soluble vitamins and changes in the deficiency rates of fat-soluble vitamins between the two groups after nutritional intervention. Secondary outcomes included the difference in blood concentrations of fat-soluble vitamins and changes in the deficiency rates of fat-soluble vitamins within each group between baseline and after the nutritional intervention.

Vitamin assessment

To accurately assess the levels of vitamins in the blood, High-Performance Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS; AB Sciex Q-Trap 4500; Applied Biosystems) was used to detect multiple vitamins in dried blood spots. Before and after the intervention trial, all subjects fasted in the morning and provided approximately 3 mL of peripheral venous blood. Blood samples were accurately pipetted onto two spots on dried blood spot cards at 20 μ L per spot. Once dried, the cards were sealed in aluminium foil bags and stored at -80°C. The preparation of dried blood spot cards was performed in a laboratory biosafety cabinet.

Statistical analyses

Sample size calculations were performed based on an expected common standard deviation of 13.9 ng/mL for vitamin D, a target improvement of 7.2 ng/mL, a significance level of 0.05, and 90% power. The required sample size was calculated to be approximately 82 participants

per group. Considering potential attrition, a total of 164 participants were enrolled in the study (Figure 1). The sample size (n) was estimated using the formula

$$n = [2(Z_{1-\alpha/2} + Z_{1-\beta})^2 \sigma^2] / \delta^2$$

with $\sigma = 13.9$, $\delta = 7.2$, $\alpha = 0.05$, and power = 90%.

Continuous variables with normal distributions are presented as means $\pm$ standard deviations (SD), while non-normally distributed variables are presented as medians with interquartile ranges (IQR). Categorical variables are expressed as frequencies and percentages. Shapiro-Wilk test was used to assess the normality of the data distribution. The Chi-square test was used to compare categorical variables between the two groups. For continuous variables, within-group comparisons (pre- and post-intervention) were performed using paired-sample t-tests or Wilcoxon signed-rank tests depending on data distribution. Based on the study design, participants were assessed at two time points (baseline and after the 4-week intervention). Within-group comparisons were conducted using paired-sample t-tests or Wilcoxon signed-rank tests, depending on data distribution. To compare the two groups while adjusting for baseline differences, we applied a Repeated Measures Analysis of Variance (RM-ANOVA). This model evaluated three effects: (1) time effect (pre- to post-intervention change across all participants), (2) group effect (Group 1 vs. Group 2), and (3) time $\times$ group interaction effect (difference in changes over time between groups). This analytical approach allowed us to assess whether the observed changes in fat-soluble vitamin levels were significantly different between the intervention and control groups, while controlling for baseline variability. The significance level was set at $p < 0.05$. Data were analyzed using Statistical Package for Social Sciences (SPSS) software v.27.

RESULTS

Characteristic of the study participants

Only one individual in Group 1 declined to participate in the study, resulting in a total of 155 individuals completing the trial: nutritional education + multivitamin supplement ($n = 77$) and nutritional education + placebo ($n = 78$) (Figure 1). The characteristics of all participants are summarized in Table 1. In Group 1, the mean (SD) age was 32.12 (8.73) years, with 61 (79.22%) female participants, most of whom were Han and employed. Similarly, in Group 2, the mean (SD) age was 30.91 (7.49) years, with 61 (78.21%) female participants, most of whom were Han and employed. There were no significant differences between the groups in terms of sex, age, height, weight, BMI, ethnicity, and educational level.

Comparisons of vitamin concentrations and deficiency rates between group 1 and group 2 at baseline

We assessed the blood concentrations of vitamins A, D, and E, and included participants with a deficiency in any one of these vitamins for the next stage of the study. In Group 1, the baseline concentrations of vitamins A, D, and E were 284.80 (240.50-346.30) µg/dL, 21.39 (15.55-28.30) ng/mL, and 3.32 (2.78-4.02) mg/dL, respectively. In Group 2, the baseline concentrations of vitamins A, D, and E were 281.55 (234.35-352.08) µg/dL, 22.69 (14.88-31.46) ng/mL, and 3.52 (2.77-4.25) mg/dL, respectively. There were no significant differences in the concentrations of the three vitamins between the two groups (all $p > 0.05$). In Group 1, the deficiency rates for vitamins A, D, and E were 57.14%, 35.06%, and 53.25%, respectively. In Group 2, the deficiency rates for vitamins A, D, and E were 55.13%, 34.62%, and 46.15%, respectively. Similarly, there were no significant differences in the deficiency rates of the three vitamins between the two groups (all $p > 0.05$) at baseline. All results are shown in Table 2.

Comparisons of Vitamin A, D, and E concentrations within groups before and after the intervention

The blood concentrations of the three vitamins significantly improved within both groups after either the nutritional education + multivitamin supplement intervention or the nutritional education alone intervention, as shown in Figure 2. In Group 1, the concentration of vitamin A increased from 284.80 (240.50-346.30) µg/dL to 374.10 (325.35-444.80) µg/dL ($p < 0.001$) (Figure 2a). In Group 2, the concentration of vitamin A increased from 281.55 (234.35-352.08) µg/dL to 345.90 (310.48-423.33) µg/dL ($p < 0.001$) (Figure 2b). In Group 1, the concentration of vitamin D increased from 21.39 (15.55-28.30) ng/mL to 30.90 (25.30-40.25) ng/mL ($p < 0.001$) (Figure 2a). In Group 2, the concentrations of vitamin D increased from 22.69 (14.88-31.46) ng/mL to 27.30 (21.88-37.91) ng/mL ($p < 0.001$) (Figure 2b). In the case of vitamin E, the concentrations increased from 3.32 (2.78-4.02) mg/dL to 3.96 (3.56-4.76) mg/dL in Group 1 ($p < 0.001$) (Figure 2a) and from 3.52 (2.77-4.25) mg/dL to 4.07 (3.65-4.72) mg/dL in Group 2 ($p < 0.001$) (Figure 2b).

Simultaneously, the deficiency rates of the three vitamins significantly decreased in both groups after the intervention, as shown in Figures 2c and 2d. The deficiency rate of vitamin A significantly decreased from 57.14% to 7.79% in Group 1 ($p < 0.001$), and from 55.13% to 15.38% in Group 2 ($p < 0.001$). The deficiency rate of vitamin D significantly decreased from 35.06% to 0% in Group 1 ($p < 0.001$), and from 34.62% to 3.84% in Group 2 ($p < 0.001$). For

vitamin E, the deficiency rate significantly decreased from 53.25% to 6.49% in Group 1 ($p < 0.001$), and from 46.15% to 1.28% in Group 2 ($p < 0.001$). The detailed results are shown in Figure 2 and Table 3.

Comparisons of vitamin concentrations, the change levels, and deficiency rates between Group 1 and Group 2 after the intervention

Finally, we compared the effectiveness of the two interventions using different statistical methods for concentration and deficiency rate, as shown in Table 3. After the 4-week intervention, repeated measures ANOVA showed no significant differences in the concentrations of vitamins A, D, and E between the two groups (all p (Group) > 0.05), as shown in Table 3. The p (Time) for within-group changes was significant (all p (Time) < 0.001), indicating that the concentrations of all vitamins significantly increased within each group. Furthermore, the p (Time $\times$ Group) for the interaction between time and group was not significant (all p (Time $\times$ Group) > 0.05), suggesting no significant differences in the time-by-group interaction effects. For deficiency rates, we used Chi-square tests and found no significant differences in the deficiency rates of vitamins A, D, and E between the two groups (all $p > 0.05$), as shown in Table 3. Additionally, there were no significant differences, in the change levels between the two groups ($p > 0.05$, showed in Supplementary Table 3).

DISCUSSION

In this randomized clinical trial, our investigation revealed that both nutritional education and multivitamin supplementation effectively improved the concentrations of vitamins A, D, and E and reduced their deficiency rates among adults. However, there were no statistically significant differences in the efficacy between the two interventions. This suggests that, while both methods are beneficial, combining multivitamin supplements with nutritional education does not provide a significant advantage over nutritional education alone.

Similar to our study, previous research has indicated the effectiveness of both multivitamin supplementation and nutritional education in improving vitamin status. A recent open-label RCT found that eight weeks of vitamin D supplementation significantly increased serum vitamin D concentrations and improved vitamin D status.²³ A meta-analysis of RCTs also indicated that supplementation with vitamin D3 had a significant and positive effect on raising serum 25(OH)D concentrations.²⁴ Multivitamin supplementation is more commonly used for specific populations to improve vitamin or disease status, such as pregnant women, depressed patients, and adults living with HIV. Current studies have reported a significant

suppressive effect of vitamin supplementation in depressed patients compared with the control group,²⁵ and multivitamin supplementation has been found to improve vitamin status and immune function in adults living with HIV.²⁶

Moreover, our findings highlight the significant role of nutrition education in improving nutritional status. A recent study reported a significant increase in vitamin D levels following a nutrition education course, demonstrating the positive effect of education on vitamin D status.²⁷ An RCT highlighted the significant positive impact of nutrition education on women's health, particularly in preconception vitamin intake, compared to a control group.²⁸ Even in specific populations, such as pregnant women, nutrition education has been proven effective in improving nutritional status.²⁹ Additionally, the importance of nutrition education in the prevention and management of common chronic conditions, such as hypertension, cardiovascular disease, and diabetes, is well documented.³⁰ This further underscores the potential of nutrition education as a primary strategy for enhancing vitamin levels and addressing nutritional deficiencies.

However, numerous studies suggest that the use of fat-soluble vitamin supplements may involve potential risks. A significant review based on the latest evidence report and recommendation statement from the U.S. Preventive Services Task Force (USPSTF) emphasized that vitamin and mineral supplements offer little benefit in preventing cancer, cardiovascular disease, and mortality, and excessive intake of certain vitamins might even increase cancer risk.³¹ Some RCTs have shown that multivitamins provide no significant benefits for health,³² and may even pose risks, such as increased total mortality.³³ Even a study conducted in the U.S. demonstrated that supplemental vitamin D3 did not result in a significantly lower risk of fractures than placebo.³⁴ These findings suggest that, under general circumstances, adopting safer and more effective strategies, such as health nutrition education, might be preferable for improving vitamin nutritional status.

At present, no study has directly compared the efficacy of multivitamin supplementation with nutritional education in improving vitamin nutritional status. To our knowledge, this is the first double-blind RCT to compare the combined effects of nutrition education and multivitamin supplementation with nutrition education alone on fat-soluble vitamin deficiencies in adults.

This study also has several limitations. First, although both groups showed significant improvements in vitamin concentrations, the four-week intervention period may have been too short to detect any additional benefits of supplementation beyond those achieved with nutrition education. Second, focusing on a relatively healthy population with specific vitamin

deficiencies might limit the generalizability of our findings to other groups or those with different nutritional needs. Additionally, while the double-blind design helped reduce bias, the placebo effect could not be entirely excluded. Future research should involve a longer follow-up period and a broader participant pool to enhance the applicability and reliability of the findings.

Conclusion

Our study provided data support from China and highlighted the importance of dietary interventions and personalized nutrition approaches to address vitamin deficiencies, rather than relying solely on supplements. Multivitamin supplements are not superior to nutrition education, nutrition education alone could be a safer and effective approach to improve vitamin A, D, and E deficiencies and could reduce the risks associated with unnecessary vitamin supplement use in the general population. It is crucial to develop safer, more effective, and tailored nutritional strategies to promote optimal health and prevent nutrient deficiencies.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

This research was supported by the Medical Science and Technology Research Foundation of Guangdong Province (B2023227) and the Xiangshan Talented Scientific Research Project of Zhuhai People's Hospital (2021XSYC-03).

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Table 1. Baseline characteristics of participants

	Group 1 [†] (n = 77)	Group 2 [†] (n = 78)	p
Age (years), mean ± SD	32.12 ± 8.73	30.91 ± 7.49	0.357 [§]
Sex (%)			
Male	16 (20.78)	17 (21.79)	0.877 [‡]
Female	61 (79.22)	61 (78.21)	
Height (m), mean ± SD	1.63 ± 0.07	1.64 ± 0.07	0.445 [§]
Weight (kg), mean ± SD	55.87 ± 8.83	55.81 ± 8.78	0.965 [§]
BMI (kg/m ²), mean ± SD	21.02 ± 2.39	20.77 ± 2.30	0.505 [§]
Ethnicity (%)			
Han	73 (94.81)	73 (93.59)	0.746 [‡]
Other	4 (5.19)	5 (6.41)	
Employment status (%)			
Employed	75 (97.40)	67 (85.90)	0.034 [‡]
Retired	0 (0)	1 (1.28)	
Unemployed	2 (2.60)	10 (12.82)	
Educational level (%)			
Primary school or below	3 (3.90)	2 (2.56)	0.805 [‡]
Junior high school	2 (2.60)	3 (3.85)	
High school	46 (59.74)	51 (65.38)	
College university or above	26 (33.77)	22 (28.21)	
Exercise (%)			
Yes	49 (63.64)	35 (44.87)	0.019 [‡]
No	28 (36.36)	43 (55.13)	

BMI, body mass index; SD, standard deviation

[†]Group 1, nutritional education + multivitamin supplement group; Group 2, nutritional education + placebo group.

[‡]The p value of Chi-square test.

[§]The p value of Student t-test.

Table 2. Comparisons of vitamin concentrations and deficiency rates between the two groups at baseline

		Group 1 [†] (n = 77)	Group 2 [†] (n = 78)	p
Vitamin A	median (IQR)	284.80 (240.50-346.30)	281.55 (234.35-352.08)	0.334
(ug/dL)	deficiency n (%)	44 (57.14)	43 (55.13)	0.800
Vitamin D	median (IQR)	21.39 (15.55-28.30)	22.69 (14.88-31.46)	0.381
(ng/mL)	deficiency n (%)	27 (35.06)	27 (34.62)	0.953
Vitamin E	median (IQR)	3.32 (2.78-4.02)	3.52 (2.77-4.25)	0.348
(mg/dL)	deficiency n (%)	41 (53.25)	36 (46.15)	0.377

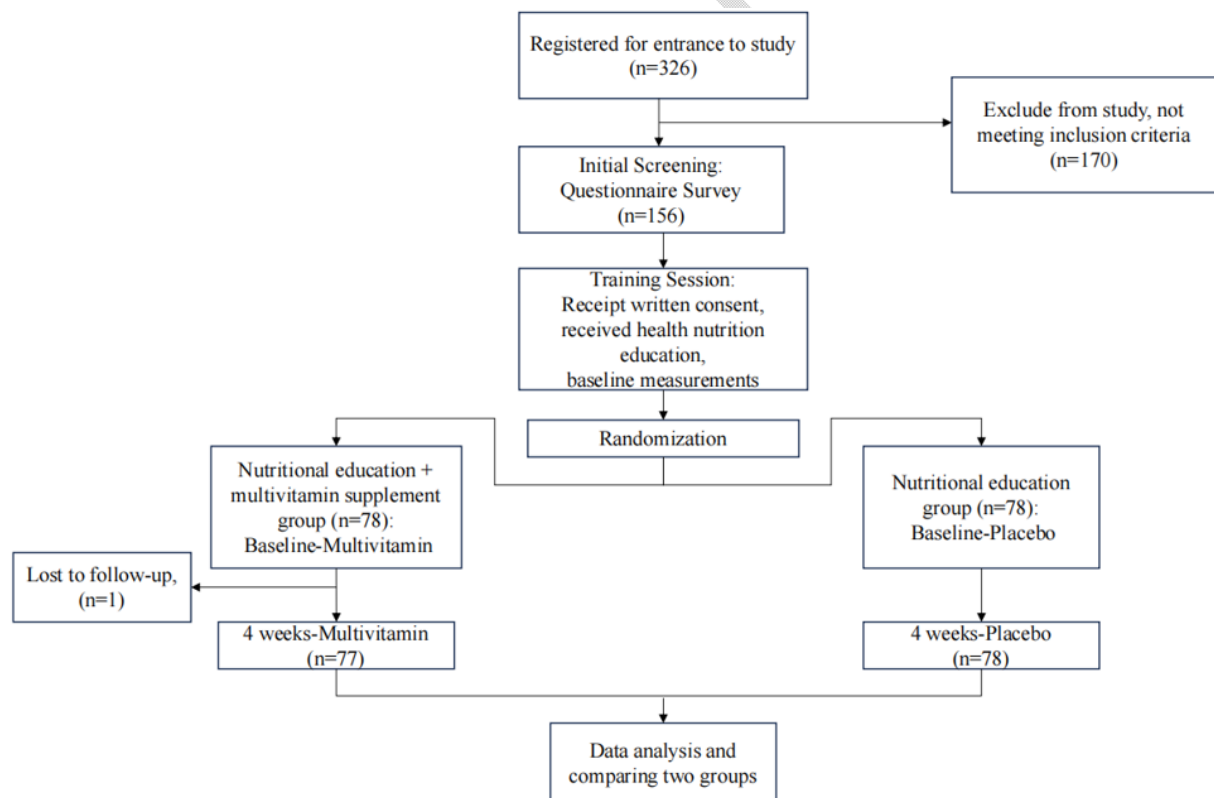
IQR, interquartile range.

[†]Group 1, nutritional education + multivitamin supplement group; Group 2, nutritional education + placebo group.

Table 3. Comparison of vitamin concentrations and deficiency rates between the two groups after the intervention

	Group 1 [†] (n = 77)	Group 2 [†] (n = 78)	<i>p</i> [‡]	<i>p</i> (Time) [§]	<i>p</i> (Group) [¶]	<i>p</i> (Time × Group) ^{††}
Vitamin A (ug/dL)						
Median (IQR)	374.10 (325.35-444.80)	345.90 (310.48-423.33)		< 0.001	0.106	0.415
Deficiency n (%)	6 (7.79)	12 (15.38)	0.140			
Vitamin D (ng/mL)						
Median (IQR)	30.90 (25.30-40.25)	27.30 (21.88-37.91)		< 0.001	0.738	0.482
Deficiency n (%)	0 (0)	3 (3.85)	0.248			
Vitamin E (mg/dL)						
Median (IQR)	3.96 (3.56-4.76)	4.07 (3.65-4.72)		< 0.001	0.700	0.483
Deficiency n (%)	5 (6.49)	1 (1.28)	0.206			

IQR, interquartile range.

[†]Group 1, nutritional education + multivitamin supplement group; Group 2, nutritional education + placebo group.[‡]*p*: From Chi-square test comparing deficiency rates between groups.[§]*p* (Time): *p*-value for time effect (within-group comparison across time points).[¶]*p* (Group): *p*-value for the main effect of group (between-group comparison).^{††}*p* (Time × Group): *p*-value for interaction between time and group.**Figure 1.** Summary of study design. A flowchart summarizing the study design and participant flow. Initially, 326 participants were registered, with 170 excluded for not meeting inclusion criteria. The remaining 156 participants experienced a questionnaire survey and a training session, where written consent was obtained and baseline measurements were taken. Participants were then randomized into two groups: the nutritional education + multivitamin supplement group (Group 1, n=78) and the nutritional education group (Group 2, n=78). One participant from Group 1 was lost to follow-up. Data analysis was performed to compare the outcomes between the two groups

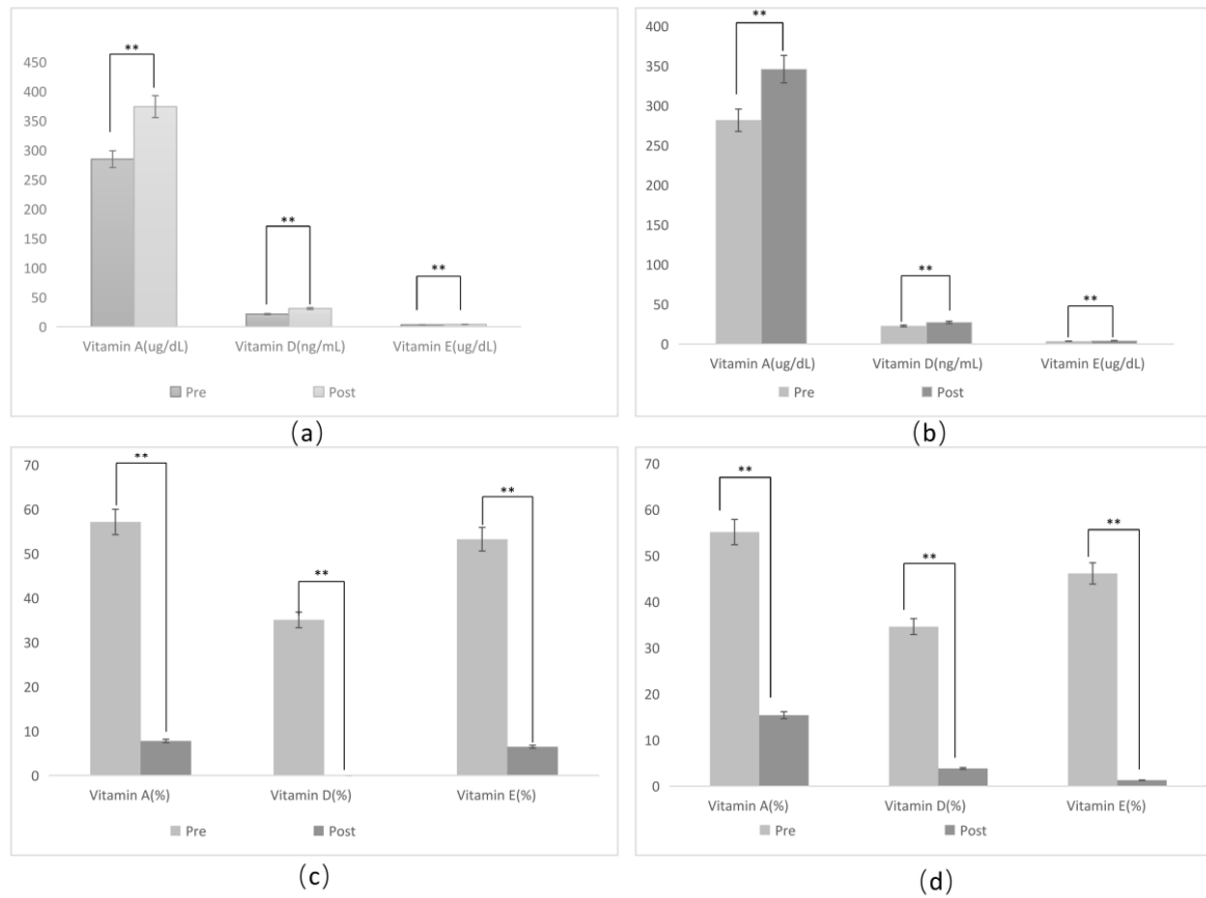


Figure 2. Comparisons of Vitamin A, D, and E concentrations and deficiency rates before and after intervention. (a) Vitamin A, D, and E concentrations in Group 1. (b) Vitamin A, D, and E concentrations in Group 2. (c) Deficiency rates of Vitamin A, D, and E in Group 1. (d) Deficiency rates of Vitamin A, D, and E in Group 2. Data are presented as mean $\pm$ standard error. Significant differences between pre- and post-intervention values are indicated by asterisks ($p < 0.001$). Vitamin concentrations were measured in $\mu\text{g/dL}$ for Vitamin A, ng/mL for Vitamin D, and $\mu\text{g/dL}$ for Vitamin E, while deficiency rates are presented as percentages. Pre- and post-intervention data reflect changes in the blood concentrations and deficiency rates following nutritional education and supplementation.