

## SUPLEMENTAÇÃO COM MICRONUTRIENTES: QUANDO, QUANTO E PARA QUEM?

VII Jornada de Atualização Técnica de Fiscais do Sistema CFN-CRN (26-28/11/2019)



Silvia M Franciscato Cozzolino smfcozzo@usp.br FCF-USP

### Sumário

- ◆ Introdução
- ◆ Saúde e Doença
- Recomendações Dieteticas
- ◆ Suplementos? Quando? Para quem?
- ◆ Estudos Científicos
- **♦** Conclusões

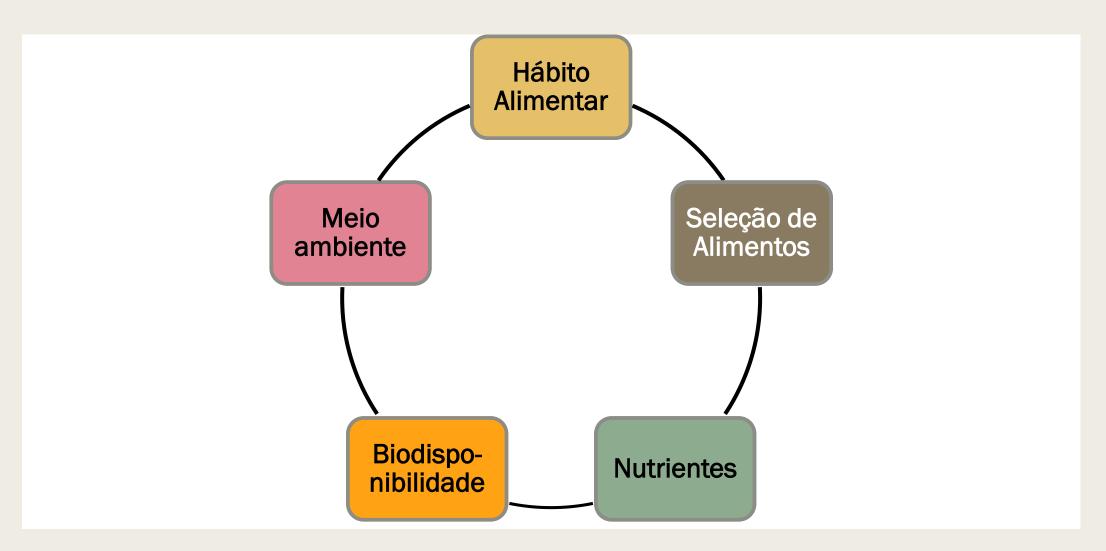


## Definição de Saúde

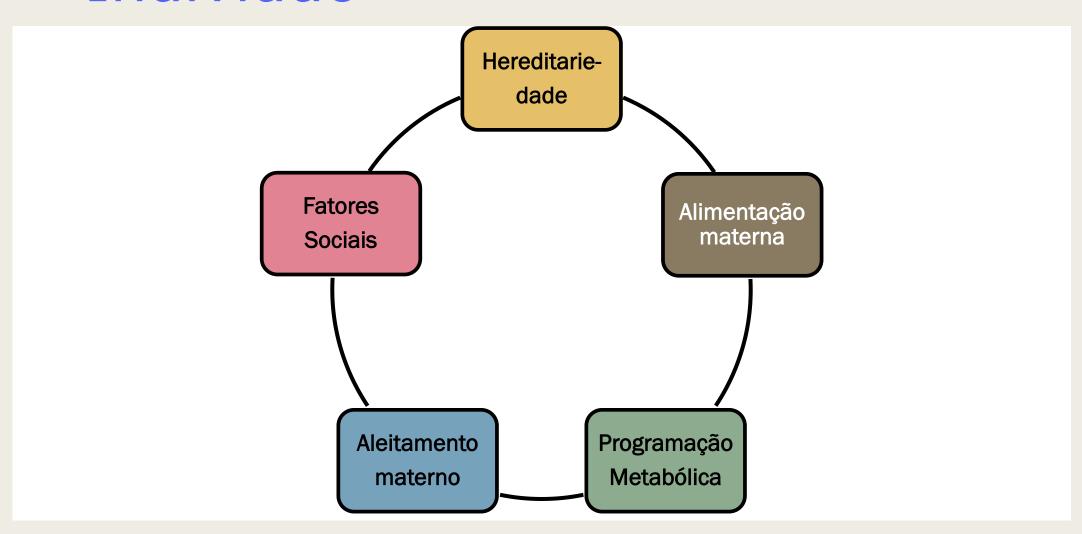
✓ Segundo WHO: "Completo estado de bem estar físico, mental e social e não meramente uma ausência de doença ou enfermidade (1948).

✓ Estado de **equilíbrio dinâmico** entre o organismo e o meio ambiente, mantendo as características estruturais e funcionais do organismo dentro dos limites normais para a fase do ciclo de vida.

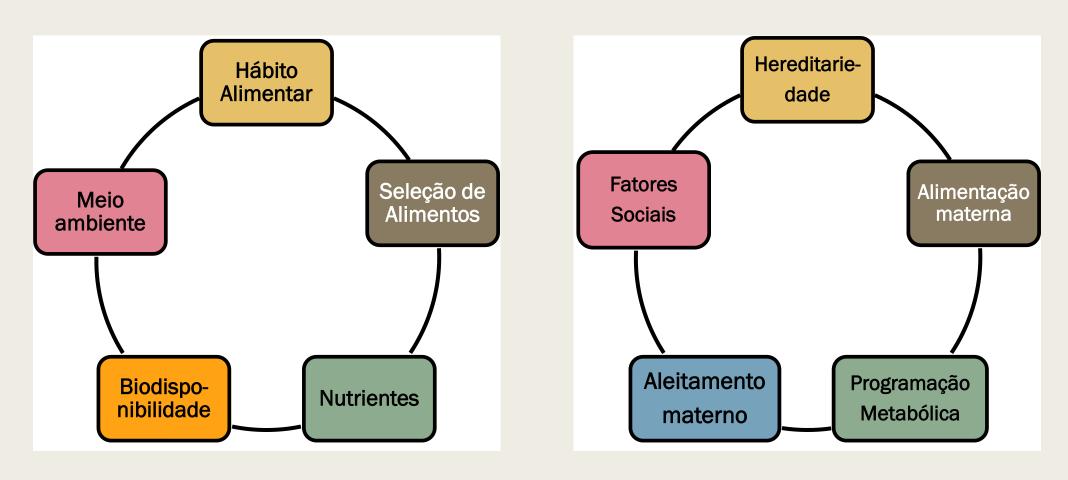
## Dieta - Fatores que interferem



## Indivíduo

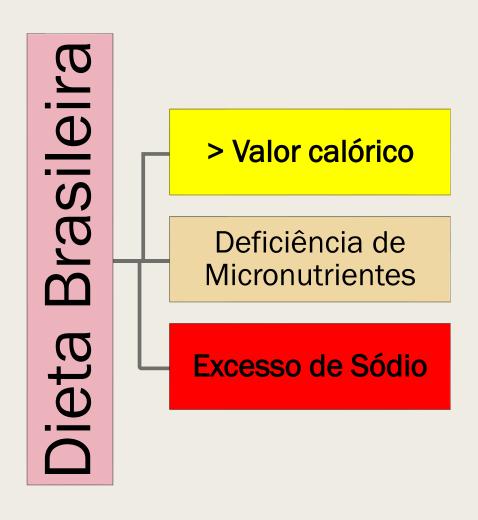


### Interação: Dieta - Indivíduo - Nutriente



SAÚDE ou DOENÇA

### Dieta Brasileira: Riscos Nutricionais



# ALIMENTAÇÃO ADEQUADA?

### Guias de Alimentação

- Dieta Mediterrânea
- Guias para Estados Unidos (FDA)
- Guias Alimentares para população brasileira
- Dentre outras......

## Fatores de risco para deficiência de Micronutrientes (1)

- Dietas monótonas com baixa densidade de micronutrientes
- Baixa ingestão de alimentos de origem animal
- Baixa prevalência de aleitamento materno
- Baixa densidade de micronutrientes na alimentação complementar para crianças > 6 meses
- Aumento da demanda fisiológica na gestação e lactação

## Fatores de risco para deficiência de Micronutrientes (2)

- Estado nutricional deficiente
- Má absorção devido a diarreias e parasitas intestinais
- Aumento da excreção
- Variações sazonais na disponibilidade de nutrientes
- Fatores sociais, pobreza, baixo nível educacional
- Doenças associadas (polifarmácia)

### Nutrientes nos alimentos

Variam com idade da planta, maturação, espécie,

variedade, cultivar, dieta

- Meio ambiente (clima, solo, chuvas, estação do ano)
  - Processamento (tempo de armazenamento,

temperatura, método de preservação, preparação)

### Alimentação Saudável?

Aquela que favorece o crescimento e desenvolvimento adequados, mantêm o organismo saudável e pode diminuir o risco de doenças crônicas não transmissíveis (DCNT)

## SUPLEMENTAÇÃO? QUANDO? QUANTO E PARA QUEM?





### Quando Suplementar?

- Grupos de risco para deficiência:
- Gestantes e Crianças
- Adolescentes
- Esportistas
- Idosos



Importante: plano alimentar direcionado para o indivíduo, respeitando suas individualidades

## Recomendações para Suplementação (1)



 Quando a ingestão alimentar de determinado nutriente estiver abaixo da recomendação média considerada para o indivíduo, associada a parametros bioquímicos que indiquem deficiência



## Recomendações para Suplementação (2)



Quando o indivíduo apresentar sinais e sintomas

compatíveis com prejuízo de função de determinado

nutriente



## Recomendações para Suplementação (3)



Quando existirem condições de doença que promovam a deficiência de um ou mais nutrientes em particular (considerando a farmacoterapia e as interações medicamentos e nutrientes)



### **Minerais em Dietas Brasileiras**

Minerais	Ca	Na	Mg	Fe	Zn	Cu	Se	Referência
Dietas	(mg)	(g)	(mg)	(mg)	(mg)	(mg)	(μ <b>g</b> )	
Nordeste	440	nd	nd	16,7	8,1	nd	nd	Pedrosa & Cozzolino
Manaus – AM	438	3,5	252	11,2	8,7	1,13	98	Yuyama & Cozzolino
Santa Catarina I	287	2,0	158	6,4	5,2	0,69	55,3	Tramonte & Cozzolino
Santa Catarina II	508	3,6	122	11,6	9,8	1,21	114,5	Tramonte & Cozzolino
Cuiabá - MT	356	nd	192	12,5	9,9	1,12	60,0	Boaventura & Cozzolino
São Paulo – idosos	377	1,2	nd	5,2	3,5	0,32	30,0	Cordeiro & Cozzolino
São Paulo – adultos	636	3,7	nd	19,0	11,6	nd	53,0	Mafra & Cozzolino
São Paulo I AG	525	nd	313	15,8	10,4	1,46	36,0	Favaro & Cozzolino
DRI	1000	0,5	320-420	8-18	8-11	0,9	55	NRC

## GESTANTES E CRIANÇAS

### Micronutrientes em Evidência

Minerais

- Ferro
- Cálcio
- lodo
- Zinco

Vitaminas

- Vitamina A
- Vitamina D
- Ácido Fólico

## GESTANTES E SUPLEMENTAÇÃO

## **Epigenetics of Inflammation, Maternal Infection, and Nutrition**<sup>1-3</sup>

Kate J Claycombe, 4\* Catherine A Brissette, 5 and Othman Ghribi 5

<sup>4</sup>USDA-Agricultural Research Service, Grand Forks Human Nutrition Research Center, Grand Forks, ND; and <sup>5</sup>Department of Basic Sciences, University of North Dakota School of Medicine and Health Sciences, Grand Forks, ND

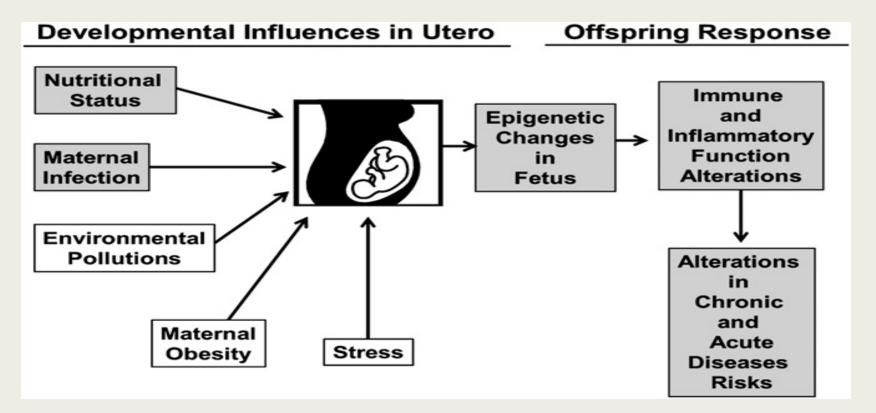
#### **Abstract**

Studies have demonstrated that epigenetic changes such as DNA methylation, histone modification, and chromatin remodeling are linked to an increased inflammatory response as well as increased risk of chronic disease development. A few studies have begun to investigate whether dietary nutrients play a beneficial role by modifying or reversing epigenetically induced inflammation. Results of these studies show that nutrients modify epigenetic pathways. However, little is known about how nutrients modulate inflammation by regulating immune cell function and/or immune cell differentiation via epigenetic pathways. This overview will provide information about the current understanding of the role of nutrients in the epigenetic control mechanisms of immune function. *J Nutr* 2015;145:1109S–15S.

**Keywords:** epigenetics, immunity, inflammation, nutrients, macrophages, obesity

Importância da alimentação materna, evitando alta ingestão de Lipideos, baixa ingestão de Proteína e de Micronutrientes (Zn, vit.D, Fe, ác.Fólico, vit.A, lodo, etc..) além de compostos bioativos, para < risco de DCNT.

*J Nutr* 2015;145:1109S–15S.



**FIGURE 1** Epigenetic regulators of immune and inflammatory functions in offspring. Maternal nutrient intake, infection, obesity, environmental pollution, and stress contribute to epigenetic changes in the fetus by DNA methylation and histone modifications. These epigenetic changes, in turn, alter immune function and inflammatory responses by activating inflammatory cytokines and chemokines, resulting in increased risk of acute and chronic diseases in offspring.

*J Nutr* 2015;145:1109S–15S.

### Multiple-micronutrient supplementation for women during pregnancy

Batool A Haider<sup>1</sup>, Zulfigar A Bhutta<sup>2</sup>

<sup>1</sup>Department of Global Health and Population, Harvard School of Public Health, Boston, MA, USA. <sup>2</sup>Centre for Global Child Health, Hospital for Sck Children, Toronto, Canada

Contact address Zulfiqar A Bhutta, Centre for Global Child Health, Hospital for Sck Children, Toronto, ON, M5G A04, Canada Zulfiqar.bhutta@sckkids.ca, zulfiqar.bhutta.bhu

Editorial group: Cochrane Pregnancy and Childbirth Group.

Publication status and date: Edited (no change to conclusions), published in Issue 4, 2017.

**Citation:** Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database of Systematic Reviews* 2017, Issue 4. Art. No.: CD 004905. DOI: 10.1002/14651858.CD 004905.pub5.

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

#### Authors' conclusions

Our findings support the effect of MMN supplements with iron and folic acid in improving some birth outcomes. Overall, pregnant women who received MMN supplementation had fewer low birthweight babies and small-for-gestational-age babies. The findings consistently observed in several systematic evaluations of evidence, provide a basis to guide the replacement of iron and folic acid with MMN supplements containing iron and folic acid for pregnant women in low and middle income countries where MMN deficiencies are common among women of reproductive age. Efforts could focus on the integration of this intervention in maternal nutrition and antenatal care programs in low and middle income countries.

Foi comparada a suplementação com Fe isolado, Fe mais ácido fólico, e suplementação com vários micronutrientes contendo Fe e Ácido Fólico (MMN) para gestantes.

Conclusão: a suplementação com MMN melhorou o baixo peso ao nascer e o tempo de gestação. Os autores enfatizam que a população estudada foi de baixa e média renda (2017)

#### Efect of vitamin A suplementation: a systematic review

Marcela Martins Soares <sup>1</sup> Mariane Alves Silva <sup>1</sup> Pauliana Pimentel Coelho Garcia <sup>2</sup> Luciana Saraiva da Silva <sup>3</sup> Glauce Dias da Costa <sup>1</sup> Raquel Maria Amaral Araújo <sup>1</sup> Rosângela Minardi Mitre Cotta <sup>1</sup>

**Abstract** To evaluate the effect of vitamin A supplementation in postpartum infants and women on serum retinol levels and breast milk. The databases Medline, PubMed, Lilacs and SciELO were consulted. The descriptors used were vitamin A, dietary supplement, child, postpartum period, infant and nutrition programs policies. Search found 7432 articles. After elimination of duplicity and application of eligibility criteria, 8 studies remained. All evaluated the effect of vitamin A supplementation on immediate postpartum, five studies used retinyl palmitate supplementation, one with retinyl palmitate and two did not specify the form of supplementation. Six studies evaluated colostrum and two included supplementation of children. It was found that supplementation in the puerperium increases the concentrations of serum retinol and breast milk, however, this result was in the short term and was relevant when the previous concentrations of the mother were low. When maternal serum concentrations are adequate, the retinol content in milk does not change, with little relevance for children. Further studies should be performed to evaluate the effect of megadoses supplementation on serum concentrations of children.

**Key words** Vitamin A, Nutritional supplements, Postpartum period, Infant

Ciência & Saúde Coletiva, 24(3):827-838, 2019

Artigo de revisão publicado esse ano, mostrando que os resultados ainda são inconclusivos. Com megadose de vitamina A (200000UI) para as mães (deficientes) houve aumento por curto período no colostro, mas não pode ser verificado benefícios para as crianças.

The studies are still inconclusive as to the real benefit of megadoses supplementation in children and nursing mothers, regarding serum retinol and human milk. In view of this, we emphasize the importance of further studies aimed at evaluating the vitamin A effectiveness megadoses supplementation program, since this deficiency causes a number of public health problems and this is a program that many countries have not adhered to.

### Adjusting total body iron for inflammation: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project

Zuguo Mei, $^{I}$  Sorrel ML Namaste, $^{2,3}$  Mary Serdula, $^{I}$  Parminder S Suchdev, $^{I,4}$  Fabian Rohner, $^{5}$  Rafael Flores-Ayala, $^{I}$ O Yaw Addo, $^{4}$  and Daniel J Raiten $^{6}$ 

<sup>1</sup>Nutrition Branch, CDC, Atlanta, GA; <sup>2</sup>Strengthening Partnerships, Results, and Innovations in Nutrition Globally, Arlington, VA; <sup>3</sup>Helen Keller International, Washington, DC; <sup>4</sup>Emory University, Atlanta, GA; <sup>5</sup>GroundWork, Fläsch, Switzerland; and <sup>6</sup>Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH, Bethesda, MD

#### **ABSTRACT**

**Background:** Total body iron (TBI) that is calculated from ferritin and soluble transferrin receptor (sTfR) allows for the evaluation of the full range of iron status from deficiency to excess. However, both ferritin and sTfR are affected by inflammation and malaria, which may require a statistical adjustment. TBI has been used to assess iron status in the United States, but its use worldwide and in settings with inflammation has been limited.

**Objective:** We examine whether inflammation-adjusted ferritin and sTfR concentrations affect TBI values and the prevalence of low TBI (<0 mg/kg) in preschool children (PSC) (age range: 6–59 mo) and women of reproductive age (WRA) (age range: 15–49 y).

**Design:** Cross-sectional data for PSC (8 surveys; n = 8413) and WRA (4 surveys; n = 4258) from the Biomarkers Reflecting the Inflammation and Nutritional Determinants of Anemia (BRINDA) project were analyzed individually and combined. TBI and the prevalence of low TBI were compared following 3 adjustment approaches for ferritin and sTfR: I) the exclusion of individuals with inflammation (C-reactive protein concentration >5 mg/L or  $\alpha$ -1-acid glycoprotein concentration >1 g/L), 2) the application of arithmetic correction factors, and 3) the use of regression correction.

**Results:** Regardless of the method that was used to adjust ferritin and sTfR for inflammation, the adjusted mean TBI decreased in both PSC and WRA compared with unadjusted values. Subsequently, inflammation-adjusted TBI increased the prevalence of low TBI by a median of 4–14 percentage points (pps) in PSC and 1–3 pps in WRA compared with unadjusted TBI. The regression approach resulted in a greater median increase than was achieved with the exclusion or correction-factor approaches, and accounting for malaria in addition to inflammation did not have an added effect on the prevalence estimates.

**Conclusion:** The prevalence of low TBI is underestimated if it is not adjusted by inflammation, particularly in children living in areas with a high prevalence of inflammation. *Am J Clin Nutr* 2017;106(Suppl):383S–9S.

Levantam a questão da inflamação, que pode subestimar os resultados bioquímicos para deficiência de Fe. Assim, autores recomendam OS biomarcadores avaliar de 08 inflamação anteriormente à suplementação, principalmente regiões onde a Malária é muito prevalente (2017).

BRINDA – Biomarcadores Refletindo Inflamação e Determinantes Nutricionais da Anemia



[Intervention Review]

### Vitamin D supplementation for women during pregnancy

Cristina Palacios<sup>1</sup>, Lia K Kostiuk<sup>2</sup>, Juan Pablo Peña-Rosas<sup>3</sup>

<sup>1</sup>Department of Dietetics and Nutrition, Robert Stempel College of Public Health and Social Work, Florida International University, Miami, Florida, USA. <sup>2</sup>Preventive Medicine, University of Wisconsin - Madison, Madison, Wisconsin, USA. <sup>3</sup>Evidence and Programme Guidance, Department of Nutrition for Health and Development, World Health Organization, Geneva, Switzerland

Contact address: Cristina Palacios, Department of Dietetics and Nutrition, Robert Stempel College of Public Health and Social Work, Florida International University, 11200 SW 8th Street, AHC 5 – 323, Miami, Florida, 33199, USA. cristina.palacios@fiu.edu.

Editorial group: Cochrane Pregnancy and Childbirth Group

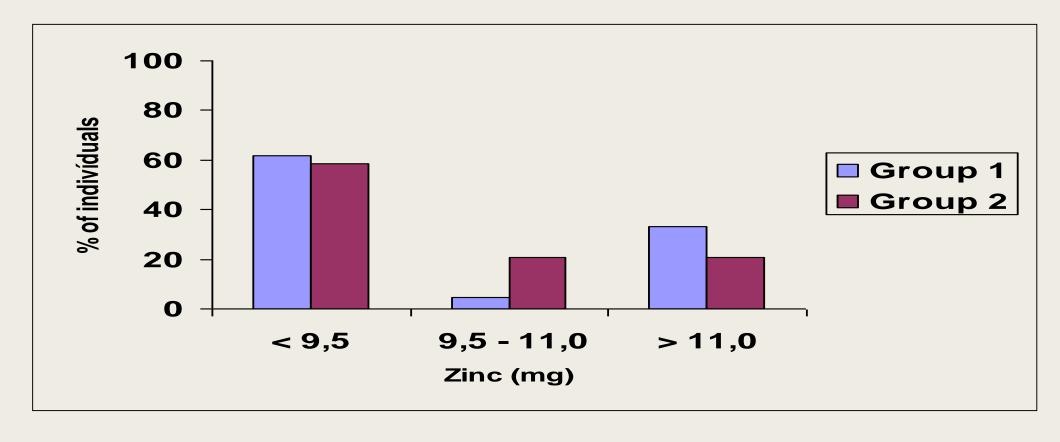
Publication status and date: New search for studies and content updated (conclusions changed), published in Issue 7, 2019.

**Citation:** Palacios C, Kostiuk LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. *Cochrane Database of Systematic Reviews* 2019, Issue 7. Art. No.: CD008873. DOI: 10.1002/14651858.CD008873.pub4.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

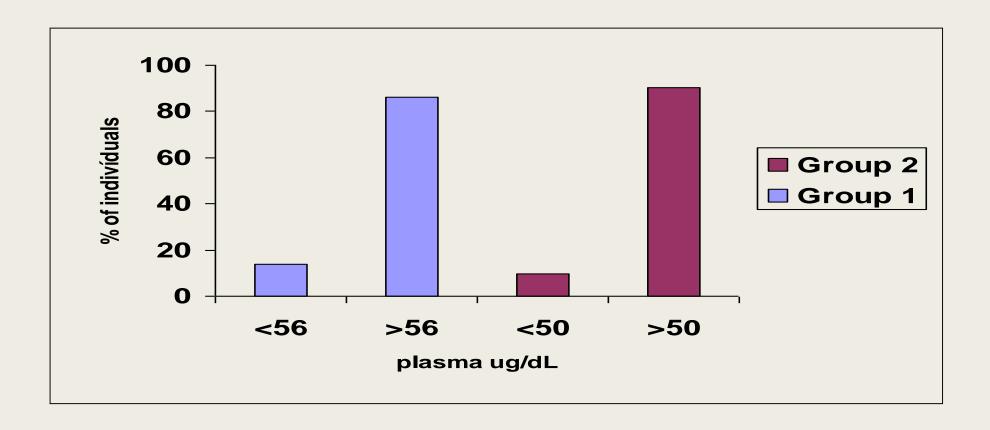
Supplementing pregnant women with vitamin D alone probably reduces the risk of pre-ecta adversos (2019) and the risk of severe postpartum haemorrhage. It may make little or no difference in the risk of having a preterm birth < 37 weeks gestation. Supplementing pregnant women with vitamin D and calcium probably reduces the risk of pre-eclampsia but may increase the risk of preterm births < 37 weeks (these findings warrant further research). Supplementing pregnant women with vitamin D and other nutrients may make little or no difference in the risk of preterm birth or low birthweight (less than 2500 g) and the effects for gestational diabetes and maternal adverse events are unclear. Additional rigorous high quality and larger randomised trials are required to evaluate the effects of vitamin D supplementation in pregnancy, particularly in relation to the risk of maternal adverse events.

Supl. Vit D de forma isolada provavelmente pode **reduzir o** risco de pre-eclampsia, diabetes gestacional, baixo peso ao nascer e risco de hemorragia pós parto. Recomendam estudos, principalmente mais em relação ao risco de efeitos Zn intake of Pregnant Women - Distribution in Relation to the Reference Values (1st and 2nd Trimester) Região de São Paulo, 2005 - Chioccola, G & Cozzolino, SMF (Dissertação Mestrado)



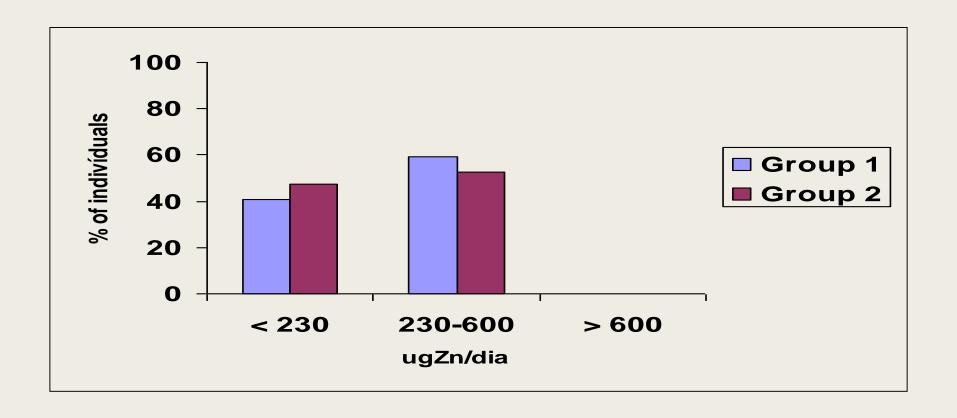
Zinc intake (mg/dia)

Pregnant Women - Distribution in Relation to the Reference for Plasma Zn (1st and 2nd Trimester) 2005, Chioccola, G & Cozzolino, SMF (Dissertação Mestrado)



Percentual distribution for plasma Zn (µg/dL)

Pregnant Women - Distribution in Relation to the Reference for Zn excretion (1st and 2nd Trimester) 2005, Chioccola, G & Cozzolino, SMF (Dissertação de Mestrado)



Percentual distribution for urinary zinc (µgZn/24h)

## SUPLEMENTAÇÃO PARA CRIANÇAS

Brazilian preschool children attending day care centers show an inadequate micronutrient intake through 24-h duplicate diet

Author links open overlay panel

<u>Isabelle NogueiraLeroux<sup>a</sup> Ana Paula Sacone da SilvaFerreira<sup>a</sup> Fernanda</u>
<u>PolloPaniz<sup>a</sup> Fábio Ferreira da Silva<sup>bc</sup> Maciel Santos Luz<sup>d</sup> Bruno Lemos Batista<sup>b</sup> Dirce
<u>Maria Marchioni<sup>e</sup> Kelly Polido Kaneshiro Olympio<sup>a</sup></u>
Show more</u>

https://doi.org/10.1016/j.jtemb.2019.04.001.

89% of children did not achieve a potassium adequate intake.

- •Calcium and Selenium were the micronutrients with highest inadequate intake rates.
- •48% of children had a Sodium intake higher than the tolerable upper level.
- •Overweight and obesity prevalence in the studied preschool group was 17%.

Journal of Trace Elements in Medicine and Biology, 54, 2019, 175-182

Nutrition 29 (2013) 405-410



#### Contents lists available at ScienceDirect

### Nutrition





#### Applied nutritional investigation

### Nutritional risk among Brazilian children 2 to 6 years old: A multicenter study

Milena Baptista Bueno Ph.D. <sup>a</sup>, Regina Mara Fisberg Ph.D. <sup>a</sup>, Priscila Maximino M.Sc. <sup>b</sup>, Guilherme de Pádua Rodrigues Ph.D. <sup>c</sup>, Mauro Fisberg Ph.D. <sup>b,\*</sup>

#### ARTICLEINFO

Article history: Received 19 July 2011 Accepted 28 June 2012

Keywords: Preschool children Dietary intake Schools Nutrients Consumption

#### ABSTRACT

Objective: To estimate the nutritional risk in children 2 to 6 y old.

Methods: The sample consisted of 3058 children enrolled in public and private schools in nine Brazilian cities. The assessment of nutrient intake was based on 1-d data combining direct individual weighing of foods and a food diary. A second evaluation of food consumption was conducted in a subsample to estimate the usual intake.

Results: There was low prevalence of inadequate intake of vitamin B6 (<0.001%), riboflavin (<0.001%), niacin (<0.001%), thiamin (<0.001%), folate (<0.001%), phosphorus (<0.1%), magnesium (<0.1%), iron (<0.5%), copper (<0.001%), zinc (<0.5%), and selenium (<0.001%). However, 22% of children younger than 4 y and 5% of children older than 4 y consumed fiber quantities larger than the adequate intake. Approximately 30% of the sample consumed more saturated fat than recommended. The prevalence of inadequate vitamin E intake ranged from 15% to 29%. More than 90% of the children had an inadequate vitamin D intake. In children older than 4 y, the prevalence of inadequate calcium intake was approximately 45%. Sodium intake was higher than the upper intake level in 90% of children younger than 4 y and 73% of children older than 4 y.

*Conclusions:* The prevalence of inadequate dietary intake was low for most nutrients. However, fiber, calcium, and vitamin D and E intakes were lower than recommended. Moreover, children consumed large amounts of sodium and saturated fat.

© 2013 Elsevier Inc. All rights reserved.

Ingestão adequada para a maioria dos nutrientes, entretanto inadequada para Ca, vitamina D e E (2013)

<sup>&</sup>lt;sup>a</sup> Nutrition Department, University of São Paulo, São Paulo, São Paulo, Brazil

<sup>&</sup>lt;sup>b</sup> Pediatric Department, Federal University of São Paulo, São Paulo, São Paulo, Brazil

<sup>&</sup>lt;sup>c</sup> Danone Research, São Paulo, São Paulo, Brazil

## The importance of vitamin D in maternal and child health: a global perspective

M Fiscaletti<sup>1\*</sup>(), P Stewart<sup>1</sup> and CF Munns<sup>1,2</sup>

### Abstract

Vitamin D and calcium are important nutrients for skeletal growth and bone health. Children and pregnant women are particularly vulnerable to 25-hydroxy vitamin D deficiency (VDD). VDD, with or without dietary calcium deficiency, can lead to nutritional rickets (NR), osteomalacia, and disturbances in calcium homeostasis. Multiple studies have linked VDD to adverse health outcomes in both children and pregnant women that extend beyond bone health. VDD remains an important global public health concern, and an important differentiation must be made between the impact of VDD on children and adults. Reports of increased incidence of NR continue to emerge. NR is an entirely preventable condition, which could be eradicated in infants and children worldwide with adequate vitamin D and calcium supplementation. The desire and necessity to put in place systems for preventing this potentially devastating pediatric disease should not elicit dispute. VDD and NR are global public health issues that require a collaborative, multi-level approach for the implementation of feasible preventative strategies. This review highlights the history, risk factors, and controversies related to VDD during pregnancy and childhood with a particular focus on global NR prevention.

Os autores chamam a atenção para os efeitos da deficiência de Vit D e Ca no **Raquitismo** e recomendam embora que muitos estudos não mostrem uma diferença significativa com a suplementação, e que os estudos devem seguir buscando resultados, mais essa deficiência não pode ser negligenciada.

Fiscaletti *et al. Public Health Reviews* (2017) 38:19 DOI 10.1186/s40985-017-0066-3

#### EVALUATION OF SOME ESSENTIAL AND TRACE ELEMENTS IN DIETS FROM 3 NURSERIES FROM JUIZ DE FORA, M.G., BRAZIL, BY NEUTRON ACTIVATION ANALYSIS.

D.I.T. Fávaro\*<sup>1</sup>, E. L. Chicourel<sup>2</sup>, V.A. Maihara<sup>1</sup>, K.C. Zangrande<sup>1</sup>, M.I. Rodrigues<sup>1</sup>, L.G. Barra<sup>2</sup>, M.B.A. Vasconcellos<sup>1</sup>, S.M.F.Cozzolino<sup>3</sup>.

<sup>1</sup>Supervisão de Radioquímica – IPEN/CNEN-SP. Caixa Postal 11049, 05422-970, São Paulo, Brasil. defavaro@curiango.ipen.br.

<sup>2</sup>Faculdade de Fármacia e Bioquímica – Departamento de Alimentos e Toxicologia, Universidade Federal de Juiz de Fora, Minas Gerais, Brasil.

<sup>3</sup>Faculdade de Ciências Farmacêuticas, Departamento de Alimentos e Nutrição Experimental, USP- São Paulo, Brasil.

#### **ABSTRACT**

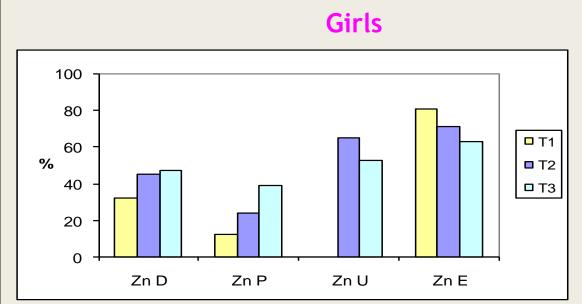
A study was made in diets offered to a group of pre-school children, whose mean age was 67 months (between 48 - 85 months) that remained the whole day in 3 public nurseries from Juiz de Fora, M.G., Brazil, eating two complete meals and snacks, with the aim of evaluating the essential and trace contents. For sampling, the duplicate portion technique was used, and the diets offered during a week were collected and analyzed separately each day, in the 3 nurseries. Instrumental Neutron activation Analysis was applied to the determination of 16 elements (Ba, Br, Ca, Cl, Co, Cr, Cs, Fe, K, Mg, Mn, Na, Rb, Sc, Se and Zn). The samples were submitted to short and long irradiations at the nuclear research reactor IEA-R1m at IPEN. The daily dietary intake values found in this work were: Ca (162, 458, 311mg); Cl (2947, 3329, 2742 mg); Fe (7.0, 8.3, 5.0 mg); K (1045, 1336, 1279 mg); Mg (119, 122, 117 mg); Mn (1.6, 1.4, 1.4 mg); Na (2083, 2137, 1746 mg); Se (12.9, 17.9, 9.1 g) and Zn (4.4, 6.0, 5.0 mg) respectively for S. Luzia, V. Ideal and Benfica nurseries. When these values were compared to the RDA(children 4–6 years old) it was verified that the diets showed to be deficient for the essential elements Ca, Fe, Se and Zn. For the elements Mg and Mn the diets showed the closest values and for Cl and Na ,higher values than recommendations. For the other elements there is no recommendation for children.

Foram analisadas em laboratório dietas de 3 creches de população de baixa renda de Juiz de Fora-MG.

Observou-se deficiência de ingestão de Ca, Fe, Se e Zn e valores altos para Na.

### Percentage of School Children with Low Zn intake and Biochemical Parameters

Michelazzo, F & Cozzolino, SMF



Boys

100
80
60
40
20
Zn D
Zn P
Zn U
Zn E

ZnD (Zn diet); Zn P (Plasma Zn); Zn E (Erythrocyte Zn) Zn U (Urinary Zn)

EAR= 7 mg/d (IOM, 2000) Zn E=  $40 - 44 \mu g Zn/g Hb$  (GUTHRIE; PICCIANO, 1995) Zn P=  $\geq 70 \mu g/dL$  (GIBSON, 1990) Zn U=  $300 - 600 \mu g/24h$  (GIBSON, 1990)

### Anemia e deficiência de vitamina A em crianças menores de cinco anos assistidas pela Estratégia Saúde da Família no Estado de Pernambuco, Brasil

Resumo O objetivo do presente estudo foi descrever a prevalência e os fatores associados à anemia e à deficiência de vitamina A (DVA) em crianças menores de cinco anos assistidas pela Estratégia Saúde da Família. Estudo transversal, realizado em Pernambuco, Brasil, em 2006, Foram selecionadas crianças entre 6 e 59 meses de idade, que tiveram realizadas dosagens de hemoglobina e retinol sérico, perfazendo amostras de 945 e 563 crianças respectivamente. A presença de anemia foi determinada pelo nível de hemoglobina < 11 g/dL e DVA pelo nível de retinol sérico < 0,70 µmol/L. Realizaram-se análises univariada e ajustada por regressão múltipla de Poisson, utilizando modelo hierarquizado. A prevalência de anemia foi de 35%, diminuindo com o aumento do número de pessoas por cômodo, idade materna e idade da criança. No que concerne à DVA, sua prevalência foi de 16%, aumentando em locais onde o destino do lixo era inadequado e em crianças que apresentaram diarreia nos últimos quinze dias. A prevalência de anemia foi maior que o dobro encontrada para a DVA, chamando atenção a influência dos fatores ambientais sobre a DVA.

Palavras-chave Anemia, Deficiência de vitamina A, Epidemiologia, Programa saúde da família, Inquéritos nutricionais Weslla Karla Albuquerque Silva de Paula <sup>1</sup> Maria de Fátima Costa Caminha <sup>1</sup> José Natal Figueirôa <sup>1</sup> Malaquias Batista Filho <sup>1</sup>

Avaliação de 1650 crianças < de 5 anos considerando Anemia (<11g/dL) e deficiência de Vitamina A (<0,7µmol) (dados de 2006)

Resultados:

35% Anemia

16% Vitamina A

População de baixa renda de

Pernambuco

Ciência & Saúde Coletiva, 19(4):1209-1222, 2014

# Estado nutricional de vitaminas A e D em crianças participantes de programa de suplementação alimentar

### Resumo

Foram avaliados as concentrações séricas de vitaminas A e D e os fatores associados em crianças beneficiárias de programa de distribuição de leite fortificado, sendo utilizados modelos de regressão linear múltiplos com seleção hierárquica de variáveis independentes (condição sociodemográfica, de saúde, alimentação, amamentação, consumo do leite fortificado, exposição solar, antropometria, retinol e calcidiol séricos). Foram consideradas insuficiência e deficiência de vitamina A e de vitamina D as concentrações séricas < 1,05µmol/L, 0,70µmo/L, 30ng/mL e 20ng/mL, respectivamente. Houve inadequação do consumo alimentar de vitaminas A e D. As prevalências de insuficiência e deficiência de vitamina A e de vitamina D foram 19%, 6%, 82% e 58%, respectivamente. Os fatores associados às menores concentrações séricas de vitamina A foram: amamentação materna exclusiva < 120 dias, ausência de trabalho materno combinada com menor escolaridade materna, maior número de pessoas que consomem leite fortificado no domicílio e menor vitamina D sérica. Para a vitamina D, foram: menor exposição ao sol e menor vitamina A sérica. Ações de educação nutricional são necessárias para melhorar a situação nutricional dessas crianças.

Aline Yukari Kurihayashi <sup>1</sup> Rosangela Aparecida Augusto <sup>1</sup> Fernanda Martins Dias Escaldelai <sup>1</sup> Lígia Araújo Martini <sup>1</sup>

Os autores observaram que mesmo com o programa de fortificação do leite a Insuficiência de Vit A e D foram significantes, da ordem de 19% de Insuficiência e 6% de Deficiência para Vitamina A e de 82% de Insuficiência e 58% de deficiência para Vitamina D.

Estudo realizado em S.Paulo em 2012/13, onde foram incluidas 84 crianças.

Cad. Saúde Pública, Rio de Janeiro, 31(3):531-542, mar, 2015



**REVIEW** 

**3** OPEN ACCESS



### Is vegetarianism healthy for children?

Nathan Cofnas

Balliol College, University of Oxford, Oxford

Conclusão: Existe evidência de que o vegetarianismo pode estar associado com sérios riscos para o cérebro e desenvolvimento tanto do feto como de crianças. Portanto não se pode dizer que mesmo com a suplementação de Fe, Zn e B12, o vegetarianismo seja seguro.(2018)

### **ABSTRACT**

According to the Academy of Nutrition and Dietetics' influential position statement on vegetarianism, meat and seafood can be replaced with milk, soy/legumes, and eggs without any negative effects in children. The United States Department of Agriculture endorses a similar view. The present paper argues that the Academy of Nutrition and Dietetics ignores or gives short shrift to direct and indirect evidence that vegetarianism may be associated with serious risks for brain and body development in fetuses and children. Regular supplementation with iron, zinc, and  $B_{12}$  will not mitigate all of these risks. Consequently, we cannot say decisively that vegetarianism or veganism is safe for children.

### **KEYWORDS**

Vegetarianism in childrenveganism in childrengrowthcognitive developmentphytoestrogens in pregnancybirth ratio

### Low prevalence of inadequate micronutrient intake in young children in the south of Brazil: a new perspective

Caroline Nicola Sangalli<sup>1</sup>, Fernanda Rauber<sup>2</sup> and Márcia Regina Vitolo<sup>3</sup>\*

<sup>1</sup>Graduate Program in Health Sciences, Universidade Federal de Ciencias da Saude de Porto Alegre, 245 Sarmento Leite, Porto Alegre, 90050-170, Brazil

<sup>2</sup>Nutrition Research Group (NUPEN), Universidade Federal de Ciencias da Saude de Porto Alegre, 245 Sarmento Leite, Porto Alegre, 90050-170, Brazil

<sup>3</sup>Department of Nutrition, Universidade Federal de Ciencias da Saude de Porto Alegre, 245 Sarmento Leite, Porto Alegre, 90050-170. Brazil

(Submitted 8 December 2015 - Final revision received 19 June 2016 - Accepted 21 June 2016 - First published online 25 July 2016)

### Abstract

In Brazil, children's eating patterns have been characterised by an increased consumption of ultra-processed foods that are fortified. Our aims were to (1) estimate the prevalence of inadequate micronutrient intake among children from low-income families and (2) to assess micronutrient intake from fortified foods. We carried out a cross-sectional study from a randomised field trial conducted at healthcare centres in Porto Alegre, Brazil, with 446 mother—child pairs, with the children aged 2–3 years. Dietary data were assessed using two 24-h recalls. The prevalence of inadequacy for six micronutrients was estimated using the proportion of individuals with intakes below the estimated average requirement (EAR). Micronutrient intakes from fortified foods were evaluated using EAR and upper tolerable level (UL). Healthy foods consumption was below the recommendations, except for beans, and 88·1% of the children consumed ultra-processed foods. A low prevalence of inadequate micronutrient intake was observed for Fe (1·2%), vitamin C (4·7%), vitamin A (5·2%), Ca (11·4%) and folate (15·2%). None of the children had intakes less than the EAR for Zn. Fortified foods contributed between 11·3 and 38·3% to micronutrient intakes, and 43·0% of the children met the EAR for Fe, 13·9% for vitamin C and 12·3% for Zn using fortified foods only. In addition, 4·0% of the children exceeded the UL for vitamin A, 3·1% for Zn, 1·1% for folic acid and 0·2% for Fe. These results highlight a low prevalence of inadequate micronutrient intakes among children and suggest that such a group could be at risk of excessive micronutrient intakes provided by ultra-processed foods.

Segundo os autores, nessa região do Brasil não ocorre deficiência de micronutrientes {Fe (1,2%), Vit C (4,7%), Vit A (5,2%), Ca (11,4%), Folato (15,2%)alimentos fortificados contribuem para micronutrientes. ingestão de Sugerem que com esse achado a suplementação poderia levar a riscos de excesso.

### **ORIGINAL ARTICLE**

### Iron fortification adversely affects the gut microbiome, increases pathogen abundance and induces intestinal inflammation in Kenyan infants

Tanja Jaeggi, <sup>1</sup> Guus A M Kortman, <sup>2</sup> Diego Moretti, <sup>1</sup> Christophe Chassard, <sup>1</sup> Penny Holding, <sup>3</sup> Alexandra Dostal, <sup>1</sup> Jos Boekhorst, <sup>4</sup> Harro M Timmerman, <sup>4</sup> Dorine W Swinkels, <sup>2</sup> Harold Tjalsma, <sup>2</sup> Jane Njenga, <sup>5</sup> Alice Mwangi, <sup>5</sup> Jane Kvalsvig, <sup>6</sup> Christophe Lacroix, <sup>1</sup> Michael B Zimmermann <sup>1</sup>

### **ABSTRACT**

**Background** In-home iron fortification for infants in developing countries is recommended for control of anaemia, but low absorption typically results in >80% of the iron passing into the colon. Iron is essential for growth and virulence of many pathogenic enterobacteria. We determined the effect of high and low dose in-home iron fortification on the infant gut microbiome and intestinal inflammation.

**Methods** We performed two double-blind randomised controlled trials in 6-month-old Kenyan infants (n=115) consuming home-fortified maize porridge daily for 4 months. In the first, infants received a micronutrient powder (MNP) containing 2.5 mg iron as NaFeEDTA or the MNP without iron. In the second, they received a different MNP containing 12.5 mg iron as ferrous fumarate or the MNP without the iron. The primary outcome was gut microbiome composition analysed by 16S pyrosequencing and targeted real-time PCR (qPCR). Secondary outcomes included faecal calprotectin (marker of intestinal inflammation) and incidence of diarrhoea. We analysed the trials separately and combined.

**Results** At baseline, 63% of the total microbial 16S rRNA could be assigned to *Bifidobacteriaceae* but there were high prevalences of pathogens, including *Salmonella Clostridium difficile*, *Clostridium perfringens*, and pathogenic *Escherichia coli*. Using pyrosequencing, +FeMNPs increased enterobacteria, particularly *Escherichial Shigella* (p=0.048), the enterobacteria/bifidobacteria ratio (p=0.020), and *Clostridium* (p=0.030). Most of these effects were confirmed using qPCR; for example, +FeMNPs increased pathogenic *E. coli* strains (p=0.029). +FeMNPs also increased faecal calprotectin (p=0.002). During the trial, 27.3% of infants in +12.5 mgFeMNP required treatment for diarrhoea versus 8.3% in -12.5 mgFeMNP (p=0.092). There were no study-related serious adverse events in either group.

**Conclusions** In this setting, provision of iron-containing MNPs to weaning infants adversely affects the gut microbiome, increasing pathogen abundance and causing intestinal inflammation.

Trial registration number NCT01111864.

#### INTRODUCTION

While infants have the highest rates of iron deficiency anaemia (IDA), they are also the group less well covered by universal fortification programmes. Micronutrient powders (MNP), added directly to

### Significance of this study

### What is already known on this subject?

- The composition of the infant gut microbiota may vary depending on dietary iron supply, but most data are from culture methods, or have come from animal experiments.
- ▶ In-home iron fortification for infants in developing countries is recommended to control anaemia, but low absorption typically results in >80% of the iron passing into the colon.
- ► Two recent iron fortification trials in infants in developing countries have raised safety concerns: in Ghana, there was an increased rate of hospitalisations possibly due to diarrhoea, and in Pakistan, a small but significant increase in overall diarrhoea prevalence.
- ► There is little known about the composition of the African infant gut microbiota during the weaning period, or the effects of iron fortification at this age.

### What are the new findings?

- ► This is the first controlled intervention trial to examine the effect of iron fortification on the African infant gut microbiome.
- Iron fortification modifies the gut microbiome in weaning African infants, increasing enterobacteria and decreasing bifidobacteria, and increases abundances of specific enteropathogens, for example, pathogenic *Escherichia coli*.
- ► Iron fortification in weaning African infants increases faecal calprotectin levels, indicating intestinal inflammation.
- These data provide a probable mechanism for the increases in diarrhoea seen in recent infant fortification studies.

### How might it impact on clinical practice in the foreseeable future?

Our findings suggest that, until safer formulations are available, iron fortification should not be given to all infants, but should be targeted only to infants with clear iron deficiency anaemia, while providing adequate protection from diarrhoea.

Jaeggi T, et al. Gut 2015;64:731-742. doi:10.1136/gutinl-2014-307720



73

Excesso Fe no intestino pode favorecer o crescimento de microorganismos patogênicos que necessitam de Fe, causando inflamação do intestino (Gut, 2015)

## RECOMENDAÇÃO DE

SUPLEMENTAÇÃO PARA

IDOSOS? E EM DCNT?

## Symposium 8: Drugs and nutrition Important drug-nutrient interactions

### Pamela Mason

The Rectory, Gwernesney, Usk, Monmouthshire NP15 1HF, UK

Drugs have the potential to interact with nutrients potentially leading to reduced therapeutic efficacy of the drug, nutritional risk or increased adverse effects of the drug. Despite significant interest in such interactions going back to over more than 40 years, the occurrence and clinical significance of many drug—nutrient interactions remains unclear. However, interactions involving drugs with a narrow therapeutic margin such as theophylline and digoxin and those that require careful blood monitoring such as warfarin are likely to be those of clinical significance. Drugs can affect nutrition as a result of changes in appetite and taste as well as having an influence on absorption or metabolism of nutrients. Moreover, foods and supplements can also interact with drugs, of which grapefruit juice and St John's wort are key examples. Significant numbers of people take both supplements and medication and are potentially at risk from interactions. Professionals, such as pharmacists, dietitians, nurses and doctors, responsible for the care of patients should therefore check whether supplements are being taken, while for researchers this is an area worthy of significant further study, particularly in the context of increasingly complex drug regimens and the plethora of new drugs.

Drugs: Nutrients: Supplements: Interactions: Cytochrome P450 enzymes

Proceedings of the Nutrition Society (2010), 69, 551–557

de medicamentos, uso principalmente de forma crônica, pode interagir com os nutrientes, < efeito do medicamento, bem biodisponibilidade do nutriente. Em geral, pacientes com câncer são aqueles que mais utilizam suplementos de minerais vitaminas. Profissionais de saúde devem ficar atentos

### Review

## The anorexia of ageing: Physiopathology, prevalence, associated comorbidity and mortality. A systematic review<sup>†</sup>

Vincenzo Malafarina a,\*, Francisco Uriz-Otano a, Lucía Gil-Guerrero b, Raquel Iniesta c

### ARTICLE INFO

Article history: Received 26 December 2012 Accepted 4 January 2013 Available online xxx

Keywords:
Anorexia of ageing
Elderly
Loss of appetite
Appetite regulation
Nutritional intervention

### ABSTRACT

The physiological processes of ageing and factors prevalent in the elderly such as comorbidities and polypharmacy often cause loss of appetite in the elderly, which we call anorexia of ageing. Social factors, together with changes in the sensory organs, can be important causes of a reduction in both appetite and ingestion. This review assesses the regulation of appetite in the elderly and the development of anorexia of ageing. It also examines the prevalence of this type of anorexia, its associated comorbidities and mortality rates. We have reviewed 27 studies, with a total of 6208 patients. These reported changes in the secretion and response of both central and peripheral hormones that regulate appetite. Anorexia, very prevalent among hospitalized and institutionalized elderly people, is associated with comorbidity and represents a predictive factor for mortality. No treatment for it has been proved to be effective. The mechanism regulating ingestion in elderly people is complex and difficult to resolve. Comorbidity as a cause or a consequence of anorexia of ageing has become a research field of great interest in geriatrics. A correct nutritional evaluation is a fundamental part of an integrated geriatric assessment.

© 2013 Elsevier Ireland Ltd. All rights reserved.

fisiológicos Fatores do envelhecimento associados polifarmácia podem ser responsáveis pela anorexia (diminuição apetite) do idoso. Fator de risco para desnutrição. Portanto existe necessidade cuidados nutricionais eventual suplementação, 2013.

<sup>&</sup>lt;sup>a</sup> Department of Geriatrics, Hospital San Juan de Dios, Calle Beloso Alto 3, 31006 Pamplona, Spain

<sup>&</sup>lt;sup>b</sup> Department of Internal Medicine, Hospital San Juan de Dios, Calle Beloso Alto 3, 31006 Pamplona, Spain

<sup>&</sup>lt;sup>c</sup> Servicio de soportes estadístico, Fundació per a la recerca Sant Joan de Deu, Carrer Santa Rosa 39-57, Level 3, 08950 Esplugues de Llobregat, Barcelona, Spain



### **REVIEW**

## The role of calcium supplementation in healthy musculoskeletal ageing

An expert consensus meeting of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the International Foundation for Osteoporosis (IOF)

```
N. C. Harvey<sup>1,2</sup> · E. Biver<sup>3</sup> · J.-M. Kaufman<sup>4</sup> · J. Bauer<sup>5</sup> · J. Branco<sup>6</sup> · M. L. Brandi<sup>7</sup> ·
```

O. Bruyère<sup>8</sup> · V. Coxam<sup>9,10</sup> · A. Cruz-Jentoft<sup>11</sup> · E. Czerwinski<sup>12</sup> · H. Dimai<sup>13</sup> ·

P. Fardellone <sup>14</sup> · F. Landi <sup>15</sup> · J.-Y. Reginster <sup>16</sup> · B. Dawson-Hughes <sup>17</sup> · J. A. Kanis <sup>18,19</sup> ·

R. Rizzoli<sup>3</sup> · C. Cooper <sup>1,2,20</sup>

Received: 24 May 2016 / Accepted: 11 September 2016 / Published online: 20 October 2016 © International Osteoporosis Foundation and National Osteoporosis Foundation 2016

**Abstract** The place of calcium supplementation, with or without concomitant vitamin D supplementation, has been much debated in terms of both efficacy and safety. There have

been numerous trials and meta-analyses of supplementation for fracture reduction, and associations with risk of myocardial infarction have been suggested in recent years. In this Estudos recentes têm desaconselhado suplementação medicamentosa com Ca isoladamente para idosos, considerando > risco DCV, cálculos renais, disturbios GI. Entretanto, quando associado com Vit.D, poderia ser utilizado considerando idosos com insuficiência de ingestão e no tratamento de osteoporose.(Osteoporos Int. 2017)

# Micronutrients supplementation and nutritional status in cognitively impaired elderly persons: a two-month open label pilot study

Christine AF von Arnim<sup>1\*</sup>, Stephanie Dismar<sup>2</sup>, Cornelia S Ott-Renzer<sup>2</sup>, Nathalie Noeth<sup>1</sup>, Albert C Ludolph<sup>1</sup> and Hans K Biesalski<sup>2</sup>

### **Abstract**

**Background:** Malnutrition is a widespread problem in elderly people and is associated with cognitive decline. However, interventional studies have produced ambiguous results. For this reason, we wanted to determine the effect of micronutrient supplementation on blood and tissue levels and on general nutritional status in persons with mild or moderate cognitive impairment.

**Methods:** We performed a 2-month, open-label trial, administering a daily micronutrient supplement to 42 memory clinic patients with mild cognitive deficits. Blood levels of antioxidants, zinc, and B vitamins were determined before and after supplementation. In addition, we assessed metabolic markers for B vitamins and intracellular (buccal mucosa cell [BMC]) antioxidant levels. Nutritional status was assessed by using the Mini Nutritional Assessment (MNA).

**Results:** Blood levels of B vitamins, folic acid, lutein,  $\beta$ -carotene,  $\alpha$ -carotene, and  $\alpha$ -tocopherol increased significantly. Decreases in homocysteine levels and the thiamine pyrophosphate effect and an increase in holotranscobalamin were observed. We found no increase in intracellular antioxidant levels of BMC. The MNA score in subjects at risk for malnutrition increased significantly, mainly owing to better perception of nutritional and overall health status.

**Conclusions:** Micronutrient supplementation improved serum micronutrient status, with improved metabolic markers for B vitamins but not for intracellular antioxidant status, and was associated with improved self-perception of general health status. Our data underline the necessity of determining micronutrient status and support the use of additional assessments for general health and quality of life in nutritional supplementation trials.

**Keywords:** B vitamins, Intracellular antioxidative status, Mini nutritional assessment, Micronutrient supplement

Suplementação de idosos necessita ser avaliada com cuidado com ajustes para grupos específicos. Dependendo do estado nutricional anterior, as doses necessitam ser ajustadas, assim como o tempo adequado para verificação do efeito.

von Arnim *et al. Nutrition Journal* 2013, **12**:148 http://www.nutritionj.com/content/12/1/148

## Vitamin D Supplementation Improves Quality of Life and Physical Performance in Osteoarthritis Patients

Pacharee Manoy <sup>1</sup>, Pongsak Yuktanandana <sup>2</sup>, Aree Tanavalee <sup>2</sup>, Wilai Anomasiri <sup>3</sup>, Srihatach Ngarmukos <sup>2</sup>, Thanathep Tanpowpong <sup>2</sup> and Sittisak Honsawek <sup>2,3,\*</sup> <sup>1</sup>

- Program in Medical Sciences, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, 1873 Rama IV Road, Pathumwan, Bangkok 10330, Thailand; pachareeman@gmail.com
- Vinai Parkpian Orthopaedic Research Center, Department of Orthopaedics, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, 1873 Rama IV Road, Pathumwan, Bangkok 10330, Thailand; ypongsak@gmail.com (P.Y.); areetana@hotmail.com (A.T.); srihatach@hotmail.com (S.N.); thanathep1@yahoo.com (T.T.)
- Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, 1873 Rama IV Road, Pathumwan, Bangkok 10330, Thailand; awilaiano@gmail.com
- \* Correspondence: sittisak.h@chula.ac.th; Tel.: +662-256-4482

Received: 3 May 2017; Accepted: 22 July 2017; Published: 26 July 2017

Abstract: (1) Background: Lower levels of serum 25-hydroxyvitamin D (25(OH)D) are common in osteoarthritis (OA) patients. However, the effect of vitamin D supplementation on muscle strength and physical performance remains unclear. This study will investigate the effects of vitamin D<sub>2</sub> supplementation on muscle strength and physical performance in knee OA patients; (2) Methods: One hundred and seventy-five primary knee OA patients with low levels of serum 25(OH)D (<30 ng/mL) received 40,000 IU vitamin D<sub>2</sub> (ergocalciferol) per week for six months. Body composition, muscle strength, physical performance, serum 25(OH)D level, leptin, interlukin-6 (IL-6), parathyroid hormone (PTH), protein carbonyl, and metabolic profile were analyzed; (3) Results: Baseline mean serum 25(OH)D levels in knee OA patients was 20.73 ng/mL. Regarding baseline vitamin D status, 58.90% of patients had vitamin D insufficiency, and 41.10% had vitamin D deficiency. After vitamin D<sub>2</sub> supplementation for six months, mean serum 25(OH)D level was 32.14 ng/mL. For post-supplementation vitamin D status, 57.10% of patients had vitamin D sufficiency and 42.90% had vitamin D insufficiency. From baseline to six months, there was a significant increase in mean serum 25(OH)D level (p < 0.001), while mean LDL cholesterol (p = 0.001), protein carbonyl (p = 0.04), and PTH (p = 0.005) all significantly decreased. Patient quality of life (SF-12) and pain (visual analog scale, VAS) both improved significantly from baseline to the six-month time point (p = 0.005 and p = 0.002, respectively). Knee OA patients demonstrated significant improvement grip strength and physical performance measurements after vitamin  $D_2$  supplementation (p < 0.05); (4) Conclusions: Vitamin  $D_2$ supplementation for six months reduced oxidative protein damage, decreased pain (VAS), improved quality of life, and improved grip strength and physical performance in osteoarthritis patients.

Keywords: vitamin D<sub>2</sub> supplementation; osteoarthritis; muscle strength; physical performance

Pacientes com osteoartrite com baixas concentrações de vitamina D (20,73ng/mL) suplementados com 40000UI de vit **D2** por semana durante 6 meses, > conc. 32,14ng/mL, melhora com dos sintomas. (Nutrients, 2017)

Endocrine (2017) 55:376–385 DOI 10.1007/s12020-016-1098-z

### **META-ANALYSIS**



### Insufficient documentation for clinical efficacy of selenium supplementation in chronic autoimmune thyroiditis, based on a systematic review and meta-analysis

Kristian Hillert Winther (1) 1,2 · Johanna Eva Märta Wichman 1,2 · Steen Joop Bonnema 1,2 · Laszlo Hegedüs 1,2

Received: 17 May 2016 / Accepted: 17 August 2016 / Published online: 28 September 2016 © The Author(s) 2016; This article is published with open access at Springerlink.com

Abstract By a systematic review and meta-analysis to investigate clinically relevant effects of selenium supplementation in patients with chronic autoimmune thyroiditis. Controlled trials in adults (≥18 years) with autoimmune thyroiditis, comparing selenium with or without levothyroxine substitution, versus placebo and/or levothyroxine substitution, were eligible for inclusion. Identified outcomes were serum thyrotropin (thyroid stimulating hormone) levels in LT4-untreated patients, thyroid ultrasound and health-related quality of life. Eleven publications, covering nine controlled trials, were included in the systematic review. Random effects model meta-analyses were performed in weighted mean difference for thyroid stimulating hormone, ultrasound and health-related quality of life. Quality of evidence was assessed per outcome, using GRADE. Meta-analyses showed no change in thyroid stimulating hormone, or improvements in health-related quality of life or thyroid echogenicity (ultrasound), between levothyroxine substitution-untreated patients assigned to selenium supplementation or placebo. Three trials found some improvement in wellbeing in patients receiving levothyroxine substitution, but could not be synthesized in a meta-analysis. The quality of evidence ranged from very low to low for thyroid stimulating hormone as well as ultrasound outcomes, and low to moderate for health-related quality of life, and was generally downgraded

due to small sample sizes. We found no effect of selenium supplementation on thyroid stimulating hormone, health-related quality of life or thyroid ultrasound, in levothyroxine substitution-untreated individuals, and sporadic evaluation of clinically relevant outcomes in levothyroxine substitution-treated patients. Future well-powered RCTs, evaluating e.g. disease progression or health-related quality of life, are warranted before determining the relevance of selenium supplementation in autoimmune thyroiditis.

**Keywords** Chronic autoimmune thyroiditis  $\cdot$  Hashimoto's thyroiditis  $\cdot$  Selenium supplementation  $\cdot$  Thyroid hormones  $\cdot$  Systematic review  $\cdot$  Meta-analysis  $\cdot$  Quality of life  $\cdot$  Thyroid ultrasound

### Introduction

Chronic autoimmune (AIT) or Hashimoto's thyroiditis affects 1–2% of the population with increasing prevalence with age and a female preponderance. In communities replete in iodine intake, it is the predominant cause of hypothyroidism [1, 2]. The etiology is multifactorial and based on genetic susceptibility in a complex interaction with numerous environmental triggers [3, 4], possibly including

Não observaram efeito com a suplementação com Se.

Sugerem mais estudos

(Endocrine, 2017)

## Calcium supplementation in osteoporosis: useful or harmful?

### Iacopo Chiodini<sup>1,2</sup> and Mark J Bolland<sup>3</sup>

<sup>1</sup>Department of Medical Sciences and Community Health, University of Milan, Milan, Italy, <sup>2</sup>Unit of Endocrinology, Fondazione IRCCS Cà Granda, Milan, Italy, and <sup>3</sup>Department of Medicine, University of Auckland, Auckland, New Zealand

Correspondence should be addressed to I Chiodini

Emai

iacopo.chiodini@unimi.it

### **Abstract**

Osteoporosis and fragility fractures are important social and economic problems worldwide and are due to both the loss of bone mineral density and sarcopenia. Indeed, fragility fractures are associated with increased disability, morbidity and mortality. It is known that a normal calcium balance together with a normal vitamin D status is important for maintaining well-balanced bone metabolism, and for many years, calcium and vitamin D have been considered crucial in the prevention and treatment of osteoporosis. However, recently, the usefulness of calcium supplementation (alone or with concomitant vitamin D) has been questioned, since some studies reported only weak efficacy of these supplementations in reducing fragility fracture risk. On the other hand, besides the gastrointestinal side effects of calcium supplements and the risk of kidney stones related to use of co-administered calcium and vitamin D supplements, other recent data suggested potential adverse cardiovascular effects from calcium supplementation. This debate article is focused on the evidence regarding both the possible usefulness for bone health and the potential harmful effects of calcium and/or calcium with vitamin D supplementation.

European Journal of Endocrinology (2018) **178**, D13–D25 Debate continua, recomendado ou não?

Tanto para Ca isoladamente como para Ca e Vit.D.

(European J Endocrinology,

2018)





Review

### Immune Function and Micronutrient Requirements Change over the Life Course

Silvia Maggini <sup>1,\*</sup>, Adeline Pierre <sup>1</sup> and Philip C. Calder <sup>2,3</sup>

- Bayer Consumer Care AG, 4002 Basel, Switzerland; adeline.pierre@bayer.com
- Human Development & Health, Faculty of Medicine, University of Southampton, Southampton SO16 6YD, UK; P.C.Calder@soton.ac.uk
- <sup>3</sup> NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust and University of Southampton, Southampton SO16 6YD, UK
- \* Correspondence: silvia.maggini@bayer.com; Tel.: +41-582-727-516

Received: 28 September 2018; Accepted: 15 October 2018; Published: 17 October 2018



Abstract: As humans age, the risk and severity of infections vary in line with immune competence according to how the immune system develops, matures, and declines. Several factors influence the immune system and its competence, including nutrition. A bidirectional relationship among nutrition, infection and immunity exists: changes in one component affect the others. For example, distinct immune features present during each life stage may affect the type, prevalence, and severity of infections, while poor nutrition can compromise immune function and increase infection risk. Various micronutrients are essential for immunocompetence, particularly vitamins A, C, D, E, B2, B6, and B12, folic acid, iron, selenium, and zinc. Micronutrient deficiencies are a recognized global public health issue, and poor nutritional status predisposes to certain infections. Immune function may be improved by restoring deficient micronutrients to recommended levels, thereby increasing resistance to infection and supporting faster recovery when infected. Diet alone may be insufficient and tailored micronutrient supplementation based on specific age-related needs necessary. This review looks at immune considerations specific to each life stage, the consequent risk of infection, micronutrient requirements and deficiencies exhibited over the life course, and the available evidence regarding the effects of micronutrient supplementation on immune function and infection.

**Keywords:** adults; age-related immunity; deficiency; elderly; immunosenescence; infants; infection; micronutrients; older people

Varios micronutrientes são essenciais para o sistema imune, principalmente Vitaminas A, C, D, E, B2, B6, B12, ác.fólico, Fe, Se e Zn. Em diferentes fases da vida pode haver necessidade de suplementação (2018)

Hindawi Journal of Diabetes Research Volume 2017, Article ID 8232863, 11 pages https://doi.org/10.1155/2017/8232863

### Clinical Study

## **Vitamin D Supplementation Improves Mood in Women with Type 2 Diabetes**

Sue Penckofer, Mary Byrn, William Adams, Mary Ann Emanuele, Patricia Mumby, Ioanne Kouba, and Diane E. Wallis<sup>2</sup>

<sup>1</sup>Loyola University Chicago, Health Sciences Campus, 2160 S. First Avenue, Maywood, IL 60153, USA

Correspondence should be addressed to Sue Penckofer; spencko@luc.edu

Academic Editor: Ilaria Campesi

Copyright © 2017 Sue Penckofer et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Objective. The aim of this study was to determine the effect of vitamin D supplementation on improving mood (depression and anxiety) and health status (mental and physical) in women with type 2 diabetes mellitus (T2DM). Methods. Fifty women with T2DM and significant depressive symptomology were enrolled into the "Sunshine Study," where weekly vitamin D supplementation (ergocalciferol, 50,000 IU) was given to all participants for six months. The main outcomes included (1) depression (Center for Epidemiologic Studies Depression, CES-D, and Patient Health Questionnaire, PHQ-9), (2) anxiety (State-Trait Anxiety), and (3) health status (Short Form, SF-12). Results. Forty-six women (92%) completed all visits. There was a significant decrease in depression (CES-D and PHQ-9, p < 0.001) and anxiety (state and trait, p < 0.001). An improvement in mental health status (SF-12, p < 0.001) was also found. After controlling for covariates (race, season of enrollment, baseline vitamin D, baseline depression (PHQ-9), and body mass index), the decline in depression remained significant (CES-D, p < 0.001). There was a trend for a better response to supplementation for women who were not taking medications for mood (antidepressants or anxiolytics) (p = 0.07). Conclusions. Randomized trials to confirm that vitamin D supplementation can improve mood and health status in T2DM women are needed.

observado Foi que suplementação por seis mêses com 50000UI Vit melhorou os sintomas depressão ansiedade, е porém autores OS recomendam mais estudos (Diabetes Research, 2017).

<sup>&</sup>lt;sup>2</sup>Advocate Medical Group, 3825 Highland Avenue, Suite 400, Downers Grove, IL 60515, USA

Nutrients 2015, 7, 3621-3651; doi:10.3390/nu7053621



Review

### Selenium and Chronic Diseases: A Nutritional Genomics Perspective

Catherine Méplan 1,2

- School of Biomedical Sciences, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne NE2 4HH, UK
- Human Nutrition Research Centre, Newcastle University, Newcastle upon Tyne NE2 4HH, UK; E-Mail: Catherine.meplan@ncl.ac.uk; Tel.: +44-191-208-7664; Fax: +44-191-208-8900

Received: 7 April 2015 / Accepted: 6 May 2015 / Published: 15May 2015

Abstract: Mechanistic data have revealed a key role for selenium (Se) and selenoproteins in biological pathways known to be altered in multifactorial diseases, such as cellular maintenance, response to oxidative stress and correct protein folding. Although epidemiological studies indicate that low Se intake is linked to increased risk for various chronic diseases, supplementation trials have given confusing outcomes, suggesting that additional genetic factors could affect the relationship between Se and health. Genetic data support this hypothesis, as risk for several chronic diseases, in particular cancer, was linked to a number of single nucleotide polymorphisms (SNP) altering Se metabolism, selenoprotein synthesis or activity. Interactions between SNPs in selenoprotein genes, SNPs in related molecular pathways and biomarkers of Se status were found to further modulate the genetic risk carried by the SNPs. Taken together, nutritional genomics approaches uncovered the potential implication of some selenoproteins as well as the influence of complex interactions between genetic variants and Se status in the aetiology of several chronic diseases. This review discusses the results from these genetic associations in the context of selenoprotein functions and epidemiological investigations and emphasises the need to assess in future studies the combined contribution of Se status, environmental stress, and multiple or individual SNPs to disease risk.

**Keywords** selenoprotein P; glutathione peroxidase; single nucleotide polymorphisms; cancer; nutritional genomics; selenium

Importante considerar a influência de fatores genéticos ligados ao Se que podem oferecer diferentes respostas entre saúde e doença.

## Calcium supplementation and cardiovascular risk: A rising concern

Aurel T. Tankeu MD<sup>1</sup> | Valirie Ndip Agbor MD<sup>2</sup> | Jean Jacques Noubiap MD<sup>3</sup>

<sup>1</sup>Department of Internal Medicine and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon

<sup>2</sup>Ibal sub-Divisional hospital, Oku, North-west Region, Cameroon

<sup>3</sup>Department of Medicine, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa

### Correspondance

Jean Jacques Noubiap, Department of Medicine, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa.

Email: noubiapjj@yahoo.fr

Over the past decade, the number of individuals taking calcium supplementation worldwide has been on the rise, especially with the emergence of new pharmaceutical companies specialized in the marketing of dietary supplements; with calcium supplementation being their main business axis. This is mostly because of the established role of calcium in the prevention and treatment of osteoporosis and, to a lesser extent, its role in the prevention of fractures. Recently, a rising body of evidence on the adverse effect of calcium supplementation on nonskeletal, especially cardiovascular, health has been a cause for concern. In fact, a significant number of studies have reported an association between calcium supplementation and adverse cardiovascular events, even though high dietary calcium intake was shown to have a protective effect. The mechanism by which calcium supplementation could cause a cardiovascular event was still unclear until a recent study published in the Journal of the American Heart Association. Combining this recent finding with available data associating calcium supplementation with cardiovascular mortality and all-cause mortality, we call on the need for an evidence-based approach to calcium supplementation, while stressing on the safety of dietary calcium intake over the former on cardiovascular health.

Artigo recente do J Am Heart
Assoc recomenda aprofundar
os estudos sobre
Suplementação de Ca e morte
por DCV. J Clin Hypertens.
2017;19:640–646

## Multivitamin use and cardiovascular disease in a prospective study of women<sup>1-3</sup>

Susanne Rautiainen, I-Min Lee, Pamela M Rist, J Michael Gaziano, JoAnn E Manson, Julie E Buring, and Howard D Sesso

### **ABSTRACT**

2015-101-144 52

**Background:** Although multivitamins are widely used, there are limited prospective studies investigating their association with both long- and short-term risk of cardiovascular disease (CVD).

**Objective:** The objective was to investigate how multivitamin use is associated with the long- and short-term risk of CVD.

**Design:** A prospective cohort study was conducted of 37,193 women from the Women's Health Study aged  $\geq$ 45 y and free of CVD and cancer at baseline who were followed for an average of 16.2 y. At baseline, women self-reported a wide range of lifestyle, clinical, and dietary factors. Women were categorized into I) no current use and 2) current use of multivitamins. Duration and updated measures over the course of the follow-up to address short-term effects were also considered. Women were followed for major CVD events, including myocardial infarction (MI), stroke, and CVD death.

Results: During the follow-up, 1493 incident cases of CVD [defined as myocardial infarction (MI), stroke, and CVD death] occurred. In multivariable analyses, multivitamin use compared with no use was not associated with major CVD events (HR: 1.01; 95% CI: 0.89, 1.15), MI (HR: 1.04; 95% CI: 0.84, 1.27), stroke (HR: 0.99; 95% CI: 0.83, 1.18), or CVD death (HR: 1.10; 95% CI: 0.84, 1.45). A nonsignificant inverse association was observed between baseline multivitamin use and major CVD events among women aged  $\geq$ 70 y (P-interaction = 0.04) and those consuming  $\leq$ 3 servings/d of fruit and vegetables (P-interaction = 0.01). When updating information on multivitamin use during the course of follow-up, no associations were observed for major CVD events (HR: 0.91; 95% CI: 0.82, 1.02), MI (HR: 0.89; 95% CI: 0.74, 1.06), stroke (HR: 0.91; 95% CI: 0.78, 1.06), and CVD death (HR: 0.91; 95% CI: 0.71, 1.16). Conclusions: In this study of middle-aged and elderly women, neither baseline nor time-varying multivitamin use was associated with the long-term risk of major CVD events, MI, stroke, cardiac revascularizations, or CVD death. Additional studies are needed to clarify the role of multivitamins on CVD. Am J Clin Nutr Conclusão: Sem diferença significativa. Am J Clin Nutr 2015. Estudo 37193 mulheres > 45 anos, que faziam ou não uso de suplementos e risco DCV. Periodo de 16 anos.

## Micronutrient (Zn, Cu, Fe)—gene interactions in ageing and inflammatory age-related diseases: Implications for treatments

Eugenio Mocchegiani\*, Laura Costarelli, Robertina Giacconi, Francesco Piacenza, Andrea Basso, Marco Malavolta

Translational Research Center in Nutrition and Ageing, Scientific and Techonologic Area, Italian National Research Centres on Ageing (INRCA), Ancona, Italy

### ABSTRACT

In ageing, alterations in inflammatory/immune response and antioxidant capacity lead to increased susceptibility to diseases and loss of mobility and agility. Various essential micronutrients in the diet are involved in age-altered biological functions. Micronutrients (zinc, copper, iron) play a pivotal role either in maintaining and reinforcing the immune and antioxidant performances or in affecting the complex network of genes (nutrigenomic approach) involved in encoding proteins for a correct inflammatory/immune response. By the other side, the genetic inter-individual variability may affect the absorption and uptake of the micronutrients (nutrigenetic approach) with subsequent altered effects on inflammatory/immune response and antioxidant activity. Interesponse, the individual micronutrient—gene interactions are rundamental to achieve healthy ageing. In this review, we report and discuss the role of micronutrients (Zn. Cu Fe)—gene interactions in relation to the inflammatory status and the possibility of a supplement in the event of a micronutrient deficiency or chelation in presence of micronutrient overload in relation to specific polymorphisms of inflammatory proteins or proteins related of the delivery of the micronutrients to various organs and tissues. In this last context, we report the protein-metal speciation analysis in order to have, coupled with micronutrient—gene interactions, a more complete picture of the individual need in micronutrient supplementation or chelation to achieve healthy ageing and longevity.

© 2012 Elsevier B.V. All rights reserved

Suplementação de Fe, Zn e
Cu para idosos deve ter
cautela,
considerando a dificuldade
de estabelecer deficiência ou
excesso.
Necessidade de
biomarcadores mais
sensíveis.

Ageing Research Reviews 11 (2012) 297–319

Association between intakes of magnesium, potassium, and calcium and risk of stroke: 2 cohorts of US women and updated meta-analyses<sup>1–4</sup>

Sally N Adebamowo, Donna Spiegelman, Walter C Willett, and Kathryn M Rexrode

### **ABSTRACT**

**Background:** Prospective data on the relation of magnesium, potassium, and calcium intakes with stroke risk are inconsistent, and to our knowledge, the effect of a combined mineral diet score has not been examined.

**Objective:** We examined associations between intakes of magnesium, potassium, and calcium and risk of incident stroke in 86,149 women in the Nurses' Health Study (NHS) I and 94,715 women in the NHS II.

**Design:** In this prospective cohort study, we calculated HRs of stroke by quintiles of intake for each mineral and for a combined diet score of all 3 minerals by using multivariate Cox proportional hazard models. In addition, we updated meta-analyses on dietary intakes of these minerals and risk of stroke.

Results: During follow-up (30 y in the NHS I; 22 y in the NHS II) a total of 3780 incident stroke cases were documented. Pooled multivariate RRs of total stroke for women in the highest compared with the lowest quintiles were 0.87 (95% CI: 0.78, 0.97) for total magnesium, 0.89 (95% CI: 0.80, 0.99) for total potassium, and 0.97 (95% CI: 0.87, 1.09) for total calcium intake. Pooled RRs for women in the highest compared with the lowest quintiles of a combined mineral diet score were 0.72 (95% CI: 0.65, 0.81) for total stroke, 0.78 (95% CI: 0.66, 0.92) for ischemic stroke, and 0.80 (95% CI: 0.61, 1.04) for hemorrhagic stroke. In the updated meta-analyses of all prospective studies to date, the combined RR of total stroke was 0.87 (95% CI: 0.83, 0.92) for a 100-mg/d increase in magnesium intake, 0.91 (95% CI: 0.88, 0.94) for a 1000-mg/d increase in potassium intake, and 0.98 (95% CI: 0.94, 1.02) for a 300-mg/d increase in calcium intake.

**Conclusions:** A combined mineral diet score was inversely associated with risk of stroke. High intakes of magnesium and potassium but not calcium were also significantly associated with reduced risk of stroke in women.

Am J Clin Nutr 2015;101:1269–77.

Associação inversa entre > consumo Mg, K, Ca e DCV

(>100mg/d Mg; 300mg/d Ca e 1000mg/d K).

Valores de consumo semelhantes à dieta mediterrânea.

*Am J Clin Nutr* 2015;101:1269–77.

## Calcium and phosphorus intake and prostate cancer risk: a 24-y follow-up study<sup>1-3</sup>

Kathryn M Wilson, Irene M Shui, Lorelei A Mucci, and Edward Giovannucci

### **ABSTRACT**

**Background:** High calcium intake has been associated with an increased risk of advanced-stage and high-grade prostate cancer. Several studies have found a positive association between phosphorus intake and prostate cancer risk.

**Objective:** We investigated the joint association between calcium and phosphorus and risk of prostate cancer in the Health Professionals Follow-Up Study, with a focus on lethal and high-grade disease.

**Design:** In total, 47,885 men in the cohort reported diet data in 1986 and every 4 y thereafter. From 1986 to 2010, 5861 cases of prostate cancer were identified, including 789 lethal cancers (fatal or metastatic). We used Cox proportional hazards models to assess the association between calcium and phosphorus intake and prostate cancer, with adjustment for potential confounding.

Results: Calcium intakes >2000 mg/d were associated with greater risk of total prostate cancer and lethal and high-grade cancers. These associations were attenuated and no longer statistically significant when phosphorus intake was adjusted for. Phosphorus intake was associated with greater risk of total, lethal, and high-grade cancers, independent of calcium and intakes of red meat, white meat, dairy, and fish. In latency analysis, calcium and phosphorus had independent effects for different time periods between exposure and diagnosis. Calcium intake was associated with an increased risk of advanced-stage and high-grade disease 12–16 y after exposure, whereas high phosphorus was associated with increased risk of advanced-stage and high-grade disease 0–8 y after exposure.

**Conclusions:** Phosphorus is independently associated with risk of lethal and high-grade prostate cancer. Calcium may not have a strong independent effect on prostate cancer risk except with long latency periods. *Am J Clin Nutr* 2015;101:173–83.

Estudo 24 anos de seguimento, observou que > ingestão Ca (2000mg/dia), poderia ter efeito na piora do câncer de próstata, com período de latência de 12 a 16 anos após exposição e diagnóstico, enquanto para P de 0-8 anos. Autores concluem que excesso de P promoveria

> risco. Am J Clin Nutr, 2015.

Vitamin supplementation on the risk of venous thrombosis: results from the MEGA case-control study<sup>1–4</sup>

Biljana A Vučković, Nienke van Rein, Suzanne C Cannegieter, Frits R Rosendaal, and Willem M Lijfering

### **ABSTRACT**

**Background:** Whether vitamin supplements decrease venous thrombosis risk is controversial. Previous reports did not all take confounding fully into account, either by randomization or by extensive adjustment.

**Objective:** The aim of our study was to determine whether vitamin supplementation decreases the risk of venous thrombosis.

**Design:** A large case-control study included 2506 patients with venous thrombosis, 2506 partner controls, and 2684 random-digit dialing (RDD) controls. When patients were compared with RDD controls, unconditional logistic regression was used to calculate ORs with 95% CIs. When patients were compared with partner controls, conditional logistic regression was used, providing further adjustment for unmeasured confounding.

Results: Vitamin use yielded a 37% lower risk of venous thrombosis than no vitamin use (OR: 0.63; 95% CI: 0.57, 0.70) when comparing patients with RDD controls. Adjustment for several putative confounders did not change the estimate (OR: 0.68; 95% CI: 0.61, 0.77). The fully adjusted ORs for vitamin A, vitamin B-6, vitamin B-12, folic acid, vitamin C, vitamin D, vitamin E, and multivitamin use were in the same range. However, when patients were compared with partner controls, ORs attenuated to unity. Results were similar for provoked and unprovoked events, as well as for deep vein thrombosis and pulmonary embolism.

**Conclusions:** After extensive adjustments, vitamin supplementation was no longer associated with a decreased risk of venous thrombosis in this study. Previous positive results may have been spurious as a result of uncontrolled confounding. *Am J Clin Nutr* 2015;101:606–12.

Nesse estudo, a suplementação com vitaminas < em 37% os eventos de Trombose venosa, entretanto quando os indivíduos foram comparados com seus pares, e feitos os ajustes estatísticos, os autores chegaram à conclusão que não houve diferenças. Am J Clin Nutr. 2015

### Flavonoid intake and all-cause mortality<sup>1–3</sup>

Kerry L Ivey, Jonathan M Hodgson, Kevin D Croft, Joshua R Lewis, and Richard L Prince

### **ABSTRACT**

**Background:** Flavonoids are bioactive compounds found in foods such as tea, chocolate, red wine, fruit, and vegetables. Higher intakes of specific flavonoids and flavonoid-rich foods have been linked to reduced mortality from specific vascular diseases and cancers. However, the importance of flavonoids in preventing all-cause mortality remains uncertain.

**Objective:** The objective was to explore the association between flavonoid intake and risk of 5-y mortality from all causes by using 2 comprehensive food composition databases to assess flavonoid intake. **Design:** The study population included 1063 randomly selected women aged >75 y. All-cause, cancer, and cardiovascular mortalities were assessed over 5 y of follow-up through the Western Australia Data Linkage System. Two estimates of flavonoid intake (total flavonoid<sub>USDA</sub> and total flavonoid<sub>PE</sub>) were determined by using food composition data from the USDA and the Phenol-Explorer (PE) databases, respectively.

**Results:** During the 5-y follow-up period, 129 (12%) deaths were documented. Participants with high total flavonoid intake were at lower risk [multivariate-adjusted HR (95% CI)] of 5-y all-cause mortality than those with low total flavonoid consumption [total flavonoid $_{\rm USDA}$ : 0.37 (0.22, 0.58); total flavonoid $_{\rm PE}$ : 0.36 (0.22, 0.60)]. Similar beneficial relations were observed for both cardiovascular disease mortality [total flavonoid $_{\rm USDA}$ : 0.34 (0.17, 0.69); flavonoid $_{\rm PE}$ : 0.32 (0.16, 0.61)] and cancer mortality [total flavonoid $_{\rm USDA}$ : 0.25 (0.10, 0.62); flavonoid $_{\rm PE}$ : 0.26 (0.11, 0.62)].

**Conclusions:** Using the most comprehensive flavonoid databases, we provide evidence that high consumption of flavonoids is associated with reduced risk of mortality in older women. The benefits of flavonoids may extend to the etiology of cancer and cardiovascular disease. *Am J Clin Nutr* 2015;101:1012–20.

Estudo realizado com 1063 indivíduos. Aumento do consumo de flavonoides (chocolate, frutas, verduras, vinho tinto, chás) avaliado durante 5 anos, foi positivo para < risco para mortalidade de DCV e câncer. Am J Clin Nutr 2015

### Recommendations on reporting requirements for flavonoids in research<sup>1–3</sup>

Douglas A Balentine, Johanna T Dwyer, John W Erdman Jr., Mario G Ferruzzi, P Courtney Gaine, James M Harnly, and Catherine L Kwik-Uribe

### **ABSTRACT**

Numerous observational and intervention-based human studies support the notion of a beneficial role for dietary flavonoids in human health. Despite these studies, it is not yet possible to make dietary recommendations with regard to the types and amounts of flavonoids to be consumed. The inherent diversity of flavonoid structure, chemistry, and natural distribution in foods lends itself to errors in reporting the types and/or amounts of flavonoids consumed, as well as incomplete recognition of requirements for intervention studies that aim to assess their benefits in a clinical setting. A need exists for guidelines that facilitate the design and reporting of flavonoid research. With a focus on clinical studies, this article 1) outlines limitations commonly encountered in the field of flavonoid research, including the inconsistent use of nomenclature, inappropriate analytic methods, inconsistent use of existing flavonoid databases, and the lack of full consideration in the design of test materials for intervention trials, and 2) provides guidance for future studies with a focus on clinical intervention trials. Adoption of this guidance will facilitate more accurate and interpretable research that will support the development of dietary recommendations regarding the intake of flavonoids. Am J Clin Nutr 2015;101:1113–25.

Considera a importância de estudos que estabeleçam valores de recomendação de ingestão para esses compostos bioativos, e que estes sejam mais precisamente definidos (quimicamente) para evitar erros de interpretação. Am J Clin Nutr 2015.

### **AHA SCIENCE ADVISORY**

# Omega-3 Polyunsaturated Fatty Acid (Fish Oil) Supplementation and the Prevention of Clinical Cardiovascular Disease

A Science Advisory From the American Heart Association

**ABSTRACT:** Multiple randomized controlled trials (RCTs) have assessed the effects of supplementation with eicosapentaenoic acid plus docosahexaenoic acid (omega-3 polyunsaturated fatty acids, commonly called fish oils) on the occurrence of clinical cardiovascular diseases. Although the effects of supplementation for the primary prevention of clinical cardiovascular events in the general population have not been examined, RCTs have assessed the role of supplementation in secondary prevention among patients with diabetes mellitus and prediabetes, patients at high risk of cardiovascular disease, and those with prevalent coronary heart disease. In this scientific advisory, we take a clinical approach and focus on common indications for omega-3 polyunsaturated fatty acid supplements related to the prevention of clinical cardiovascular events. We limited the scope of our review to large RCTs of supplementation with major clinical cardiovascular disease end points; meta-analyses were considered secondarily. We discuss the features of available RCTs and provide the rationale for our recommendations. We then use existing American Heart Association criteria to assess the strength of the recommendation and the level of evidence. On the basis of our review of the cumulative evidence from RCTs designed to assess the effect of omega-3 polyunsaturated fatty acid supplementation on clinical cardiovascular events, we update prior recommendations for patients with prevalent coronary heart disease. and we offer recommendations, when data are available, for patients with other clinical indications, including patients with diabetes mellitus and prediabetes and those with high risk of cardiovascular disease, stroke, heart failure, and atrial fibrillation.

David S. Siscovick, MD, MPH, FAHA, Chair Thomas A. Barringer, MD, FAHA

Amanda M. Fretts, PhD, MPH

Jason H.Y. Wu, PhD, MSc, FAHA

Alice H. Lichtenstein, DSc, FAHA

Rebecca B. Costello, PhD, FAHA

Penny M. Kris-Etherton, PhD, RD, FAHA

Terry A. Jacobson, MD, FAHA

Mary B. Engler, PhD, RN, MS. FAHA

Heather M. Alger, PhD

Lawrence J. Appel, MD, MPH, FAHA

Dariush Mozaffarian, MD, DrPH, FAHA

On behalf of the American
Heart Association Nutrition Committee of the
Council on Lifestyle and
Cardiometabolic Health;
Council on Epidemiology
and Prevention; Council
on Cardiovascular Disease
in the Young; Council on
Cardiovascular and Stroke
Nursing; and Council on
Clinical Cardiology

Foram avaliados inúmeros trabalhos e as conclusões dos *experts* sobre o tema foram de que as evidencias são muito pequenas com relação à prevenção, entretanto em algumas situações de eventos secundários (ex. MI) poderia ser indicado, com uma eficiência de 8 a 10% para < mortes.



### LIPID ABNORMALITIES AND CARDIOVASCULAR PREVENTION (G DE BACKER, SECTION EDITOR)

### Does Supplementation with Omega-3 PUFAs Add to the Prevention of Cardiovascular Disease?

Evangelos C. Rizos 1,2 · Moses S. Elisaf3

Published online: 21 April 2017

© Springer Science+Business Media New York 2017

#### Abstract

Purpose of Review Omega-3 fatty acids are increasingly used for the protection of cardiovascular disease. The main but not the sole mechanism of action is the reduction of triglyceride levels. In this review, we summarize the effect of omega-3 supplements on all-cause and cardiovascular mortality, myocardial infarction, and stroke from the relevant randomized controlled trials.

Recent Findings Twenty-one randomized controlled trials assessed omega-3 supplementation on mortality and cardiovascular-related outcomes. From these studies, as well as from the relevant meta-analyses, we found that omega-3 supplements do not exert a consistent benefit for cardiovascular protection.

Summary There is uncertainty of a clear profit from omega-3 supplementation in cardiovascular disease.

**Keywords** Omega 3 · Polyunsaturated fatty acids · Fish oil · Cardiovascular · Myocardial infarction · Death

This article is part of the Topical Collection on *Lipid Abnormalities and Cardiovascular Prevention* 

Moses S. Elisaf egepi@cc.uoi.gr

Evangelos C. Rizos

### Introduction

Omega-3 polyunsaturated fatty acids (PUFAs) are commonly used for a variety of conditions ranging from Alzheimer's or Parkinson's disease to cancer. During the last 2 decades, omega-3 PUFAs have been extensively studied mainly for the prevention or even treatment of cardiovascular disease (CVD). Nowadays, omega-3 PUFAs constitute as one of the ingredients for a healthy diet, and their consumption through diet or even as supplements is commonly proposed from a variety of organizations, but most of all from advertisements of fish-oil compounds. These supplements are usually sold as over the counter formulations in supermarkets and pharmacies, as well as in large amounts through the internet market.

Systematic reviews and meta-analyses with commentaries of randomized clinical trials published in the field of cardio-vascular (CV) protection provide conflicting reports and failed to support a net benefit on CVD development [1•, 2–5]. Even the summary of product characteristics for omega-3 supplements or the indication for the marketing authorization varies, while the current guidelines from major societies on CV prevention and treatment are generally in favor of their use, mostly through dietary consumption, especially in post-myocardial infarction (MI) subjects [6–10].

In this review we summarize the evidence for the role of omega-3 supplementation on CVD emphasizing on the results from the higher quality relevant reports.

Ainda existe incertezas quanto a efetividade da suplementação com omega-3 (Curr Cardiol Rep, 2017, 19: 47)

### Selenium Supplementation and Prostate Cancer Mortality

Stacey A. Kenfield, Erin L. Van Blarigan, Natalie DuPre, Meir J. Stampfer, Edward L. Giovannucci\*, June M. Chan\*

Affiliations of authors: Department of Urology, University of California, San Francisco, San Francisco, CA (ELVB, SAK, JMC); Department of Epidemiology, Harvard School of Public Health, Boston, MA (SAK, ND, MJS, EG); Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA (ELVB, JMC); Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA (MJS, EG); Department of Nutrition, Harvard School of Public Health, Boston, MA (MJS, EG).

\*Authors contributed equally to this work.

Correspondence to: Stacey A. Kenfield, ScD, Helen Diller Family Cancer Research Building, MC 3110, 1450 3rd Street, University of California, San Francisco, CA 94158–9001 (e-mail: KenfieldS@urology.ucsf.edu).

### Abstract

**Background:** Few studies have evaluated the relation between selenium supplementation after diagnosis and prostate cancer outcomes.

Methods: We prospectively followed 4459 men initially diagnosed with nonmetastatic prostate cancer in the Health Professionals Follow-Up Study from 1988 through 2010 and examined whether selenium supplement use (from selenium-specific supplements and multivitamins) after diagnosis was associated with risk of biochemical recurrence, prostate cancer mortality, and, secondarily, cardiovascular disease mortality and overall mortality, using Cox proportional hazards models. All P values were from two-sided tests.

Results: We documented 965 deaths, 226 (23.4%) because of prostate cancer and 267 (27.7%) because of cardiovascular disease, during a median follow-up of 8.9 years. In the biochemical recurrence analysis, we documented 762 recurrences during a median follow-up of 7.8 years. Crude rates per 1000 person-years for prostate cancer death were 5.6 among selenium nonusers and 10.5 among men who consumed 140 or more  $\mu$ g/day. Crude rates per 1000 person-years were 28.2 vs 23.5 for all-cause mortality and 28.4 vs 29.3 for biochemical recurrence, for nonuse vs highest-dose categories, respectively. In multivariable analyses, men who consumed 1 to 24  $\mu$ g/day, 25 to 139  $\mu$ g/day, and 140 or more  $\mu$ g/day of supplemental selenium had a 1.18 (95% confidence interval [CI] = 0.73 to 1.91), 1.33 (95% CI = 0.77 to 2.30), and 2.60-fold (95% CI = 1.44 to 4.70) greater risk of prostate cancer mortality compared with nonusers, respectively,  $P_{trend}$  = .001. There was no statistically significant association between selenium supplement use and biochemical recurrence, cardiovascular disease mortality, or overall mortality.

Conclusion: Selenium supplementation of 140 or more  $\mu g/day$  after diagnosis of nonmetastatic prostate cancer may increase risk of prostate cancer mortality. Caution is warranted regarding usage of such supplements among men with prostate cancer.

Autores chamam a atenção para a suplementação de Se (>140 µg/d) após diagnostico de câncer de prostata, pode > risco mortalidade.

JNCI J Natl Cancer Inst (2015) 107(1): dju360

Nutrients 2015, 7, 3621-3651; doi:10.3390/nu7053621



Review

### Selenium and Chronic Diseases: A Nutritional Genomics Perspective

Catherine Méplan 1,2

- School of Biomedical Sciences, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne NE2 4HH, UK
- Human Nutrition Research Centre, Newcastle University, Newcastle upon Tyne NE2 4HH, UK; E-Mail: Catherine.meplan@ncl.ac.uk; Tel.: +44-191-208-7664; Fax: +44-191-208-8900

Received: 7 April 2015 / Accepted: 6 May 2015 / Published: 15May 2015

Abstract: Mechanistic data have revealed a key role for selenium (Se) and selenoproteins in biological pathways known to be altered in multifactorial diseases, such as cellular maintenance, response to oxidative stress and correct protein folding. Although epidemiological studies indicate that low Se intake is linked to increased risk for various chronic diseases, supplementation trials have given confusing outcomes, suggesting that additional genetic factors could affect the relationship between Se and health. Genetic data support this hypothesis, as risk for several chronic diseases, in particular cancer, was linked to a number of single nucleotide polymorphisms (SNP) altering Se metabolism, selenoprotein synthesis or activity. Interactions between SNPs in selenoprotein genes, SNPs in related molecular pathways and biomarkers of Se status were found to further modulate the genetic risk carried by the SNPs. Taken together, nutritional genomics approaches uncovered the potential implication of some selenoproteins as well as the influence of complex interactions between genetic variants and Se status in the aetiology of several chronic diseases. This review discusses the results from these genetic associations in the context of selenoprotein functions and epidemiological investigations and emphasises the need to assess in future studies the combined contribution of Se status, environmental stress, and multiple or individual SNPs to disease risk.

**Keywords** selenoprotein P; glutathione peroxidase; single nucleotide polymorphisms; cancer; nutritional genomics; selenium

Importante considerar a influência de fatores genéticos ligados ao Se que podem oferecer diferentes respostas entre saúde e doença.

### Selenium status in elderly: Relation to cognitive decline

Bárbara Rita Cardoso<sup>a,\*</sup>, Verônica Silva Bandeira<sup>a</sup>, Wilson Jacob-Filho<sup>b</sup>, Silvia Maria Franciscato Cozzolino<sup>a</sup>

#### ARTICLE INFO

### Keywords: Cognitive decline Alzheimer's disease Mild cognitive impairment Oxidative stress Selenium

### ABSTRACT

Studies show that decreased antioxidant system is related to cognitive decline. Thus we aimed to measure selenium (Se) status in Alzheimer's disease (AD) and mild cognitive impairment (MCI) elderly and compared them with a control group (CG). 27 AD, 17 MCI and 28 control elderly were evaluated. Se concentration was determined in plasma and erythrocyte by using hydride generation atomic absorption spectroscopy. Erythrocyte Se concentration in AD group was lower than CG  $(43.73 \pm 23.02 \,\mu\text{g/L})$ and  $79.15 \pm 46.37 \,\mu\text{g/L}$ ; p = 0.001), but not statistically different from MCI group (63.97  $\pm$  18.26  $\mu\text{g/L}$ ; p = 0.156). AD group exhibited the lowest plasma Se level  $(34.49 \pm 19.94 \,\mu\text{g/L})$  when compared to MCI  $(61.36 \pm 16.08 \,\mu\text{g/L}; p = 0.000)$  and to CG  $(50.99 \pm 21.06 \,\mu\text{g/L}; p = 0.010)$ . It is observed that erythrocyte Se decreases as cognition function does. Since erythrocyte reflects longer-term nutritional status, the data point to the importance of the relation between Se exposure and cognitive function. Our findings suggest that the deficiency of Se may contribute to cognitive decline among aging people.

© 2014 Published by Elsevier GmbH.

μcg/mL μcg/mL Control z MCI ⋈AD Control MCI Control AD

**Fig. 1.** Se levels in control, MCI and AD groups. (A) Plasma; (B) erythrocyte. \*\*p < 0.001.

Journal of Trace Elements in Medicine and Biology 28 (2014) 422–426

<sup>&</sup>lt;sup>a</sup> Faculty of Pharmaceutical Sciences, University of São Paulo, Brazil

<sup>&</sup>lt;sup>b</sup> Division of Geriatrics, University of São Paulo Medical School, Brazil

### Fontes de Variabilidade e de Incertezas

### Variabilidade

- Inter-individual
  - Diferenças de:
- Adaptação
- Funcionalidade
- Polimorfismos
- Programing
- Idade
- Sexo
- Maturação fisiológica

### Incertezas

- Fatores desconhecidos ou imprecisos
- Dieta
- Exposição
- Dose
- Biodisponibilidade
- Medidas avaliadas (metodologia utilizada)
- Extrapolações

## Suplementação e DCNT

- Estudos de suplementação com vitaminas, minerais, compostos bioativos, visando a redução do risco de doenças (ex: Obesidade, DCV, Câncer, Diabetes...) tem apresentado resultados conflitantes
- A maioria deles mostra que havendo deficiência os resultados poderiam ser positivos. Entretanto, em populações cujos indivíduos apresentam estado nutricional adequado, o excesso poderia ter efeitos adversos



## Conclusões

- □ A suplementação com micronutrientes, compostos bioativos, devem continuamente ser avaliadas, em vista da possibilidade de eventuais riscos de efeitos adversos
- ☐ Há necessidade de biomarcadores mais sensíveis para identificação tanto da deficiência como de excessos
- □ O nutricionista ao prescrever o uso de suplementos, deve se basear no diagnóstico nutricional adequado e ter a sensibilidade crítica para avaliar tanto os prós como os contra, e além disso, deve acompanhar e avaliar a eficácia da sua conduta.
- Embora nos países mais desenvolvidos existam controversias com relação à suplementação, no Brasil há necessidade de atenção para melhoria das dietas e fortificação e/ou suplementação com micronutrientes, principalmente para a população mais vulnerável.

## SMFCOZZO@USP.BR