Insufficient consumption of micronutrients and common mental disorders in Brazilian adolescents

ABSTRACT
The study aimed to estimate the association of insufficient consumption of vitamins A, C, E, B\textsubscript{12} and zinc on the pathogenesis of Common Mental Disorders (CMD) in Brazilian adolescents who participated in the Estudo de Riscos Cardiovasculares em Adolescentes - ERICA (Study of Cardiovascular Risks in Adolescents) from February 2013 to November 2014. The sample corresponded to the number of students (71,971) who answered the the 24-hour dietary recall and the questionnaire that addressed mental health. Pearson’s chi-square test and multivariate logistic regression analysis were performed between the CMD variable and insufficient micronutrient consumption, adjusting for sex, type of school and age group variables. The level of significance adopted was \( p<0.05 \). Associations between the existence of CMD and insufficient consumption of Vitamin B12 and zinc were significant. Zinc, when consumed in small quantities, was the element that most influenced the CMD variable. Therefore, it was found that insufficient consumption of Vitamin B12 and zinc influences the presence of CMD in adolescents.

Keywords: Adolescent; Cross-Sectional Studies; Mental disorders; Micronutrients; Zinc deficiency.

RESUMEN
El objetivo de este estudio fue estimar la asociación del consumo insuficiente de vitaminas A, C, E, B\textsubscript{12} y zinc en la patogénesis de los trastornos mentales comunes (TMC) en adolescentes brasileños que participaron en el Estudio de Riesgos...
Cardiovasculares en Adolescentes (ERICA), en el período de febrero de 2013 a noviembre de 2014. La muestra correspondió al número de estudiantes (71,971) que respondieron una encuesta de alimentación recordatorio de 24 horas y un cuestionario que abordaba aspectos de la salud mental. La prueba de chi-cuadrado y el análisis de regresión logística multivariada se aplicaron entre la variable TMC y el consumo insuficiente de micronutrientes, ajustando por sexo, tipo de escuela y grupo de edad. El nivel de significación aceptado fue del p<0.05. Las asociaciones entre la existencia de TMC y el consumo insuficiente de vitamina B12 y zinc fueron significativas. El zinc, cuando se consume en pequeñas cantidades, fue el elemento que más influyó en la variable TMC. Por lo tanto, se encontró que el consumo insuficiente de vitamina B12 y zinc influye en la presencia de TMC en adolescentes.

**INTRODUCTION**

Mental disorders can affect anyone and at any age. There are several types, with different presentations, which are generally understood by a combination of thoughts, perceptions, emotions and abnormal behaviors, which can interfere in relationships with people.

Common Mental Disorders (CMD) refer to a set of non-psychotic symptoms such as insomnia, fatigue, irritability, forgetfulness, difficulty concentrating and somatic complaints, which designate situations of mental suffering. Globally, CMDs include anxiety and depression.

CMDs represent major health problems and are responsible for 16% of the global burden of illness and injury in people aged 10 to 19 years. Half of the cases do not appear until the age of 14, but the majority are not detected or treated.

Anxiety and depression are affected by several genetic, hormonal, immunological, biochemical, neurodegenerative and nutritional factors. More and more research shows the relationship between diet quality and mental disorders. Deficiencies of B complex vitamins, minerals, amino acids and other nutrients are often seen in patients with CMD.

Found in relatively high concentrations in the limbic system, zinc has many neurological implications that extend throughout life, which has been observed from brain growth in childhood to the development of neurodegenerative diseases.

B complex vitamins play an important role in the metabolic pathway involved in the synthesis processes of neurotransmitters in the central nervous system, in addition to participating in the metabolism of homocysteine. Those in high concentrations significantly increase oxidation by free radicals.

Thus, the decrease in the synthesis of neurotransmitters, the increase in the concentration of homocysteine and/or the deleterious effects caused by oxidative stress can be prevented by antioxidants such as vitamins A, C, E, B12 and zinc.

Based on these considerations, this investigation aimed to estimate the association of insufficient consumption of vitamins A, C, E, B12 and zinc on the pathogenesis of CMDs in Brazilian adolescents.

**MATERIALS AND METHODS**

**Study characterization**

We conducted a cross-sectional study with data from the Estudo de Riscos Cardiovasculares em Adolescentes - ERICA (Study of Cardiovascular Risks in Adolescents), a multicenter, nationwide survey carried out with adolescents aged 12 to 17, from elementary or high school, from public and private schools, between February 2013 and November 2014.

**Population of interest and sample**

The ERICA population was stratified into 32 geographic strata, with 27 capitals and five groups with the other municipalities in each macro-region. Schools from 124 municipalities were selected, corresponding to a total of 3,753 classes, in 1,247 schools.

Of the 102,327 eligible adolescents registered in the selected schools, 71,971 (70.3%) participated in this investigation, who answered the 24-hour dietary recall (R24h) and the questionnaire regarding mental health. Adolescents who did not belong to the age group of interest, pregnant adolescents and those who were unable to answer the questionnaires because they were mentally disabled were excluded from the analysis.

**Data collection**

Data were collected using a self-administered questionnaire. For the present study, the following variables were explored: sex, age, type of school, CMD and intake of the following micronutrients: vitamins A, C, E, B12 and zinc. The age variable was used categorically, considering two groups: 12-14 years and 15-17 years.

To assess CMD, the General Health Questionnaire, 12 item version, was used. The scores of the individual items present in the questionnaire were coded as “absent” or “present” (0 or 1, respectively) and then added together; adolescents with a score of three or more were classified as cases of CMD. Food intake was estimated by applying a R24h. Specific software was used to enter food consumption data and the interview technique applied was the multiple-pass method, which aims to reduce the underreport of food consumption. Nutrient intake data did not include consumption of supplements or medications.

**Statistical analysis**

The prevalence of inadequate consumption of micronutrients (vitamins A, C, E, B12 and zinc) was based on R24h data and estimated as the proportion of adolescents with intake below the estimated average need, using the Estimated Average Requirement - EAR method, as recommended by the Institute of Medicine. For the calculation of inadequacy,
the sample weight and the complexity of the sample design were considered, using the Balanced Repeated Replication technique with Fay modification. The intra-individual variability was corrected according to the method proposed by the National Cancer Institute (NCI)\textsuperscript{16}.

Data analysis was performed using the Stata\textsuperscript{®} software (Statacorp, College Station, Texas, USA), version 12.0, using the survey module, considering complex sample data analysis. The Pearson chi-square test was used to assess the existence of an association between the variables of insufficient consumption of vitamins A, C, E, B\textsubscript{12} and zinc with sex, type of school and age group. The Odds Ratio (OR) was calculated, with a 95\% confidence interval (CI), estimated by the logistic regression model, to measure the strength of association between the variables. Crude OR’s were estimated and adjusted for sex, type of school and age group. Multivariate logistic regression analysis was performed between the dependent variable (CMD) and insufficient micronutrient consumption (crude model) and then adjusted for sex, type of school and age group variables (adjusted model). The variables that showed statistical significance in the crude and adjusted models made up the final model. The level of significance adopted was 5%.

**Ethical aspects**

The ERICA was approved by the Research Ethics Committee of the Institute of Studies in Collective Health, from the Federal University of Rio de Janeiro (Opinion n° 01/2009; Process 45/2008) and by the Research Ethics Committees of each 27 participating institutions, one in each unit of the Brazilian federation. The adolescents who agreed to participate and whose parents signed the informed consent form participated in the study.

**RESULTS**

The results show: CMD associations with sex, type of school and age group; associations of insufficient consumption of micronutrients in relation to sex, type of school, age group and CMD; and a multiple logistic regression model, which estimates which micronutrients contribute to the presence of CMD, when consumed insufficiently.

Mental disorders were more prevalent in female adolescents, from public schools and aged 15 to 17 years. Significant associations were found between CMD, sex and age group (Table 1).

High prevalence of insufficient nutrient consumption was observed, which was significantly associated with sex, with the exception of Vitamin C. The highest percentages of inadequate consumption of Vitamins E, B\textsubscript{12} and zinc occurred among females (Table 2).

Public school students had higher percentages of insufficient consumption of Vitamins A, C and B\textsubscript{12} compared with private school students. Associations of these nutrients with the type of school variable were significant (p<0.001). However, although the association has not been shown significant for vitamin E and zinc, attention is paid to the high percentages of insufficient consumption of these elements in public and private schools, table 2.

Older adolescents had higher percentages of insufficient consumption of micronutrients, except zinc. Significant differences were observed in relation to the low consumption of Vitamin E and B\textsubscript{12} and age group (Table 2).

Significant associations between CMD and insufficient consumption of Vitamin A, B\textsubscript{12} and zinc were observed (Table 3).

| Table 1. Common Mental Disorders according to sex, type of school and age group. ERICA, Brazil, 2013-2014. |
| Variables | CMD |
|-----------|-----|
|           | Yes (%) | No (%) | p - value |
| Sex       |       |       |           |
| Female    | 64.0  | 43.7  | <0.001*   |
| Male      | 36.0  | 56.3  |           |
| Type of school |       |       |           |
| Public    | 82.7  | 82.6  | 0.870     |
| Private   | 17.3  | 17.4  |           |
| Age group |       |       |           |
| 12 to 14  | 46.9  | 55.2  | <0.001*   |
| 15 to 17  | 53.1  | 44.8  |           |

CMD: Common Mental Disorders; * Pearson chi-square test: p<0.05.
Using univariate logistic regression (Table 3), the data showed that, in a crude model, students with insufficient consumption of vitamin B$_{12}$ and zinc had higher chances of CMD, when compared to those who consumed a sufficient amount (Vitamin B$_{12}$: crude OR: 1.09; CI: 1.01-1.19 and Zinc: crude OR: 1.17; CI: 1.10 -1.27). In contrast, adolescents with insufficient consumption of vitamin A were less likely to have CMD (crude OR: 0.79; CI: 0.69-0.91).

In an adjusted model, vitamin B$_{12}$ and zinc lost their significance in the association, while vitamin A maintained the previously observed relationship (Table 3).

Analyzing the statistical data of multiple logistic regression (Table 4), it was possible to observe that the insufficient consumption of vitamin A and zinc were the ones that most influenced the CMD variable.

In a crude model, consumers with an insufficient amount of food sources of zinc had higher chances of CMD (OR: 1.18; 95% CI: 1.06-1.33; p-value: 0.004), while consumers with an insufficient amount of vitamin A were less likely (OR: 0.76; 95% CI: 0.68-0.86).

When the model was adjusted by sex, type of school and age group, insufficient consumption of vitamin A maintained the relation of the crude model while zinc lost its significance. In addition, it was observed that women and those aged between 15 and 17 years were more likely to have CMD.

In the analysis of the final model, it was observed that insufficient consumption of zinc returned to have significance in the association with CMD, being the element that, when consumed in small quantities, most influenced the existence of CMD.

Table 2. Consumption of micronutrients by adolescents participating in ERICA, according to sex, type of school and age group. ERICA, Brazil, 2013-2014.

| Insufficient micronutrient consumption | Sex | p-value | Type of school | p-value | Age group | p-value |
|--------------------------------------|-----|---------|----------------|---------|-----------|---------|
| | Male | Female | | Pub | Priv | 12 to 14 | 15 to 17 |
| Vitamin A | | | | | | | |
| Yes | 92.4 | 90.2 | <0.001* | 91.9 | 8.3 | <0.001* | 90.9 | 91.8 | 0.040* |
| No | 7.6 | 9.8 | | 8.1 | 11.7 | | 9.1 | 8.2 | |
| Vitamin C | | | | | | | |
| Yes | 53.8 | 53.5 | 0.806 | 55.5 | 44.7 | <0.001* | 52.6 | 54.7 | 0.130 |
| No | 46.2 | 46.5 | | 44.5 | 55.3 | | 47.4 | 45.3 | |
| Vitamin E | | | | | | | |
| Yes | 96.6 | 97.6 | <0.001* | 97.1 | 97.1 | 0.937 | 96.5 | 97.8 | <0.001* |
| No | 3.4 | 2.4 | | 2.9 | 2.9 | | 3.5 | 2.2 | |
| Vitamin B$_{12}$ | | | | | | | |
| Yes | 23.6 | 28.5 | <0.001* | 27.2 | 20.3 | <0.001* | 24.7 | 27.5 | <0.001* |
| No | 76.4 | 71.5 | | 72.8 | 79.7 | | 75.3 | 72.5 | |
| Zinc | | | | | | | |
| Yes | 22.2 | 69.9 | <0.001* | 73.8 | 74.0 | 0.880 | 74.1 | 73.9 | 0.699 |
| No | 77.8 | 30.1 | | 26.2 | 26.0 | | 25.9 | 26.1 | |

Pub: public; Priv: private. *The Pearson chi-square test: p<0.05.
Table 3. Association between insufficient consumption of micronutrients and Common Mental Disorders. ERICA, Brazil, 2013-2014.

| Insufficient micronutrients consumption (IMC) | IMC distribution in the total sample (%) | Prevalence of CMD according to IMC(%) | p-value \( \chi^2 \) | Crude OR | 95% CI | Adjust. OR | 95% CI |
|---------------------------------------------|------------------------------------------|--------------------------------------|-----------------|-----------|---------|-----------|---------|
| Vitamin A                                  | 91.3                                     | 29.4                                 | <0.001*         | 0.70      | 0.69 – 0.91 | 0.82      | 0.70 – 0.96 |
| Vitamin C                                  | 53.6                                     | 30.0                                 | 0.666           | 1.01      | 0.94 – 1.09 | 1.01      | 0.94 – 1.09 |
| Vitamin E                                  | 97.1                                     | 29.8                                 | 0.533           | 0.92      | 0.72 – 1.19 | 0.81      | 0.63 – 1.06 |
| Vitamin B\(_{12}\)                         | 26.0                                     | 31.3                                 | 0.044*          | 1.09      | 1.01 -1.19  | 1.03      | 0.94 – 1.12 |
| Zinc                                        | 26.1                                     | 32.4                                 | <0.001*         | 1.17      | 1.10 – 1.27 | 1.08      | 0.99 – 1.18 |

IMC: Insufficient micronutrients consumption; CMD: Common Mental Disorders; Crude OR: Crude Odds ratio; Adjusted OR: Odds ratio adjusted by sex, type of school and age group; Univariate logistic regression model. CI: Confidence interval.

Table 4. Modeling the association of insufficient micronutrient consumption with Common Mental Disorders. ERICA, Brazil, 2013-2014.

| Insufficient consumption | Crude model OR | p-value | Adjusted model OR | p-value | Final model OR | 95% CI | p-value |
|--------------------------|----------------|---------|--------------------|---------|----------------|--------|---------|
| Vitamin A                | 0.76           | 0.68 – 0.86 | <0.001*           | 0.82    | 0.71 – 0.95   | 0.007  | 0.80    | 0.69 – 0.94 | 0.007* |
| Vitamin C                | 1.01           | 0.93 – 1.08 | 0.852             | 1.01    | 0.94 – 1.10   | 0.723  |         |         |
| Vitamin E                | 0.95           | 0.74 – 1.20 | 0.660             | 0.84    | 0.66 – 1.07   | 0.155  |         |         |
| Vitamin B\(_{12}\)      | 1.02           | 0.91 – 1.15 | 0.673             | 0.99    | 0.88 – 1.12   | 0.942  |         |         |
| Zinc                     | 1.18           | 1.06 – 1.33 | 0.004*            | 1.11    | 0.98 – 1.24   | 0.089  | 1.10    | 1.01 – 1.20 | 0.027* |

Sex
- Female
- Type of school
  - Private
- Age group
  - 15 to 17

OR: Odds ratio; CI: Confidence interval; *Multivariate logistic regression.
DISCUSSION
Associations found between micronutrient intake and CMD have been, in general, derived from investigations carried out in adults or the elderly. This is the first study developed, based on ERICA, which analyzed data on mental morbidity in adolescents and its relationship with insufficient consumption of micronutrients.

Inadequate eating habits may reflect insufficient consumption of micronutrients, which, in turn, can trigger several metabolic changes that can result in various pathologies, including psychopathies6.

Population-based review studies conducted in different parts of the world show that approximately one-third of adolescents experience some CMD throughout their lives. These studies point to higher prevalence of CMD among girls, while boys have higher rates of behavioral and conduct mental disorders varying with the degree of income and development of countries17,18,19.

Anxiety and depression are the most common psychiatric disorders induced by increased oxidative stress and damage to brain cells. Non-enzymatic antioxidants, such as vitamins E (alphatocopherol), C (ascorbic acid), β-carotene, zinc, among others, minimize the production of free radicals that damage cells and, thus, to combat excessive oxidation, in addition to the antioxidant defense in the biological system20,21. Studies associate CMD with reduced concentrations of antioxidant compounds and suggest that supplementation of these elements may be useful as adjunctive therapy in patients with stress-induced mental disorders, as they suppress neuroinflammation and oxidative stress20,22,23.

The result obtained in the present investigation, regarding the association of vitamin A and CMD, was different to what has been reported in the literature20,21,22,23. Methodological differences may justify this finding, such as: instruments and methods used to determine food consumption and mental disorders, age group of the participants, sample and statistical analysis. On the other hand, our results that report the positive association between insufficient consumption of Vitamin B12, zinc and CMD in adolescents, are concordant with research carried out in children, adults and the elderly in different countries24,25,26.

Vitamin B12 is a methyl donor in many methylation reactions in the brain. According to the hypomethylation hypothesis, it is essential for the transmethylation of neuroactive substances such as myelin and monoamine neurotransmitters. Thus, the lack of synthesis and/or changes in the cobalamin-dependent metabolic cycle has been implicated as pathogenic mechanisms in central nervous system disorders, associated with depression, bipolar disorder, panic disorder psychosis and phobias27,28,29,30.

Recent studies emphasize the possible role of zinc in neurotransmitter systems, particularly serotonergic and glutamatergic systems, as well as in antioxidant mechanisms, neurotrophic factors and neuronal precursor cells. Thus, zinc deprivation influences cerebral zinc homeostasis leading to psychiatric symptoms, including, in addition to depression, impaired cognition and learning difficulties31,32,33,34.

Some investigations corroborate the inverse relationships between dietary zinc intake and depression in female individuals found in the present study35,36.

A new study, conducted at the University of California, points out that females are almost twice as chances to develop depression. The researchers found that women who had received small doses of endotoxins (substances that promote controlled brain inflammation) had a reduction in the activity of a set of structures that promote the sensation of pleasure and that, in depression, is inhibited. The same did not happen with the men who took the endotoxins and with the entire placebo group36.

Finally, although this study used validated instruments for diagnosing CMD and food intake, limitations should be considered, namely: other variables that may influence the mental health of individuals such as body mass index, activity physical practice, alcohol and drug use, medications and hours of sleep were not included in our models. The adjustments used in the statistical analyses were different from other studies- some adjusted for BMI, physical activity, energy, while others did not; and the methods of assessing CMD were different from other original studies, which were based on rating scales.

In conclusion, the present investigation showed that insufficient consumption of Vitamin B12, zinc and CMD were different from other original studies, which were based on rating scales. Furthermore, carrying out prospective and controlled studies would be important to obtain a more precise interpretation of the relationship between micronutrient consumption and CMD in this population subgroup.

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