


# Malnutrition in Bariatric Surgery Candidates: Multiple Micronutrient Deficiencies Prior to Surgery

Leigh A. Peterson<sup>1</sup>  · Lawrence J. Cheskin<sup>2,3,4</sup> · Margaret Furtado<sup>5</sup> · Konstantinos Papas<sup>6</sup> · Michael A. Schweitzer<sup>1</sup> · Thomas H. Magnuson<sup>1</sup> · Kimberley E. Steele<sup>1</sup>

Published online: 22 August 2015  
© Springer Science+Business Media New York 2015

## Abstract

**Background** Over 78 million American adults have obesity. Bariatric surgery is the leading means of durable weight loss. Nutritional deficiencies are commonly treated post-operatively but are often undiagnosed pre-operatively. Malnutrition is correlated with adverse surgical outcomes.

**Objectives** The aim of this study is to assess pre-operative nutritional status in our bariatric surgery candidates in a cross-sectional study.

**Methods** We recruited 58 bariatric candidates approved to undergo the Roux-en Y gastric bypass. Nutritional status was determined for vitamins A, B<sub>12</sub>, D, E- $\alpha$ , and E- $\beta/\gamma$  as well as thiamine, folate, and iron. We used clinical as well as frank deficiency cut-offs based on the Institute of Medicine and the World Health Organization guidelines.

**Results** This cohort was largely female (77.6 %) and white (63.8 %). Median age was 42.2 years. Median body mass index (BMI) was 46.3 kg/m<sup>2</sup>. Multiple comorbidities (MCM) were present in 41.4 %, 54.0 % hypertension, 42.0 % diabetic, 34.0 % sleep apnea. Men had more comorbidities, 69.2 % with MCM. Folate and iron saturation varied significantly by sex. Vitamins A, D, E- $\alpha$ , and thiamine significantly varied by race. Vitamin D negatively correlated with BMI ( $p=0.003$ ) and age ( $p=0.030$ ). Vitamin A negatively correlated with age ( $p=0.001$ ) and number of comorbidities ( $p=0.003$ ). These pre-operative bariatric candidates had significant malnutrition, particularly in vitamin D (92.9 %) and iron (36.2 to 56.9 %). Multiple micronutrient deficiency (MMND) was more common in blacks (50.0 versus 39.7 % overall). Number of comorbidities did not correlate with MMND.

**Conclusions** Malnutrition in one or multiple micronutrients is pervasive in this pre-operative bariatric cohort. The effect of pre-operative supplementation, especially vitamin D and iron, should be explored.

✉ Leigh A. Peterson  
leighpeterson@jhmi.edu

✉ Lawrence J. Cheskin  
cheskin@jhu.edu

Margaret Furtado  
MargaretF@auamed.net

Konstantinos Papas  
guspapas@gmail.com

Michael A. Schweitzer  
mschwei7@jhmi.edu

Thomas H. Magnuson  
tmagnus@jhmi.edu

Kimberley E. Steele  
ksteel3@jhmi.edu

<sup>1</sup> The Johns Hopkins Center for Bariatric Surgery, 4940 Eastern Avenue, Baltimore, MD 21224, USA

<sup>2</sup> The Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, USA

<sup>3</sup> The Johns Hopkins Weight Management Center, The Global Obesity Prevention Center at Johns Hopkins, Baltimore, MD 21205, USA

<sup>4</sup> The Johns Hopkins Bloomberg School of Public Health, 550 N Broadway, Baltimore, MD 21205, USA

<sup>5</sup> The Johns Hopkins Bayview Department of Clinical Nutrition, American University of Antigua School of Medicine, 4940 Eastern Avenue, Baltimore, MD 21224, USA

<sup>6</sup> PO Box 572, Jonesborough, TN 37659, USA

**Keywords** Bariatric surgery · Nutritional status · Multiple micronutrient deficiency · Malnutrition

## Introduction

More than 78 million American adults have obesity [1] (body mass index (BMI)  $\geq 35$  kg/m<sup>2</sup>), costing an estimated \$147 billion annually due to medical care alone [2–4]. Non-Hispanic blacks and Hispanics are disproportionately affected with obesity rates of 47.8 and 42.5 %, respectively, compared to 32.6 % for non-Hispanic whites [5].

Currently, sustained long-term weight loss is most successfully obtained with bariatric surgery. Since the inception of modern weight loss surgery in 1977 with the development of the Roux-en Y gastric bypass procedure, bariatric surgeons have attempted to optimize patient care by improving techniques and post-operative care, including nutritional counseling [5]. Pre-operative nutrition, on the other hand, is largely uncultivated.

Nutritional deficiencies after surgery are commonly treated, particularly following malabsorptive procedures like the Roux-en Y gastric bypass. If deficiencies are present prior to surgery, it stands to reason that remedying them prior to surgery could be beneficial and certainly easier than after a malabsorptive procedure. Furthermore, malnutrition has been linked to adverse surgical outcomes in many studies [5].

In this study, we assessed the baseline nutritional status of our patients who were approved and scheduled to undergo Roux-en Y gastric bypass. Our aim was to determine the prevalence of micronutrient deficiencies in our patient population prior to surgery. We have focused on vitamins A, B<sub>12</sub>, D, E- $\alpha$ , E- $\beta/\gamma$ , thiamine, folate, and iron as these are the micronutrient deficiencies we see most commonly in our post-operative patient population.

## Methods

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

We determined the nutritional status in 58 consecutive patients in this prospective, cross-sectional study (a 20 % sample of our annual surgeries). Patients were included if they were aged 18 to 65 years and were approved to undergo the Roux-en Y gastric bypass procedure. We excluded other procedures such as adjustable gastric band and vertical sleeve gastrectomy in an attempt to limit differences within the group due to BMI and other factors that may contribute to procedure selection. While we did not exclude those taking a standard multivitamin, we excluded those taking high dose supplements such as bariatric multivitamins, which some patients choose to begin prior to surgery.

As part of the standard of care and preparation for surgery, all patients underwent routine history and physical examination. On the day of surgery in the pre-operative holding area, we collected blood specimens to determine the nutritional status of vitamins A, B<sub>12</sub>, D, E- $\alpha$ , E- $\beta/\gamma$ , thiamine, folate, and iron (iron, total iron binding capacity (TIBC), and iron saturation). The  $\alpha$  form (most biologically active form) and  $\beta/\gamma$  form (most dietary abundant form) of vitamin E were determined separately as  $\beta/\gamma$  has been shown to decrease with  $\alpha$  supplementation [6]. High pressure liquid chromatography was used for vitamins A, E- $\alpha$ , and E- $\beta/\gamma$  liquid chromatography with tandem mass spectrometry for thiamine and immunoassays for vitamins B<sub>12</sub>, D, and folate. Spectrophotometry was used for iron and turbidity for transferrin.

Statistical analysis was performed using Stata 12.1 (StataCorp, College Station, TX, USA). Missing data was treated as missing at random. We set  $\alpha=0.05$  and  $\beta=0.20$  for all analysis and used two-sided tests. Descriptive univariate and bivariate analysis was utilized to describe the nutritional status and comorbidities of our patient cohort. Results are expressed as median  $\pm$  standard deviation.

This research study was approved by our Institutional Review Board. All patients underwent informed consent prior to participation.

## Results

This cohort was 77.6 % female and 63.8 % white (Table 1). The median age was 42.5 years (range 24 to 65 years) with no significant difference by sex or race/ethnicity. The males were heavier and taller. Median BMI was 46.3 kg/m<sup>2</sup> (range 33.5 to 64.6 kg/m<sup>2</sup>), which varied only by race/ethnicity. Hispanics and blacks tended to present with higher BMIs than whites. Comorbidities were highly prevalent in this cohort with multiple comorbidities present in 41.4 % of patients; 54 % had hypertension, 42.0 % were diabetic, and 34.0 % had sleep apnea. The highest rate of multiple comorbidities was seen in males, which was largely driven by a higher rate of diabetes and sleep apnea.

Group status for each nutrient is reported in Table 2. Median group status indicates deficiency in vitamin D in total and in all strata. Folate and iron saturation were significantly higher in males than females. Nutritional status was poorer in blacks and Hispanics with vitamins A, D, E- $\alpha$ , and thiamine being significantly lower than in whites. Vitamin D was strongly correlated with BMI ( $p=0.003$ ) and age ( $p=0.030$ ). Vitamin A strongly correlated with age ( $p=0.001$ ) and number of comorbidities ( $p=0.003$ ).

To further explore the differences in this cohort, we dichotomized nutritional status into normal versus clinical deficiency (Table 3) and frank deficiency cut points (Table 4). We

**Table 1** Pre-operative characteristics of patients presenting for bariatric surgery

Cohort demographics by sex			
	Total	Female	Male
Demographics			
Age (years)	42.5±10.9	41.9±11.0	43.0±11.1
Female	77.6 %	n=45	n=13
White	63.8 %	60.0 %	76.9 %
Weight (lbs)	288.9±46.6	281.5±43.1	316.6±50.5 *
Height (in.)	66.3±3.4	65.2±2.8	70.3±2.4 *
BMI (kg/m <sup>2</sup> )	46.3±6.9	46.63±7.0	45.0±6.8
Medical history			
Hypertension	54.0 %	48.7 %	72.7 %
Diabetes	42.0 %	30.8 %	81.8 % *
High cholesterol	32.7 %	29.0 %	45.5 %
Gastroesophageal reflux	32.0 %	30.8 %	36.4 %
Sleep apnea	34.0 %	25.6 %	63.6 % *
Cancer	4.0 %	0.0 %	18.2 % *
Irritable bowel syndrome	4.0 %	0.0 %	18.2 % *
Cholecystectomy	14.0 %	10.3 %	27.3 %
Multiple comorbidities	41.4 %	33.3 %	69.2 % *
Cohort demographics by race/ethnicity			
	White	Black	Hispanic
Demographics			
Age (years)	43.8±11.7	40.4±9.2	32.7±12.5
Female	73.0 %	83.3 %	100 %
White	n=32	n=14	n=3
Weight (lbs)	283.4±42.5	298.4±56.6	302.7±33.1
Height (in.)	66.8±3.2	65.8±3.7	62.3±1.5
BMI (kg/m <sup>2</sup> )	44.6±6.3	48.3±6.8	55.0±8.5 *
Medical history			
Hypertension	51.5 %	57.1 %	66.7 %
Diabetes	45.5 %	28.6 %	66.7 %
High cholesterol	37.5 %	21.4 %	33.3 %
Gastroesophageal reflux	45.5 %	0.0 %	33.3 % *
Sleep apnea	39.4 %	21.4 %	33.3 %
Cancer	6.1 %	0.0 %	0.0 %
Irritable bowel syndrome	6.1 %	0.0 %	0.0 %
Cholecystectomy	15.2 %	7.1 %	33.3 %
Multiple comorbidities	43.2 %	38.9 %	33.3 %

\*p<0.05

found significant malnutrition, particularly in vitamin D and iron. Deficiency was more prominent in blacks. Multiple micronutrient deficiency (MMND) was more common in blacks, 50.0 % versus 39.7 % overall. Number of comorbidities did not significantly correlate with MMND.

**Table 2** Pre-operative nutritional status of patients presenting for bariatric surgery

Nutritional status by sex			
	Total	Female	Male
Vitamin A (µg/dL)	55.5±21.1	54.4±22.1	59.5±17.4
Vitamin B <sub>12</sub> (pg/ml)	451.9±235.6	444.0±240.6	481.3±223.2
Vitamin D (ng/mL)	16.8±6.6	16.7±7.1	17.3±4.3
Vitamin E-α (mg/L)	11.4±4.8	11.0±4.9	12.7±4.6
Vitamin E-β/γ (mg/L)	2.1±0.9	2.2±0.9	1.7±0.7
Thiamine (nmol/L)	133.7±47.0	132.1±51.5	139.6±24.5
Folate (ng/mL)	15.3±6.2	14.3±5.7	19.2±6.7 *
Iron (µg/dL)	75.3±47.9	70.4±36.0	92.6±75.5
TIBC (µg/dL)	360.0±80.1	369.9±79.8	325.7±74.0
Iron saturation (%)	22.5±16.8	19.4±9.6	33.4±28.9 *
Nutritional status by race/ethnicity			
	White	Black	Hispanic
Vitamin A (µg/dL)	62.9±21.1	42.9±15.0	40.0±2.6 *
Vitamin B <sub>12</sub> (pg/ml)	434.9±224.5	464.4±185.0	591.0±580.9
Vitamin D (ng/mL)	18.2±5.6	14.6±7.8	10.7±7.4 *
Vitamin E-α (mg/L)	12.7±5.3	9.0±2.8	9.9±1.9 *
Vitamin E-β/γ (mg/L)	2.2±1.0	1.9±0.7	2.2±0.1
Thiamine (nmol/L)	150.6±47.6	105.9±30.3	103.0±32.2 *
Folate (ng/mL)	15.9±6.1	14.3±6.8	14.1±0.9
Iron (µg/dL)	83.6±56.1	59.2±23.3	70.0±20.8
TIBC (µg/dL)	356.4±78.7	367.7±90.5	358.7±33.1
Iron saturation (%)	25.4±20.0	17.0±6.6	19.7±7.2

\*p<0.05

**Discussion**

The American Society for Metabolic & Bariatric Surgery (ASMBS) reports that 80 % of bariatric surgery patients are female [5], similar to this cohort (77.6 % female). Patients are typically between the ages of 40 and 64 years of age [7–11]; our median age was 42.5 years (IQR 33 to 50 years of age). The majority of surgeries are performed on whites despite higher burden of obesity in blacks and Hispanics. We observed this as well (63.8 % white).

The highest risk of morbidity and mortality in obesity is class 3+ obesity (BMI≥40 kg/m<sup>2</sup>). Class 3+ obesity was present in 81.0 % of this pre-operative bariatric surgery cohort and was more frequent in blacks and Hispanics. Multiple comorbidities were less common in class 3+ obesity (37.5 versus 63.6 % in BMI<40 kg/m<sup>2</sup>). This is likely due to the approval process for the surgery itself. Patients with a BMI under 40 kg/m<sup>2</sup> are considered candidates for bariatric surgery if they have “high-risk comorbid conditions such as life-threatening cardiopulmonary problems (for example, severe sleep apnea,

**Table 3** Frequency of clinical deficiency prior to bariatric surgery by sex and race

	Cut-point	Total	Female	Male	White	Black	Hispanic	
Vitamin A	<20 ug/dL	1.7 %	2.2 %	0 %	0 %	5.6 %	0 %	
Vitamin B <sub>12</sub>	<180 ng/L	3.5 %	2.2 %	7.7 %	2.7 %	5.6 %	0 %	
Vitamin D	<30 ng/mL	92.9 %	90.9 %	100 %	91.9 %	93.8 %	100 %	
Vitamin E- $\alpha$	<5.5 mg/L	5.2 %	6.7 %	0 %	0 %	16.7 %	0 %	*
Thiamine	<78 nmol/L	1.8 %	2.3 %	0 %	0 %	0 %	33.3 %	*
Folate	<7.2 ug/L	5.3 %	6.7 %	0 %	2.7 %	11.8 %	0 %	
Iron								
	Female	<50 ug/dL	36.2 %	35.4 %	38.5 %	37.8 %	38.9 %	0 %
	Male	<65 ug/dL						
TIBC	>400 ug/dL	22.4 %	26.6 %	7.7 %	24.3 %	22.2 %	0 %	
Iron saturation	<20 %	56.9 %	62.2 %	38.5 %	51.4 %	66.7 %	66.7 %	
Multiple micronutrient deficiencies	$\geq 3$	39.7 %	40.0 %	38.5 %	35.1 %	50.0 %	33.3 %	

\* $p < 0.05$ 

pickwickian syndrome, or obesity-related cardiomyopathy) or uncontrolled type 2 diabetes mellitus” or “obesity-induced physical problems interfering with lifestyle (for example, joint disease treatable but for the obesity, or body size problems precluding or severely interfering with employment, family function, and ambulation)” [12–16]. Such considerations may also explain the high rate of multiple comorbidities (41.4 %) as well as for hypertension (54 %), diabetes (42.0 %), and sleep apnea (34.0 %) since these likely improve the chance a patient will be approved for bariatric surgery.

Males presented with the highest rate of multiple comorbidities, driven by a higher rate of diabetes and sleep apnea. This is despite the fact that class 3+ obesity was present in 69.2 % of males compared to 84.4 % of females. This also may be due to the approval process for bariatric surgery. It may be due to the differing motivations for males versus females. Females undergoing bariatric surgery more frequently cite physical appearance as a motivator [17, 18]. Additionally, males have a higher rate of sleep apnea largely due to greater central adiposity [19–25].

Sleep apnea also adds to the metabolic syndrome, e.g., insulin resistance, hypertension, and dyslipidemia [26].

While most comorbidities present in this cohort did not vary by race, the rate of gastroesophageal reflux disease (GERD) was significantly lower in blacks. None of the 14 blacks reported GERD, while 45.5 % of whites and 1 out of 3 Hispanics reported GERD. Caucasians are known to be at greater risk of GERD [27].

Racial disparities also exist in this cohort in nutritional status with minorities (blacks and Hispanics) having significantly lower status in vitamins A, D, E- $\alpha$ , and thiamine. The primary deficiency in minorities is in vitamin D, which was present in all Hispanics ( $n=3$ ) in this cohort. Slightly fewer blacks (81.3 %) presented with frank vitamin D deficiency and even fewer whites (64.9 %) fell into this category. Race is indicative of melanin concentration, and increased melanin concentration in the skin is a risk factor for vitamin D deficiency. Since melanin prevents ultraviolet (UV)-B solar radiation from photoproducing vitamin D in the skin, darker skin

**Table 4** Frequency of frank deficiency prior to bariatric surgery by sex and race

	Cut-point	Total	Female	Male	White	Black	Hispanic	
Vitamin A	<10 ug/dL	0 %	0 %	0 %	0 %	0 %	0 %	
Vitamin B <sub>12</sub>	<150 ng/L	1.8 %	2.2 %	0 %	2.7 %	0 %	0 %	
Vitamin D	<20 ng/mL	71.4 %	72.7 %	66.7 %	64.9 %	81.3 %	100 %	
Vitamin E- $\alpha$	<3 mg/L	0 %	0 %	0 %	0 %	0 %	0 %	
Thiamine	<70 nmol/L	1.8 %	2.3 %	0 %	0 %	0 %	33.3 %	*
Folate	<4 ug/L	0 %	0 %	0 %	0 %	0 %	0 %	
Iron								
	Female	<35 ug/dL	36.2 %	35.6 %	38.5 %	37.8 %	38.9 %	0 %
	Male	<50 ug/dL						
TIBC	>400 ug/dL	22.4 %	26.6 %	7.7 %	24.3 %	22.2 %	0 %	
Iron saturation	<14 %	19.0 %	22.2 %	7.7 %	13.5 %	33.3 %	0 %	
Multiple micronutrient deficiencies	$\geq 3$	20.7 %	22.2 %	15.4 %	21.6 %	22.2 %	0.0 %	

\* $p < 0.05$

tones (blacks and Hispanics) are less able to photoproduce vitamin D given identical sun exposure. In addition to frank deficiency, clinical MMND was more frequent in blacks (50.0 versus 39.7 % for the cohort).

Overall, vitamin D and iron were the chief nutritional deficiencies found in pre-operative bariatric surgery patients. Vitamin D was negatively correlated with BMI ( $p=0.003$ ) and age ( $p=0.030$ ), a common finding in the literature [19–24, 28, 29]. Vitamin A negatively correlated with age ( $p=0.001$ ) and number of comorbidities ( $p=0.003$ ). Since vitamin A is an acute phase reactant, one would expect illness and chronic inflammation to correlate with vitamin A status.

The National Health and Nutrition Examination Survey (NHANES) 2003–2006 was used to develop the body iron model, which predicts that 9 % of females will have iron deficiency in the US population [28, 29]. The rate of iron deficiency in our cohort is higher than this prediction. We found 22.4 to 56.9 % deficiency in all patients. This breaks down to 26.6 to 62.2 % females and 7.7 to 38.5 % males. According to serum iron concentration, 36.2 % of our cohort are deficient, while TIBC indicates that 22.4 % are deficient. An interesting finding is that more males were deficient than females, according to serum iron concentration (38.5 versus 35.6 %).

The median vitamin D status in this cohort indicates frank deficiency as a group and in each subgroup (stratified by sex and race). According to NHANES 2005–2006 survey, the mean serum 25(OH)D in the USA is 22.4 ng/ml (56 nmol/L) [20, 24, 28–31], higher than the 16.8 ng/ml (42 nmol/L) mean in this cohort of pre-operative bariatric surgery patients. Obesity is a known risk factor for vitamin D deficiency due to an inherent need for more vitamin D to exhibit the same serum 25(OH)D concentration [5]. This greater need is due to sequestration of this fat soluble hormone in adipose tissue [32, 33]. As fat mass increases, an individual will require greater amounts of vitamin D (via photoproduction from sun exposure, dietary intake, and/or supplementation).

## Limitations

Limited numbers of males and minorities, especially Hispanics, were included in this study. A larger study would be able to include more subjects from these groups, which currently undergo fewer bariatric surgeries.

## Strengths

Our population is generalizable to most academic centers of excellence with the majority of patients being female and white. Our study assessed a broad range of micronutrients

and identified two chief deficiencies for future study: iron and vitamin D.

## Conclusions

Malnutrition in one or multiple micronutrients is pervasive in this pre-operative bariatric cohort, chiefly in vitamin D and iron. Minorities tended to have greater malnutrition. Further studies should be carried out to determine whether these deficiencies increase the risk of adverse surgical outcomes. Furthermore, the effect of pre-operative supplementation, especially vitamin D and iron, should be explored.

**Conflicts of Interest Disclosure Statement** The authors declare that they have no competing interests.

**Statement of Informed Consent** Informed consent was obtained from all individual participants included in the study.

**Statement of Human and Animal Rights** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## References

1. Baker MT. The history and evolution of bariatric surgical procedures. *Surg Clin N Am*. 2011;91:1181–201. viii.
2. Burden S, Todd C, Hill J, et al. Pre-operative nutrition support in patients undergoing gastrointestinal surgery. *Cochrane Database Syst Rev*. 2012;11:CD008879.
3. Dempsey DT, Mullen JL, Buzby GP. The link between nutritional status and clinical outcome: can nutritional intervention modify it? *Am J Clin Nutr*. 1988;47:352–6.
4. Evans DC, Martindale RG, Kiraly LN, et al. Nutrition optimization prior to surgery. *Nutr Clin Pract*. 2014;29:10–21.
5. Mechanick JI, Kushner RF, Sugerman HJ, et al. American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery Medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient. *Obesity (Silver Spring)*. 2009;17(1):S1–70.
6. Handelman GJ, Epstein WL, Peerson J, et al. Human adipose alpha-tocopherol and gamma-tocopherol kinetics during and after 1 y of alpha-tocopherol supplementation. *Am J Clin Nutr*. 1994;59:1025–32.
7. Kirkness JP, Schwartz AR, Schneider H, et al. Contribution of male sex, age, and obesity to mechanical instability of the upper airway during sleep. *J Appl Physiol (1985)*. 2008;104:1618–24.
8. Kritikou I, Basta M, Tappouni R, et al. Sleep apnoea and visceral adiposity in middle-aged male and female subjects. *Eur Respir J*. 2013;41:601–9.
9. Schwartz AR, Patil SP, Laffan AM, et al. Obesity and obstructive sleep apnea: pathogenic mechanisms and therapeutic approaches. *Proc Am Thorac Soc*. 2008;5:185–92.
10. Schwartz AR, Patil SP, Squier S, et al. Obesity and upper airway control during sleep. *J Appl Physiol (1985)*. 2010;108:430–5.

11. Schwartz AR, Schneider H, Smith PL, et al. Physiologic phenotypes of sleep apnea pathogenesis. *Am J Respir Crit Care Med*. 2011;184:1105–6.
12. Iftikhar IH, Khan MF, Das A, et al. Meta-analysis: continuous positive airway pressure improves insulin resistance in patients with sleep apnea without diabetes. *Ann Am Thorac Soc*. 2013;10:115–20.
13. Lam JC, Mak JC, Ip MS. Obesity, obstructive sleep apnoea and metabolic syndrome. *Respirology*. 2012;17:223–36.
14. Pallayova M, Steele KE, Magnuson TH, et al. Sleep apnea predicts distinct alterations in glucose homeostasis and biomarkers in obese adults with normal and impaired glucose metabolism. *Cardiovasc Diabetol*. 2010;9:83.
15. Punjabi NM, Sorkin JD, Katzell LI, et al. Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. *Am J Respir Crit Care Med*. 2002;165:677–82.
16. Tasali E, Ip MS. Obstructive sleep apnea and metabolic syndrome: alterations in glucose metabolism and inflammation. *Proc Am Thorac Soc*. 2008;5:207–17.
17. Spechler SJ, Sharma P, Souza RF, et al. American gastroenterological association medical position statement on the management of Barrett's esophagus. *Gastroenterology*. 2011;140:1084–91.
18. Hirota WK, Zuckerman MJ, Adler DG, et al. ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. *Gastrointest Endosc*. 2006;63:570–80.
19. Fish E, Beverstein G, Olson D, et al. Vitamin D status of morbidly obese bariatric surgery patients. *J Surg Res*. 2010;164:198–202.
20. McGill AT, Stewart JM, Lithander FE, et al. Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. *Nutr J*. 2008;7:4.
21. Parikh SJ, Edelman M, Uwaifo GI, et al. The relationship between obesity and serum 1,25-dihydroxy vitamin D concentrations in healthy adults. *J Clin Endocrinol Metab*. 2004;89:1196–9.
22. Salehpour A, Hosseinpanah F, Shidfar F, et al. A 12-week double-blind randomized clinical trial of vitamin D(3) supplementation on body fat mass in healthy overweight and obese women. *Nutr J*. 2012;11:78.
23. Saneei P, Salehi-Abargouei A, Esmaillzadeh A. Serum 25-hydroxy vitamin D levels in relation to body mass index: a systematic review and meta-analysis. *Obes Rev* 2013
24. Vimalaswaran KS, Berry DJ, Lu C, et al. Causal relationship between obesity and vitamin D status: bi-directional Mendelian randomization analysis of multiple cohorts. *PLoS Med*. 2013;10:e1001383.
25. Lee P, Greenfield JR, Seibel MJ, et al. Adequacy of vitamin D replacement in severe deficiency is dependent on body mass index. *Am J Med*. 2009;122:1056–60.
26. Centers for Disease Control and Prevention. FastStats—Anemia. <http://www.cdc.gov/nchs/fastats/anemia.htm> . 7-14-2014. 12-22-2014.
27. Institute of Medicine Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academy Press; 2010.
28. Liel Y, Ulmer E, Shary J, et al. Low circulating vitamin D in obesity. *Calcif Tissue Int*. 1988;43:199–201.
29. Wortsman J, Matsuoka LY, Chen TC, et al. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr*. 2000;72:690–3.
30. Earthman CP, Beckman LM, Masodkar K, et al. The link between obesity and low circulating 25-hydroxyvitamin D concentrations: considerations and implications. *Int J Obes (Lond)*. 2012;36:387–96.
31. Goldner WS, Stoner JA, Thompson J, et al. Prevalence of vitamin D insufficiency and deficiency in morbidly obese patients: a comparison with non-obese controls. *Obes Surg*. 2008;18:145–50.
32. Holick MF. Deficiency of sunlight and vitamin D. *BMJ*. 2008;336:1318–9.
33. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96:1911–30.