

# Body Mass Index and Risk of Suicide Among Men

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**Background:** Body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) has been linked to depression and the risk of suicide attempts and deaths in conflicting directions.

**Methods:** In a prospective cohort study of 46 755 men free of cancer enrolled in the Health Professionals Follow-up Study, participants reported their height, weight, diet, and physical activity on repeated occasions beginning in 1986 and were followed up until death or until February 2002. A subsample of 1829 men reported their mental health–related quality of life with the Mental Component Summary Scale of the 36-Item Short-Form Health Survey in 1998.

**Results:** A total of 131 men died from suicide during follow-up. A higher BMI was related to a graded decline in the suicide mortality rate, from 52 per 100 000 person-years among men with a BMI of less than 21 to 13 per

100 000 among men with a BMI of 30 or higher; the adjusted hazard ratio per 1-U BMI increment was 0.89 (95% confidence interval, 0.84-0.95;  $P < .001$ ). The relationship was consistent when baseline or updated measures of BMI were used and with adjustment for medical illness, dietary factors, antidepressant use, physical activity, or social support. Height and physical activity were not strongly associated with risk. Analyses of mental health–related quality of life showed a similar positive relationship with BMI.

**Conclusions:** Among men, risk of death from suicide is strongly inversely related to BMI, but not to height or to physical activity. Although obesity cannot be recommended on the basis of its detrimental effects, further research into the mechanisms of lower risk among overweight and obese men may provide insights into effective methods of suicide prevention.

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**O**BESITY AND DEPRESSION, extremely common causes of morbidity,<sup>1,2</sup> have an intriguing and complex interrelationship.<sup>3,4</sup> Although depression has been associated with subsequent obesity in some studies,<sup>5</sup> obesity has also been associated with depressive symptoms<sup>6</sup> that may improve with weight loss.<sup>7,8</sup> Antidepressant-related weight changes<sup>9</sup> and activation of the hypothalamic-adrenal axis in both disorders<sup>4</sup> complicate this interrelationship even further.

Another complicating factor in the association of obesity with depression is the “jolly fat” hypothesis, first proposed 3 decades ago, which suggests that overweight is inversely related to anxiety and depressive symptoms.<sup>10-12</sup> Although the mechanism of this relationship is unclear, some have speculated that a high intake of carbohydrates may ameliorate or prevent depressive symptoms but also lead to weight gain.<sup>13</sup>

Despite interest in the relationship of weight and depression, the relationship of weight and body habitus with the risk of suicide has received far less attention. Suicide remains the 11th leading cause of death in the United States,<sup>14</sup> but identification of remediable risk factors for suicide has been difficult. Based on the links between obe-

sity and depression, it might be hypothesized that overweight and obese individuals would have a higher risk of suicide. A small number of studies with limited information on anthropomorphic measures and potentially confounding factors have suggested exactly the opposite, at least among men,<sup>15,16</sup> although an inverse association has not been detected in all studies.<sup>17,18</sup>

To determine the associations of body mass index (BMI) and other anthropomorphic measures with the risk of death from suicide (hereafter referred to as *suicide death*), we studied more than 45 000 participants of the Health Professionals Follow-up Study (HPFS). The HPFS is a prospective cohort study of male health care professionals in the United States for whom 16-year follow-up on mortality,<sup>19</sup> including death related to suicide, and repeated, validated information on BMI, diet, and physical activity is available.

## METHODS

The HPFS is a prospective investigation of 51 529 US male dentists, pharmacists, veterinarians, optometrists, osteopathic physicians, and podiatrists aged 40 to 75 years who returned a mailed questionnaire regarding diet and medical history in 1986. Follow-up questionnaires were sent biennially to update in-

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formation on exposures and newly diagnosed illnesses. For this analysis, we excluded men with cancer (other than nonmelanoma skin cancer) at baseline (n=2002) and men whose initial questionnaires were missing information on BMI (n=1094) or had inadequate dietary information or other technical deficiencies (n=1678), leaving 46 755 men available for analysis.

## ANTHROPOMORPHIC MEASURES

Participants reported body weight and height at baseline in 1986 and body weight alone in every biennial questionnaire afterward. At baseline, participants also reported their estimated weight 5 years previously (ie, in 1981) and their estimated weight at 21 years of age. As a measure of weight cycling, participants also reported the difference in their maximal and minimal weight in the preceding 2 years beginning in 1990.

Information on waist and hip circumference was collected in a brief follow-up questionnaire sent out in 1987<sup>20</sup> that included paper tape measures, detailed instructions, and illustrations to assist the men in measuring standing waist and hip circumferences. Participants were instructed to measure their waist circumference at the umbilicus and their hip circumference as the largest diameter between the waist and thighs.

We calculated the BMI (measured as weight in kilograms divided by height in meters squared) and waist-hip ratio for each participant. Self-reported anthropomorphic measures have been compared with standardized measures conducted by a technician in a subset of this cohort.<sup>21</sup> Self-reported and measured weight were strongly correlated ( $r=0.97$ ); the mean difference was an underreporting by 1.06 kg. The corresponding correlation coefficients between self-reported and measured waist and hip circumferences were 0.95 and 0.88, respectively.

We categorized BMI into 6 categories spanning approximately 2 U each as in previous analyses<sup>22</sup>; in sensitivity analyses, we also examined it in quintiles, in World Health Organization (WHO) categories, and as a continuous variable after winsorization at the upper 95th percentile to minimize the influence of outliers.<sup>23</sup> We examined the height and waist-hip ratio in quintiles.

## PHYSICAL ACTIVITY

Physical activity was derived from the biennial questionnaires, which included a series of questions on the average total time per week spent on specific activities during the previous year. Total weekly energy expenditure was expressed as metabolic equivalent-hours.<sup>24</sup> The validity and reproducibility of physical activity measurements were determined with a past-week recall, four 1-week activity diaries, and a step test among a subset of participants, as reported elsewhere.<sup>25</sup> The correlations between diary-based and questionnaire-based activity scores were 0.28 for nonvigorous activity and 0.58 for vigorous activity. We categorized physical activity into approximate quintiles as in previous analyses.<sup>26</sup>

## OTHER COVARIATES

We assessed dietary factors using a 131-item food frequency questionnaire, which has been validated with dietary records.<sup>27</sup> In 1988, participants responded to a series of questions regarding social support, including the number of close friends and close relatives they had, the number of friends and relatives they saw at least monthly, how often they attended religious gatherings, and how many hours per week they spent in community or social groups.<sup>28</sup> Participants reported use of antidepressant medication every 2 years, beginning with the 1990 questionnaire; doses were not reported. As in previous analy-

ses,<sup>29</sup> region of residence was categorized into the following 4 geographic regions, according to US Census definitions: West, Midwest, South, and Northeast. Participants reported prevalent and incident illnesses at every questionnaire; cases of cancer, coronary heart disease, and diabetes are subsequently adjudicated by physicians blinded to questionnaire information.<sup>20,22,30</sup> Participants also reported their employment and marital status every 2 years; response options were full-time, part-time, retired, or disabled for employment, and married, divorced, widowed, or never married for marital status.

## ASSESSMENT OF SUICIDE DEATHS

We confirmed deaths when reported by families, postal officials, or the National Death Index, with a combined follow-up rate in a companion study exceeding 98%.<sup>31</sup> Physicians reviewed death certificates and hospital or pathology reports to classify individual causes of death and were unaware of participants' reported questionnaire results. Deaths caused by self-inflicted or external injury were classified according to the underlying causes listed on the death certificate. For this study, we included deaths classified with codes E950 through E959 of the *International Classification of Diseases, Eighth Revision*. We also separately examined suicide deaths associated with firearm use (code E955) and other causes.

## QUALITY OF LIFE

In 1998, a supplemental questionnaire was administered to men with prostate cancer and control participants who were free of prostate cancer<sup>32-34</sup>; the questionnaire included the Medical Outcomes Study 36-Item Short-Form Health Survey.<sup>35</sup> For each case, 2 healthy controls matched on age were selected; the response rate among the controls was 93%. Of the 2217 controls who returned questionnaires, 2103 had baseline information on BMI and nutrient intake, and 1829 had complete information on the Mental Component Summary (MCS) and Physical Component Summary scales, summary measures of mental and physical health-related quality of life, respectively. The scales have population means of 50 and SDs of 10, with higher scores indicating better quality of life in that domain.

## STATISTICAL ANALYSIS

We calculated person-years for each participant from the date of return of the 1986 questionnaire to the date of death or to February 2002. Analyses incorporating the waist-hip ratio or social support began at the return of the 1988 questionnaire, and the corresponding analyses of antidepressant use began at the return of the 1990 questionnaire.

We calculated incidence rates by dividing the number of suicides in each category by person-years of follow-up in that category. In multivariate analyses, we simultaneously controlled for age, smoking (never, former, and 1-14, 15-24, and  $\geq 25$  cigarettes per day),<sup>36</sup> alcohol use (in 4 categories), geographic region, physical activity (in 5 categories), and marital status (in 4 categories). In sensitivity analyses, we also adjusted individually for intakes of energy, glycemic load,<sup>37</sup> caffeine,<sup>38</sup> and  $\omega$ -3 fatty acids<sup>39</sup> (all in quintiles); profession (in 6 categories); measures of social support (in 5 categories each); employment status; or incident major illnesses (cancer, diabetes, and coronary heart disease).

Nutrient intakes were updated every 4 years; other covariates (other than region and profession) were updated every 2 years. For multivariate analysis, we used Cox regression with time-dependent covariates; we noted no violations of the proportional hazards assumption. Our analyses used updated mea-

**Table 1. Selected Characteristics of 46 755 Male Health Care Professionals by BMI in 1986\***

Characteristic	Baseline BMI					
	<21.0	21.0-22.9	23.0-24.9	25.0-27.4	27.5-29.9	≥30.0
No. of participants	1755	6772	13 177	15 246	5955	3850
Age, y	54.4	53.8	54.1	54.8	54.8	54.3
Height, cm	179.8	178.0	178.3	178.0	178.3	177.0
Estimated BMI at age 21 y	19.5	20.7	21.7	22.8	24.1	26.3
Waist-hip ratio	0.90	0.92	0.93	0.94	0.96	0.98
Current cigarette smoker, %	18.6	13.1	12.8	13.8	14.1	12.9
Past cigarette smoker, %	32.6	36.8	40.7	43.6	44.5	47.0
Married, %	86	89	91	92	93	92
Physical activity, MET-hours/wk	23	26	23	20	16	13
Diabetes, %	3.1	2.7	2.8	2.7	3.7	5.9
Hypertension, %	14.1	15.4	18.1	22.2	29.4	37.5
Mean daily intakes						
Total energy, kcal/d	2035	1999	1979	1971	1988	2019
Caffeine, mg/d†	199	214	226	251	265	261
Dietary fiber, g/d†	22.4	22.0	21.5	20.7	20.2	20.0
ω-3 Fatty acid, mg/d†	292	314	318	304	297	301
Alcohol intake, g/d	10.3	10.8	11.6	11.6	11.5	10.2

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); MET-hours, metabolic equivalent-hours.  
 \*All variables except for age were standardized to the age distribution of the study population. Unless otherwise indicated, data are expressed as means.  
 †Caffeine, fiber, and ω-3 fatty acid intakes adjusted for total energy intake.

asures of BMI, in which we prospectively assessed the relative risk of suicide death in 2-year increments, based on the weight reported in the preceding questionnaire. Thus, we used the 1986 questionnaire to determine the risk of suicide death during the 1986-1988 period, the 1988 questionnaire for the 1988-1990 period, etc. In all analyses, we excluded men with prevalent malignancy at baseline and stopped updating BMI at the diagnosis of incident malignancy; in sensitivity analyses, we further excluded follow-up after diagnosis of malignancy during follow-up. We also examined baseline BMI alone and with a 2-year lag to minimize the inclusion of individuals with pre-existing illnesses.

For quality of life, we used linear regression to examine the relationship of BMI in 1986 or 1998 with MCS and Physical Component Summary scores, adjusting for the same covariates as in Cox models; however, of these covariates, only age and BMI were independently associated with MCS scores.

## RESULTS

Baseline characteristics of the HPFS cohort according to BMI are shown in **Table 1**; similar characteristics according to physical activity have been reported previously.<sup>26</sup>

A total of 131 men died of suicide during follow-up, ie, a suicide mortality rate of 19 per 100 000 person-years. The median age at suicide death was 64 years (interquartile range, 56-74 years). **Table 2** shows incidence rates and hazard ratios (HRs) for suicide according to BMI. There was a stepwise decrease in the suicide mortality rate with increasing BMI, with a roughly 4-fold gradient in risk even after adjustment. Additional adjustment for incident disease or social support did not influence the results; incident cancer was strongly related to suicide risk (HR, 2.23; 95% confidence interval [CI], 1.27-3.93), but diabetes was not (HR, 1.31; 95% CI, 0.68-2.53), even without adjustment for BMI (HR, 1.23; 95% CI, 0.64-2.36). Results also tended to be similar for suicide deaths related to firearms

and other causes. Additional adjustment for energy intake, caffeine, or ω-3 fatty acid intake also did not influence our findings (data not shown).

Analyses restricted to nonsmokers, those using a 2-year lag or baseline BMI, and those adjusted for antidepressant use (a potential intermediate) all attenuated the HRs to a moderate degree, although at least 2-fold gradients in risk remained in all cases. Antidepressant use itself was also strongly associated with risk (HR, 5.94; 95% CI, 3.03-11.64).

Table 2 further shows analyses using alternate cut points for BMI. Using the WHO definition of normal weight, there was an inverse association of BMI and risk through BMI values below 35.0; risk did not appear to be lower at the highest levels of BMI, but only 5 cases of suicide occurred in this subgroup.

**Table 3** shows the relationships of waist-hip ratio, height, and physical activity with risk of suicide. There was an inverse trend between waist-hip ratio and suicide risk, although it was less strong than that seen for BMI and not statistically significant. There was no evidence of any association between height or physical activity and risk.

**Table 4** shows the relationship of a 1-U increase in BMI with risk of suicide, overall and in sensitivity analyses. Risk was 11% lower for each 1-U increase in the full cohort. Neither censoring at the time of incident malignancy nor incorporating a 4-year lag between the assessment of exposure and onset of follow-up altered this finding. Even in analyses excluding men in the lowest BMI category to minimize confounding related to comorbid illness, there was a 10% lower risk for a 1-U increase in BMI. The inverse association of BMI with suicide was also not altered by additional adjustment for glycemic load (HR, 0.89; 95% CI, 0.84-0.95), and it did not differ in

**Table 2. Adjusted HRs for Suicide Mortality Among 46 755 HPFS Participants by BMI\***

Variable	Updated BMI						P Value†
	<21.0	21.0-22.9	23.0-24.9	25.0-27.4	27.5-29.9	≥30.0	
No. of cases of suicide death	13	25	37	32	15	9	
Related to firearms	7	11	18	22	13	4	
Unrelated to firearms	6	14	19	10	2	5	
Follow-up, person-years	24 911	89 950	177 980	216 899	101 496	71 881	
Incidence rate per 100 000 person-years	52	28	21	15	15	13	
Adjusted HR‡	1.39 (0.69-2.81)	1 [Reference]	0.78 (0.46-1.31)	0.52 (0.31-0.89)	0.52 (0.27-1.01)	0.42 (0.19-0.92)	<.001
Adjusted for cancer, diabetes, coronary heart disease	1.42 (0.70-2.89)	1 [Reference]	0.76 (0.45-1.29)	0.51 (0.30-0.87)	0.51 (0.26-0.98)	0.41 (0.19-0.90)	<.001
Never/distant smokers (n = 51)	0.89 (0.22-3.54)	1 [Reference]	0.72 (0.31-1.65)	0.69 (0.31-1.56)	0.52 (0.18-1.52)	0.47 (0.13-1.77)	.17
2-y Lag (n = 126)	1.21 (0.54-2.71)	1 [Reference]	0.96 (0.57-1.65)	0.59 (0.34-1.03)	0.57 (0.29-1.14)	0.57 (0.26-1.24)	.01
Adjusted for social support (n = 126)§	1.13 (0.51-2.48)	1 [Reference]	0.83 (0.49-1.41)	0.56 (0.32-0.97)	0.52 (0.26-1.03)	0.43 (0.20-0.96)	.003
Related to firearms (n = 75)	1.46 (0.52-4.08)	1 [Reference]	0.93 (0.43-2.01)	0.79 (0.38-1.67)	0.98 (0.42-2.25)	0.43 (0.13-1.39)	.11
Unrelated to firearms (n = 56)	1.26 (0.46-3.41)	1 [Reference]	0.65 (0.32-1.32)	0.30 (0.13-0.68)	0.13 (0.03-0.60)	0.40 (0.14-1.16)	<.001
Adjusted for antidepressant use (n = 107)	0.91 (0.37-2.22)	1 [Reference]	0.84 (0.47-1.47)	0.49 (0.27-0.89)	0.57 (0.28-1.15)	0.42 (0.18-0.97)	.01

  

Variable	Baseline BMI						P Value†
	<21.0	21.0-22.9	23.0-24.9	25.0-27.4	27.5-29.9	≥30.0	
Adjusted HR	1.59 (0.78-3.25)	1 [Reference]	0.80 (0.48-1.34)	0.53 (0.31-0.90)	0.60 (0.30-1.17)	0.61 (0.29-1.31)	.007
Adjusted for baseline disease	1.56 (0.76-3.19)	1 [Reference]	0.79 (0.47-1.32)	0.52 (0.30-0.89)	0.59 (0.30-1.16)	0.62 (0.29-1.32)	.007
No baseline disease (n = 65)	0.98 (0.34-2.82)	1 [Reference]	0.70 (0.36-1.40)	0.36 (0.17-0.80)	0.99 (0.41-2.34)	0.17 (0.02-1.37)	.05

  

Variable	WHO Categories of BMI					P Value†
	<18.5	18.5-24.9	25.0-29.9	30.0-34.9	≥35.0	
Adjusted HR	3.58 (0.89-14.39)	1 [Reference]	0.59 (0.40-0.86)	0.29 (0.10-0.79)	1.05 (0.41-2.70)	.003

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; WHO, World Health Organization.

\*Unless otherwise indicated, data are expressed as HR (95% CI).

†Derived from tests of linear trend.

‡All HRs are adjusted for age, smoking, alcohol consumption, geographic region, average daily exertion, and marital status. In the row headings, numbers in parentheses indicate cases of suicide mortality included in these sensitivity analyses.

§Social support includes number of close friends, number of close relatives, and time spent in religious activities.

||Baseline disease includes rheumatoid arthritis, renal failure, liver disease, inflammatory bowel disease, asthma, and periodontal disease.

**Table 3. Adjusted HR for Suicide Mortality by BMI, Waist-Hip Ratio, Height, and Physical Activity**

Variable	Quintiles, Adjusted HR (95% CI)*					P Value
	Q1	Q2	Q3	Q4	Q5	
BMI	1 [Reference]	0.74 (0.46-1.20)	0.49 (0.29-0.85)	0.47 (0.27-0.81)	0.42 (0.24-0.74)	<.001
Waist-hip ratio (n = 126)	1 [Reference]	0.75 (0.39-1.46)	0.75 (0.37-1.49)	0.84 (0.44-1.62)	0.72 (0.37-1.41)	.13
Height	1 [Reference]	0.85 (0.48-1.49)	0.97 (0.57-1.64)	1.01 (0.57-1.77)	0.66 (0.30-1.45)	.61

  

Variable	Physical Activity, MET-hours/wk					P Value
	<6.33	6.33-14.49	14.50-25.08	25.09-41.98	>41.99	
Adjusted HR (95% CI)	1 [Reference]	0.82 (0.46-1.45)	0.86 (0.48-1.52)	0.83 (0.46-1.49)	1.01 (0.61-1.68)	.86

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; HR, hazard ratio; MET-hours, metabolic equivalent-hours.

\*All HRs are adjusted for age, smoking, alcohol consumption, geographic region, average daily exertion, and marital status.

men whose glycemic load was above or below the median level; glycemic load per se was not associated with risk. The association was also identical when adjusted for work status, although disability itself was associated with a higher risk (HR, 3.20; 95% CI, 1.20-8.58).

Stratified analyses suggested generally similar relationships in all subgroups, with no statistically significant in-

teractions; although the association appeared to be stronger in younger men, even when BMI and age were modeled as continuous variables, the interaction was not significant (P=.14). When we analyzed change in BMI during follow-up controlling for previous BMI, a 1-U increase in BMI was associated with a nonsignificant 11% lower subsequent risk. When we further excluded decreases in BMI

**Table 4. Adjusted HRs for Suicide Mortality Among HPFS Participants per 1-U Increase in BMI**

Participant Characteristic	BMI, HR (95% CI)	P Value*	P Value (Interaction)
<b>Updated BMI</b>			
Overall	0.89 (0.84-0.95)	<.001	NA
Censored at diagnosis of malignancy	0.91 (0.85-0.97)	<.001	NA
BMI <21 excluded	0.90 (0.84-0.97)	.005	NA
Age <60 y	0.81 (0.73-0.90)	<.001	.41
Age ≥60 y	0.95 (0.88-1.03)	.19	
Exertion <14.5 MET-hours/wk	0.89 (0.81-0.98)	.02	.80
Exertion ≥14.5 MET-hours/wk	0.90 (0.82-0.98)	.02	
Height <177.8 cm	0.93 (0.84-1.04)	.21	.17
Height ≥177.8 cm	0.87 (0.80-0.94)	<.001	
Unmarried	0.82 (0.69-0.97)	.02	.15
Married	0.91 (0.85-0.98)	.01	
BMI with 4-y lag	0.92 (0.86-0.98)	.02	
2-y Change in BMI	0.89 (0.75-1.06)	.20	
<b>Baseline BMI</b>			
Overall	0.90 (0.85-0.96)	.001	NA
BMI <21 excluded	0.91 (0.85-0.98)	.02	NA

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; MET-hours, metabolic equivalent-hours; NA, not applicable.

\*Derived from tests of linear trend.

**Table 5. Age- and Multivariate-Adjusted Differences in 1998 Mental Component Summary Scale Scores According to BMI**

Variable	BMI, HR (95% CI)						Linear Trend P Value
	<21.0	21.0-22.9	23.0-24.9	25.0-27.4	27.5-29.9	≥30.0	
Age-adjusted							
1986 BMI	-0.1 (-1.2 to 1.1)	1 [Reference]	-0.3 (-0.9 to 0.3)	0.3 (-0.3 to 0.9)	0.9 (0.1 to 1.7)	1.8 (0.8 to 2.8)	<.001
1998 BMI	-0.5 (-1.6 to 0.5)	1 [Reference]	0.1 (-0.6 to 0.7)	0.5 (-0.1 to 1.1)	1.0 (0.2 to 1.7)	1.7 (0.9 to 2.6)	<.001
Multivariate-adjusted*							
1986 BMI	0.004 (-1.1 to 1.2)	1 [Reference]	-0.3 (-0.9 to 0.3)	0.3 (-0.3 to 0.9)	1.0 (0.2 to 1.8)	1.8 (0.8 to 2.8)	<.001
1998 BMI	-0.5 (-1.6 to 0.5)	1 [Reference]	0.04 (-0.6 to 0.7)	0.5 (-0.1 to 1.1)	1.0 (0.2 to 1.7)	1.7 (0.9 to 2.6)	<.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; HR, hazard ratio.

\*Multivariate-adjusted regression coefficients are adjusted for age, smoking, alcohol consumption, geographic region, average daily exertion, and marital status.

of 0.5 U or more to minimize the contribution of weight loss among participants before suicide, a 1-U increase in BMI was associated with a nonsignificant 17% lower subsequent risk (HR, 0.83; 95% CI, 0.56-1.21;  $P = .32$ ).

We also evaluated the association of self-reported BMI at 21 years of age with risk of suicide mortality during follow-up. The HR associated with a 1-U increase in BMI at 21 years of age was 0.95 (95% CI, 0.89-1.01); the corresponding HR for a 1-U gain in BMI from 21 years of age to baseline was 0.93 (95% CI, 0.87-1.00). Large amounts of weight change within a 2-year period tended to be associated with a higher risk, although estimates were not statistically significant (HR for the maximal weight difference within the last 2 years of  $\geq 6.8$  kg vs  $\leq 1.8$  kg, 1.61; 95% CI, 0.79-3.31) and did not alter the association of BMI with risk (HR per 1-U increment in BMI, 0.90; 95% CI, 0.84-0.97).

**Table 5** shows the relationship of BMI and mental health-related quality of life using the baseline BMI in 1986 or the BMI at the time of the questionnaire in 1998.

The Pearson correlation coefficients of 1986 and 1998 BMI with MCS scores were 0.11 and 0.09, respectively ( $P < .001$  for both). Similar to the results seen for suicide risk, MCS scores tended to be higher with increasing BMI, even when measured at baseline 12 years before the administration of the 36-Item Short-Form Health Survey. In contrast, 1986 and 1998 BMIs were inversely correlated with Physical Component Summary scores, with Pearson correlation coefficients of  $-0.15$  and  $-0.11$ , respectively ( $P < .001$  for both).

#### COMMENT

In this prospective cohort study of male health care professionals, higher BMI was associated with a lower risk of suicide mortality. There was a stepwise gradient in risk, the results were largely unchanged in sensitivity analyses, and there was a similar relationship of BMI with mental health-related quality of life.

A small number of previous studies support an inverse relationship of BMI with risk of suicide death, although data on suicide attempts generally suggest the opposite. In a case-control analysis of the General Practice Research Database, hypertensive adults with a BMI of 25 or higher had an adjusted odds ratio for suicide of 0.33 (95% CI, 0.11-0.98) compared with leaner hypertensive adults.<sup>15</sup> Using the military records of nearly 1.3 million Swedish male teens, Magnusson and colleagues<sup>16</sup> found an inverse association of teenage BMI with the risk of suicide, with an HR of 0.85 (95% CI, 0.79-0.91) for each 5-U increment in BMI, although no information on adult anthropometric measures was available. However, suicide attempts tended to be positively associated with BMI in a representative German sample<sup>40</sup> and among teenagers<sup>41</sup> and female physicians<sup>42</sup> in the United States. Dong and colleagues<sup>43</sup> also found positive associations of marked obesity with suicide attempts in 2 parallel studies, but more typical levels of obesity were not assessed. The increased prevalence of overweight and obesity in the United States in the 1990s was accompanied by a 6% decrease in suicide mortality rates but little apparent change in the rate of suicide attempts.<sup>44</sup>

The mechanisms by which adult BMI could be inversely linked to the risk of suicide death are as yet uncertain. One possibility is the role of insulin in dictating mood. The drop in maternal insulin levels after birth has been hypothesized to precipitate postpartum depression,<sup>45</sup> perhaps related to the ability of insulin to stimulate hypothalamic serotonin release.<sup>46</sup> In a study of 30 patients with type 2 diabetes, 4 weeks of insulin administration led to marked improvements in depressive symptoms and subjective well-being, even with minimally altered glycemic control.<sup>47</sup> Given that BMI has a continuous and positive relationship with insulin levels at all levels of weight,<sup>48</sup> even among children,<sup>49</sup> and that weight gain over time has a similar relationship,<sup>50</sup> it is plausible that BMI could be linked to lower risk of suicide through circulating levels of insulin.

At the same time, we generally found little evidence to support the hypothesis that specific dietary factors mediate the relationship of obesity and suicide. Although carbohydrate intake in particular has been postulated to improve mood and increase weight, adjustment for glycemic load had no effect on our estimates of risk. Glycemic load is a measure of the acute glycemic response<sup>51</sup> and is not necessarily related to fasting insulin levels.<sup>52</sup> Taken with our findings on BMI, these results suggest that physiological responses to glycemic load may be less relevant for suicide than is adiposity per se.

Our findings in this population of men may not readily generalize to all women. For example, in an analysis of the 1992 National Longitudinal Alcohol Epidemiologic Survey, Carpenter and colleagues<sup>53</sup> found that a 10-U increment in BMI was associated with increased odds of suicide attempts among women (odds ratio, 1.22; 95% CI, 0.91-1.63), but significantly decreased odds among men (odds ratio, 0.45; 95% CI, 0.40-0.51). Several cross-sectional studies have suggested that men and women differ in their relationship between BMI and depressive symptoms.<sup>10,12,54</sup> It is possible that the stigma attached to obesity may be particularly acute among women,<sup>55</sup> al-

though this has not been borne out in all studies.<sup>56</sup> Alternately, the association between endogenous estrogen levels and depression may complicate the picture for women. Estrogen alters serotonergic neurotransmission and receptor distribution<sup>57,58</sup> and has been suggested to ameliorate depression in some clinical trials.<sup>59</sup> In support of this hypothesis, BMI may be inversely associated with depressive symptoms among postmenopausal but not premenopausal women.<sup>11</sup>

The relationship of BMI and suicide tended to be stronger among younger than older men, although a formal test of interaction did not yield significant results. This may reflect the role of chance, as in any subgroup analysis. We also could not readily evaluate suicide among men in their third and fourth decades of life, in whom suicide accounts for a disproportionately large proportion of deaths, albeit at a lower absolute rate than among older men. However, BMI tends to be a better measure of adiposity in the young, whereas it is disproportionately influenced by underlying illness and changes in muscle mass in older adults.<sup>60</sup> If the weaker relation in older men is confirmed, it would tend to support further the importance of adiposity per se in lowering the risk of suicide.

The potential interrelationships of BMI, depressive symptoms and major depressive disorders, antidepressant medication, and risk of suicide are complex and likely bidirectional. On the one hand, BMI may have direct positive effects on mood that mediate the observed association of BMI with suicide, such as through elevated insulin levels. On the other hand, depression and the medications used to treat it may influence eating and exercise habits and subsequently BMI. This bidirectionality is also likely to be true for other emotional and relational factors for which we did not have information. We had information on antidepressant use, a potential contributor to suicide even in adults,<sup>61</sup> and social support, neither of which appeared to confound the association of BMI with the risk of suicide death to any substantial degree. However, we did not have systematic information on depression or depressive symptoms. Future studies that incorporate repeated measures of both depression and BMI in large samples of participants and methodological approaches that account for the possibility that depression acts as both a mediator and a confounder for the effect of BMI on suicide risk<sup>62,63</sup> will ultimately be required to clarify these relationships definitively.

The HPFS is also subject to other limitations. We did not have information on suicide attempts, and hence we could not ascertain whether BMI is related to the risk of suicide attempts or their case-fatality rate in this population. This latter issue will require additional study, given the somewhat contradictory results of previous studies relating BMI to suicide attempts and suicide death.

Participants in the HPFS are not necessarily representative of the total US population, which limits the generalizability of our results but provides a sample of uniform sex, educational attainment, and occupational status. Moreover, the rate of suicide death among these middle-aged and older men is similar to that found in other large cohort studies.<sup>64</sup>

As in other cohort studies, our definition of suicide death was based on death certificates, an approach that appears to be valid.<sup>65</sup> However, treating practitioners may

have misclassified some cases of suicide death, particularly in cases where other causes of death may have been plausible (eg, among men with known chronic disease), although cases of suicide death related to firearm use may be less prone to underreporting and were related inversely with BMI.

Although we relied on self-reported measures of height and weight in this study, we have previously validated them in this population and all assessments were made prospectively. A related limitation is the relatively truncated range of BMI noted among these men, and we cannot evaluate the possibility that greater degrees of obesity (eg, BMI of  $\geq 40$ ) are associated with a higher risk of suicide, as suggested elsewhere.<sup>43</sup>

Our analyses were necessarily limited by the relative rarity of death related to suicide. Although our primary analyses yielded reasonably precise results, our stratified analyses—and particularly stratified analyses that examined categories of BMI—yielded considerably wider CIs. Larger studies with greater numbers of cases of suicide mortality will be needed to overcome this limitation.

In conclusion, higher BMI was strongly associated with a lower risk of suicide mortality among men, with a clear gradient in risk between the highest and lowest BMI levels. Given the strength of this relationship, research to identify its mechanisms could lead to important insights into prevention of this important cause of death.

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