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Nutritional Risks in Adolescents After Bariatric Surgery

Stavra A. Xanthakos, M.D., M.S.[1], **Jane C. Khoury, Ph.D.**[2], **Thomas H. Inge, M.D., Ph.D.**[3], **Todd M. Jenkins, Ph.D.**[4], **Avani C. Modi, Ph.D.**[5], **Marc P. Michalsky, M.D.**[6], **Mike K. Chen, M.D.**[7], **Anita P. Courcoulas, M.D.**[8], **Carroll M. Harmon, M.D., Ph.D.**[9], **Mary L. Brandt, M.D.**[10], **Michael A. Helmrath, M.D.**[4], **Heidi J. Kalkwarf, Ph.D.**[1] **Teen Longitudinal Assessment of Bariatric Surgery Consortium**

[1]Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio

[2]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio

[3]Department of Surgery, University of Colorado, Denver and Children's Hospital Colorado, Aurora, Colorado

[4]Division of Pediatric Surgery, Cincinnati Children's Hospital Medical Center, Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio

[5]Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio

[6]Department of Pediatric Surgery, The Ohio State University College of Medicine and Nationwide Children's Hospital, Columbus, Ohio

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Correspondence: Stavra Xanthakos, MD, MS, Division of Gastroenterology, Hepatology and Nutrition, MLC 2010, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio 45229, Phone: 513-636-4415, Fax: 513-803-2785, stavra.xanthakos@cchmc.org.

Author contributions:
Stavra Xanthakos: study concept and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content.
Jane Khoury: statistical analysis and interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content.
Thomas Inge: obtained funding, administrative and technical support, study supervision, critical revision of the manuscript for important intellectual content.
Todd Jenkins: administrative and technical support, acquisition of data, analysis and interpretation of data, critical revision of the manuscript for important intellectual content.
Avani Modi: Critical revision of the manuscript for important intellectual content
Marc Michalsky: study supervision, acquisition of data, critical revision of the manuscript for important intellectual content
Mike Chen: study supervision, acquisition of data, critical revision of the manuscript for important intellectual content
Anita Courcoulas: study supervision, acquisition of data, critical revision of the manuscript for important intellectual content
Carroll Harmon: study supervision, acquisition of data, critical revision of the manuscript for important intellectual content
Mary Brandt: study supervision, acquisition of data, critical revision of the manuscript for important intellectual content
Michael Helmrath: study supervision, acquisition of data, critical revision of the manuscript for important intellectual content
Heidi Kalkwarf: study concept and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content.

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[7]Department of Surgery, University of Alabama at Birmingham, Birmingham, AL

[8]Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

[9]Division of Pediatric Surgery, John R. Oishei Children's Hospital and Jacobs School of Medicine and Biosciences--SUNY University at Buffalo, Buffalo, NY

[10]Division of Pediatric Surgery, Texas Children's Hospital, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Texas

Abstract

Background & Aims: Little is known about prevalence and risk factors for nutritional deficiencies in adolescents after metabolic bariatric surgery. We performed a 5-year prospective cohort study of these.

Methods: Adolescents who had Roux-en-Y gastric bypass (RYGB, n=161) or vertical sleeve gastrectomy (VSG, n=67) were enrolled at 5 tertiary-care centers from March 2007 through February 2012. The final analysis cohort included 226 participants (161 who had RYGB and 65 who had VSG). We measured serum levels of ferritin; red blood cell folate; vitamins A, D, B1, B12; and parathyroid hormone at baseline and annually for 5 years. General linear mixed models were used to examine changes over time and identify factors associated with nutritional deficiencies.

Results: The participants were 75% female and 72% white, with a mean age of 16.5±1.6 years and mean body mass index of 52.7±9.4 kg/m^2 at surgery. Mean body mass index decreased 23% at 5 years, and did not differ significantly between procedures. After RYGB, but not VSG, serum concentrations of vitamin B12 significantly decreased whereas serum levels of transferrin and parathyroid hormone increased. Ferritin levels decreased significantly after both procedures. Hypo-ferritinemia was observed in 2.5% of patients before RYGB and 71% at 5 y after RYGB (P<.0001), and 11 % of patients before VSG and 45% 5 y after VSG (P=.002). No significant changes in serum levels of folate or vitamins A, B1, or D were found between baseline and 5 y after either procedure. By 5 y, 59% of RYGB and 27% of VSG recipients had 2 or more nutritional deficiencies. Risk factors associated with specific deficiencies included surgery type, female sex, black race, supplementation intake, weight regain, and for females, pregnancy.

Conclusions: In a prospective study of adolescents who underwent RYGB or VSG, we observed nutritional deficiencies by 5 y after the procedures—particularly in iron and B12 after RYGB. Ongoing nutrient monitoring and supplementation are recommended for all patients, but surgery type, supplementation intake, sex, and race might affect risk.

ClinicalTrials.gov number, NCT00474318.

Keywords

BMI; PTH; long-term; outcome

INTRODUCTION

Nutritional deficiencies are a significant concern following metabolic bariatric surgery, and may lead to osteoporosis, chronic anemia and/or permanent neurological deficits if unrecognized or inadequately managed.[1, 2] Lifelong micronutrient supplementation is therefore recommended.[3] While prevalence of nutritional deficiencies has been estimated largely from adult cohorts[4], bariatric surgery is an increasingly accepted treatment for severe obesity in youth.[5] Yet, lower adherence to supplementation[6] and anticipated longer lifespan with altered gastrointestinal physiology may increase risk of adverse nutritional outcomes in these youth.

Earlier studies investigating nutritional deficiencies after adolescent bariatric surgery were retrospective, single center studies.[7, 8] In 2015, the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) consortium, a multicenter prospective observational study, reported worsening iron and B12 status, but no significant changes in vitamin A, D, B1, folate or albumin levels, in adolescents 3 years after Roux-en-y gastric bypass (RYGB) or vertical sleeve gastrectomy (VSG).[9] However, deficiencies may progress over longer duration, as nutrient stores are further depleted. A recent multicenter prospective study following 81 adolescents after RYGB found nutritional deficits in 72% by 5 years. Yet this study lacked VSG recipients, now the predominant procedure performed in adolescents and adults and presumed to carry lower nutritional risk.[10] Further, no prior studies have examined specific clinical or demographic factors associated with nutritional deficiencies after surgery. Identifying high-risk youth and risk factors could inform screening, prevention, and earlier intervention.

We therefore aimed to characterize longitudinal changes in iron status, vitamins B12, B1, folate, A, D, albumin, and calcium homeostasis (PTH) in adolescents over 5 years after VSG or RYGB and to determine factors associated with nutritional deficiencies. We hypothesized that deficiencies would increase over time, particularly after RYGB, and that lower supplement intake and female sex would be independent risk factors.

METHODS AND MATERIALS

Population

The observational Teen-LABS cohort study (NCT00474318) enrolled 242 adolescents, 13-19 years old, undergoing laparoscopic bariatric surgery (March 2007 - February 2012) at five U.S. centers. Methodological details and CONSORT diagram have been previously described.[9] The study was approved by each center's Institutional Review Board. All parents/guardians and adolescents provided written informed consent or assent.

The analysis cohort included 226 participants (RYGB n=161, VSG n=65), excluding 14 who underwent adjustable gastric banding and 2 who underwent VSG with preexisting conditions that could impact nutritional biomarkers (see Supplemental Material).

Measures

Age, sex, race, ethnicity, household demographics, height, weight, BMI, and comorbidities, were collected within 30 days of operation at in-person visits.[9]

Blood samples and clinical data were obtained at baseline and 6, 12, 24, 36, 48 and 60 months post-surgery. The Northwest Lipid Metabolism and Diabetes Research Laboratories, (Seattle, Washington) measured serum ferritin, transferrin, vitamin B12, erythrocyte transketolase activity coefficient (B1 status), red blood cell folate, vitamin A, 25-hydroxyvitamin D (25-OH-D), parathyroid hormone (PTH), and albumin.[9] High sensitivity C-reactive protein (hs-CRP) was measured to account for systemic inflammation.

Abnormal values were defined as: hypoferritinemia, females <10 μg/L and males <20 μg/L; high transferrin, females >382 mg/dL and males >392 mg/dL; low vitamin B12 <145 pg/mL; low B1 status, erythrocyte transketolase activity coefficient ≥1.30; low folate ≤5.8 ng/mL; low vitamin A <301 μg/L; low vitamin D deficiency <20.1 ng/mL; elevated PTH >88 pg/mL; hypoalbuminemia <3.5 g/dL, elevated hs-CRP>1.0 mg/dL.[9,11]

Multivitamin, iron, calcium, vitamin D and B12 supplements were recommended at each visit, following standard of care guidelines. [4] Participants reported intake of these nutritional supplements at each visit, and frequency taken per week was estimated. We assessed metformin and acid suppression intake (histamine blockers and proton pump inhibitors) as they may influence iron and B12 status.[12–14]

For females, we recorded pregnancy history and categorized menstrual frequency as amenorrhea (≤3 menses per year), oligomenorrhea (4-9 menses per year) or normal menses (≥10 menses per year).

Statistical Analysis

The distributions of all variables were assessed. Non-normally distributed nutrient biomarkers were log transformed (ferritin, B12, PTH and hs-CRP). Categorical variables are presented using frequencies and percentages, while continuous variables are presented as means and standard deviations or medians and 25th and 75th percentiles (as interquartile range [IQR]). We examined nutrient concentrations over time (visit) for each surgery group, focusing on changes during 3 intervals: 1) baseline to year 1, the period of rapid weight loss; 2) the linear trend between year 1 to 5, the period of relative weight stabilization; and 3) baseline to year 5, the net change. Visit was treated categorically for the baseline to years 1 and 5 comparisons, whereas the trend across visits was fitted for years 1 to 5 comparison using a linear model. Tukey-Kramer adjustment was used when testing categorical differences over time. The same approach was used for determining change in prevalence of abnormal nutritional biomarker levels over time. We used generalized linear mixed models (GLMM) to examine change over time for both continuous and categorical outcome variables. A logit link was used for categorical outcome variables. Subject was used as the repeated variable with random terms of intercept and site.

The GLMM approach also was used to identify predictors of nutritional status 1 to 5 years post-operatively. Prespecified variables included visit, surgery type, sex, race, caregiver educational level and baseline nutritional level as fixed effects, and study center as a random effect. Weight change between visits and self-reported multivitamin use were included as time-varying covariates. Additional variables (see Supplemental Material) were included for specific models.

We also analyzed potential effects of pregnancy and irregular menses on nutritional status in females. Pregnancy at each visit was defined as being either currently pregnant or within 6-months post-partum.

A p<0.05 was considered statistically significant. Sensitivity analyses and analyses to account for missing data are described in Supplemental Material.[15] All authors had access to the study data and reviewed and approved the final manuscript.

RESULTS

Participant characteristics

The cohort (Table 1) was predominantly female (75%), white (72%) and non-Hispanic (93%). At baseline, mean age (±SD) was 16.5 (±1.6) years and mean BMI was 52.7 (±9.4) kg/m^2. The mean BMI declined similarly in RYGB and VSG over 5 years (Table 2), with no appreciable changes in height.

Median levels and IQR of all nutrition related-biomarkers over the 5-year period by surgery group are shown in Figure 1 and Table 2. Prevalence with 95% confidence intervals of abnormal nutritional biomarkers are shown in Figure 2 and Supplemental Table 1.

Iron status

By 5 years, ferritin levels had decreased and hypoferritinemia had increased significantly after both RYGB and VSG. In the first year, iron status worsened significantly only after RYGB, but thereafter, significant changes occurred after both procedures. Correspondingly, transferrin levels increased significantly across all periods after RYGB, while prevalence of high transferrin increased significantly after year 1. Transferrin levels increased significantly 1 to 5 years after VSG, though the prevalence of high transferrin remained low, with non-estimable changes.

Because inflammation can increase ferritin, we assessed hs-CRP levels, which declined significantly in the first year after both RYGB and VSG then remained stable thereafter.

B vitamins and folate

After RYGB, net vitamin B12 levels declined significantly (Figure 1), after a non-significant decline in the first year (p=0.06). Though prevalence of low B12 increased significantly after year 1, the net increase was not significant (p=0.06, Figure 2). In contrast, after VSG, there was no significant net decline in vitamin B12 levels, despite a significant decline in the first year. Changes in prevalence of low vitamin B12 were not estimable or non-significant after VSG due to the small proportion of low values.

Vitamin B1 status (erythrocyte transketolase activity) did not change following either surgery, with low prevalence of abnormal activity at all time points.

After RYGB, there was a transient decline in folate levels and an increase in low folate at 6 months (Figures 1 and 2) but no net change at 1 year. Thereafter, folate levels increased significantly, resulting in a significant net increase from baseline. There was no net change in prevalence of low folate from baseline to year 5, despite a significant decline after year 1. After VSG, folate levels significantly declined by 1 year, then stabilized with no significant overall change. There was also no net change in prevalence of low folate.

Vitamins A and D, and parathyroid hormone

There was no significant net or interval change in vitamin A levels or low vitamin A after RYGB or VSG, despite a transient increase in low vitamin A levels 6 months after RYGB (Figure 2).

There was no net change in 25OH-vitamin D levels after either procedure, though levels significantly declined from year 1 onwards. Likewise, there was no net change in prevalence of vitamin D deficiency after either procedure, despite an upwards trend 1 year after RYGB.

Conversely, PTH levels increased significantly over 5 years after RYGB. The prevalence of elevated PTH also increased between 1 and 5 years. After VSG, PTH levels were unchanged and prevalence of elevated PTH remained very low, with no estimable differences.

Serum albumin

Serum albumin levels increased in the first year after RYGB, then remained stable. There were no significant changes after VSG. The proportion of patients with hypoalbuminemia was very low after both procedures.

Multiple nutritional deficiencies

The proportion of patients with ≥2 nutritional deficiencies increased over 5 years after RYGB (from 12% to 59%, p<0.0001), but not VSG (from 6% to 27%, p=0.09) [Supplemental Figure 1]. Likewise, the prevalence of ≥3 nutritional deficiencies increased following RYGB (from 3% to 19%, p=0.0005), but remained very low after VSG (from 2% to 2.3%).

Nutritional supplements and nutritionally-relevant medications

Reported intake of recommended nutritional supplements (multivitamin, calcium, vitamin D, iron, B12) varied by supplement type and over time (Supplemental Table 2). Multivitamin use declined from 74% at baseline to 53% by year 5. Intake of other supplements was lower at baseline (range 14% to 38%), increased by 6 months, but then steadily declined by year 5, except for iron.

Acid suppressant medication was taken by 15% of participants at baseline, increased to 32% at 6 months, then declined steadily to 7% at 5 years. Metformin usage decreased from 26% at baseline to ≤4% thereafter.

Risk factors associated with nutritional deficiencies

Multivariable models identified factors associated with nutritional biomarker levels (Table 3) and odds of abnormal nutritional values (Table 4) from 1 to 5 years post-operatively. Models predicting abnormal B12 values did not converge.

Compared to VSG, RYGB was associated with lower ferritin and higher transferrin levels, lower vitamin B12, vitamin A and PTH levels, and higher risk of abnormal values of ferritin, transferrin, vitamin A, and PTH.

Compared to male sex, female sex was associated with lower ferritin and higher transferrin levels, but higher folate and 25OH-vitamin D levels. There was no difference in risk of abnormal values by sex.

Compared to white race, black race was associated with higher ferritin and lower transferrin, but lower folate, vitamin A and 25OH-D, and higher PTH levels.

Weight gain (+5 kg/year) between visits was associated with lower ferritin and higher transferrin levels, but not with higher odds of abnormal values. Interval weight gain also was associated with lower 25OH-D and higher PTH levels, and higher odds of vitamin D deficiency. Conversely, interval weight gain was associated with higher folate and vitamin A levels and lower odds of low folate.

Acid suppression medication intake was not associated with iron or vitamin B12 status. Higher hs-CRP was significantly associated with higher ferritin, lower transferrin levels and reduced odds of low ferritin.

Greater multivitamin intake was associated with higher ferritin, vitamin B12, folate, vitamin A, and 25OH-D levels and reduced odds of vitamin D deficiency. Increasing frequency of oral vitamin B12 supplementation was positively associated with higher B12 levels. Similarly, increasing intake of vitamin D was associated with higher 25OH-D levels and lower odds of vitamin D deficiency. Vitamin D and calcium supplementation were not associated with PTH levels or abnormal PTH.

Among the 170 female participants, 49 visits occurred ≤6 months of a pregnancy: 36 visits after GB and 13 visits after VSG. Pregnancy was associated with higher transferrin (beta estimate ± standard error 26.0 ± 7.03, p=0.0002), higher odds of high transferrin (odds ratio 4.65, 95% CI: 1.95, 11.1, p=0.01) and lower vitamin B12 (beta estimate −0.26 ± 0.10, p=0.01), but no other nutrient markers. Menstrual frequency and iron status were not associated.

DISCUSSION

Bariatric surgery is increasingly recommended for adolescents suffering from severe obesity to achieve significant, sustained weight loss and resolve comorbid diseases.[9, 10, 16] However, the considerable metabolic benefits are tempered by a risk of developing nutritional deficiencies due to altered gastrointestinal physiology and dietary intake. Systematic assessment in adolescents has been limited, particularly after VSG, now the most commonly performed procedure across all ages.[9, 10] Yet, adolescents may be at heightened risk due to low adherence to supplementation and a longer potential lifespan with altered physiology.[6] Associated clinical and demographic risk factors, needed to inform screening, prevention and treatment strategies, are unknown. We addressed these gaps by examining nutritional outcomes over 5 years in a large multicenter prospective cohort of adolescents who received RYGB or VSG.

The most prevalent abnormality we observed was hypoferritinemia, which affected nearly twice as many RYGB recipients by year 5 compared to VSG. Vitamin B12 status likewise worsened disproportionately after RYGB, despite similar trajectories of weight loss after VSG. This suggests that the differential risk is due to anatomical and physiological differences between procedures, rather than weight loss alone. In aggregate, RYGB was associated with a striking 5-fold increase in ≥2 deficiencies and 6-fold increase in ≥3 deficiencies by 5 years. VSG resulted in a 4-fold, though non-significant, increase in ≥2 deficiencies, supporting a lower, but not negligible, nutritional risk.

The increase in iron and B12 deficiencies after RYGB in our cohort are aligned with those reported in a 5-year longitudinal Swedish cohort of 81 adolescents undergoing RYGB.[10] In that cohort, the prevalence of low ferritin and/or iron increased from 24% at baseline to 66% at 5 years, compared to a hypoferritinemia prevalence of 71% at 5 years in our RYGB group. Vitamin B12 deficiency was rare preoperatively (≤1%) in both cohorts, but increased to 22% in the Swedish study vs. 12% in our cohort. Vitamin D deficiency was common at baseline in both cohorts and did not appreciably change.

High rates of iron and vitamin B12 deficiency have also been reported in adults after bariatric surgery.[3] Reported iron deficiency ranged from 22-45% after RYGB and 18-36% after VSG in adults, somewhat lower than in our study. The prevalence of vitamin B12 deficiency in adults is comparable, and generally higher after RYGB (9%-42%) than VSG (5-15%).[4] In addition to adherence to supplementation[6], multiple factors can impact nutritional status, including inadequate dietary intake, supplement formulation, coadministration with other supplements (e.g. vitamin C with iron), impaired digestion or absorption resulting from bypassing the proximal small intestine, small intestinal bacterial overgrowth, and reduced gastric acid production.[17, 18] Over time, deficiencies in iron and B12 can lead to anemia, fatigue, exercise intolerance, neurological dysfunction, and infertility, but the long-term risk of these outcomes among adolescent recipients remains unknown.[19]

Both adults and adolescents have high rates of vitamin D deficiency pre- and post-operatively, raising long-term concern for impaired bone health and fracture risk.[2, 20] The preoperative prevalence of vitamin D deficiency in our cohort (37%) was lower than rates reported in adult bariatric cohorts (range 60-80%)[3, 4], which may, in part, reflect age-specific or secular trends in increased vitamin D supplementation.[21] Other preoperative micronutrient deficiencies were uncommon in our cohort, in contrast with higher preoperative rates reported in adults (B12, thiamin, folate and iron).[3, 4]

Our study is the first to assess comparative nutritional outcomes in adolescents after both VSG and RYGB. VSG is now the predominant bariatric surgery in adolescents and adults due to limited anatomical alteration, lower operative risk, and presumed lower risk of nutritional deficits.[22] Our results now provide critical evidence that VSG does in fact carry significantly lower nutritional risk than RYGB, but can still worsen iron status.

Some nutrient levels declined acutely only during the 6-12 months of rapid weight loss, and then either improved (folate) or remained low (vitamin A after RYGB). We previously found that dietary intakes of calcium, iron, folate, zinc and vitamins A and D were reduced in the first year after bariatric surgery.[23] Our findings support the recommendation to avoid pregnancy in the first 1-2 years after surgery and to carefully monitor nutritional status, dietary intake and supplementation during pregnancy.[24]

Recognizing that dietary intake and composition in the first postoperative year may not reflect long-term intake[23, 25], we also assessed changes in nutritional status from 1 to 5 years to determine if risk evolves over time. The continued increase in iron, B12 (RYGB only), vitamin D deficiencies and abnormal PTH (RYGB only) after the first postoperative year is particularly worrisome, given the longer potential lifespan of these youth. Additionally, we identified risk factors associated with worsening nutritional status after the first year. These included RYGB (iron, B12, vitamin A and PTH status), female sex (iron), interval weight regain after the first year (iron, vitamin D, PTH), and black race (vitamin A, vitamin D, PTH). We hypothesize that higher risk associated with weight regain could in part be due to higher intake of high calorie, nutrient-poor processed foods, and for low vitamin D, the known association with worsening obesity.[26] Racial variation in iron and vitamin D status have been reported in other cohorts and merits investigation to determine mechanisms.[26, 27] Pregnancy was also a risk factor for worse iron and vitamin B12 status. Notably, acid suppression was not related to iron or vitamin B12 measures. Inflammation, as measured by hs-CRP, was related to higher ferritin and lower transferrin levels, emphasizing the need to account for inflammation when using these measures. As expected, increased intake of multivitamin, B12 and D supplements was associated with better nutritional measures, underscoring the importance of adequate supplementation and promoting adherence.

Strengths of our study include the multicenter prospective design, high retention, standardized data collection and use of a central laboratory. Limitations included some missing data, however we employed a robust statistical approach. We were also limited to available nutritional measures, which precluded fully characterizing iron and vitamin B12 nutriture. In addition, other nutrients including copper, zinc and vitamin E were not assessed.[3] Self-reported supplement intake is likely to have appreciable error, possibly biasing findings towards the null, and data on dietary intake and non-recommended supplement intake were lacking.

In summary, bariatric surgery in adolescents was associated with increasing prevalence of several nutritional deficiencies over 5 years, with greater risk after RYGB, particularly for iron and B12 deficiency. In addition to surgical type and inadequate supplement intake, weight regain, black race and pregnancy were associated with heightened risk for selected deficiencies. Our findings underscore the importance of long-term nutritional monitoring in adolescents after bariatric surgery and the need to examine impact on health outcomes and quality of life as these youth advance into adulthood, including systematic assessment of anemia and bone health. The lower, albeit not negligible, nutritional risk of VSG also highlights the importance of examining nutritional outcomes in recipients of endoscopic sleeve and other bariatric procedures, as their use is likely to increase.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

BMI	body mass index
RYGB	Roux-en-Y gastric bypass
GERD	gastroesophageal reflux disease
hs-CRP	high sensitivity c-reactive protein
NAFLD	nonalcoholic fatty liver disease
PTH	parathyroid hormone
PCOS	polycystic ovarian syndrome
VSG	vertical sleeve gastrectomy
25-OH-D	25-hydroxyvitamin D

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What You Need to Know

Background:

Little is known about nutritional deficiencies in adolescents after metabolic bariatric surgery.

Findings:

In a prospective study of adolescents who underwent RYGB or VSG, we observed nutritional deficiencies by 5 y after the procedures—particularly in iron and B12 after RYGB.

Implications for patient care:

Adolescents who undergo bariatric surgery should be monitored for nutrient deficiencies.

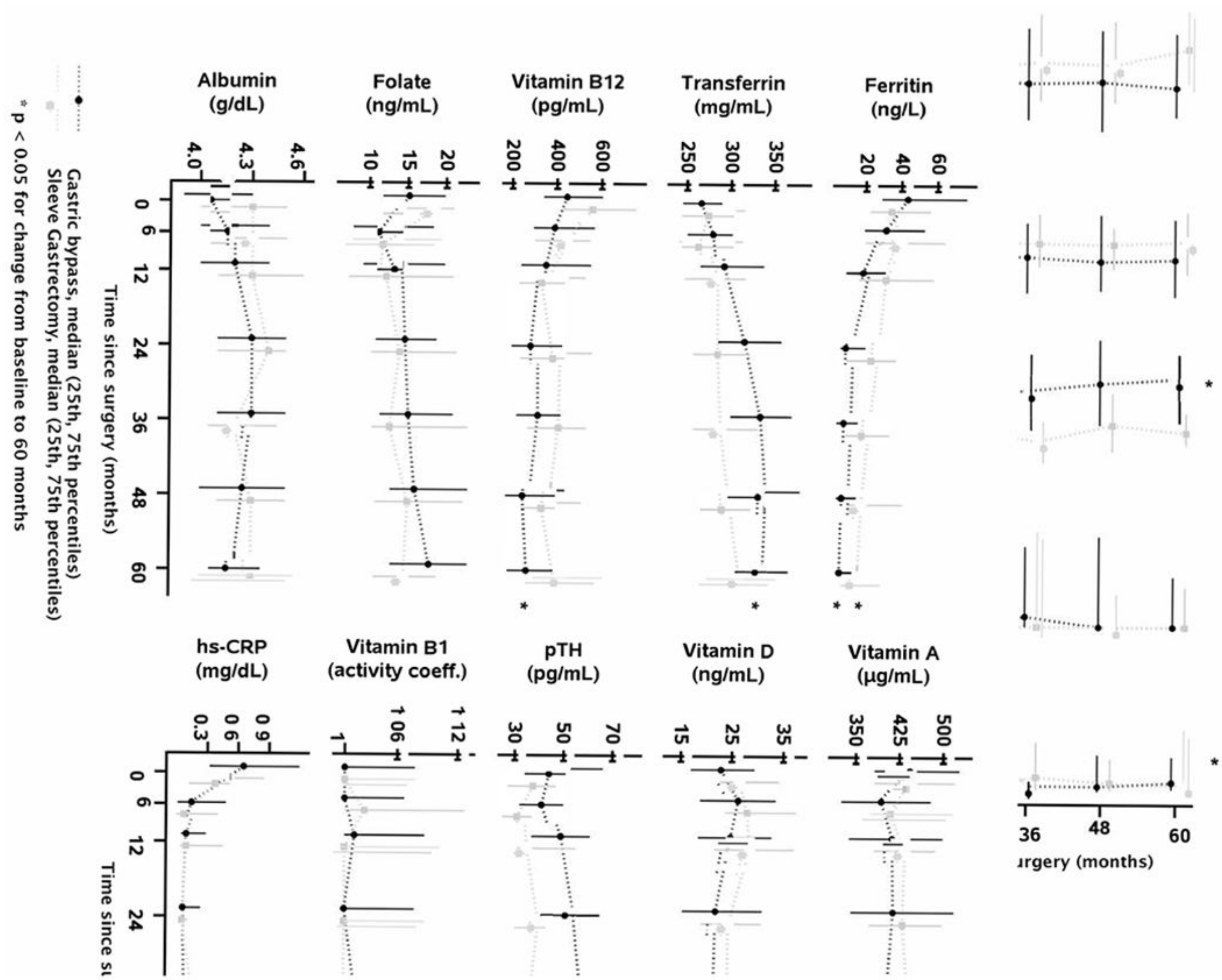

Figure 1:

Nutritional measures by surgery group over time. * change from baseline to 5 years p<0.05.

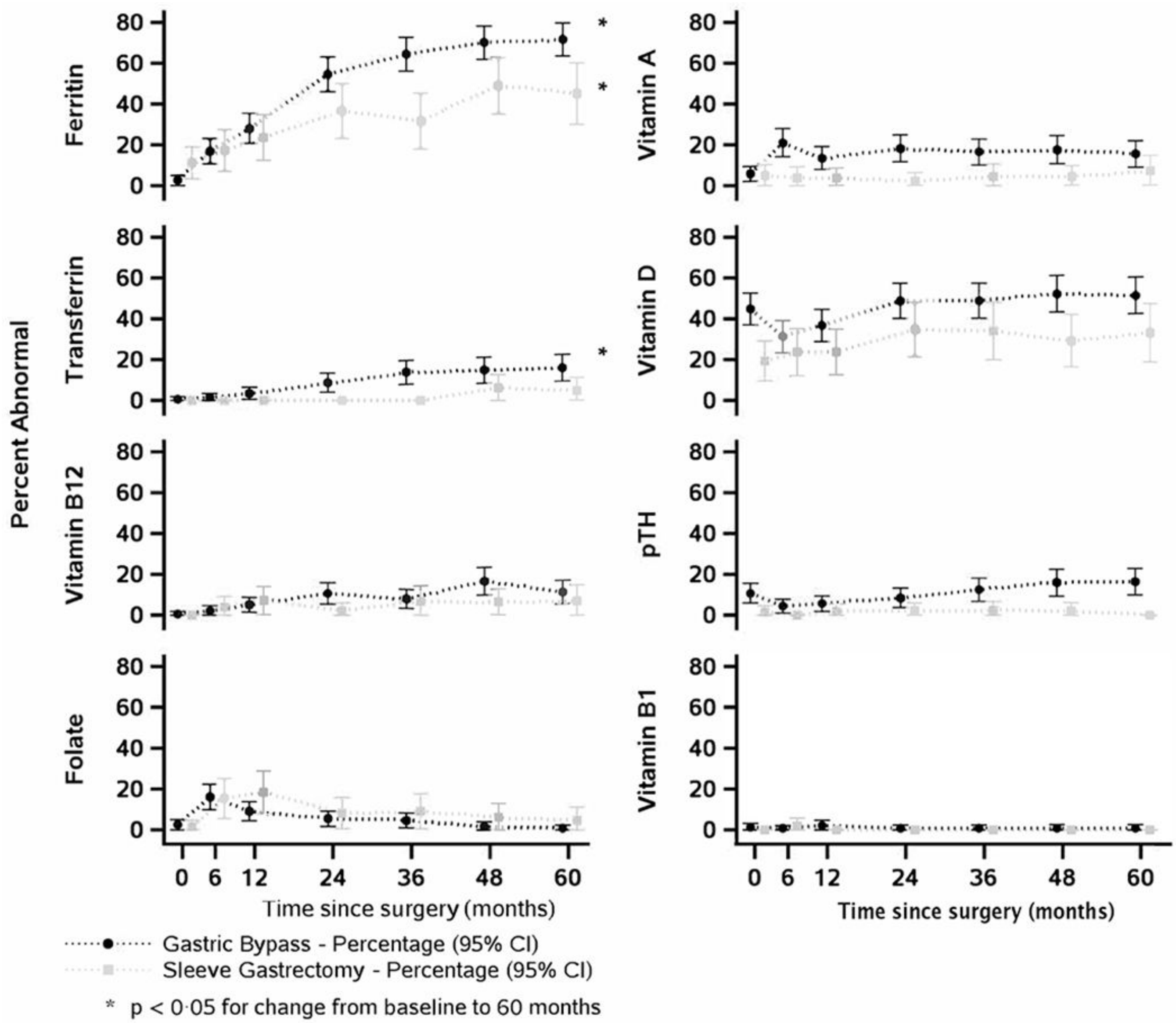

Figure 2:

Prevalence of abnormal values by surgery group. * change from baseline to 5 years p<0.05.

Table 1:
Participant characteristics of the analysis cohort by surgery type.

Data presented as mean (standard deviation) or n (%).

Variable	Gastric Bypass (n=161)*	Sleeve Gastrectomy (n=65)
Age at surgery (years)	16.6 (1.6)	16.4 (1.6)
Sex (Female)	126 (78.3)	44 (67.7)
Race:		
White	119 (73.9%)	44 (67.7%)
Black	35 (21.7%)	14 (22.5%)
Asian	1 (0.6%)	0
American Indian or Alaskan Native	0	1 (1.5%)
More than one race	6 (3.7%)	6 (9%)
Hispanic	15 (9.3%)	1 (1.5%)
Household income:		
<$25,000	51 (32.7%)	30 (50.0%)
$25,000-$49,999	31 (19.9%)	13 (21.7%)
$50,000-$74,999	28 (18.0%)	10 (16.7%)
≥$75,000	46 (29.5%)	7 (11.7%)
Missing	5	5
Caregiver level of education:		
<high school	11 (7%)	12 (19%)
High school graduate	47 (30%)	21 (34%)
Some college	67 (42%)	20 (32%)
College graduate	32 (20%)	9 (14%)
Missing	4	3
Insurance:		
Caregiver has insurance	136/156 (87%)	53/62 (86%)
Patient covered by this insurance	93/136 (68%)	39/53 (74%)
Weight (kg)	150.9 (30.3)	144.4 (32.8)
Height (cm)	167.5 (8.5)	169.0 (10.2)
BMI (kg/m^2)	53.7 (9.6)	50.2 (8.3)
Baseline diagnoses		
Diabetes	25/161 (16%)	7/161 (11%)
Dyslipidemia	126/160 (79%)	44/63 (70%)
Elevated blood pressure	73/159 (46%)	23/63 (36%)
Abnormal kidney function	28/153 (18%)	7/59 (12%)
NAFLD	70/161 (44%)	18/64 (28%)
GERD	19/161 (12%)	10/64 (16%)
PCOS (females only)	27/125 (22%)	6/44 (14%)

*The denominator is provided [n=] when the data were not available on all subjects

Table 2:

Trends in nutritional biomarkers over five years after gastric bypass or sleeve gastrectomy surgery in adolescents.

	Baseline	6 months	Year 1	Year 2	Year 3	Year 4	Year 5	*P*-value for comparison of values between visits†		
Nutritional biomarker	**Median***	**Median***	**Median***	**Median***	**Media***	**Median***	**Median***	**Baseline to 1y**	**1y to 5y linear trend**	**Baseline to 5y**
BMI (kg/m²)										
Gastric Bypass	52.9 (45.8, 59.9) N=161	39.4 (32.8, 46.3) N=143	35.8 (30.6, 42.7) N=144	35.5 (30.5, 44.0) N=135	36.4 (30.4, 44.9) N=130	37.5 (31.6, 43.2) N=129	39.0 (32.0, 48.2) N=134	<0.0001	0.002	<0.0001
Sleeve Gastrectomy	48.0 (45.1, 52.9) N=65	35.8 (32.5, 39.7) N=53	33.7 (29.7, 37.7) N=58	33.7 (29.3, 38.1) N=51	34.7 (29.5, 40.3) N=45	34.7 (30.9, 39.8) N=51	37.0 (32.1, 40.8) N=49	<0.0001	0.008	<0.0001
Ferritin (ug/L)										
Gastric Bypass	39.0 (24.5, 72.0) N=160	27.0 (15.0, 48.5) N=136	18.5 (9.0, 31.0) N=142	9.0 (6.0, 20.0) N=132	8.0 (4.0, 16.0) N=129	7.0 (4.0, 15.0) N=120	6.0 (4.0, 13.0) N=122	<0.0001	<0.0001	<0.0001
Sleeve Gastrectomy	30.0 (18.0, 52.0) N=63	36.0 (15.5, 60.0) N=52	27.0 (12.0, 54.0) N=55	23.0 (9.0, 37.0) N=49	18.0 (9.0, 33.5) N=44	14.0 (6.0, 37.0) N=49	12.0 (7.0, 29.0) N=42	ns 0.98	0.0002	0.002
Transferrin (mg/mL)										
Gastric Bypass	266 (245, 290) N=160	280 (250, 302) N=136	284 (257, 329) N=142	308 (278, 350) N=132	326 (292, 362) N=129	332 (298, 372) N=120	330 (307, 367) N=122	0.0008	<0.0001	<0.0001
Sleeve Gastrectomy	274 (242, 307) N=63	263 (233, 305) N=51	277 (239, 308) N=55	277 (249, 314) N=49	281 (250, 324) N=44	291 (267, 324) N=49	304 (266, 345) N=42	ns 0.99	0.0006	ns 0.09
Vitamin B12 (pg/mL)										
Gastric Bypass	411 (305, 571) N=159	356 (262, 537) N=136	318 (207, 519) N=142	282 (198, 426) N=132	286 (188, 387) N=129	251 (174, 408) N=120	268 (183, 390) N=122	ns 0.06	0.01	<0.0001
Sleeve Gastrectomy	525 (382, 722) N=63	417 (268, 517) N=52	330 (233, 497) N=55	384 (238, 527) N=49	378 (240, 504) N=44	336 (245, 484) N=49	396 (267, 579) N=42	0.004	ns 0.41	ns 0.35
Vitamin B1 (erythrocyte transketolase activity coefficient)										
Gastric Bypass	1.0 (1.0, 1.07) N=154	1.00 (1.00, 1.06) N=133	1.01 (1.00, 1.08) N=137	1.00 (1.00, 1.07) N=126	1.01 (1.00, 1.08) N=127	1.00 (1.00, 1.09) N=116	1.00 (1.00, 1.05) N=113	ns 0.67	0.04	ns 0.99
Sleeve Gastrectomy	1.00 (1.00, 1.07) N=61	1.02 (1.00, 1.12) N=51	1.00 (1.00, 1.10) N=56	1.00 (1.00, 1.08) N=48	1.00 (1.00, 1.10) N=44	1.00 (1.00, 1.04) N=43	1.00 (1.00, 1.04) N=39	ns 0.99	ns 0.07	ns 0.83

Nutritional biomarker	Baseline Median*	6 months Median*	Year 1 Median*	Year 2 Median*	Year 3 Media*	Year 4 Median*	Year 5 Median*	*P*-value for comparison of values between visits† Baseline to 1y	1y to 5y linear trend	Baseline to 5y
Folate (ug/mL)										
Gastric Bypass	14.2 (10.7, 18.9) N=158	11.2 (6.9, 17.4) N=136	13.2 (8.2, 18.9) N=142	13.7 (9.9, 17.8) N=131	14.2 (10.4, 20.0) N=129	15.0 (11.8, 22.0) N=120	17.0 (11.9, 22.0) N=122	ns 0.60	<0.0001	0.03
Sleeve Gastrectomy	17.4 (11.7, 20.0) N=62	11.6 (6.8, 18.4) N=52	11.2 (6.3, 20.0) N=54	13.0 (9.3, 20.4) N=49	11.8 (9.5, 22.0) N=44	14.1 (9.8, 21.4) N=48	13.6 (9.7, 17.9) N=42	0.03	ns 0.12	ns 0.75
Vitamin A (ug/L)										
Gastric Bypass	430 (370, 515) N=158	382 (313, 466) N=134	400 (327, 487) N=142	402 (330, 507) N=131	393 (331, 488) N=127	396 (312, 484) N=120	386 (336, 479) N=121	ns 0.85	ns 0.31	ns 0.38
Sleeve Gastrectomy	436 (369, 508) N=61	398 (362, 505) N=50	422 (370, 474) N=55	419 (362, 487) N=48	429 (362, 512) N=44	425 (361, 500) N=49	453 (393, 520) N=43	ns 0.99	ns 0.58	ns 0.99
25-OH Vitamin D (ng/mL)										
Gastric Bypass	21.4 (15.5, 28.0) N=159	24.8 (17.4, 32.2) N=134	23.4 (17.0, 31.4) N=142	20.5 (14.0, 29.6) N=131	20.2 (13.1, 26.8) N=129	19.3 (13.6, 28.4) N=120	19.7 (12.5, 27.6) N=119	ns 0.22	0.02	ns 1.00
Sleeve Gastrectomy	25.0 (21.2, 32.7) [N=62	26.6 (22.2, 36.3) N=51	27.1 (20.2, 35.8) N=55	23.0 (17.7, 29.4) N=49	22.8 (18.3, 28.6) [N=44	22.6 (17.8, 25.8) N=48	23.2 (16.9, 29.1) N=42	ns 0.99	0.008	ns 0.41
PTH (pg/mL)										
Gastric Bypass	44.0 (34.0, 63.0) N=159	41.0 (32.0, 50.0) N=135	46.0 (34.0, 58.0) N=142	51.0 (41.0, 65.0) N=131	54.0 (41.0, 72.0) N=129	57.0 (40.0, 75.0) N=118	59.0 (44.0, 72.0) N=122	ns 0.99	<0.0001	0.0002
Sleeve Gastrectomy	37.5 (27.0, 47.0) N=62	31.0 (25.0, 37.0) N=62	32.0 (28.0, 52.0) N=55	37.0 (30.0, 43.0) N=49	33.5 (27.5, 44.5) N=44	40.0 (29.0, 53.0) N=47	37.0 (32.0, 45.0) N=41	ns 0.99	ns 0.52	ns 0.94
Albumin (g/dL)										
Gastric Bypass	4.1 (3.9, 4.3) N=160	4.2 (4.0, 4.4) N=138	4.2 (4.0, 4.4) N=142	4.3 (4.1, 4.5) N=133	4.3 (4.1, 4.5) N=128	4.2 (4.0, 4.5) N=122	4.2 (4.1, 4.4) N=122	0.003	ns 0.76	0.03
Sleeve Gastrectomy	4.3 (4.0, 4.5) [N=63	4.3 (4.1, 4.5) N=52	4.3 (4.1, 4.6) N=55	4.4 (4.1, 4.5) N=49	4.2 (4.0, 4.4) N=44	4.3 (4.1, 4.5) N=49	4.3 (4.0, 4.6) N=44	ns 0.98	ns 0.11	ns 1.00
hs-CRP (mg/dL)										
Gastric Bypass	0.65 (0.32, 1.20) N=160	0.22 (0.08, 0.55) N=137	0.09 (0.04, 0.29) N=142	0.06 (0.03, 0.24) N=131	0.08 (0.03, 0.19) N=129	0.07 (0.02, 0.38) N=121	0.12 (0.05, 0.36) N=121	<0.0001	ns 0.40	<0.0001

Nutritional biomarker	Baseline Median*	6 months Median*	Year 1 Median*	Year 2 Median*	Year 3 Media*	Year 4 Median*	Year 5 Median*	*P*-value for comparison of values between visits† Baseline to 1y	1y to 5y linear trend	Baseline to 5y
Sleeve Gastrectomy	0.45 (0.19, 0.85) N=63	0.14 (0.06, 0.47) N=52	0.09 (0.03, 0.45) N=55	0.05 (0.03, 0.12) N=49	0.16 (0.04, 0.50) N=44	0.11 (0.04, 0.34) [N=49	0.09 (0.05, 0.63) N=43	0.001	ns 0.06	0.01

*Median (25^{th}, 75^{th} percentile)

†P-values are from generalized linear mixed models performed using log transformed (ferritin, B12, PTH, hs-CRP) or untransformed data (all others). Tukey-Kramer adjustment used when testing differences between baseline and year 1 and baseline and year 5 time-points. A linear model was fitted to test for trend between year 1 and year 5.

Table 3.

Clinical and demographic predictors of nutrient levels*

	Ferritin (log)	Transferrin	Vitamin B12 (log)	Folate	Vitamin A	Vitamin D	PTH (log)
Surgery type:							
Gastric Bypass	−0.26 (0.08)	17.2 (4.28)	−0.28 (0.06)	−0.06 (0.49)	−26.9 (10.4)	0.18 (0.86)	0.24 (0.04)
Sleeve Gastrectomy	0 p=0.002	0 p<0.0001	0 p<0.0001	0 p=0.89	0 p=0.01	0 p=0.83	0 p<0.0001
Visit:							
Year 1	0	0	0	0	0	0	0
Year 2	−0.26 (0.10)	6.76 (5.13)	−0.04 (0.07)	0.47 (0.59)	−10.3 (13.2)	−0.06 (1.08)	0.02 (0.05)
Year 3	−0.53 (0.10)	21..2 (5.32)	−0.03 (0.07)	1.18 (0.61)	−14.4 (13.6)	0.38 (1.12)	0.02 (0.05)
Year 4	−0.62 (0.11)	30.0 (5.40)	−0.10 (0.07)	2.06 (0.62)	−26.9 (13.7)	0.11 (1.13)	0.07 (0.05)
Year 5	−0.69 (0.11) p<0.0001	34.1 (5.45) p<0.0001	−0.03 (0.07) p=0.74	2.54 (0.62) p<0.0001	−15.7 (13.9) p=0.40	0.31 (1.14) p=0.99	0.12 (0.05) p=0.13
Sex:							
Female	−0.62 (0.07)	24.9 (3.64)	0.003 (0.05)	1.00 (0.42)	5.46 (9.24)	1.89 (0.76)	0.01 (0.04)
Male (reference)	0 p<0.0001	0 p<0.0001	0 p=0.95	0 p=0.02	0 p=0.55	0 p=0.01	0 p=0.70
Race:							
Black	0.19 (0.08)	−15.3 (3.95)	0.03 (0.05)	−0.94 (0.45)	−35.5 (10.0)	−5.02 (0.84)	0.13 (0.04)
Other	0.22 (0.13)	−14.6 (6.77)	0.13 (0.09)	−1.54 (0.80)	1.47 (17.0)	−3.26 (1.44)	0.04 (0.07)
White (reference)	0 p=0.02	0 P=0.0002	0 p=0.37	0 p=0.03	0 P=0.002	0 p<0.0001	0 P=0.001
Education:							
HS graduate	0.17 (0.12)	1.49 (5.90)	0.12 (0.08)	0.05 (0.67)	19.4 (15.0)	−0.94 (1.23)	−0.04 (0.06)
College	−0.01 (0.12)	8.12 (5.86)	0.14 (0.08)	−0.07 (0.67)	6.73 (14.8)	−0.58 (1.22)	0.004 (0.06)
College graduate	0.18 (0.13)	1.58 (6.43)	0.13 (0.09)	0.51 (0.74)	26.5 (16.2)	−0.88 (1.34)	−0.05 (0.06)
<High school (reference)	0 p=0.04	0 p=0.23	0 p=0.35	0 p=0.72	0 p=0.19	0 p=0.87	0 p=0.54
Weight change (+5 kg/y)	−0.03 (0.01) p=0.04	2.42 (0.71) p=0.0007	0.009 (0.01) p=0.37	0.32 (0.08) p=0.0001	5.17 (1.81) p=0.004	−0.47 (0.15) p=0.002	0.02 (0.01) p=0.02
Acid suppression	−0.03 (0.10) p=0.74	2.14 (5.00) p=0.67	−0.002 (0.07) p=0.98	NA	NA	NA	NA
hsCRP	0.31 (0.05) p<0.0001	−9.45 (2.50) p=0.0002	NA	NA	NA	NA	NA

	Ferritin (log)	Transferrin	Vitamin B12 (log)	Folate	Vitamin A	Vitamin D	PTH (log)
Multivitamin supplements/wk:							
<7							
7-14	−0.07 (0.09)	1.97 (4.44)	0.008 (0.07)	1.41 (0.51)	−8.85 (11.3)	3.26 (0.98)	−0.02 (0.05)
14+	−0.07 (0.08)	−1.26 (3.89)	0.10 (0.06)	2.35 (0.45)	6.77 (9.95)	4.00 (0.90)	−0.06 (0.05)
0 (reference)	0.22 (0.10) 0 p=0.05	−2.39 (5.26) 0 p=0.85	0.26 (0.07) 0 p=0.003	2.57 (0.60) 0 p<0.0001	34.4 (13.3) 0 p=0.02	5.47 (1.15) 0 p<0.0001	−0.09 (0.06) 0 p=0.43
Vitamin D supplements/wk:	NA	NA	NA	NA	NA		
<7						1.17 (1.02)	−0.10 (0.05)
7+						4.51 (0.95)	0.005 (0.05)
0 (reference)						0 p<0.0001	0 p=0.12
Vitamin B12 supplements/wk:	NA	NA		NA	NA	NA	NA
<7							
7+			0.07 (0.07)				
0 (reference)			0.30 (0.07) 0 p<0.0001				
Calcium supplements/wk:	NA	NA		NA	NA	NA	
<7							−0.07 (0.06)
7-14							0.02 (0.05)
14+							0.01 (0.05)
0 (reference)							0 p=0.53

* Nutrient level is modelled as either raw or log value showing beta estimate (standard error). P-values reflect test for overall significance of each variable.

Table 4.

Clinical and demographic predictors of abnormal nutrient values*

	Ferritin	Transferrin	Folate	Vitamin A	Vitamin D	PTH
Surgery type:						
Gastric Bypass	2.88 (1.57, 5.26)	3.76 (1.19, 11.9)	0.49 (0.21, 1.13)	4.57 (1.91, 10.9)	1.93 (0.99, 3.77)	5.91 (2.03, 17.2)
Sleeve Gastrectomy (reference)	1.0 p=0.001	1.0 p=0.008	1.0 p=0.15	1.0 p=0.0005	1.0 p=0.06	1.0 P=0.0005
Visit:						
Year 1	1.0	1.0	1.0	1.0	1.0	1.0
Year 2	2.10 (1.12, 3.94)	2.14 (0.38, 12.0)	0.95 (0.34, 2.65)	1.64 (0.65, 4.12)	0.95 (0.48, 1.90)	1.33 (0.46, 3.86)
Year 3	2.66 (1.27, 5.57)	4.21 (0.74, 23.8)	1.08 (0.30, 3.90)	1.42 (0.53, 3.82)	0.70 (0.31, 1.62)	1.93 (0.61, 6.04)
Year 4	4.39 (2.09, 9.22)	4.68 (0.85, 26.0)	0.40 (0.08, 2.07)	1.69 (0.59, 4.84)	0.77 (0.36, 1.69)	2.07 (0.64, 6.64)
Year 5	4.94 (2.36, 10.3) p<.0001	5.56 (1.05, 29.5) p=0.01	0.19 (0.03, 1.28) p=0.009	1.65 (0.51, 5.39) p=0.61	0.87 (0.39, 1.92) p=0.68	2.38 (0.75, 7.55) p=0.31
Sex:						
Female	1.47 (0.80, 2.68)	3.58 (0.85, 15.1)	0.68 (0.28, 1.67)	1.07 (0.53, 2.15)	0.73 (0.43, 1.26)	1.90 (0.79, 4.97)
Male (reference)	1.0 p=0.22	1.0 p=0.08	1.0 p=0.44	1.0 p=0.86	1.0 p=0.26	1.0 p=0.13
Race:						
Black	1.07 (0.52, 2.17)	0.55 (0.15, 2.02)	0.33 (0.09, 1.27)	2.47 (1.11, 5.51)	4.12 (2.04, 8.34)	2.03 (0.74, 5.56)
Other	1.07 (0.38, 2.98)	0.51 (0.12, 2.13)	2.03 (0.55, 7.53)	1.42 (0.29, 6.95)	1.35 (0.31, 5.95)	1.78 (0.24, 12.9)
White (reference)	1.0 p=0.97	1.0 p=0.30	1.0 p=0.045	1.0 p=0.06	1.0 P=0.0002	1.0 p=0.29
Education:						
HS graduate	0.74 (0.30, 1.82)	1.92 (0.12, 31.8)	1.23 (0.20, 7.46)	0.87 (0.16, 4.79)	1.75 (0.56, 5.41)	0.60 (0.12, 2.90)
College	0.92 (0.38, 2.26)	4.26 (0.29, 63.5)	0.93 (0.19, 4.55)	2.05 (0.41,10.1)	1.26 (0.44, 3.59)	0.82 (0.21, 3.26)
College graduate	0.66 (0.25, 1.76)	3.14 (0.20, 50.5)	0.43 (0.06, 3.07)	0.60 (0.09, 3.88)	1.27 (0.39, 4.14)	0.33 (0.06, 1.94)
<High school (reference)	1.0 p=0.63	1.0 p=0.19	1.0 p=0.33	1.0 p=0.04	1.0 p=0.59	1.0 p=0.30
Weight change (+5 kg/y)	1.08 (0.99, 1.17) p=0.08	1.01 (0.86, 1.20) p=0.87	0.83 (0.73, 0.94) p=0.01	0.92 (0.82, 1.02) p=0.12	1.14 (1.04, 1.25) p=0.005	1.08 (0.93, 1.25) p=0.34
Acid suppression	1.19 (0.63, 2.27) p=0.59	0.51 (0.13, 1.92) p=0.24	NA	NA	NA	NA
hsCRP	0.47 (0.33, 0.68) p=0.0006	0.80 (0.45, 1.41) p=0.39	NA	NA	NA	NA

	Ferritin	Transferrin	Folate	Vitamin A	Vitamin D	PTH
Multivitamin supplements/wk:						
<7	1.02 (0.52, 1.96)	0.88 (0.33, 2.34)	0.87 (0.30, 2.51)	0.97 (0.38, 2.47)	0.49 (0.23, 1.02)	0.80 (0.19, 3.37)
7-14	0.76 (0.43, 1.34)	0.93 (0.36, 2.42)	0.61 (0.23, 1.66)	0.87 (0.38, 2.02)	0.38 (0.19, 0.74)	1.01 (0.27, 3.75)
14+	0.51 (0.24, 1.07)	0.63 (0.16, 2.59)	0.73 (0.20, 2.68)	0.73 (0.28, 1.91)	0.38 (0.16, 0.91)	0.68 (0.16, 2.82)
0 (reference)	1.0 p=0.11	1.0 p=0.77	1.0 p=0.66	1.0 p=0.85	1.0 p=0.004	1.0 p=0.71
Vitamin D supplements/wk:	NA	NA	NA	NA		
<7					0.47 (0.21, 1.04)	0.38 (0.10, 1.37)
7+					0.50 (0.26, 0.95)	0.93 (0.27, 3.25)
0 (reference)					1.0 p=0.01	1.0 p=0.15
Vitamin B12 supplements/wk:	NA	NA	NA	NA	NA	NA
<7						
7+						
0 (reference)						
Calcium supplements/wk:	NA	NA	NA	NA	NA	
<7						0.38 (0.02, 5.89)
7-14						1.19 (0.37, 3.83)
14+						0.91 (0.22, 3.72)
0 (reference)						1.0 p=0.45

* P-values reflect test for overall significance of each variable.