

## Multivitamin and dietary supplements, body weight and appetite: results from a cross-sectional and a randomised double-blind placebo-controlled study

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Two studies were conducted to compare characteristics of consumers and non-consumers of vitamin and/or dietary supplements (study 1) and to assess the effect of a multivitamin and mineral supplementation during a weight-reducing programme (study 2). Body weight and composition, energy expenditure, and Three-Factor Eating Questionnaire scores were compared between consumers and non-consumers of micronutrients and/or dietary supplements in the Québec Family Study (study 1). In study 2, these variables and appetite ratings (visual analogue scales) were measured in forty-five obese non-consumers of supplements randomly assigned to a double-blind 15-week energy restriction ( $-2930$  kJ/d) combined with a placebo or with a multivitamin and mineral supplement. Compared with non-consumers, male consumers of vitamin and/or dietary supplements had a lower body weight ( $P<0.01$ ), fat mass ( $P<0.05$ ), BMI ( $P<0.05$ ), and a tendency for greater resting energy expenditure ( $P=0.06$ ). In women, the same differences were observed but not to a statistically significant extent. In addition, female supplements consumers had lower disinhibition and hunger scores ( $P<0.05$ ). In study 2, body weight was significantly decreased after the weight-loss intervention ( $P<0.001$ ) with no difference between treatment groups. However, fasting and postprandial appetite ratings were significantly reduced in multivitamin and mineral-supplemented women ( $P<0.05$ ). Usual vitamin and/or dietary supplements consumption and multivitamin and mineral supplementation during a weight-reducing programme seems to have an appetite-related effect in women. However, lower body weight and fat were more detectable in male than in female vitamin and/or dietary supplements consumers.

**Obesity: Weight loss: Micronutrients: Energy expenditure: Appetite**

Above the fundamental roles of physical activity and a macro-nutrient-balanced diet in the maintenance of a healthy body weight, evidence is pointing toward other dietary factors, admittedly of a lower impact range, that could affect energy balance on a long-term basis and therefore represent an avenue worth considering under obesity treatment circumstances. Ca is a good example of this, as low consumption of this micronutrient has been shown to be inversely associated with body weight and adiposity in many studies<sup>(1–3)</sup>. More recently, it was observed in a large cohort of 15 655 individuals that overweight or obese men and women who had a high consumption of multivitamins, vitamin B<sub>6</sub>, vitamin B<sub>12</sub> or Cr had gained less weight than those who had not consumed these supplements over 8–12 years<sup>(4)</sup>.

How vitamins and minerals could be implicated in the regulation of body energy stores is not known. For instance, one could propose that they influence the control of food intake through their roles in neurotransmitter synthesis and regulation in the central nervous system. Vitamins C and B<sub>6</sub> are good examples of this, since they are respectively involved in the

hydroxylation and decarboxylation of tryptophan for the synthesis of serotonin<sup>(5)</sup> which is known to control food intake through the melanocortin pathways<sup>(6)</sup>. Low status of vitamin B<sub>6</sub> and its consequent decrease in brain serotonin synthesis<sup>(7)</sup> could result in an increased appetite and presumably food intake and favour a positive energy imbalance. On the other side of the equation, the role of micronutrients as enzyme cofactors necessary for energy transformation within cells<sup>(5)</sup> suggests that they could also influence the regulation of energy expenditure. In support to these hypothesis, Singh *et al.* have shown that vitamins C and E deficiency was a risk factor for higher percentage body fat and central obesity in Indian men<sup>(8)</sup>. Moreover, high percentages of vitamin C and B<sub>2</sub> deficiency<sup>(9)</sup>, lower bioavailability of vitamin D<sup>(10)</sup>, lower serum vitamins A, C and E<sup>(11)</sup> and folic acid concentrations<sup>(12)</sup> have been found in overweight and obese individuals compared with non-obese subjects. Interestingly, high serum folic acid level was also recently found to be a significant predictor of body-weight loss in morbidly obese patients<sup>(13)</sup>. Finally, an effect of vitamin C status<sup>(14)</sup> and of

**Abbreviations:** AUC, area under the curve; CS, consumers; FFM, fat-free mass; FM, fat mass; MMS, multivitamin + mineral supplement; NCS, non-consumers; REE, resting energy expenditure.

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Cr supplementation on lipid oxidation and fat-mass (FM) loss<sup>(15,16)</sup> have been observed in intervention studies.

Taken together, these results suggest that a certain level of availability of vitamins and minerals might influence energy balance regulation and, thus, that an adequate intake could be associated with lower body weight or even determine the success of weight-reducing programmes. In order to investigate this issue, we report data from two separate studies. The objective of study 1 was to determine whether regular consumers (CS) of vitamin and/or dietary supplements were characterised by lower body weight and adiposity values than non-consumers (NCS) of these supplements using data from the Québec Family Study<sup>(17)</sup>. The aim of study 2 was to assess in a different group of participants the effect of a weight-loss intervention, combined with either a multivitamin + mineral supplement (MMS) or with a placebo on body-weight and FM loss, energy expenditure and appetite.

## Methods

### Study 1

Adult men (*n* 267) and women (*n* 320) aged 20–65 years with complete data from the dietary questionnaire (explained in the next section) were selected among the subjects who participated in phase 2 (1991–8) of the Québec Family Study<sup>(17)</sup>. Families of French descent from the greater Québec City area were recruited to participate in this study which received approval from the Laval University Medical Ethics Committee.

**Vitamins and dietary supplements.** A questionnaire was used to gather dietary information. One of the questions of interest for this study was as follows: ‘Do you consume vitamin/dietary supplements?’ Since this was the only question asked to record the participants’ supplement consumption habits, the dose and the type of vitamins and/or dietary supplements cannot be addressed in this study. The present study therefore pertains to differences between consumers (CS) and NCS of vitamins and/or dietary supplements.

**Three-day dietary record and physical activity diary measurement.** Dietary habits were determined by a 3 d dietary record which has been previously shown to provide reliable results<sup>(18)</sup>. All subjects were requested to record their dietary intake during two week days and one weekend day. Nutritionists explained to each subject how to accurately complete the forms. All subjects were supplied with a balance, measuring cups and spoons to facilitate the measuring procedures. A nutritionist reviewed the records together with subjects during an interview. The Canadian Nutrient File<sup>(19)</sup> was used to assess macro- as well as micronutrient content of foods. Daily physical activities were evaluated with a 3 d physical activity diary, as previously described<sup>(20)</sup>. Briefly, subjects recorded the number of 15 min periods during 24 h that they were engaged in activities classified on a 1–9 scale, 1 corresponding to activities of very low energy expenditure such as sleeping and 9 to activities of very high energy expenditure such as running. The 3 d mean of the number of periods in activities 7 to 9 (activity periods) was used as an indication of physical activity practice.

**Eating behaviour measurements.** A subgroup of participants completed the Three-Factor Eating Questionnaire<sup>(21)</sup> as

validated for the French population<sup>(22)</sup>. Since this questionnaire was included in the Québec Family Study only at the end of the second phase, data from only 119 men and 174 women were available. The Three-Factor Eating Questionnaire evaluates ‘dietary restraint’, which measures the actual restrictive eating as well as the intention to restrain eating, ‘disinhibition’, which measures how easily external factors, that is, environmental events and emotional reactions, disinhibit the control of eating, and ‘susceptibility to hunger’, which measures the ability to cope with the sensation of hunger<sup>(23)</sup>. The Three-Factor Eating Questionnaire has been shown to have acceptable reliability and validity<sup>(21,24)</sup>.

**Anthropometric measurements.** Body weight was measured with a standard beam scale. Body density was determined by hydrodensitometry<sup>(25)</sup>. The closed circuit He-dilution method<sup>(26)</sup> was used to assess the residual lung volume. The Siri formula<sup>(27)</sup> was used to estimate the percentage of body fat from body density. FM was calculated from the percentage of body fat and total body weight while fat-free mass (FFM) was estimated as the difference between FM and body weight.

**Measure of resting energy expenditure.** Resting energy expenditure (REE) was measured early in the morning while participants were in a fasted state (12 h overnight fast). Subjects were asked to refrain from physical activity on the day before this measurement. Indirect calorimetry was performed over a 30 min period through an open-circuit system with a ventilated hood. Data from the last 10 min of this measurement period were used for the calculation of respiratory quotient and REE. Gas analyses were assayed with an IR CO<sub>2</sub> analyser (Ametek CD-3A; Thermox Instruments Division, Pittsburgh, PA, USA) and an IR O<sub>2</sub> analyser (Ametek S-3A; Thermox Instruments Division). Analysers were calibrated before each test. The Weir formula<sup>(28)</sup> was used to determine the energy equivalent of O<sub>2</sub> volume.

**Statistical analysis.** Statistical analyses were performed using SAS software (version 9.1.2; SAS Institute, Cary, NC, USA). Since most of the participants were from three generations of the same family<sup>(17)</sup>, analyses were performed to verify whether there were generation × supplement consumed status interaction effects and none were found. All subjects were thus pooled together for further analyses although sexes were analysed separately. A one-way analysis of covariance (CS and NCS) taking into account potential covariates (age, height, daily energy intake, percentage dietary fat and activity periods) which have been shown to affect energy balance and/or body-weight control was performed for body weight, FM, FFM, fat percentage and BMI. A one-way ANOVA (CS and NCS) was performed on all other dependent variables. Differences were considered as significant at *P* < 0.05 and data are presented as mean values and standard deviations.

### Study 2

**Screening.** Study 2 was approved by the Laval University Ethics Committee and participants were recruited through diverse media sources such as local newspapers, radio stations and email communications. A sample of sixty-three individuals coming from the Québec City metropolitan area met the study inclusion and exclusion criteria which were as follows: aged 25–45 years, BMI 30–40 kg/m<sup>2</sup>, good health,

waist circumference  $\geq 90$  cm, stable body weight during 6 months before the study, premenopausal, less than 1 h/week of continuous physical activity, normal blood pressure values, normal blood glucose levels, normal thyroid hormone levels, non-smoker, no use of medication that could potentially interfere with the study's objectives and no use of vitamin and mineral supplements 6 months before the beginning of the study. Breast-feeding or pregnant women, verified by a urine-based pregnancy test, were excluded from the study.

Participants came to the laboratory for a screening evaluation in order to confirm their eligibility and for explanation of the study consent form. During this visit, blood samples were collected after a 12 h overnight fast to measure a biochemical profile. Body weight, height and blood pressure were also measured during this visit. Another session was fixed for a medical examination and for explanation of the 3 d dietary record by a nutritionist (as described for study 1). Fasting blood samples were taken and a 75 g oral glucose tolerance test over 3 h was also performed.

**Protocol.** Following the screening procedures, forty-five obese otherwise healthy men and women were initially enrolled and randomised in a double-blind manner to receive the MMS or the placebo coupled to a 15-week energy restriction. MMS capsules were the Premium Multi-Cap with Ester-C from Quest, Canada (composition of the supplement can be found at [www.questvitamins.com](http://www.questvitamins.com)), and placebo was lactose monohydrate in gelatine capsules. Dosage was one tablet taken before breakfast. Among the initial participants, five dropped out (three placebo and two MMS); four because of personal reasons and one became pregnant.

The sequence of measurements happened as follow and is described in more detail in the following paragraphs. Measurements were spread over two consecutive days. On day 1, REE and respiratory quotient were measured in the fasting state; appetite ratings were assessed before and after a standardised breakfast test and participants were asked to fill in the Three-Factor Eating Questionnaire. On day 2, 24 h energy expenditure was measured. Day 1 and 2 measurements were realised at baseline (week 0) and were repeated at the end of the 15-week intervention (week 15).

**Weight-loss intervention.** The subjects followed a non-macronutrient-specific energy-restricted diet for 15 weeks. Prescribed daily energy intake was determined by subtracting 2930 kJ (700 kcal) from the daily energy expenditure calculated by multiplying the REE by an activity factor of 1.4. A 3 d dietary record was also used to estimate energy and macronutrient intake of each subject. Following the baseline visit (week 0), a nutritionist explained to the participants how to reach the targeted daily 2930 kJ (700 kcal) non-macronutrient-specific energy deficit using the food exchange system for diabetics from the Association Diabète Québec<sup>(29)</sup>. During this visit, treatment tablets (MMS or placebo) were given to participants who started the energy restriction and the consumption of the treatment tablets the next morning. The intervention lasted 15 weeks, during which participants met the nutritionist every 2 weeks. In order to assess compliance to the weight-reducing programme, a count of remaining treatment tablets, a 24 h dietary recall assessed with the nutritionist and visual analogue scales evaluating satisfaction with the diet, hunger, and rigor in following the treatment were filled in by the participants

during the interview. On the week between these meetings, participants received a phone call from the nutritionist to answer any questions and ensure that participants were following treatment. Each staff member and participants were blinded to treatment assignment for the duration of the study.

**Anthropometry.** Height, body weight and waist circumference were determined following the procedures recommended at the Airlie Conference<sup>(30)</sup>, and BMI was then calculated. FM, FFM and percentage of fat were determined as described in the Study 1 methods section.

**Resting and 24 h energy expenditure.** REE was measured by indirect calorimetry after a 12 h overnight fast and a 24 h period without alcohol consumption and intense physical activity. Participants had to arrive in the morning at the laboratory and to keep an activity level as low as possible in between their wake-up time and their arrival to the laboratory. A questionnaire was filled in by the subjects upon their arrival to ensure they were meeting these criteria. After resting for 15 min, expired gas collection was performed through a mouthpiece for 15 min while the nose was clipped during the whole measurement. O<sub>2</sub> and CO<sub>2</sub> concentrations were determined by non-dispersive IR analysis (Uras 10 E; Hartmann & Braun, Frankfurt, Germany) whereas pulmonary ventilation determination was assessed with an S430A measurement system (KL Engineering, Ventura, CA, USA). The Weir formula<sup>(28)</sup> was used to determine the energy equivalent of O<sub>2</sub> volume. The determination of substrate oxidation was assessed through the calculations previously described by Frayn<sup>(31)</sup> while assuming that protein oxidation contributes 10% of total energy expenditure measured under these conditions.

The next day, 24 h total energy expenditure was measured with a whole-body indirect calorimeter, which has been shown to provide highly reproducible data in our laboratory<sup>(32)</sup>. Subjects came back to the laboratory early in the morning and had to have respected the same criteria for fasting, alcohol consumption and physical activity as for the REE measurement. During this stay, subjects were maintained in energy balance by using the REE performed at the initial visit and by extrapolating this value over a 24 h period and then multiplying this value by an activity factor of 1.32. The same energy intake was maintained for the two measurements of 24 h energy expenditure (weeks 0 and 15). Moreover, the nutrient composition of the diet (daily food quotient 0.85), the sedentary lifestyle pattern (watching television, computer use, reading, etc) and the meal pattern, as well as the period of sleep, were also standardised in each session. It was not permitted to eat or drink any other foods than those provided and therefore no foods or beverages containing caffeine were allowed during the metabolic chamber stay. Sleeping metabolic rate was also measured in the chamber and was determined as the mean of the two consecutive hours of the night when the subject had the lowest O<sub>2</sub> consumption. This value was then extrapolated over 24 h. Women were tested between days 0 and 8 of their menstrual cycle, because energy metabolism-related factors have been shown to be affected by sex steroid levels<sup>(33)</sup>.

**Standardised breakfast and appetite ratings.** A standardised breakfast which has previously been described<sup>(34)</sup> was served to participants after a 12 h overnight fast. The energy

**Table 1.** Characteristics of regular consumers and non-consumers of supplements in study 1 (Mean values and standard deviations)

	Men							Women						
	Consumers			Non-consumers			<i>P</i>	Consumers			Non-consumers			<i>P</i>
	<i>n</i>	Mean	SD	<i>n</i>	Mean	SD		<i>n</i>	Mean	SD	<i>n</i>	Mean	SD	
Age (years)	51	41.4	14.8	216	40.9	13.9	0.82	105	41.3	13.7	215	38.5	13.0	0.08
Body weight (kg)*	51	75.0	15.5	216	82.3	19.4	0.009	105	67.0	14.6	215	70.1	21.5	0.40
BMI (kg/m <sup>2</sup> )*	51	24.9	4.6	216	27.4	6.3	0.008	105	26.2	5.7	215	27.1	8.3	0.38
Fat mass (kg)*	51	16.1	9.7	216	20.9	13.4	0.02	105	22.5	10.9	215	24.2	15.9	0.47
Fat-free mass (kg)*	51	59.0	7.8	216	61.4	8.3	0.04	105	44.5	5.5	215	45.9	7.1	0.31
Fat (%)*	51	20.2	8.0	216	23.7	9.1	0.01	105	32.0	9.0	215	31.8	10.9	0.90
Resting energy expenditure (kJ/kg per d)	50	92.6	5.3	216	89.1	11.8	0.06	104	83.6	13.2	213	86.2	15.2	0.13
Activity periods ( <i>n</i> )†	49	4.0	5.5	207	3.6	5.4	0.72	99	2.2	3.3	207	1.5	2.8	0.07
Energy intake (kJ/d)	51	11 427.8	2272.7	215	11 423.2	2958.9	0.99	105	8159.6	1841.0	210	8568.8	2028.8	0.08
Dietary fat (%)	51	34.4	5.6	215	34.6	6.4	0.87	105	33.3	6.2	210	34.9	6.1	0.03
Dietary carbohydrates (%)	51	47.6	7.6	215	46.2	6.6	0.20	105	48.7	7.0	210	47.3	6.0	0.06
Dietary proteins (%)	51	15.4	2.5	215	16.0	3.1	0.19	105	16.3	3.0	210	16.2	3.2	0.72
Alcohol (%)	51	2.7	5.0	215	3.2	5.4	0.49	105	1.7	3.0	210	1.7	3.4	0.96
Dietary restraint	29	5.9	3.4	90	5.5	3.6	0.59	65	7.9	5.0	109	8.3	4.6	0.67
Disinhibition	29	4.6	3.5	90	4.8	2.9	0.80	65	6.0	3.4	109	7.1	3.7	0.05
Susceptibility to hunger	29	3.9	3.9	90	4.4	3.2	0.51	65	3.4	3.0	109	4.7	3.6	0.02

\* Adjusted for age, height, daily energy intake, percentage dietary fat and activity periods.

† Mean daily number of 15 min periods of activity level 7–9 assessed with a physical activity diary.

**Table 2.** Characteristics of multivitamin and mineral supplementation (MMS) and placebo groups of men before (week 0) and after (week 15) the weight-loss intervention in study 2 (Mean values and standard deviations)

	Placebo						MMS						Statistical significant effect of		
	Week 0			Week 15			Week 0			Week 15			Time	Treatment	Time x treatment interaction
	n	Mean	SD	Mean	SD	n	Mean	SD	Mean	SD					
Age (years)	8	35	8	103.8	21.9	10	39.2	7.4	96.4	9.2	<0.001	0.33	0.67		
Body weight (kg)	8	106.7	19.0	103.8	21.9	10	100.1	8.4	96.4	9.2	<0.001	0.33	0.67		
BMI (kg/m <sup>2</sup> )	8	35.3	5.9	34.3	6.6	10	32.2	2.9	31.02	3.1	<0.001	0.17	0.74		
Waist circumference (cm)	8	117.8	11.9	113.1	13.5	10	110.5	7.5	105.6	8.6	<0.0001	0.15	0.88		
Fat (%)	8	35.8	6.2	34.2	6.2	10	31.2	5.4	29.3	6.2	<0.01	0.11	0.70		
Fat mass (kg)	8	38.7	12.1	36.2	13.4	10	31.6	8.0	28.6	8.4	<0.01	0.15	0.73		
Fat-free mass (kg)	8	68.0	10.2	67.5	10.9	10	68.5	3.06	67.8	4.3	0.10	0.92	0.76		
Resting energy expenditure (kJ/kg per d)	7	80.0	7.4	82.3	7.3	9	80.8	8.0	83.6	8.3	0.29	0.75	0.89		
Resting respiratory quotient	7	0.82	0.04	0.81	0.03	9	0.81	0.04	0.85	0.04	0.19	0.51	0.09		
Sleeping metabolic rate energy expenditure (kJ/kg per d)	6	82.7	11.3	88.7	12.4	8	88.4	13.4	89.2	7.0	0.15	0.59	0.27		
24 h Energy expenditure (kJ/kg per d)	6	109.6	11.8	114.4	12.5	8	116.9	16.5	113.0	9.9	0.88	0.66	0.18		
24 h Respiratory quotient	6	0.93	0.06	0.91	0.03	8	0.91	0.06	0.94	0.04	0.94	0.75	0.27		
Lipid oxidation (g/d)	6	66.5	56.7	80.6	23.0	8	85.7	76.0	56.0	33.7	0.70	0.89	0.32		

content of the breakfast was 3067 kJ (733 kcal) and 2506 kJ (599 kcal) for men and women, respectively, and had a food quotient of 0.85. All participants were instructed to eat within 30 min or less. Before, immediately after and every 10 min for a period of 1 h after the breakfast, subjects were asked to fill in visual analogue scales adapted from Blundell & Hill<sup>(35)</sup>. The answer to the following questions were used to determine their 'desire to eat', 'hunger', 'fullness' and 'prospective food consumption', respectively: (1) 'How strong is your desire to eat?' (very weak – very strong); (2) 'How hungry do you feel?' (not hungry at all – as hungry as I have ever felt); (3) 'How full do you feel?' (not full at all – very full); (4) 'How much food do you think you could eat?' (nothing at all – a large amount), respectively. Appetite ratings measured before breakfast were considered as the fasting measurement, and appetite ratings in response to the breakfast were evaluated by calculating the post-meal area under the curve (AUC) with the trapezoid method as previously described<sup>(36)</sup>. AUC was calculated considering appetite rating responses at 0, 10, 20, 30, 40, 50 and 60 min after the breakfast. Breakfast was consumed and visual analogue scale measurements performed in the same room kept quiet and away from different visual, hearing and olfactory stimuli that might have influenced the measurements. Under these conditions, visual analogue scale measurements in our laboratory have been shown to be highly reliable both before and in response to a meal<sup>(36,37)</sup>. During this visit, participants were also asked to complete the Three-Factor Eating Questionnaire as described in study 1.

**Statistical analysis.** Statistical analyses were performed using SAS software (version 9.1.2; SAS Institute, Cary, NC, USA). A two-way ANOVA with repeated measurements on one factor (time) was used to assess the effects of treatment (placebo and MMS) and time, and their interaction on all dependent variables within each sex. In order to adjust the appetite variables for change in body weight, a two-way ANOVA was repeated using residual scores for appetite ratings and the Three-Factor Eating Questionnaire scores derived from linear regression analysis considering body weight as the independent variable. Three-Factor Eating Questionnaire scores that included unanswered questions were corrected for the specific eating behaviour total score. Differences were considered significant at  $P < 0.05$  and data are presented as mean values and standard deviations.

**Results**

*Study 1*

Results from study 1 showed that men CS had significantly lower body weight, BMI, FM, percentage body fat and FFM than men NCS after adjustments were made for age, height, daily energy intake, percentage dietary fat and activity periods. Men CS also had a trend toward a greater REE expressed per kg body weight compared with men NCS ( $P = 0.06$ ). The same trend was found for anthropometric measurements between CS and NCS in women but the differences were less pronounced and statistically non-significant. Variables related to food intake as well as daily physical activity level were all comparable between both groups of men (Table 1). However, the CS group of women had a

**Table 3.** Characteristics of multivitamin and mineral supplementation (MMS) and placebo groups of women before (week 0) and after (week 15) the weight-loss intervention in study 2 (Mean values and standard deviations)

	Placebo				MMS				Statistical significant effect of		
	Week 0		Week 15		Week 0		Week 15		Time	Treatment	Time × treatment interaction
	n	Mean	SD	Mean	SD	n	Mean	SD			
Age (years)	11	36	9	37	6	11	37	11	–	–	–
Body weight (kg)	11	94.4	14.2	90.4	11.2	11	90.4	11	<0.001	0.65	0.10
BMI (kg/m <sup>2</sup> )	11	35.2	3.7	33.1	3.5	11	35.1	11	<0.001	0.82	0.13
Waist circumference (cm)	11	103.1	9.4	97.3	9.6	11	103.6	11	<0.0001	0.67	0.06
Fat (%)	11	42.2	5.1	40.1	4.8	11	46.8	11	<0.01	0.26	0.30
Fat mass (kg)	11	40.3	10.1	36.1	9.1	11	39.7	11	<0.001	0.87	0.12
Fat-free mass (kg)	11	54.1	6.4	52.8	6.3	11	50.7	11	<0.01	0.25	0.29
Resting energy expenditure (kJ/kg per d)	11	74.9	6.6	77.2	9.0	11	72.6	11	0.81	0.10	0.23
Resting respiratory quotient	11	0.81	0.04	0.81	0.02	11	0.82	11	0.93	0.53	0.74
Sleeping metabolic rate energy expenditure (kJ/kg per d)	8	85.1	12.3	86.6	6.02	10	78.0	10	0.49	0.16	0.93
24 h Energy expenditure (kJ/kg per d)	8	108.8	15.9	106.4	9.0	10	103.4	10	0.56	0.37	0.77
24 h Respiratory quotient	8	0.89	0.05	0.91	0.04	10	0.91	10	0.24	0.44	0.67
Lipid oxidation (g/d)	8	86.2	37.9	65.2	32.6	10	64.9	10	0.16	0.25	0.57

lower fat intake and tended to be older and to have a lower overall energy intake, greater carbohydrate consumption and to be more physically active (Table 1). Women CS also had a significantly lower disinhibition and hunger scores than NCS women ( $P < 0.05$ ), while in CS men the slightly lower scores observed for these variables were not statistically different from those in NCS men.

### Study 2

Baseline daily vitamin and mineral consumption, assessed with the 3 d dietary record, was similar between placebo and MMS groups in both men and women (results not shown). Anthropometric variables, REE and 24 h energy expenditure mean values are presented in Tables 2 and 3 for men and women, respectively. Means for these variables were similar in MMS and placebo groups before intervention. Body weight, BMI, waist circumference, FM and percentage of fat were significantly decreased at week 15 in men and women in both MMS and placebo groups. In women only, a significant decrease in FFM was also observed, with no difference between MMS and placebo groups.

Appetite ratings measured in the fasting state before breakfast and postprandial appetite rating AUC measured after the breakfast are presented in Table 4. In men, no significant between-group difference was observed for these variables. In women, baseline value for fasting desire to eat was significantly lower in the placebo than in the MMS group. However, a significant time × treatment interaction effect was observed for this variable, revealing a significant decrease in the MMS group and a non-significant increase in the placebo group. Significant time × treatment interaction effects were observed in women for desire to eat, hunger and prospective food consumption AUC, revealing a significant decrease in these variables in the MMS group only, and an AUC value for these three variables that was significantly lower in the MMS group compared with the placebo group at week 15 (Table 4). These differences were observed after statistical adjustments for body-weight change. In both men and women, a significant increase in dietary restraint and a significant decrease in disinhibition and susceptibility to hunger were observed following the programme with no difference between treatment groups (Table 5).

### Discussion

Results obtained in study 1 showed that men regularly consuming micronutrients and dietary supplements had a lower body weight and FM than men who did not. This agrees with the recently reported lower 8–12 years body-weight gain in overweight or obese CS of multivitamins, vitamins B<sub>6</sub>, vitamin B<sub>12</sub> and Cr compared with NCS<sup>(4)</sup>. From a body-weight-regulation standpoint, these observations suggest that a sufficient intake of micronutrients, which have fundamental roles in energy metabolism<sup>(5)</sup>, might be needed to achieve energy balance stability. Sufficient intake of micronutrients could thus be important in the context of obesity treatment, where micronutrient intake may be decreased along with macronutrients during reduced-energy diets<sup>(38,39)</sup>. This hypothesis was investigated in study 2, and no difference in the changes in body weight, FM, energy expenditure and

**Table 4.** Appetite ratings measured before and after a standardised breakfast meal before (week 0) and after (week 15) the weight-loss intervention in study 2 (Mean values and standard deviations)

	Placebo				MMS				Statistical significant effect‡ of				
	n	Week 0		Week 15		n	Week 0		Week 15		Time	Treatment	Time × treatment interaction
		Mean	SD	Mean	SD		Mean	SD	Mean	SD			
<b>Men</b>													
Fasting desire to eat (mm)	8	73.1	43.9	83.1	38.4	10	76.8	40.7	89.9	31.0	0.60	0.74	0.94
Fasting hunger (mm)	8	100.8	37.2	102.0	24.3	10	99.8	37.6	105.7	32.1	0.60	0.83	0.77
Fasting fullness (mm)	8	23.0	17.6	32.1	17.2	10	27.8	19.0	35.0	25.8	0.08	0.60	0.84
Fasting PFC (mm)	8	97.3	22.1	97.3	30.9	10	100.4	34.8	111.2	20.6	0.60	0.63	0.48
AUC desire to eat (mm × min)	8	1854	1571	1740	1074	10	1775	1554	1985	1333	0.94	0.88	0.73
AUC hunger (mm × min)	8	2001	1490	2139	1667	10	1891	1522	1983	1394	0.68	0.90	0.96
AUC fullness (mm × min)	8	4895	1790	5535	1726	10	5875	2171	5807	2161	0.82	0.45	0.44
AUF PFC (mm × min)	8	2505	1082	2226	857	10	3022	2518	2463	1916	0.36	0.71	0.81
<b>Women</b>													
Fasting desire to eat (mm)	11	71.6	43.7	92.1	48.5	11	116.8†	28.8	76.4*	39.4	0.13	0.39	0.001
Fasting hunger (mm)	11	81.3	45.1	86.2	45.6	11	96.7	43.8	90.0	44.5	0.69	0.60	0.74
Fasting fullness (mm)	11	35.6	30.4	21.8	26.1	11	19.9	19.3	36.4	37.6	0.54	0.90	0.06
Fasting PFC (mm)	11	95.5	45.5	92.1	34.9	11	110.1	30.7	88.9	38.4	0.73	0.11	0.31
AUC desire to eat (mm × min)	11	1184	1369	1616	1593	11	1548	1397	900*†	807	0.58	0.72	0.028
AUC hunger (mm × min)	11	1398	1584	1717	1974	11	1562	1509	1007*†	1081	0.33	0.62	0.048
AUC fullness (mm × min)	11	6308	1936	6390	2184	11	5584	2006	6905	2211	0.10	0.85	0.09
AUF PFC (mm × min)	11	2404	1925	2310	2059	11	1952	1490	1004*†	941	0.029	0.23	0.028

MMS, multivitamin and mineral supplementation; PFC, prospective food consumption; AUC, area under the curve.

\* Mean value was significantly different from that in week 0 ( $P < 0.05$ ).

† Mean value was significantly different from that in the placebo group ( $P < 0.05$ ).

‡ Adjusted for body-weight change.

**Table 5.** Three-Factor Eating Questionnaire mean scores before (week 0) and after (week 15) the weight-loss intervention in men and women in study 2 (Mean values and standard deviations)

	Placebo						MMS						Statistical significant effect* of		
	Week 0			Week 15			Week 0			Week 15					Treatment
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD			
<b>Women</b>															
Dietary restraint	8	8.5	4.2	13.8	4.6	4.6	9	7.8	4.8	5.5	11.9	5.5	0.0004	0.51	0.60
Disinhibition	8	10.1	3.3	8.2	3.4	3.4	9	10.0	3.2	3.8	7.9	3.8	0.003	0.88	0.67
Susceptibility to hunger	8	4.8	3.7	2.6	2.5	2.5	9	5.7	3.6	2.1	3.8	2.1	0.008	0.35	0.96
<b>Men</b>															
Dietary restraint	6	3.2	2.9	7.7	5.4	5.4	7	5.5	2.5	4.1	10.8	4.1	0.0009	0.16	0.74
Disinhibition	6	7.7	1.9	5.3	0.87	0.87	7	8.6	4.2	3.6	7.0	3.6	0.0003	0.28	0.36
Susceptibility to hunger	6	6.1	4.0	2.0	0.9	0.9	7	4.6	4.6	3.3	3.3	3.3	0.005	0.98	0.09

MMS, multivitamin and mineral supplementation.  
\* Adjusted for body-weight change.

lipid oxidation was observed between obese individuals supplemented with a MMS or with a placebo in the context of a weight-reducing programme. However, the supplementation in micronutrients had a beneficial effect on appetite-rating variables in women as shown by the significantly lower AUC for desire to eat, hunger and prospective food consumption in MMS-supplemented women compared with baseline and compared with the placebo group. A significant decrease in fasting desire to eat was also observed in MMS-supplemented women, although this result could be considered less powerful since the baseline value for this variable was significantly higher in this group compared with placebo. These differences remained significant when change in body weight was taken into account, suggesting that an adequate intake in vitamins and minerals might influence satiety.

Appetite is increased in response to body-weight loss<sup>(36,40)</sup> due to variations in hormone levels implicated in the regulation of energy balance such as insulin, leptin and cortisol<sup>(36,41,42)</sup>. Since some vitamins and minerals are involved in the synthesis of these and other peptides and neurotransmitters that control food intake, a decreased micronutrient availability could affect peptide hormone levels and thus interfere with the signalling pathways that control food intake, as was observed in Zn-deprived rats<sup>(43)</sup>. From a more peripheral perspective, it is well known that variations in energy substrate availability can also impact on hunger and energy intake. Studies in animals<sup>(44,45)</sup> and in human subjects<sup>(46,47)</sup> have shown that inhibition of glucose utilisation and fatty acid oxidation resulted in an increased appetite and energy intake, as does a decrease in blood glucose concentrations<sup>(48,49)</sup>. Since micronutrients are essential to energy substrate oxidation and must be supplied by the diet<sup>(5)</sup>, one can speculate that their intake is also regulated. As such, a lower consumption could result in signalling to feeding centres to increase energy intake in order to satisfy the body's micronutrient needs<sup>(50)</sup>. This hypothesis is supported by the recently described evidence for the existence of an appetite for Ca, Na, Mg and Se<sup>(51–54)</sup>, and is concordant with the lower susceptibility to hunger and disinhibition observed in women CS compared with NCS in study 1. This could also explain the significant decrease in appetite ratings at the end of the programme in MMS women but not in the placebo group in study 2. Interestingly, some studies have shown that postprandial prospective food consumption, which was significantly reduced in MMS women, is the most consistent predictor of energy intake<sup>(36,55,56)</sup>. Thus, these results strengthen the plausible role for vitamins and minerals in the control of appetite and ultimately energy intake.

In this regard, the absence of any significant effect of the MMS supplement on body weight, energy expenditure and lipid oxidation in study 2 cannot be ignored. It could perhaps be explained by the fact that participants were not selected on the basis of a low micronutrient intake status. Indeed, vitamin and mineral consumption by the participants was in a normal range before intervention, and the appetite for minerals as described above has been reported mainly in circumstances of deprivation in these minerals<sup>(50–54)</sup>. Moreover, several cross-sectional studies have reported a link between a high body weight and intake of a micronutrient when the latter is inadequate or a deficiency is evident<sup>(1–3,8,9,11,12,57)</sup>. In accordance with this, Volpe *et al.* found no effect from supplementation



of Cr, an essential trace element involved in energy substrate metabolism<sup>(5)</sup>, on body composition or REE in obese women whose vitamin and mineral consumption was in a normal range before intervention<sup>(58)</sup>. Overall, this suggests that an appetite-modulating effect of vitamin and mineral supplements could be more significant in individuals characterised by inadequate intake in micronutrients.

It is also possible that the energy restriction in study 2 masked the effect that the vitamin and mineral supplementation could have had on body weight. Indeed, all participants were instructed to reduce their energy intake in proportion to their baseline consumption. This could explain, at least partly, why a decrease in body weight above that attributed to the weight-reducing programme was not seen in supplemented individuals, but that a lower body weight was observed in free-living long-term vitamin and/or dietary supplement CS (study 1 and Nachtigal *et al.*<sup>(4)</sup>) in whom no *a priori* dietary restriction interfered with the proposed micronutrient-induced appetite-reduction effect. Further research in this issue should focus on large groups of individuals characterised by inadequate vitamin and mineral intake.

It is intriguing that in study 1, the possible influence of vitamin and dietary supplements on body weight was observed only in men (and in women to a lesser extent) while in study 2, significant appetite effects were observed only in women, as for the suggested behavioural effect in study 1. In this last study, this could be due to the fact that other factors affecting energy balance and body weight (see Table 1) were not as closely matched in women as they were in men. Moreover, CS women were older and had a significant lower dietary fat intake than NCS women. With respect to study 2 findings, because appetite control is under the influence of central and peripheral as well as behavioural signals and social factors<sup>(36,41,42)</sup>, dietary restraint typically more present in women than in men<sup>(57,59)</sup> could have influenced appetite ratings. However, in both sexes, changes that occurred during the programme followed the same trend upward for restraint and downward for disinhibition and susceptibility to hunger. Moreover, these changes as well as these variables' scores before and after the programme were similar between treatment groups, suggesting that they probably do not account for the differences in appetite ratings in women and in men. However, it has to be recognised that although we took into consideration the most obvious confounding variables (physical activity, macronutrient composition of the diet), and verified that the education level and total annual familial income was not affecting the results (results not shown), other lifestyle factors we did not measure might have exerted an influence and have partly accounted for the differences between CS and NCS in study 1. This is especially true for the type and composition of the vitamin and/or dietary supplement in study 1 for which we had no detailed information. Although study 2 was based on a much stronger experimental design to control for potential confounders, the number of participants was low. On one hand this indicates that effects were substantial since statistical significance was achieved despite small group sizes but on the other hand, the present results and conclusions need to be treated with caution unless replicated in larger groups of participants.

### Conclusion

In conclusion, cross-sectional observations have shown that men regularly consuming vitamin and dietary supplements had a lower body weight and FM and tended to have a higher relative RMR compared with men who did not report consuming such supplements, independently from physical activity level and dietary factors. This trend was also seen in women together with a reduced hunger level. A double-blind randomised controlled study showed no direct evidence that multivitamin and mineral supplementation during a weight-reducing programme in a relatively small number of obese individuals could enhance body-weight and FM loss. However, the multivitamin and mineral supplement was found to significantly decrease appetite ratings in women after weight loss, compared with a placebo group which also lost weight. This therefore suggests that vitamin and mineral supplements could attenuate, in women, the increase in appetite that often accompanies body-weight loss. This issue should be further investigated as should the underlying mechanisms of vitamins and minerals in appetite control.

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