

# Prospective Study of Body Mass Index, Weight Change, and Fatigue in Acute Infectious Mononucleosis

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**ABSTRACT. Objective:** To examine the influence of body mass index (BMI) and weight change on fatigue severity and failure to recover in individuals with acute infectious mononucleosis.

**Methods:** We prospectively studied 148 individuals presenting with a positive monospot test. We obtained measured weights and vitality subscale scores from the Short Form-36 Health Survey (SF-36) at the index visit and at 6 months.

**Results:** The mean age of the participants was 21 years and 24% were overweight or obese. During acute illness, overweight and obese participants had an adjusted odds ratio for low vitality scores of 2.9 (confidence interval 1.2-7.1) compared to normal weight subjects. Neither index BMI nor 6-month weight gain was significantly associated with prolonged fatigue or failure to recover.

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**Conclusion:** Overweight and obese patients with acute infectious mononucleosis are more likely to experience severe fatigue. In contrast, neither baseline weight nor weight gain appear to impede recovery. doi:10.1300/J092v14n03\_03 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <<http://www.HaworthPress.com>> © 2007 by The Haworth Press. All rights reserved.]

**KEYWORDS.** Infectious mononucleosis, chronic fatigue, fatigue, obesity, weight gain

### INTRODUCTION

Acute infectious mononucleosis (AIM) due to Epstein-Barr viral infection is characterized by excessive fatigue, somnolence, other physical symptoms, and limitations in functioning. For most patients with AIM, these symptoms are transient (1, 2). In a minority of patients, however, the fatigue and increased need for sleep linger (1, 3, 4), and in about 10% of cases symptoms persist at 6 months (5, 6). Persistent fatigue syndromes have been shown to be independent of mood disorders (4, 7). They are differentiated from mood disorders by the lack of associated premorbid psychiatric disease (8). Instead, markers of disease, such as a positive monospot (8), and premorbid health status, such as poor physical fitness (8) and physical functioning limitations (6), have been shown to predispose individuals to long-term symptoms. In this study we examine the influence of weight gain and/or obesity on fatigue severity and failure to recover in individuals with AIM, a topic that has received virtually no previous attention.

Fatigue is one of several components of health care-related quality of life that are affected by obesity (9-13). The lower energy levels and increased fatigue reported by obese persons are especially prominent among women (14-16). Furthermore, energy is reduced and fatigue increased in chronically ill obese patients compared to their non-obese counterparts (15). The questions we ask in this prospective, observational study are: (1) Does a high BMI or weight gain increase the risk for severe fatigue from AIM? and (2) Does a high BMI or weight gain increase the risk for prolonged fatigue or failure to recover?

## METHODS

*Setting, Participant Enrollment and Follow-Up.* The setting for this study was a large health maintenance organization in the Puget Sound area. This plan serves a heterogeneous socioeconomic population whose age and gender composition are similar to the region as a whole. Enrollees who met the following criteria were considered eligible: (1) were  $\geq 16$  years of age; (2) had a positive monospot; (3) had no record of a previous monospot; (4) reported the onset of symptoms within 14 days of having the monospot; (5) were not suffering from a chronic medical condition; (6) were not being treated with steroids for AIM; and (7), had serological evidence of acute, primary infection with EBV. Using tri-weekly review of laboratory records, we prospectively identified all outpatients who had a monospot performed. Next, enrollees were screened for eligibility criteria using a computerized record system and telephone interview; if eligible, they were asked to participate. Final determination of each person's eligibility occurred after enrollment based on their interview, chart review, and evidence of acute infection (e.g., IgM), as previously described (2). Overall, 150 patients were examined during the acute illness and 6 months later. At each visit, we assessed fatigue and energy and performed a physical examination. All participants, or the parents of those  $< 18$  years of age, provided written informed consent. The appropriate institutional review boards approved recruitment procedures and study protocols.

*Measures of Height and Weight.* The research nurse or a research assistant measured weight during the physical examination performed at the index visit. The same digital scale was used at all visits. Height was self-reported at each visit. Body mass index ( $\text{kg}/\text{m}^2$ ) was calculated and participants classified according to guidelines published by the National Institutes of Health as follows: underweight ( $\text{BMI} < 18.5 \text{ kg}/\text{m}^2$ ), normal weight ( $\text{BMI} 18.5\text{-}24.9 \text{ kg}/\text{m}^2$ ), overweight ( $\text{BMI} 25.0\text{-}29.9 \text{ kg}/\text{m}^2$ ), and obese ( $\text{BMI} > 30 \text{ kg}/\text{m}^2$ ) (17). Weight and BMI change were calculated by subtracting the value at the index visit from that obtained at the 6-month visit. Weight change was categorized as  $\geq 5$  pound loss, no appreciable weight change (4.9 pound loss to 4.9 pound gain), 5 to 9.9 pound gain, and  $\geq 10$  pound gain.

*Measures of Fatigue, Recovery, and Psychiatric Diagnoses.* The 4-item vitality subscale of the Medical Outcomes Study SF-36 health survey was used to measure fatigue (18). Scores range from 0 to 100 with higher scores indicating less fatigue. The SF-36 and its subscales are well characterized with high reliability and validity in a wide variety

of patient populations (18). The SF-36 and its vitality subscale also have been used to assess fatigue in studies of patients with chronic fatigue, AIM (19, 20), and obese patients (10, 11, 15).

As in previous publications (5, 6), recovery status was assessed by self-report as no well-accepted objective measures of outcome exist for AIM. At the 6-month visit, participants were asked to compare their current health with their condition at the time the AIM was diagnosed. Responses included “worse,” “the same,” “better but not recovered,” or “completely recovered.” The recovered group consisted only of participants reporting complete recovery; all others were classified as not recovered.

The National Institute of Mental Health Diagnostic Interview Schedule (21) was administered to all participants at the index visit by a research assistant trained in its use. This reliable and valid structured psychiatric interview was used to identify the following current and lifetime DSM-III-R psychiatric diagnoses: somatization disorder, panic and generalized anxiety disorder, depression, and alcoholism (22).

*Statistical Analysis.* Descriptive statistics for continuous variables were calculated as mean values ( $\pm$  standard deviation); percents were computed for categorical variables. Logistic regression analysis was used to examine associations between outcomes and predictors of interest. Tests for trend were performed by including continuous predictor variables in the regression model. Outcome measures included fatigue during the acute illness and recovery, as measured by SF-36 vitality subscale, and self-reported 6-month recovery status. The vitality subscale scores at both the index and 6-month visits were dichotomized, with patients in the lowest quartile being classified as “low vitality.” Predictors of interest were BMI at the index visit and subsequent 6-month weight change. Covariates in the regression models included gender, age, race/ethnicity, and the presence of  $\geq 1$  psychiatric condition. All analyses were conducted using Stata 7.0 (Stata Corporation, College Station, TX).

## RESULTS

Of the 333 eligible enrollees, 33% ( $n = 111$ ) refused to participate, 22% ( $n = 72$ ) could not be contacted, and 150 (45%) were enrolled in the study; of the latter, 142 (95%) completed the 6-month follow-up visit.

Two participants (1%) were missing weight measurements and were excluded from analyses.

Age and gender were similar among participants and non-participants. Study participants were young, predominantly Caucasian, with approximately equal representation of women and men (Table 1). The initial mean BMI was in the normal range (23.2 kg/m<sup>2</sup>). At the 6-month visit, the mean BMI increased to 23.8 kg/m<sup>2</sup>. Neither weight gain nor increase in BMI was associated with initial BMI. The SF-36 physical role functioning scores at baseline did not differ between the normal (mean 21.8 ± 29.2) and overweight/obese group (mean 22.9 ± 34.0).

Mean vitality scores at index visit indicated marked fatigue with significant improvement over the 6-month course of the illness, and this was true across weight categories (Table 2). At the index visit, the odds of having low vitality scores were significantly higher in obese patients compared to normal weight patients (Table 3). In contrast, at the 6-month visit the odds of noteworthy, persistent fatigue were not in-

TABLE 1. Characteristics of patients with acute infectious mononucleosis

Characteristics at Index Visit	Total (n = 148)
<b>Demographic</b>	
Age, mean years (± SD)	21.3 (6.7)
Women, %	53
Caucasian, %	90
Education, mean years (± SD)	12.6 (2.6)
<b>Weight</b>	
BMI, mean kg/m <sup>2</sup> (± SD)	23.2 (4.1)
Underweight,* %	6
Normal weight, %	70
Overweight, %	20
Obese, %	4
<b>Clinical</b>	
≥ 1 current psychiatric condition, %	7
<b>Characteristics at 6 Month Follow-up Visit</b>	
<b>Weight</b>	
BMI, mean kg/m <sup>2</sup> (± SD)	23.8 (4.3)
Underweight,* %	4
Normal weight, %	69
Overweight, %	21
Obese, %	6
<b>Weight Change Since Index Visit</b>	
BMI, mean kg/m <sup>2</sup> (± SD)	0.6 (1.3)
Weight, mean pounds (± SD)	4.5 (8.6)
≥ 5.0 pound loss, %	9
No weight change,† %	52
5.0 – 9.9 pound gain, %	21
≥ 10.0 pound gain, %	19
<b>Clinical</b>	
Recovery, %	88

\* Underweight (BMI < 18.5 kg/m<sup>2</sup>), normal weight (BMI 18.5 – 24.9 kg/m<sup>2</sup>), overweight (BMI 25.0 – 29.9 kg/m<sup>2</sup>), obese (BMI ≥ 30.0 kg/m<sup>2</sup>); † no weight change = 4.9 pound loss to 4.9 pound gain; SD = standard deviation

TABLE 2. Mean vitality scores for young adults, obese adults and during acute infectious mononucleosis according to BMI group

Mean vitality scores							
Population norms		Acute infectious mononucleosis	Index visit		6-month follow-up visit		
N	Mean ( $\pm$ SD)		N	Mean ( $\pm$ SD)	N	Mean ( $\pm$ SD)	
Adults 18-34 years*	366	49.14 (9.75)	All subjects	148	32.8 (18.0)	140	66.2 (18.7)
			Underweight	9	32.8 (17.0)	8	73.1 (18.1)
			Normal weight	103	34.0 (18.7)	100	66.6 (18.9)
Obese†	312	47.4 (20.9)	Overweight/obese	36	29.6 (20.1)	32	63.4 (22.5)

\* From Ware Medical Outcomes Study 1996 population [25]. † From Fontaine, obese persons seeking treatment for weight [24]; SD = standard deviation.

creased as a function of higher initial BMI. Patients who gained either 5-9.9 pounds or  $\geq 10$  pounds during the 6-month interval more often reported low vitality at the 6-month visit than patients without an appreciable weight change, but these results were not significant.

At 6 months, 88% of the participants self-reported recovery. The mean initial BMI of non-recovered patients was somewhat higher than that of their recovered counterparts (24.9 versus 22.9 kg/m<sup>2</sup>,  $P = 0.07$ ). However, adjusted logistic regression analysis showed no difference in the odds of recovery according to increasing BMI ( $P_{\text{trend}} = 0.36$ ). We found no difference in the odds of recovery among participants who gained weight in the 6 months after the index visit compared to those with no weight change (Table 3).

## DISCUSSION

Prior research has shown that obesity exacerbates fatigue in patients with chronic illnesses (15). Our findings suggest that overweight and obesity can also impact reported symptoms during an acute illness. Specifically, overweight and obese individuals had higher odds of reporting severe fatigue early in the course of AIM. It is possible that differences in physical fitness might explain the association. Physical conditioning is related to long-term fatigue in AIM (23), but we did not have data to assess the role of fitness during acute fatigue. However, baseline physical role functioning did not differ between the normal weight and the overweight or obese subjects.

TABLE 3. The association of BMI and change in weight with fatigue severity and recovery status in patients with acute infectious mononucleosis

	Unadjusted		Adjusted <sup>*</sup>	
	Odds Ratio	95% CI	Odds Ratio	95% CI
<b>Low Vitality, Obesity, and Weight Change</b>				
<b>Low Vitality Score at Index Visit<sup>†</sup></b>				
Underweight <sup>‡</sup>	1.3	0.3–7.0	1.5	0.3–8.2
Normal weight	1.0	–	1.0	–
Overweight / Obese	2.7	1.1–6.2	2.9	1.2–7.1
<b>Low Vitality Score at 6 Month Follow-up Visit</b>				
Underweight	1.0	0.2–5.6	1.4	0.2–8.5
Normal weight	1.0	–	1.0	–
Overweight / Obese	1.4	0.6–3.5	1.0	0.4–2.6
<b>Low Vitality Score at 6 Month Follow-up Visit</b>				
≥ 5.0 pound loss	0.6	0.1–3.1	0.7	0.1–4.2
No weight change <sup>§</sup>	1.0	–	1.0	–
5.0–9.9 pound gain	1.4	0.5–3.6	1.7	0.6–4.7
≥ 10.0 pound gain	1.1	0.4–3.1	1.5	0.5–4.6
<b>Recovery and Weight Change</b>				
<b>Recovered at 6 Month Follow-up Visit<sup>¶</sup></b>				
≥ 5.0 pound loss	1.5	0.2–13.5	1.8	0.2–19.4
No weight change	1.0	–	1.0	–
5.0–9.9 pound gain	0.9	0.2–3.1	0.8	0.2–3.2
≥ 10.0 pound gain	1.1	0.3–4.3	0.9	0.2–3.9

\* Adjusted for age, gender, race/ethnicity, and presence of psychiatric conditions at illness onset. † Low vitality is the lowest quartile of vitality scores. ‡ Underweight (BMI < 18.5 kg/m<sup>2</sup>), normal weight (BMI 18.5–24.9 kg/m<sup>2</sup>), overweight (BMI 25.0–29.9 kg/m<sup>2</sup>), obese (BMI ≥ 30.0 kg/m<sup>2</sup>). § No weight change = 4.9 pound loss to 4.9 pound gain. ¶ All 10 participants with psychiatric conditions at illness onset recovered from mononucleosis, therefore the model did not adjust for this covariate. CI = confidence interval.

Our findings did not appear to be due to chronic low vitality scores in overweight and obese subjects for several reasons. First, items on the SF-36 refer to the preceding month and participants entered the study while symptomatic. Second, published average vitality scores in obese individuals (11, 24), although below U.S. population norms (25), are still considerably higher than those obtained at the index visit in our obese participants (see Table 2). Third, vitality scores rebounded similarly during recovery in all weight categories. These factors support the interpretation that fatigue was exacerbated by obesity and was not a pre-existing condition.

Neither overweight and obese subjects nor subjects with weight gain over the 6 months of the study had increased odds of prolonged fatigue or failure to recover. Previous research that did not assess weight has found failure to recover from AIM to be associated with female sex, a greater number of life events in the 6 months preceding infection, and more baseline family social support (6). Others have proposed that the response to illness, both in illness attributions and physical activity

level, is the primary mediator of sustained fatigue symptomatology (26). In this regard, a brief psycho-educational intervention focused on resuming activity showed promise in reducing prolonged symptoms in one small randomized-controlled trial (27). This research supports the conclusion that acute fatigue severity is more closely related to disease markers and health status, whereas other factors such as response to illness may be more important in sustained symptoms.

This study has several limitations. We did not measure height, and adolescents have been shown to overestimate their heights (28), leading to potential misclassification of overweight or obese individuals. Yet, prior studies have not assessed BMI (6) or used self-reported weight gain (4). Similarly, due to the age and good health of our AIM participants, relatively few were overweight or obese, especially in the non-recovered group. This may have reduced our ability to detect small differences in the rates of recovery among overweight and obese groups. The assessment of recovery status was also of concern, but standardized measures do not exist for recovery in AIM or other viral infections. We also note that many of the young adults in our study may still have been physically maturing. Therefore, the lack of an age-matched comparison group makes the interpretation of weight gain during AIM more difficult. Finally, participants had sought medical care, thus our results may not be applicable to those experiencing less severe or fewer symptoms. Despite these caveats, strengths of this study include its prospective approach and the direct examination of the influence of overweight and obesity, an increasingly common health issue among adolescents and young adults (29), on the acute and convalescent stage of AIM.

In sum, this is the first study to directly assess the relation of BMI and weight changes to acute and persistent fatigue following AIM. It provides useful information for clinicians assessing patients with AIM. Compared to their normal weight counterparts, overweight and obese patients with AIM may experience more severe fatigue, but high BMI does not appear to impede full recovery. Clinicians may also reassure individuals that weight gain is not inevitable during AIM (60% of subjects maintained or lost weight), and that when weight gain occurs it does not preclude a full recovery. Interesting topics for future research include the relation of obesity to symptom severity in other acute illnesses, the mechanisms by which obesity affects perceived energy levels in acute and chronic disease states and, specifically, whether factors such as physical activity or diet during episodes of AIM mediate the association of fatigue severity and BMI.

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