

**Risk of malnutrition and zinc deficiency in community-living elderly men and women.
The Tromsø Study**

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Abbreviations: BMI, Body Mass Index; SCL-10, Symptoms Check List 10; MUST, Malnutrition Universal Screening Tool;

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Abstract

Objective: Elderly people may be at particular risk of zinc deficiency due to an increased prevalence of malnutrition. The aim of this study was to evaluate the zinc status in community-living elderly people at risk of malnutrition.

Design: Cross-sectional population-based survey. Individuals at risk of malnutrition were identified by the Malnutrition Universal Screening Tool. Zinc status was assessed by measuring serum zinc. Logistic regression was performed to evaluate the association between the risk of malnutrition and zinc deficiency.

Setting: Municipality of Tromsø, Norway

Subjects: Random sample of 743 men and 778 women aged 65-87 years old.

Results: Zinc deficiency was found in 10.1% of the participants, including 13.1% of the men and 7.3% of the women. Among the men and women at risk of malnutrition, 31% and 12.7%, respectively, had zinc deficiency. In a model adjusted for age, gender, serum albumin and smoking status, zinc deficiency was positively associated with the risk of malnutrition (odds ratio 2.2 [95% confidence interval 1.3-3.6]).

Conclusion: Overall, zinc deficiency was found in one out of ten community-living elderly people and was associated with the risk of malnutrition. Our results encourage the assessment of zinc status in elderly people at risk of malnutrition, with a special emphasis on elderly men.

Introduction

Zinc is an essential micronutrient present in all body tissues and fluids. It is contained in a large number of enzymes. Second only to iron, zinc is the most abundant trace element in humans (1). Mild zinc deficiency may be associated with impaired taste and smell, reduced immunity and increased risk of pneumonia (2, 3). In cases of severe zinc deficiency, skin lesions, anaemia, diarrhoea, anorexia, decreased lymphocyte function, impaired visual function and mental retardation may be observed (4). An increased risk of depression in individuals with zinc deficiency has been previously reported (5). However, community-based research on the impact of zinc deficiency on mental health is scarce.

Important causes of reduced body zinc include a low intake of zinc-containing foods and a decreased absorption of zinc due to intestinal malabsorption (2). Worldwide, zinc deficiency is regarded as a significant contributor to the disease burden, especially among children in developing countries (6). In the developed part of the world, elderly people may be at particular risk for zinc deficiency due to an increased prevalence of malnutrition (7). However, previous studies exploring the relationship between malnutrition and zinc deficiency in elderly individuals have yielded conflicting results (8, 9).

Moreover, previous studies addressing zinc status in the general population of elderly men and women have mostly included a limited number of participants; only a few larger population-based studies of zinc status in elderly people have been conducted. The prevalence of zinc deficiency has been found to be between 6 and 15% (10).

Therefore, in the present study, we aimed to evaluate both the zinc status and the association between zinc deficiency and risk of malnutrition in a large sample of community-living elderly individuals.

Methods

Study population

The Tromsø Study is a population-based health study of the population of Tromsø, a town with 70,000 inhabitants in Northern Norway (11). The 6th Tromsø Survey was conducted between October 2007 and December 2008 (12). We restricted our analysis to participants between 65 and 87 years of age, and all inhabitants in the eligible age group were invited. A

total of 4017 men and women were included in the study, yielding an overall participation rate of 66%. Serum from all participants was frozen, and the serum zinc and albumin were later analysed in a random selection of 1765 individuals. Information on weight loss, height or weight was missing for 200 subjects. Due to laboratory technical problems, 44 samples were discarded. Consequently, a population of 1521 men and women were included in the analysis.

Zinc and albumin analysis

Non-fasting venous blood samples were collected for the measurement of zinc and albumin using trace metal-free tubes to avoid contamination. The samples were frozen and stored at -70°C, and the serum zinc was analysed later using flame atomic absorption at a wavelength of 213.9 nm (Perkin Elmer AAnalyst 800 Atomic Absorption Spectrophotometer). Serum zinc concentrations have diurnal variations, with the highest values present in the morning and slightly reduced values present after food intake later in the day (13). The International Zinc Nutrition Consultative Group (IZiNCG) recommended different serum zinc cut-off values according to gender (men or women), fasting state (non-fasting or fasting) and time of measurement (AM or PM) (13). In the present study, the participants visited the research centre between 8 AM and 5:30 PM. According to the IZiNCG guidelines, we applied the non-fasting AM or PM cut-off values for men and women depending on attendance time, i.e., cut-offs of 10.7 µmol/L (AM) and 9.3 µmol/L (PM) for men and 10.1 µmol/L (AM) and 9.0 µmol/L (PM) for women. Zinc deficiency was defined as a serum zinc level below these cut-off values.

Because a large proportion of zinc in the serum is bound to albumin (13), an additional assessment of the serum albumin was necessary using the bromocresol green method (Hitachi Modular P, Roche). The lower reference for serum albumin was 34.0 g/L.

Nutritional assessment

Height and weight were measured without shoes and in light clothing. Body mass index (BMI) was calculated as weight divided by the square of height (kg/m^2). The participants were asked if they had involuntarily lost weight during the last six months and, if so, how many kilograms (kg) they had lost. The weight loss was grouped as either below 5%, between 5% and 10% or above 10% of body weight prior to weight loss. Based on both the BMI and degree of weight loss, we categorised each subject as being at low, medium or high risk of malnutrition, according to the Malnutrition Universal Screening Tool (MUST) (Figure 1).

This tool also has an acute disease component (associated with a lack of nutritional intake for >5 days) that, in our analyses, was set to zero because all of the participants presented at the research centre and were thus regarded as not acutely ill. The weight loss question in the present study was slightly modified to address weight loss over a time span of the “last 6 months”, but this encompass the time span of the “last 3-6 months” in the original ‘MUST’ tool. The British Society of Parenteral and Enteral nutrition (www.bapen.org.uk) developed the ‘MUST’ tool (14) and is one of the nutritional screening instruments recommended by the European Society for Parenteral and Enteral nutrition for use in non-institutionalised elderly (15).

Other variables

We also aimed to study the association between zinc deficiency and mental health. The Hopkins Symptoms Check List-10 (SCL-10) was utilised to assess mental health distress. The SCL-10 is a self-administered instrument that primarily explores symptoms of anxiety and depression (16) and has been widely used in epidemiological studies. The ten items of the SCL-10 were part of the questionnaire that was included in the invitation to participate in the survey. A higher SCL-10 score indicates a greater number of symptoms (score ranging between 1.0 and 4.0). An SCL-10 score of ≥ 1.85 has been proposed as the cut-off for predicting diagnosed mental disorders (16). An important source of zinc in the Western diet is meat (17). Frequency of meat intake, smoking habits and sociodemographic variables were also obtained from the self-administered questionnaires.

Statistical analysis

Differences in baseline variables between both men and women and participants according to zinc status were analysed using the t-test, chi-square test or Mann-Whitney U test (Tables 1 and 3). The associations between risk of malnutrition (medium and high risk combined) and zinc deficiency were analysed using logistic regression, yielding odds ratio (OR) estimates with 95% confidence intervals (CIs) (Figure 2). The OR estimates were adjusted for age, smoking status and serum albumin. The SCL-10 score was positively skewed, and the median SCL-10 values with 25-75% interquartile (IQ) ranges are reported. Two-sided p-values <0.05 were considered statistically significant. The analyses were performed using SPSS statistical software version 19.0 (SPSS Inc., Chicago, Illinois, USA).

Each participant provided written informed consent. The study was conducted according to the guidelines of the Declaration of Helsinki.

Results

A total of 743 men and 778 women were included in the analysis. A risk of malnutrition (medium and high risk combined) was found in 8.0% of the participants, more often in women (10.4%) than in men (5.5%). BMI did not differ between men and women; however, former smoking was more common in men than in women (Table 1).

The prevalence of zinc deficiency was 10.1% among all participants, with rates of 13.1% in men and 7.3% in women. Among participants at risk of malnutrition, zinc deficiency was found in 31.7% of the men and 12.3% of the women (Figure 2). With increasing age, zinc deficiency was more prevalent in both men and women (Table 2). The mean serum zinc value was 11.9 $\mu\text{mol/L}$ in both men and women (range 4.8-20 $\mu\text{mol/L}$) (Table 1). The mean albumin level was 45.1 g/L (range 35.7-51.9 g/L), and the albumin level was slightly lower in zinc-deficient individuals (Table 3).

The association between zinc deficiency and risk of malnutrition was further analysed using logistic regression. Zinc deficiency was positively associated with the risk of malnutrition both in a model adjusted for gender only (OR 2.6 [1.6-4.2]) and in a model adjusted for gender, age, smoking status and serum albumin (OR 2.2 [95% CI 1.3-3.6]).

Meat is one of the most important sources of zinc in Northern Europe. The reported weekly frequency of meat intake was not lower in the participants with zinc deficiency (Table 3). Mental health distress, as assessed by the SCL-10 score, was reported more frequently by women than by men (Table 1). However, no significant differences in mental health distress were found between the two categories of zinc status in men or women (Table 3).

Discussion

In this population-based study of elderly men and women, we found that one out of ten individuals had zinc deficiency. However, in elderly men at risk of malnutrition, one out of three had zinc deficiency. In women, the corresponding proportion was lower, but the value was still increased compared with that in women not at risk of malnutrition.

Prevalence of zinc deficiency

Previous studies of zinc status in elderly individuals largely explored smaller populations, and various cut-offs for zinc deficiency have been applied. A Norwegian study of home-living elderly individuals revealed that 4 out of 97 participants had serum zinc levels below 8 $\mu\text{mol/L}$ (18). In a European multicentre study that included 853 elderly individuals, a slightly higher cut-off (11.0 $\mu\text{mol/L}$) was used, resulting in the classification of 31% of the participants as zinc-deficient (5). Applying the same cut-off value to the present study sample would have revealed a similar zinc deficiency prevalence rates (28%).

With increasing age, the prevalence of zinc deficiency increases significantly (Table 2). Some previous studies of zinc deficiency compared the old and oldest old subjects, but most studies included a small number of participants. In the Zenith study of 387 participants, the prevalence of zinc deficiency was similar between old and oldest old subjects (19). However, in a study from Italy, the oldest old had significantly lower levels of zinc compared with the old (20). This age-associated increase in zinc deficiency may be explained by several factors, including both an age-related decline in the absorptive capacity of the small bowel and a general decline in energy and food intake in the oldest old (10).

Risk of malnutrition and zinc deficiency

The relationship between the risk of malnutrition and serum zinc was previously explored in a study of 50 hospitalised patients using the Mini Nutritional Assessment tool (8). In that study, no association was found between zinc status and the risk of malnutrition. A population-based study of elderly individuals using the 'MUST'-tool showed lower mean zinc values in individuals at risk of malnutrition (9). However, the proportion of malnourished elderly individuals with zinc deficiency was not estimated.

Several mechanisms may explain the observed associations between malnutrition and zinc deficiency. First, zinc deficiency may produce altered taste and smell, resulting in reduced

appetite and consequent weight loss and malnutrition (21). Second, a reduced intake of zinc-containing food in malnourished elderly individuals may result in reduced body zinc. In Western diets, meat (beef and pork) is the most important source of zinc, contributing approximately 50% of the total zinc intake.

The recommendations for the intake of zinc are similar for elderly and other adult individuals. In the present study, no association was found between the reported intake of meat per day and zinc deficiency. However, more detailed information regarding the intake of zinc-containing foods was not available; in general, it may be difficult to obtain valid data concerning food habits from self-administered questionnaires (22).

One strength of the present study is the strictly population based design and the relatively large study population. A potential problem is the assessment of zinc status by serum zinc as only a small proportion of the body zinc is present in the serum pool. The assessment of zinc status is challenging and several biomarkers and methods have been suggested, such as the measurement of zinc in hair, erythrocytes and serum or plasma. However, serum (or plasma) zinc is the recommended method for the assessment of zinc status in larger populations (23, 24).

The level of serum zinc may be related to that of serum albumin. The majority of zinc in the serum is bound to albumin, and it has been proposed that a reduction of zinc-binding sites in hypoalbuminaemia may influence the serum zinc level. However, a reduced zinc status may also inhibit albumin synthesis (25). Although albumin is not a reliable marker of nutritional status, a reduction in serum albumin can be observed in some patients with malnutrition. This reduction may be explained by coexisting comorbidity and inflammation (26). We therefore compared serum albumin levels between the low and normal zinc groups. The albumin levels were lower in both men and women with zinc deficiency. However, no individuals exhibited an albumin level below 35 g/L, which is regarded as the cut-off value defining a significant effect of albumin level on serum zinc concentration (13). Moreover, the inclusion of albumin in the model of the relationship between zinc deficiency and malnutrition only slightly changed the odds ratio estimate.

No significantly high levels of zinc were detected in this study sample. High levels of serum zinc occur only during supplementation with zinc (13), and in Norway, supplements

containing significant amounts of zinc are primarily obtained by prescription. The toxicity of zinc is low.

Zinc is not often analysed in clinical practice, as other micronutrients are more closely associated with specific functions. As an example, iron and folate are required for haemoglobin production, the deficiency of which can be manifested by anaemia and is thus more easily detected. In contrast, zinc is necessary for general metabolism, and manifestations of any deficiency may therefore be more elusive than those associated with other micronutrients (25).

Impact of zinc deficiency

The impact of mild to moderate zinc deficiency has not been fully explored. Previous research has provided evidence for the impairment of the T-lymphocyte balance due to such deficiency, resulting in an impaired immune system and moderate zinc deficiencies in elderly men and women (27). Studies of nursing home residents suggested an increased level of pneumonia in zinc-deficient individuals and a reduction in the risk of pneumonia following zinc supplementation (28).

Furthermore, some studies have linked zinc deficiency to depression and other psychiatric disorders, mostly based on studies of psychiatric in- and out-patients (29, 30). However, in the present study, we found no association between zinc deficiency and symptoms of anxiety or depression in community-living elderly individuals.

Conclusion

In this population-based study, we found zinc deficiency to be associated with the risk of malnutrition. Overall, zinc deficiency was found in one out of ten community-living elderly people. Our results support the assessment of zinc status in elderly people at risk of malnutrition, particularly elderly men.

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JMK performed the analysis and wrote the first draft of the paper. All authors contributed to the critical revision of the article and approved the final version to be published.

Ethics of human subject participation: Each participant provided written informed consent prior to inclusion in the study. The Tromsø 6 study was approved by the Regional Board of Research Ethics in Northern Norway

(http://helseforskning.etikkom.no/xnet/public/side?p_dim=11928; approval number 200605174-12/IAY/400). The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki.

Table 1 Baseline characteristics of participating elderly men and women, The Tromsø study*

	Men (n=743)	Women (n=778)	<i>p</i> -value [†]
Age, mean (SD)	71.3 (5.3)	72.4 (5.8)	<0.01 [‡]
Smoking status			
Never smoked % (n)	22.8 (167)	47.8 (361)	
Previous smokers % (n)	62.2 (456)	37.0 (280)	<0.01 [§]
Current smokers % (n)	15.0 (110)	15.2 (115)	
Nutritional status			
BMI (kg/m ²), mean (SD)	27.0 (3.5)	26.9 (4.6)	0.89 [‡]
Medium/high risk of malnutrition, % (n)	5.5 (41)	10.4 (81)	<0.01 [§]
Laboratory values			
Serum zinc (μmol/L), mean (SD)	11.9 (1.78)	11.9 (1.74)	0.94 [‡]
Serum zinc (μmol/L), range	4.8-18.3	7.6-20.0	
Serum zinc deficiency, % (n)	13.1(97)	7.3 (57)	<0.01 [§]
Albumin (g/L), mean (SD)	45.3 (2.2)	44.8 (2.3)	<0.01 [‡]
Mental health score			
SCL-10 score, median (interquartile range)	1.1 (1.0-1.3)	1.2 (1.1-1.5)	<0.01

*There are minor differences in the number of evaluated individuals due to variations in missing values on the self-administered questionnaire regarding smoking

[†] *p*-value for differences between groups according to the [‡]t test, [§]chi-square test or ^{||}Mann-Whitney U test

Table 2 Prevalence (%) of zinc deficiency in different age categories of elderly men and women, The Tromsø study.

Age range (years)	Men	Women
64-71	12.0 (53/441) [†]	5.5 (22/402)
72-78	12.0 (26/217)	7.1 (17/239)
79-87	21.2 (18/85)	13.1 (18/137)
<i>p</i> -value*	0.07	0.005

**p*-value for linear by linear association between age categories

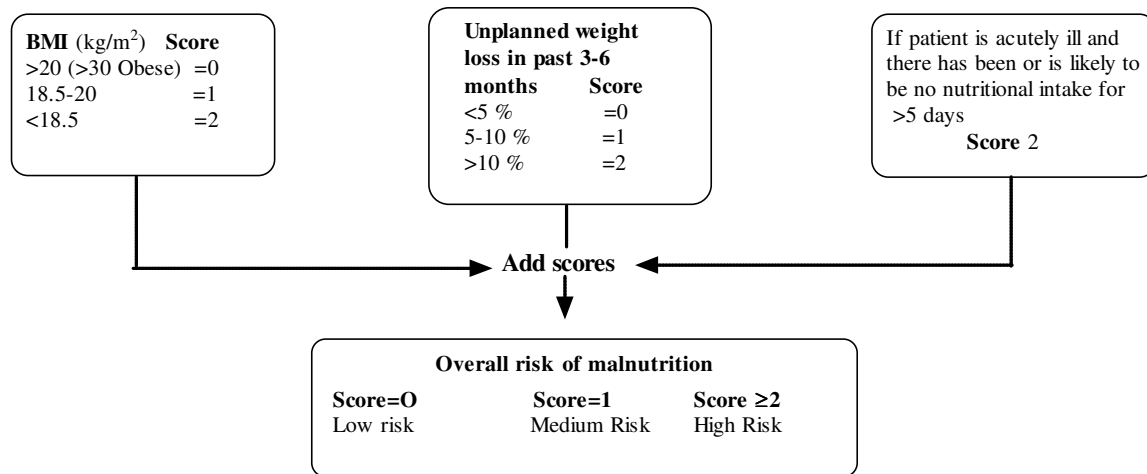
[†] % (number of subjects with zinc deficiency/number of subjects in the age group)

Table 3 Characteristics of the participating elderly men and women* according to zinc status, The Tromsø study.

	Men (n=743)			Women (n=778)		
	Zinc status			Zinc status		
	Zn-deficient (n=97)	Zn-normal (n=646)	<i>p</i> -value [†]	Zinc-deficient (n=57)	Zn-normal (n=721)	<i>p</i> -value [†]
Age, mean (SD)	72.2 (5.9)	71.2 (5.2)	0.02 [‡]	74.7 (6.5)	72.2 (5.7)	0.07 [‡]
Single marital status, % (n)	26.8 (26)	22.4 (145)	0.41 [§]	63.2 (36)	49.8 (359)	0.07 [§]
Smoking status						
Never, % (n)	27.7 (26)	22.1 (141)		56.4 (31)	47.1(330)	
Previous, % (n)	58.5 (55)	62.8 (401)	0.48 [§]	30.9 (17)	37.5 (263)	0.41 [§]
Current, % (n)	13.8 (13)	15.2 (97)		12.7 (7)	15.4(108)	
Nutritional status						
Medium/high risk of malnutrition, % (n)	13.4 (13)	4.3 (28)	0.01 [§]	17.5 (10)	9.8 (17)	0.07 [§]
Nutritional intake						
Meat intake ≤ 3 times/week, % (n)	20.2 (18)	18.8 (114)	0.85 [§]	34.7 (17)	28.1 (181)	0.41 [§]
Mental health						
SCL-10 score, median (interquartile range)	1.1 (1.0-1.3)	1.1 (1.0-1.2)	0.93 [‡]	1.2 (1.1-1.5)	1.2 (1.1-1.4)	0.77 [‡]
Supplementary laboratory values						
Albumin (g/L), mean (SD)	44.3 (2.4)	45.5 (2.2)	<0.05 [‡]	43.6 (2.7)	44.9 (2.2)	<0.05 [‡]

*There are minor differences in the number of evaluated individuals due to variations in missing values on the self-administered questionnaire regarding smoking.

[†] *p*-value for differences between groups according to the [‡]t test, [§]chi-square test or [‡]Mann-Whitney U test



The "Malnutrition Universal Screening Tool" is reproduced here with the kind permission of BAPEN (British Association for Parenteral and Enteral Nutrition). For further information on 'MUST' and management guidelines, see www.bapen.org.uk.

Figure 1 The Malnutrition Universal Screening Tool (MUST) is composed of a BMI score, a weight-loss score and an acute illness component. The risk of malnutrition can be assessed based on the sum of these scores.

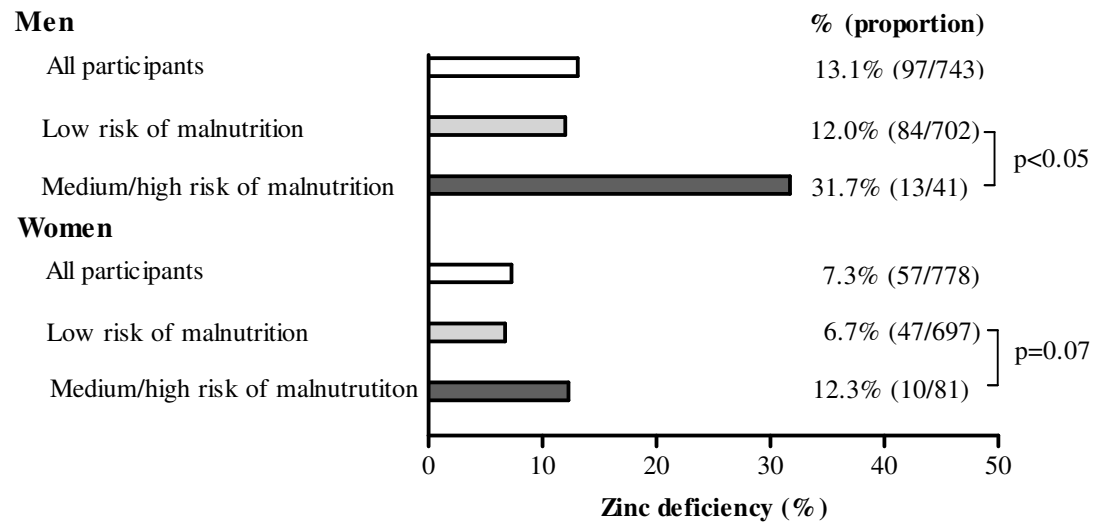


Figure 2 Zinc deficiency given as % (proportions) for all men and women, as well as for low and medium/high risk categories of malnutrition, The Tromsø study.

References

- (1) Kaplan LA, Pesce AJ, Kazmierczak SC (2003). *Clinical Chemistry. Theory, Analysis, Correlation*. 4th ed. ed. St. Louis: Mosby.
- (2) Tuerk MJ, Fazel N (2009). Zinc deficiency. *Curr Opin Gastroenterol* **25**, 136-143.
- (3) Barnett JB, Hamer DH, Meydani SN (2010). Low zinc status: a new risk factor for pneumonia in the elderly? *Nutr Rev* **68**, 30-37.
- (4) McClain CJ, McClain M, Barve S, Boosalis MG (2002). Trace metals and the elderly. *Clin Geriatr Med* **18**, 801-18.
- (5) Marcellini F, Giuli C, Papa R, Gagliardi C, Dedoussis G, Herbein G, et al. (2006) Zinc status, psychological and nutritional assessment in old people recruited in five European countries: Zincage study. *Biogerontology* **7**, 339-345.
- (6) Walker CF, Ezzati M, Black R (2008). Global and regional child mortality and burden of disease attributable to zinc deficiency. *Eur J Clin Nutr* **63**, 591-597.
- (7) High KP. Micronutrient supplementation and immune function in the elderly (1999). *Clinical infectious diseases* **28**, 717.
- (8) Pepersack T, Rotsaert P, Benoit F, Willems D, Fuss M, Bourdoux P, et al. Prevalence of zinc deficiency and its clinical relevance among hospitalised elderly (2011). *Arch Gerontol Geriatr* **33**, 243-253.
- (9) Margetts BM, Thompson RL, Elia M, Jackson AA (2003). Prevalence of risk of undernutrition is associated with poor health status in older people in the UK. *Eur J Clin Nutr* **57**, 69-74.
- (10) Haase H, Rink L (2009). The immune system and the impact of zinc during aging. *Immun Ageing* **6**, 9.
- (11) Jacobsen BK, Eggen AE, Mathiesen EB, Wilsgaard T, Njølstad I (2012). Cohort profile: the Tromsø study. *Int J Epidemiol* **41**, 961-967.
- (12) Eggen AE, Mathiesen EB, Wilsgaard T, Jacobsen BK, Njølstad I (2013). The sixth survey of the Tromsø Study (Tromsø 6) in 2007-08: collaborative research in the interface between clinical medicine and epidemiology: study objectives, design, data collection procedures, and attendance in a multipurpose population-based health survey. *Scand J Public Health* **41**, 65-80.
- (13) International Zinc Nutrition Consultative Group (IZiNCG), Brown KH, Rivera JA, Bhutta Z, Gibson RS, King JC, et al. (2004) International Zinc Nutrition Consultative Group (IZiNCG) technical document #1. Assessment of the risk of zinc deficiency in populations and options for its control. *Food Nutr Bull* **25**, S99-203.

- (14) Elia M (2003) The "MUST" Report. Nutritional screening of adults: a multidisciplinary responsibility. Worcs, UK: Malnutrition Advisory Group/The British Association for Parenteral and Enteral Nutrition.
- (15) Kondrup J, Allison SP, Elia M, Vellas B, Plauth M (2003). ESPEN guidelines for nutrition screening 2002. *Clin Nutr* **22**, 415-421.
- (16) Strand BH, Dalgard OS, Tambs K, Rognerud M (2003). Measuring the mental health status of the Norwegian population: a comparison of the instruments SCL-25, SCL-10, SCL-5 and MHI-5 (SF-36). *Nord J Psychiatry* **57**, 113-118.
- (17) Maret W, Sandstead HH (2006) Zinc requirements and the risks and benefits of zinc supplementation. *Journal of Trace Elements in Medicine and Biology* **20**, 3-18.
- (18) Lundgren B, Mowe M, Norseth J, Bohmer T (2002) Zinc deficiency is of limited clinical importance in the elderly (>69 y) of Oslo. *J Nutr Health Aging* **6**, 243-244.
- (19) Andriollo-Sanchez M, Hininger-Favier I, Meunier N, Toti E, Zaccaria M, Brandolini-Bunlon M, et al. (2005) Zinc intake and status in middle-aged and older European subjects: the ZENITH study. *Eur J Clin Nutr* **59**, S37-S41.
- (20) Ravaglia G, Forti P, Maioli F, Nesi B, Pratelli L, Savarino L, et al. (2000) Blood micronutrient and thyroid hormone concentrations in the oldest-old. *Journal of Clinical Endocrinology & Metabolism* **85**, 2260-2265.
- (21) Yagi T, Asakawa A, Ueda H, Ikeda S, Miyawaki S, Inui A (2013) The Role of Zinc in the Treatment of Taste Disorders. *Recent Pat Food Nutr Agric* **5**, 44-51.
- (22) Rothman KJ, Greenland S, Lash TL (2008) Nutritional Epidemiology. In *Modern Epidemiology*, 3rd ., pp. 580-597. Philadelphia: Lippincott Williams & Wilkens.
- (23) Lowe NM, Fekete K, Decsi T (2009) Methods of assessment of zinc status in humans: a systematic review. *Am J Clin Nutr* **89**, 2040S-2051S.
- (24) de Benoist B, Darnton-Hill I, Davidsson L, Fontaine O, Hotz C (2007) Conclusions of the Joint WHO/UNICEF/IAEA/IZiNCG Interagency Meeting on Zinc Status Indicators. *Food Nutr Bull* **28**, S480-4.
- (25) King JC (2011) Zinc: an essential but elusive nutrient. *Am J Clin Nutr* **94**, 679S-684S.
- (26) Omran ML, Morley JE (2000). Assessment of protein energy malnutrition in older persons, Part II: Laboratory evaluation. *Nutrition* **16**, 131-140.
- (27) Uciechowski P, Kahmann L, Plümäkers B, Malavolta M, Mocchegiani E, Dedoussis G, et al. (2008) TH1 and TH2 cell polarization increases with aging and is modulated by zinc supplementation. *Exp Gerontol* **43**, 493-498.
- (28) Barnett JB, Hamer DH, Meydani SN (2010) Low zinc status: a new risk factor for pneumonia in the elderly? *Nutr Rev* **68**, 30-37.

(29) Swardfager W, Herrmann N, Mazereeuw G, Goldberger K, Harimoto T, Lanctôt KL (2013) Zinc in depression: a meta-analysis. *Biol Psychiatry* **74**, 872-878.

(30) Grønli O, Kvamme JM, Friberg O, Wynn R (2013) Zinc deficiency is common in several psychiatric disorders. *PloS one* **8**, E82793.