

1 Social Jetlag, Obesity and Metabolic Disorder: Investigation in a Cohort Study

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24 **Running title:** Social Jetlag, Obesity and Metabolic Disorder

25 **Abstract:**

26 **Background:** Obesity is one of the leading causes of preventable death worldwide. Circadian  
27 rhythms are known to control both sleep timing and energy homeostasis, and disruptions in  
28 circadian rhythms have been linked with metabolic dysfunction and obesity-associated disease. In  
29 previous research, social jetlag, a measure of chronic circadian disruption caused by the discrepancy  
30 between our internal versus social clocks, was associated with elevated self-reported Body Mass  
31 Index (BMI), possibly indicative of a more generalized association with obesity and metabolic  
32 dysfunction.

33 **Methods:** We studied participants from the population-representative Dunedin Longitudinal Study  
34 (N = 1037) to determine if social jetlag was associated with clinically assessed measurements of  
35 metabolic phenotypes and disease indicators for obesity-related disease; specifically, indicators of  
36 inflammation and diabetes.

37 **Results:** Our analysis was restricted to N = 815 non-shift workers in our cohort. Among these  
38 participants, we found that social jetlag was associated with numerous clinically assessed measures  
39 of metabolic dysfunction and obesity. We distinguished between obese individuals who were  
40 metabolically healthy versus unhealthy, and found higher social jetlag levels in metabolically  
41 unhealthy obese individuals. Among metabolically unhealthy obese individuals, social jetlag was  
42 additionally associated with elevated glycated hemoglobin and an indicator of inflammation.

43 **Conclusions:** The findings are consistent with the possibility that “living against our internal clock”  
44 may contribute to metabolic dysfunction and its consequences. These findings suggest the  
45 hypothesis that reducing social jetlag might help prevent obesity. Further research aimed at  
46 understanding the physiology and social features of social jetlag may inform obesity prevention and  
47 have ramifications for policies and practices that contribute to increased social jetlag, such as work  
48 schedules and daylight savings time.

49 **Keywords:** Social jetlag, obesity, metabolism, inflammation, diabetes, population cohort

50 **INTRODUCTION**

51 Obesity is one of the biggest public health concerns facing industrialized societies (ref. 1-3).  
52 Many factors affect the risk for obesity, including sleep duration (ref. 4-8). Circadian output  
53 rhythms, including sleep-wake timing, are modified through signals from the internal circadian clock  
54 which is in turn synchronized to external environmental cues (ref. 9). The circadian clock is also  
55 known to regulate energy metabolism (ref. 10), and disruption of circadian rhythms has been shown  
56 to alter obesity and metabolic-associated phenotypes in mice and humans (ref. 11-15).

57 Social jetlag is a measure of the discrepancy in sleep timing between our work days and free  
58 days (ref. 16-17). Social jetlag was so named due to the similarity in the time discrepancy for many  
59 individuals between work and free days to that of travel-induced jetlag caused by taking a flight to  
60 the west on Friday evening and a return flight on Monday morning. Unlike travel-induced jetlag,  
61 social jetlag occurs chronically throughout an individual's working life. As travel-induced jetlag  
62 results in a misaligned circadian system that in turn causes temporary problems with metabolism, it  
63 is likely for social jetlag to have chronic consequences for metabolism, due to the manifestations of a  
64 misaligned circadian system. Recently, individuals who have more social jetlag, and thus a greater  
65 discrepancy between their internal and social clocks, were found to also have higher self-reported  
66 Body Mass Index scores (BMI) in a large European sample (N>65,000) (ref. 14). This association  
67 persisted after controlling for sleep duration and sleep timing (chronotype).

68 If social jetlag is not only associated with BMI, but more generally with other measures of  
69 obesity and metabolic dysfunction as well as with the health consequences of obesity, then this  
70 would be consistent with the hypothesis that our internal clocks being at odds with our external  
71 schedules may partially underlie the increased obesity seen in recent decades. This would be in line  
72 with a number of studies suggesting that sleep disruptions, including short sleep duration and sleep  
73 debt, may be a contributing factor to obesity (ref. 18-19).

74 We studied participants in the population-representative Dunedin Longitudinal Study in  
75 order to further explore the link between social jetlag and metabolic dysfunction in three ways. First,

76 although our sample is smaller than the original discovery sample, it has the advantage of containing  
77 a number of clinically assessed measurements of metabolic phenotypes: BMI, fat mass, waist  
78 circumference, obesity and the metabolic syndrome. We were additionally able to control not only  
79 for additional sleep measures, but also for lifestyle and demographic factors such as smoking and  
80 socioeconomic status. Second, obesity is typically associated with metabolic dysfunction and  
81 increased inflammation which have, in turn, been hypothesized to underlie an increased risk for  
82 cardiovascular disease and diabetes seen in obese individuals (ref. 20-23). In order to investigate  
83 whether social jetlag is also associated with these consequences of obesity, we investigated whether  
84 social jetlag was associated with disease indicators for obesity-related disease; specifically, indicators  
85 of inflammation and diabetes. Third, recent obesity research has shown that there is a subset of  
86 obese individuals who are metabolically healthy (ref. 24). There is controversy about whether or not  
87 these metabolically healthy obese individuals are at increased risk of developing cardiovascular  
88 disease and dying from related disorders (ref. 24-26). We thus tested whether social jetlag is  
89 specifically associated with unhealthy obesity, defined as obese individuals who exhibit at least three  
90 risk factors for metabolic syndrome.

91

## 92 **MATERIALS AND METHODS**

### 93 **Sample**

94 Participants are members of the Dunedin Multidisciplinary Health and Development Study, a  
95 longitudinal investigation of health and behaviour in a complete birth cohort. Study members  
96 (N=1,037; 91% of eligible births; 52% male) were all individuals born between April 1972 and March  
97 1973 in Dunedin, New Zealand, who were eligible for the longitudinal study based on residence in  
98 the province at age 3 and who participated in the first follow-up assessment at age 3. The cohort  
99 represents the full range of socioeconomic status in the general population of New Zealand's South  
100 Island and is primarily white (ref. 27). Assessments were carried out at birth and at ages 3, 5, 7, 9, 11,

101 13, 15, 18, 21, 26, 32, and, most recently, 38 years, when 95% of the 1,007 study members still alive  
102 took part. At each assessment wave, study members are brought to the Dunedin research unit for a  
103 full day of interviews and examinations. The Otago Ethics Committee approved each phase of the  
104 study and informed consent was obtained from all study members. We excluded all shift workers  
105 (n=131) as the standard Munich Chronotype Questionnaire (MCTQ) would only provide an estimate  
106 of their social jetlag for a single shift and thus may not give an accurate measurement of social jetlag  
107 for shift-workers on variable shift schedules. Exclusion of shift workers is standard practice when  
108 using the MCTQ (ref. 14,28).

109

#### 110 **Sleep duration, chronotype and social jetlag measures**

111 At age 38, the Munich Chronotype Questionnaire was used to assess social jetlag as well as  
112 sleep duration and chronotype (ref. 29). Social jetlag, the discrepancy between our internal timing  
113 and external timing, was measured by subtracting each participant's midpoint of sleep on work days  
114 (MSW) from their midpoint of sleep on free days (MSF). Sleep duration was calculated by averaging  
115 the sleep duration on work days and free days, assuming 5 work days and 2 free days a week as  
116 standard. Chronotype, the preference in sleep timing, was assessed using sleep-debt-corrected MSF  
117 (MSF<sub>sc</sub>) (see (ref. 17)). A detailed protocol for calculating the complete set of MCTQ variables can be  
118 found elsewhere (ref. 14). Social jetlag was significantly correlated with chronotype ( $r = 0.40, p <$   
119  $0.01$ ), but not with sleep duration ( $r = -0.04, p = 0.28$ ). The mean social jetlag among participants in  
120 our cohort was 0.88 hours with a standard deviation of 0.96 (n=815) (see Supplemental Figure 1). All  
121 analyses were conducted using the absolute value of social jetlag.

122

#### 123 **Obesity Phenotypes at age 38**

124           **Measures of being overweight.** Height was measured to the nearest millimeter using a  
125 portable Harpenden Stadiometer (Holtain, Crymych, UK). Weight was recorded to the nearest 0.1kg  
126 using calibrated scales. Individuals were weighed in light clothing. BMI was computed as weight  
127 (kg)/height (m<sup>2</sup>). Obesity was defined as BMI≥30. Of the participants, 23.4% (n=192) were obese.  
128 Waist circumference (girth) was measured in centimeters. Fat mass was measured using a body  
129 composition analyser (Tanita BC 418, Tokyo, Japan) to assess bio-electrical impedance.

130           **Metabolic syndrome.** Metabolic syndrome was assessed from measurements of five  
131 biomarkers: (i) high waist circumference (≥88cm for women, ≥102cm for men), (ii) high blood  
132 pressure (≥130/85 mmHg), (iii) low high density lipoprotein (HDL) cholesterol (<50mg/dl for women,  
133 <40mg/dl for men), (iv) high glycated hemoglobin (≥5.7%), and (v) high triglycerides (≥200 mmol/l).  
134 Biomarker assessments have been described in detail previously (ref. 30). Cohort members with  
135 high-risk values on three or more biomarkers were defined as having the metabolic syndrome (ref.  
136 31). Of the participants, 15.9% met criteria for the metabolic syndrome.

137           **Inflammation.** Elevated systemic inflammation was assessed using high sensitivity assays of  
138 C-reactive protein (hsCRP) in blood. HsCRP was measured on a Hitachi 917 analyzer (Roche  
139 Diagnostics, GmbH, D-68298, Mannheim, Germany) using a particle enhanced immunoturbidimetric  
140 assay. The CDC/AHA definition of high cardiovascular risk (hsCRP>3 mg/L) was adopted to identify  
141 the risk group (ref. 32).

142           **Glycated hemoglobin.** Glycated hemoglobin concentrations (expressed as a percentage of  
143 total hemoglobin) were measured by ion exchange high performance liquid chromatography  
144 (Variant II; Bio-Rad, Hercules, Calif) (coefficient of variation, 2.4%), a method certified by the US  
145 National Glycohemoglobin Standardization Program  
146 (<http://www.missouri.edu/~diabetes/ngsp.html>). The American Diabetes Association definition of  
147 "pre diabetes" high glycated hemoglobin (≥5.7) was adopted to identify the risk group (ref. 33).

148           **Unhealthy obesity.** We created a measure for obesity status with three levels: non-obese,  
149 BMI < 30, healthy obese individuals, BMI  $\geq$ 30 but no metabolic syndrome (see above), and  
150 unhealthy obese, BMI  $\geq$ 30 and metabolic syndrome. Of the 186 obese individuals, 101 were  
151 healthy obese and 85 were unhealthy obese.

152

### 153 **Potentially confounding variables**

154           **Current smoking** was defined as smoking at least 1 cigarette daily for at least 1 month in the  
155 previous year (0 = non-smoker, 1 = <10/day, 2 = 10-19/day, 3 = 20+/day). Of the participants, 77.3%  
156 were non-smokers. Current smoking was included as a potential confounder because it is positively  
157 associated with social jetlag (in the Dunedin study,  $r=0.24$ ,  $p < 0.0001$ ) and because smoking may  
158 keep weight low (ref. 34-35).

159           **Socioeconomic status.** At age 38, study members were asked about their current or most  
160 recent occupation. The SES of the study members was measured on a 6-point scale that assessed  
161 self-reported occupational status and allocates each occupation to 1 of 6 categories (1 = unskilled  
162 laborer, 6 = professional). Homemakers and those not working were pro-rated based on their  
163 educational status according to criteria included in the New Zealand Socioeconomic Index (ref. 36).  
164 SES was included as a covariate in the analyses because lower social status is linked to greater social  
165 jetlag (in the Dunedin Study,  $r = .17$ ,  $p < .001$ ) and because of the SES-health gradient (ref. 37).

### 166 **Analysis**

167           We conducted linear regressions for continuous outcomes (BMI, fat mass and waist  
168 circumference) and logistic regressions for dichotomous outcomes (obesity and metabolic  
169 syndrome). Social jet lag was treated as a continuous variable in all analyses. In model 1, we  
170 controlled for social jetlag, sex, chronotype ( $MSF_{sc}$ ), and sleep duration. In model 2, we controlled  
171 for the model 1 covariants and additionally added a covariant for smoking. In model 3, we  
172 controlled for the model 2 covariants and additionally added a covariant for SES. For linear  
173 regression models, we assessed violations of linearity, normality, and homoscedasticity using visual

174 inspection of histograms, residual-versus-fitted plots, and Q-Q plots, as well as skewness and  
175 kurtosis statistics ( $p < 0.05$ ). All assumptions were met. The variance inflation factor (VIF) score for  
176 the covariants used only differed slightly across models and ranged between 1.04 and 1.35. As an  
177 example the VIF scores for the covariants in model 3 with fat mass as the dependent variable are as  
178 follows: sex (1.06), social jetlag (1.34),  $MSF_{sc}$  (1.33), sleep duration (1.04), SES (1.18) and current  
179 smoking (1.20).

180 We used multinomial logistic regression to determine if social jetlag predicted metabolically  
181 unhealthy vs. healthy obesity status. For the biomarkers of inflammation (hsCRP) and diabetes  
182 (glycated hemoglobin), we first conducted the analyses as stated above and then repeated them  
183 after excluding the remaining healthy obese individuals ( $n=100$ ).

184 Six individuals had extreme values of social jetlag (values  $> 5$  hours). To address these  
185 individuals, we conducted the above analyses both with these individuals removed and with these  
186 individuals recoded to a social jetlag score of 5 hours. These two approaches yielded nearly identical  
187 results; we present the data with the recoded values.

188 Our study members are still relatively young (age 38) and only a few are taking diabetes  
189 medication ( $n = 4$ ) or statins ( $n = 18$ ). Study members were assessed for their use of medications  
190 with anti-inflammatory effect, including: systemic steroids, respiratory steroids, nonsteroidal anti-  
191 inflammatory drugs, prophylactic aspirin, anti-gout medications, anti-rheumatic medications, and  
192 estrogens. Use of anti-inflammatory drugs was not related to social jetlag ( $r = .01$ ,  $p = .68$ ). In  
193 sensitivity analyses (via statistical control and via exclusion), we verified that medication use did not  
194 influence the statistical or substantive findings reported in this article.

195 All analyses were conducted using SPSS (IBM SPSS Statistics for Windows, Version 22.0.  
196 Armonk, NY: IBM Corp).

197

## 198 **RESULTS**



199 Social jetlag was significantly associated with overweight phenotypes and phenotypes  
200 indexing metabolic dysfunction (**see Figure 1**), even after taking into account chronotype and sleep  
201 duration (**see Table 1**). Individuals with greater social jetlag scores had higher average BMIs ( $\beta = 0.10$   
202 hours/(kg/m<sup>2</sup>), s.e. = 0.2,  $p = .012$ ) and more fat mass ( $\beta = 0.08$  hours/kg, s.e. = 0.5,  $p = .031$ ), were  
203 more likely to be obese (odds ratio (OR) = 1.2 [95% confidence interval (95% CI): 1.0 to 1.5],  $p = .045$ )  
204 and to meet criteria for the metabolic syndrome (OR = 1.3 [95% CI: 1.0 to 1.6],  $p = .031$ ). There was  
205 also a trend for these individuals to have larger waist circumference ( $\beta = 0.07$  hours/cm, s.e. = 5.1,  $p$   
206 = .052). We thus found that greater social jetlag was generally associated with elevated measures of  
207 obesity and metabolic dysfunction.

208 As tobacco smoking has a suppression effect on weight, we added current smoking levels to  
209 our statistical models, anticipating that doing so would strengthen the associations between social  
210 jetlag and these measures. Consistent with this expectation, in smoking-adjusted models the  
211 associations between social jetlag and overweight phenotypes and phenotypes indexing metabolic  
212 dysfunction increased in strength by 15-30% (summarized in **Table 2**). We thus found that the  
213 suppression effect of smoking on weight was likely masking the association between social jetlag  
214 and obesity.

215 Socioeconomic status (SES) is known to predict health outcomes, with people of lower SES  
216 generally having worse scores on indicators of health, such as obesity (ref. 38). Additionally, as  
217 irregular working hours may be related to occupational status and can affect social jetlag, we added  
218 SES to the linear regression models. Overall, social class differences slightly attenuated the  
219 associations between social jetlag and both the overweight phenotypes and the phenotypes  
220 indexing metabolic dysfunction, although associations with BMI, fat mass, waist circumference and  
221 obesity remained significant (summarized in **Table 2**).

222 As social jetlag was a significant predictor of the metabolic measures, we investigated  
223 whether it was also associated with biomarkers of inflammation (hsCRP levels), and diabetes  
224 (glycated hemoglobin). Although both analyses suggested that individuals with higher social jet lag

225 scores had marginally elevated levels of hsCRP and glycated hemoglobin, the association did not  
226 reach significance for hsCRP (OR = 1.2 [95% CI: 1.0 to 1.4],  $p = .12$ ) and there was only a trend  
227 towards significance for glycated hemoglobin (OR = 1.1 [95% CI: 1.0 to 1.4],  $p = .073$ ).

228           Recent obesity research has suggested it is useful to distinguish between obese individuals  
229 who are metabolically healthy versus unhealthy (ref. 24,26). Using metabolic syndrome to  
230 differentiate between healthy and unhealthy obese individuals, we conducted a multinomial logistic  
231 regression to determine if social jetlag predicted obesity status. We found that social jetlag did  
232 predict obesity status such that higher social jetlag levels predicted increased risk for being in the  
233 metabolically unhealthy obese group (OR = 1.4 [95% CI: 1.1 to 1.8],  $p = .008$ , summarized in **figure 2**).  
234 High levels of social jetlag did not, however, predict increased risk for being in the metabolically  
235 healthy obese group (OR = 1.1 [95% CI: 0.8 to 1.4],  $p = .60$ ).

236           As the healthy obese individuals may not have an increased risk of developing and dying  
237 from obesity-related disorders, possibly because they do not have high levels of inflammation and  
238 diabetes-related pathophysiology (ref. 24-26), they might be masking associations of social jetlag  
239 with biomarkers of inflammation and diabetes in the metabolically unhealthy obese. We thus  
240 excluded the healthy obese individuals and re-estimated the associations between social jetlag,  
241 hsCRP levels and glycated hemoglobin. Upon removing these individuals we found that individuals  
242 with higher social jetlag scores were more likely to have clinically-elevated levels of hsCRP (OR = 1.3  
243 [95% CI: 1.0 to 1.6],  $p = .046$ ) and glycated hemoglobin (OR = 1.3 [95% CI: 1.0 to 1.6],  $p = .018$ ),  
244 though these associations became weaker once we controlled for smoking ((OR = 1.2 [95% CI: 1.0 to  
245 1.5],  $p = .102$ ) and (OR = 1.2 [95% CI: 1.0 to 1.6],  $p = .053$ ), respectively) and SES ((OR = 1.2 [95% CI:  
246 1.0 to 1.5],  $p = .092$ ) and (OR = 1.2 [95% CI: 1.0 to 1.5],  $p = .112$ ), respectively) (summarized in **Figure**  
247 **3 and Table 3**).

248

249 **DISCUSSION**

250 We successfully replicated the association of social jetlag with BMI in an independent cohort  
251 (ref. 14). We additionally found that social jetlag was associated with a number of clinically assessed  
252 metabolic measures, albeit modestly. Furthermore, we found that social jetlag was associated with  
253 disease indicators for obesity-related disorders, especially in “unhealthy obese” participants. Taken  
254 together these data show that social jetlag is likely a risk indicator for both obesity and the  
255 metabolic consequences frequently associated with obesity.

256 As social jetlag is a measure of the discrepancy between our internal clock and our external  
257 environment, it is possible that circadian disruption underlies these associations. A number of  
258 studies have shown that circadian disruption leads to similar metabolic consequences. Sleep  
259 restriction and circadian disruption caused decreases in resting metabolic rate, increased plasma  
260 glucose concentrations after eating and inadequate pancreatic insulin secretion (ref. 39). Chronic  
261 circadian disruption in mice led to metabolic disruption, weight gain, increased leptin and insulin  
262 levels (ref. 40-41). Furthermore, disruption of a circadian gene led to the disruption of hepatic lipid  
263 homeostasis in mice (ref. 42), while myeloid cell specific disruption of *Per1* and *Per2* expression in  
264 mice exacerbates both diet-induced inflammation and insulin resistance (ref. 43). A recent study  
265 found that mistimed sleep disrupts the daily regulation of global gene expression in humans (ref.  
266 44). As social jetlag disrupts sleep timing, it is thus possible that social jetlag has similar effects on  
267 gene expression. Taken together these studies suggest that our findings may be explained by the  
268 circadian disruption caused when our internal clocks are at odds with our external schedules,  
269 possibly by affecting the timing of gene expression. In addition, it is also likely that social jetlag  
270 disrupts healthy habits (e.g., diet) that may compromise health.

271 The nature of our observational design prevents us from making causal inferences.  
272 Additionally, reverse causation could in theory apply, if poor health associated with obesity dictates  
273 lifestyle choices, such as occupation type, that increase social jetlag. In order to control for potential  
274 confounding effects we added both smoking and SES to our statistical models, and found that  
275 afterwards social jetlag was still significantly associated with most of the metabolic measures.

276 Interestingly, controlling for smoking increased the strength of the association between social jetlag  
277 and the metabolic measures, which is in line with previous findings that nicotine acts as an appetite  
278 suppressant and smoking keeps weight low (ref. 34-35). As people with social jetlag have previously  
279 been shown to be more likely to smoke (ref. 16), it is important to consider this confound in any  
280 future replication studies, particularly as it may mask real associations of social jetlag and metabolic  
281 measures. Controlling for SES conversely decreased the strength of these associations, possibly  
282 because lower SES is associated with poor health, including obesity (ref. 38).

283           While the obesity epidemic has traditionally been thought to be caused primarily by changes  
284 in decreased levels of activity and food marketing, recent research has suggested that a number of  
285 alternative factors, including sleep debt and sleep duration, also play a role (ref. 18-19, 40-42). This  
286 multi-determinant hypothesis for obesity is compatible with our findings. Moreover, as obesity  
287 phenotypes likely have multiple determinants, large effect sizes would not be expected for any  
288 single risk factor; it is thus not surprising that the effect sizes associated with social jetlag are  
289 relatively modest in size.

290           This is the first study to find that social jetlag is associated with biomarkers for diabetes and  
291 inflammation. Given the association of social jetlag with obesity, it is not surprising to find a similar  
292 association with inflammation as inflammation has long been known to be associated with obesity  
293 (ref. 20). Although we cannot make causal inferences from our data, the fact that on average  
294 individuals with a social jetlag of 2 hours had similarly increased CRP levels as those with even higher  
295 levels of social jetlag suggests that there may be a threshold of social jetlag required for these  
296 associations. Interestingly, a similar threshold-like pattern was seen for both BMI and fat mass. It  
297 should be noted that the associations of social jetlag with these biomarkers became weaker or non-  
298 significant once we controlled for smoking and SES, suggesting that these factors may partially  
299 underlie these associations.

300           We additionally found that a higher social jetlag predicted an increased risk for being in the  
301 metabolically unhealthy obese group, but not in the metabolically healthy obese group. Regardless

302 of the causality underlying this association, this finding suggests that an individual's social jetlag may  
303 be a marker for whether individuals are at risk for obesity with adverse metabolic consequences.  
304 This points to the need, and potential benefit, of directing health campaigns at social jetlag.

305

## 306 **CONCLUSIONS**

307 In conclusion, we found that greater social jetlag was associated with unfavorable metabolic  
308 symptoms and disease indicators for obesity-related disorders. The findings are compatible with  
309 evidence that circadian disruption causes unfavorable metabolic symptoms in animals and humans.  
310 These novel findings are consistent with the hypothesis that the conflict between our internal clocks  
311 and our external schedules in modern life may be a contributory factor in the recent obesity  
312 epidemic. Further research aimed at determining the physiological mechanisms underlying these  
313 associations may give insight into the management of obesity, possibly by altering factors that  
314 promote social jetlag and by aligning our internal clocks with our social clocks.

315

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325

## 326 **CONFLICT OF INTEREST**

327 The authors have no conflicts of interest to report.

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477 **Figure 1.** Social jetlag associated with metabolic measures.

478 Social jetlag is significantly associated with: A) body mass Index ( $\text{kg}/\text{m}^2$ ); B) fat mass (kgs); D)

479 obesity and E) Metabolic Syndrome, but not with C) waist circumference (mm). The bars

480 represent the mean values or percent of specific measures organized into 1 hour bins, with the

481 number inside the bar representing N. The error bars represent standard errors. \* p-values <

482 0.05.

483 **Figure 2.** Social jetlag differs between metabolically healthy and unhealthy obese individuals.

484

485 Social jetlag predicted obesity status such that there were higher social jetlag levels in  
486 metabolically unhealthy obese individuals compared to non-obese individuals. There were no  
487 significant differences between healthy obese individuals and either non-obese or unhealthy  
488 obese individuals. The bars represent social jetlag scores of non-obese, healthy obese, and  
489 unhealthy obese individuals, with the number inside the bars representing N. The error bars  
490 represent standard errors. \* p-values < 0.05.

491 **Figure 3.** Social Jetlag associated with obesity-related biomarkers for inflammation and diabetes.  
492 Social jetlag was associated with the obesity-related disease indicators for A) inflammation, C-  
493 Reactive Protein levels (CRP) and B) diabetes, glycated hemoglobin (p-values < 0.05 see Table 3).  
494 The bars represent the mean values of specific measures organized into 1 hour bins, with the  
495 number inside the bar representing N. The error bars represent standard errors. \* p-values <  
496 0.05.

497 **Table 1. Social jetlag is associated with metabolic measures: BMI, Fat Mass, Waist Circumference,**  
498 **Obesity and Metabolic Syndrome.**

499

500 **Table is in landscape format, so is an additional document (called Table 1).**

501

502 We used linear regression models to test associations with continuous outcome measures of BMI  
503 ( $\text{kg/m}^2$ ), fat mass (kg), and waist circumference (cm). We used logistic regressions to test  
504 associations with binary outcome measures of obesity and the metabolic syndrome. Significant p-  
505 values ( $p < 0.05$ ) are shown in bold. The units for the covariants are: sex was coded as female =1,  
506 male =2; chronotype is unitless, sleep duration (hours) and social jetlag (hours).

507



508 **Table 2. Associations between social jetlag and weight and metabolic measures are increased by**  
 509 **controlling for smoking and decreased by controlling for socioeconomic status (SES).**

Weight and Metabolic measures	Controlling for Sex, Chronotype, and Sleep Duration		And controlling for smoking <sup>1</sup>		And controlling smoking and SES <sup>2</sup>	
	$\beta$ (s.e.)	p-value	$\beta$ (s.e.)	p-value	$\beta$ (s.e.)	p-value
BMI	0.10 (0.24)	<b>0.012</b>	0.13 (0.24)	<b>0.002</b>	0.12 (0.24)	<b>0.004</b>
Fat mass	0.084 (0.48)	<b>0.031</b>	0.11 (0.48)	<b>0.005</b>	0.10 (0.48)	<b>0.009</b>
Waist circumference	0.072 (5.2)	0.052	0.09 (5.2)	<b>0.017</b>	0.08 (5.2)	<b>0.034</b>
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Obesity	1.2 (1.0 to 1.5)	<b>0.045</b>	1.3 (1.0 to 1.5)	<b>0.019</b>	1.2 (1.0 to 1.5)	<b>0.035</b>
Metabolic Syndrome	1.3 (1.0 to 1.6)	<b>0.031</b>	1.3 (1.0 to 1.6)	<b>0.043</b>	1.2 (1.0 to 1.5)	0.063

510 We used linear regression models to test associations between social jetlag and continuous outcome  
 511 measures of BMI, fat mass, and waist circumference; the table shows the standardized coefficient  
 512 ( $\beta$ ), standard error (s.e.) and p-values for social jetlag as a predictor variable. The units for  $\beta$  for BMI,  
 513 fat mass and waist circumference are hours/(kg/m<sup>2</sup>), hours/kg and hours/cm, respectively. We used  
 514 logistic regressions to test associations between social jetlag and binary outcome measures of  
 515 obesity and the metabolic syndrome; the table shows the odds ratio (OR), 95% confidence interval  
 516 for the odds ratio (95% CI) and p-values for social jetlag as a predictor variable.

517 <sup>1</sup>Individuals who smoked had lower BMI ( $r = -.13, p < .001$ ), less fat mass ( $r = -0.14, p < .001$ ), smaller  
 518 waist circumference ( $r = -.09, p = .003$ ) and lower risk for obesity ( $r = -.08, p = .02$ ). Smoking was not  
 519 associated with risk for metabolic syndrome ( $r = .02, p = .51$ ).

520 <sup>2</sup>Lower SES status was significantly associated with higher BMI ( $r = -.09, p = .009$ ), greater waist  
 521 circumference ( $r = -.08, p = .02$ ), and higher risk for obesity ( $r = -.08, p = .03$ ). Lower SES status was  
 522 also marginally significantly associated with more fat mass ( $r = -.06, p = .09$ ) but not with risk for the  
 523 metabolic syndrome ( $r = -.05, p = .13$ ).

524 **Table 3. Social jetlag is associated with obesity-related disease indicators for inflammation and**  
 525 **diabetes.**

Obesity related disease indicators	Controlling for Sex, Chronotype, Sleep duration		And controlling for smoking <sup>1</sup>		And controlling for smoking and SES <sup>2</sup>	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>High sensitivity C-reactive protein levels (hsCRP)</b>	1.3 (1.0 to 1.6)	<b>.046</b>	1.2 (1.0 to 1.5)	.102	1.2 (1.0 to 1.5)	.092
<b>Glycated Hemoglobin</b>	1.3 (1.0 to 1.6)	<b>.018</b>	1.2 (1.0 to 1.6)	.053	1.2 (1.0 to 1.5)	.112

526 This table shows the odds ratio (OR), 95% confidence interval for the odds ratio (95% CI) and p-  
 527 values for social jetlag as a predictor in logistic regression models after excluding the healthy obese  
 528 individuals (n=100).

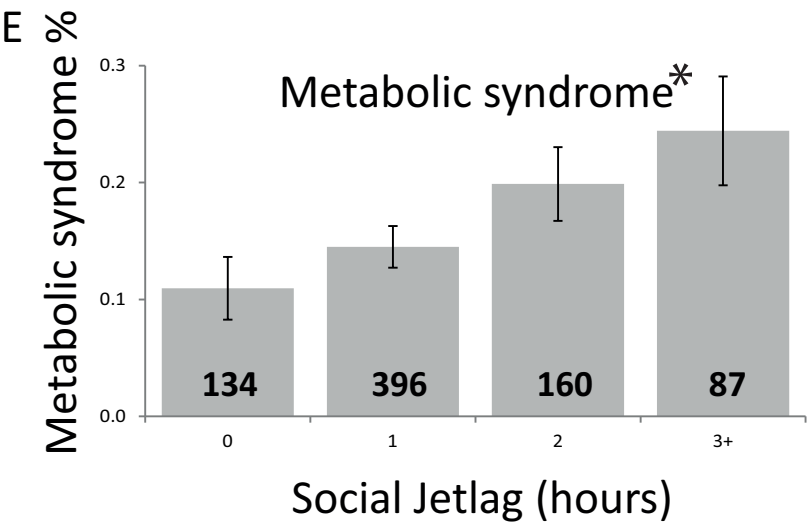
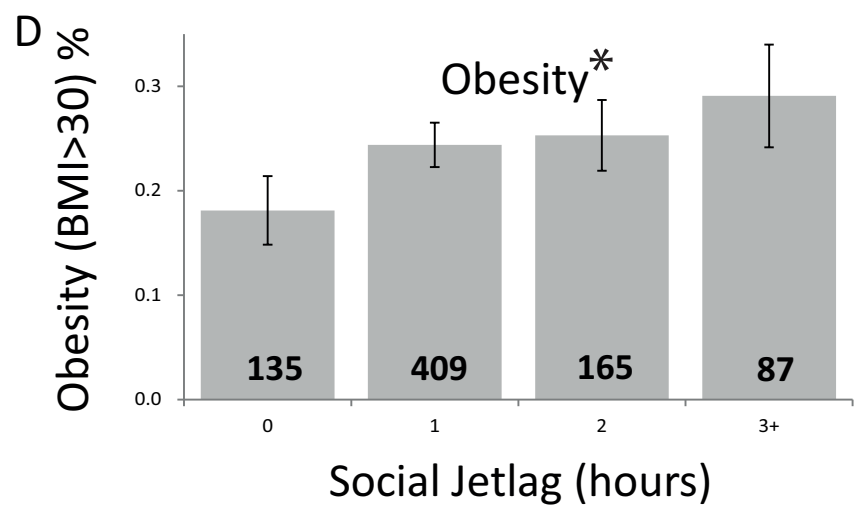
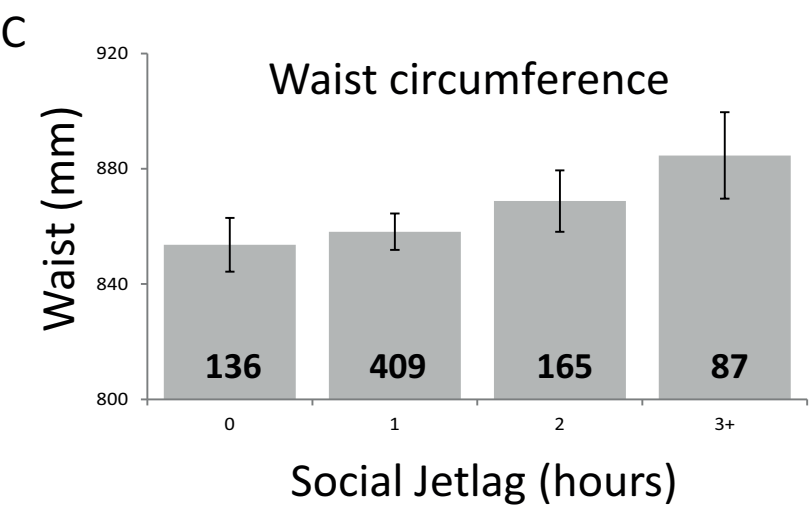
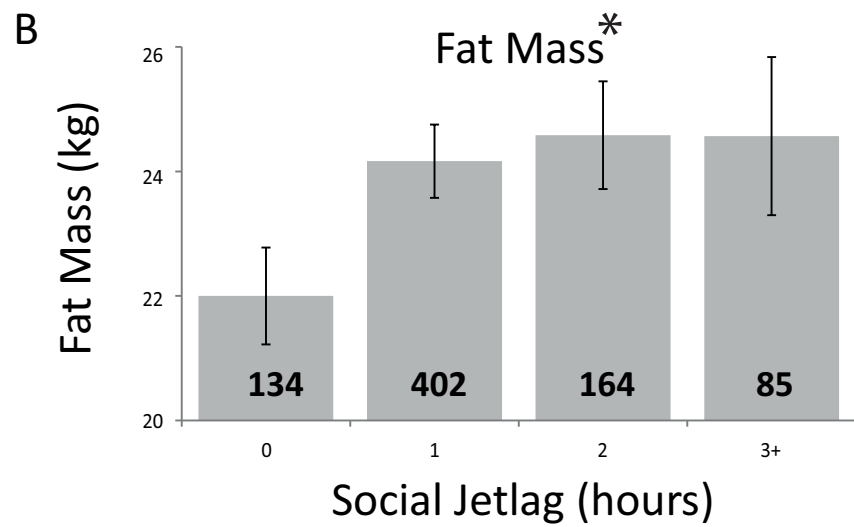
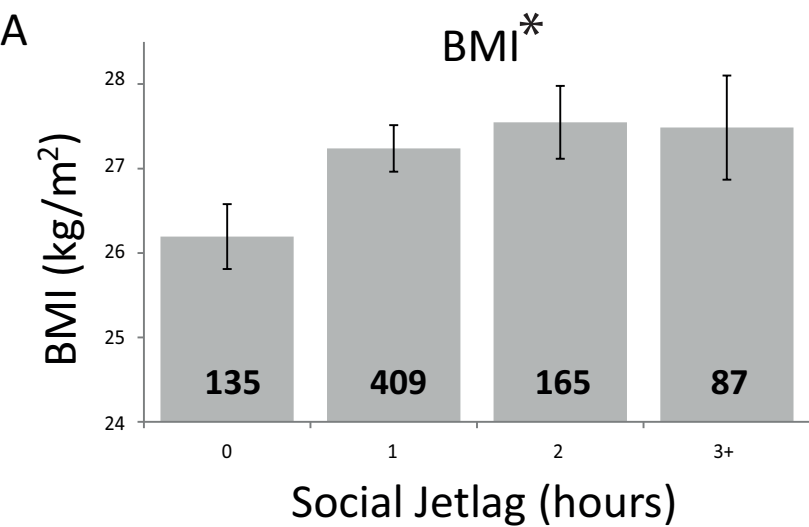
529 <sup>1</sup>Individuals who smoked were more likely to have high glycated hemaglobin levels ( $r = .11, p < .001$ )  
 530 but not high hsCRP levels ( $r = .03, p = .33$ ).

531 <sup>2</sup>Lower SES status was related to high glycated hemaglobin levels ( $r = -.10, p = .007$ ) but not high  
 532 hsCRP levels ( $r = -.02, p = .58$ ).

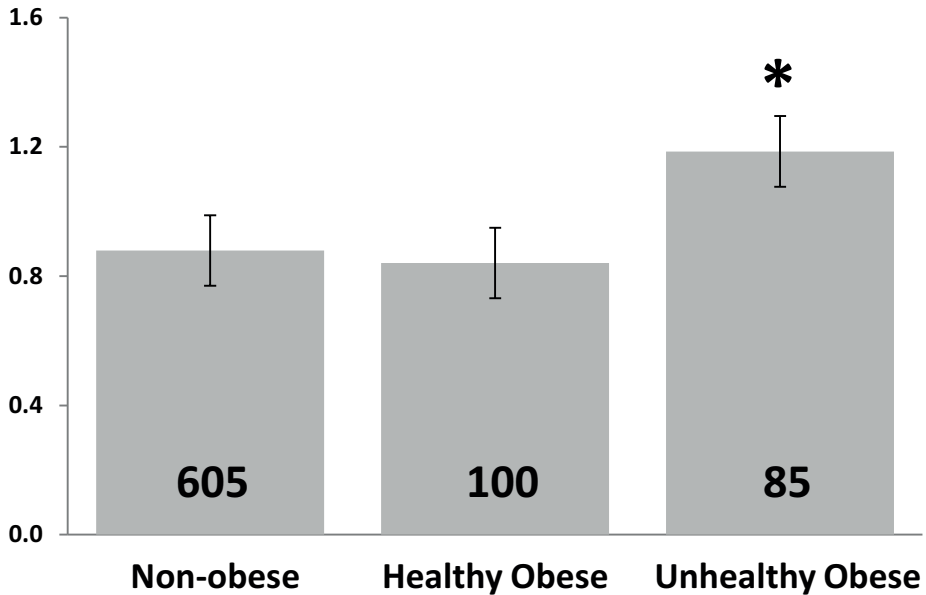
**Table 1. Social jetlag is associated with metabolic measures: BMI, Fat Mass, Waist Circumference, Obesity and Metabolic Syndrome.**

Predictor Variable	BMI (kg/m <sup>2</sup> )		Fat Mass (kg)		Waist (mm)		Obesity		Metabolic Syndrome	
	β (s.e.)	p-value	β (s.e.)	p-value	β (s.e.)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Sex</b>	0.07 (0.4)	.056	-0.27 (0.8)	<b>.000</b>	0.39 (8.4)	<b>.000</b>	1.0 (0.7 to 1.3)	0.806	2.1 (1.4 to 3.2)	<b>0.000</b>
<b>Chronotype</b>	-0.06 (0.2)	.166	-0.03 (0.4)	.528	-0.04 (4.3)	.289	0.9 (0.8 to 1.1)	0.353	1.2 (1.0 to 1.4)	0.121
<b>Sleep Duration</b>	-0.04 (0.2)	.333	-0.02 (0.4)	.432	-0.05 (4.3)	.123	0.9 (0.8 to 1.1)	0.192	1.0 (0.8 to 1.2)	0.679
<b>Social Jetlag</b>	0.10 (0.2)	<b>.012</b>	0.08 (0.5)	<b>.031</b>	0.07 (5.1)	.052	1.2 (1.0 to 1.5)	<b>0.045</b>	1.3 (1.0 to 1.6)	<b>0.031</b>

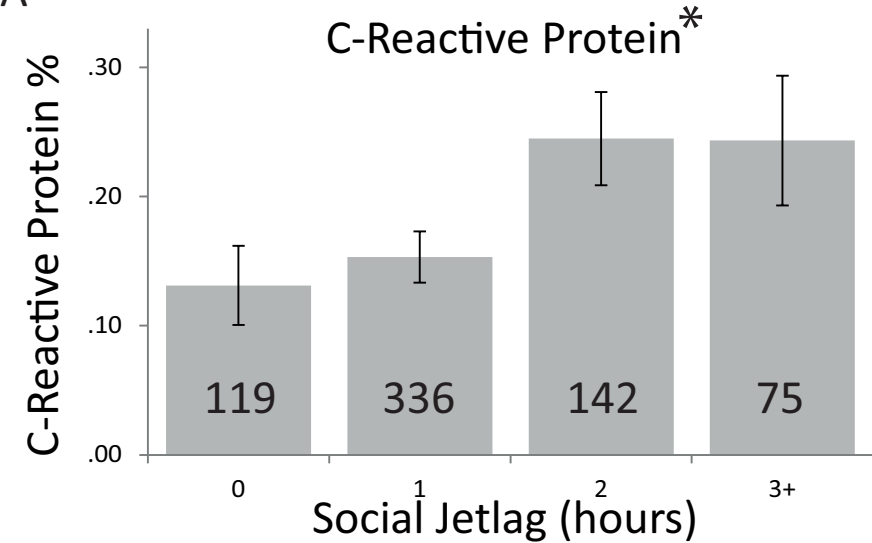
We used linear regression models to test associations with continuous outcome measures of BMI (kg/m<sup>2</sup>), fat mass (kg), and waist circumference (cm). We used logistic regressions to test associations with binary outcome measures of obesity and the metabolic syndrome. Significant p-values ( $p < 0.05$ ) are shown in bold. The units for the covariants are: sex was coded as female =1, male =2; chronotype is unitless, sleep duration (hours) and social jetlag (hours).



**Social Jetlag (hours)**



A



B

