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Original Contribution

Association of Adult Body Mass Index and Height with Anxiety, Depression, and Suicide in the General Population

The HUNT Study

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A prospective cohort of 74,332 men and women was used to investigate the association of body mass index and height with suicide, anxiety, and depression. Participants in the Nord-Trøndelag Health Study (Norway, 1984–1986) (HUNT 1) were aged 20 years or more and followed up until December 31, 2002. Anxiety and depression were measured with the Hospital Anxiety and Depression Rating Scale (HADS) in 1995–1997. There were 183 suicides. Suicide risk decreased with increasing body mass index at baseline (1984–1986) in men and women. In models controlling for a range of psychological, social, and lifestyle factors, the hazard ratio per standard deviation increase in body mass index was 0.82 (95% confidence interval: 0.68, 0.98). In contrast, in the subset of participants ($n = 44{,}396$) with HADS measures, body mass index at baseline (1984–1986) was positively associated with depression. In fully adjusted models, the odds ratio for depression per standard deviation increase in body mass index (HADS-D: $\geq$8) was 1.11 (95% confidence interval: 1.07, 1.15). In fully adjusted models, there was no association of height with the incidence of suicide or depression. Raised body mass index is associated with an increased risk of depression but reduced risk of suicide in men and women. The mechanisms underlying these different associations require clarification.

anxiety; body height; body mass index; depression; Norway; prospective studies; suicide

Abbreviations: CI, confidence interval; HADS, Hospital Anxiety and Depression Rating Scale consisting of seven items for depression (HADS-D) and seven for anxiety (HADS-A); HR, hazard ratio; HUNT, Nord-Trøndelag Health Study; SD, standard deviation.

An individual's risk of developing mental illness is influenced by factors acting throughout the life course (1–3). Studying the role of preadult exposures on mental health is challenging, because few cohort studies have prospectively recorded measures of possibly relevant exposures such as childhood illness, diet, and socioeconomic adversity. In the absence of such measures, a number of studies have examined disease associations with birth weight, height, and body mass index (4), which are indirect markers of these possible risk factors. Height, for example, is influenced by genes, diet, health, and psychosocial adversity throughout the growing years (5). Body mass index, a measure of weight that is relatively independent of height, is an indicator of ill health, diet, exercise, disturbed energy

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balance, and insulin resistance. Factors that influence growth may also affect neurodevelopment, neuroendocrine systems, and hence the risk of developing mental illness.

Some (6, 7), but not all (8), recent studies have reported that taller men have a reduced risk of suicide. The association was partly explained by lifestyle and socioeconomic factors in one study (7). Body mass index was inversely related to suicide in two recent studies, one of young conscripts (6) and the other of middle-aged health professionals (8), and the association was unchanged when a range of possible confounding factors were controlled for. These studies were based on cohorts of males and have not fully investigated the possible mediating influence of common mental disorder. The association of body weight with depression, suicidal ideation, or suicide attempts has been investigated mainly in those classified as overweight or obese (9–12). Here, we investigated the association of adult height and body mass index with mood and suicide in a large cohort of Norwegian men and women who participated in the Nord-Trøndelag Health Study (HUNT).

MATERIALS AND METHODS

The HUNT Study

HUNT is one of the world's largest population surveys. The first wave (HUNT 1) was carried out in 1984–1986 (13). The methods are described in detail on the HUNT website (http://www.hunt.ntnu.no/index.php?side=english). In brief, all residents of Nord-Trøndelag County in Norway aged 20 or more years were invited to participate in the study, which included a physical examination and self-completed questionnaires. Questionnaire 1 was attached to the clinic invitation, and 74,977 (88.1 percent) of the 85,100 eligible persons completed and returned it when they attended the clinical investigation. Of these, 74,332 (99.1 percent) had reliable height and weight measurements recorded in light clothes and without shoes by a specially trained nurse. These participants constitute our study cohort. After the clinical investigation, participants were given a second questionnaire to complete and return by mail. This second questionnaire collected information mainly on education, alcohol intake, smoking, other lifestyle issues, and functional impairment and was returned by 53,016 (70.7 percent) of the study members. Nonresponse to this questionnaire is the main reason for missing data in our multivariable analyses. Compared with responders, nonresponders were more likely to be male (54 vs. 50 percent), older (54 vs. 48 years), and shorter (168 vs. 170 cm); had a higher body mass index (25.5 vs. 25.1 kg/m^2); and reported more physical illness (9.8 vs. 6.2 percent). Information concerning age, place of residence, and marital status was obtained from Norway's National Population Registry.

The second wave of HUNT (HUNT 2) was carried out in the same geographic area as HUNT 1 between 1995 and 1997 (14). A total of 47,048 (72 percent) of the participants in HUNT 2 had also participated in HUNT 1. Participants in HUNT 2 completed the 14-item Hospital Anxiety and Depression Rating Scale (HADS) (15). A total of 44,396 (59.7 percent) HUNT 1 participants also attended HUNT 2 and had a valid HADS-D score.

The Norwegian Data Inspectorate, the Regional Committee for Ethics in Medical Research, and the HUNT Publication Review Board approved the protocols for HUNT 1, HUNT 2, and this study. All participating subjects provided written consent.

Suicide mortality

The Death Registry, Statistics Norway, identified all deaths in HUNT study members up to December 31, 2002. Suicides were defined as deaths coded as E950–E959 (suicide) and E980–E989 (excluding code E988.8, undetermined intent) using the *International Classification of Diseases*, Ninth Revision, or as codes X60–84 (suicide) and Y10–34 (undetermined intent) using the Tenth Revision. Forensic autopsies are conducted in most cases of sudden unexpected deaths where suicide cannot be ruled out. The National Mortality Registry also sends a questionnaire clarifying the cause of death to the police and to the general practitioner involved.

Measurement of depression and anxiety

HADS was used to measure depression and anxiety in HUNT 2. HADS consists of seven items for depression (HADS-D) and seven for anxiety (HADS-A), each with a four-point ordinal scale to describe symptom severity from 0 to 3. HADS has been validated across a wide range of health-care settings and age groups (16). The psychometric properties of the Norwegian version of HADS have been found to be excellent in HUNT 2 (15).

Four questions concerning anxiety and depression symptoms—nervousness, calmness, mood, and vitality—were included in both HUNT 1 and HUNT 2. These variables constituted a crude baseline measure of common mental symptoms in HUNT 1. A compound index, the Anxiety Depression Index, based on these four variables was validated against the total HADS score in the HUNT 2 population, and it appeared to be an acceptable indicator of psychiatric caseness (sensitivity = 0.51; specificity = 0.93; Cohen's kappa = 0.55) (17).

Statistical analysis

Using linear regression models, we investigated the associations of possible confounding factors with height and body mass index. To study associations between height/body mass index and suicide, we used Cox proportional hazards models with calendar time as the time axis. We controlled for age (in 5-year bands) and investigated whether associations varied in the different age groups and in men compared with women by fitting appropriate interaction terms. We calculated sex-specific z scores for height and body mass index as the number of standard deviations that an individual's measurement was above (positive values) or below (negative values) the mean for his or her sex.

Participants were categorized into four approximately equally sized groups (quartiles) on the basis of their sex-specific z scores for height. According to World Health Organization criteria, body mass index was categorized into four groups:

underweight ($\leq$18.4 kg/m^2), normal weight (18.5–24 kg/m^2), overweight (25–29 kg/m^2), and obese ($\geq$30 kg/m^2). Caseness for anxiety on HADS-A and for depression on HADS-D in HUNT 2 was defined by a score of $\geq$8 on each subscale (16).

Our initial models controlled for age and sex. We then examined the effect on associations of controlling for the following factors measured in HUNT 1:

- Lifestyle measures and markers of socioeconomic position that may confound associations of anthropometry with suicide: 1) smoking, 2) frequency of alcohol use monthly, 3) education, 4) marital status, 5) physical activity;
- Self-reported measures of symptoms related to common mental disorder (vitality, nervousness, calmness, mood, and use of tranquilizers) that may lie on the causal pathway linking anthropometric measures with suicide risk.

To investigate the possibility that severe mental illness both resulted in low weight at the baseline examination and increased suicide risk, we performed additional sensitivity analysis, first, excluding all suicides occurring in the first 2 years of follow-up; and second, excluding subjects who were Anxiety Depression Index positive at the baseline survey. For the analyses, we used STATA, version 9, software (StataCorp LP, College Station, Texas).

RESULTS

Characteristics of cohort members

The HUNT 1 cohort consisted of 36,515 males (49 percent) and 37,817 females. The mean age of study members at recruitment was 48.8 years for males and 49.8 years for females (table 1). Males were taller than females, and obesity was more common in females (13.5 percent) than males (7.7 percent). Levels of symptoms related to common mental disorder and tranquilizer use were higher in females than males. Age- and sex-adjusted analyses showed no difference in suicide risk between those with complete self-report health and lifestyle data ($n = 53{,}016$ in the second questionnaire) and those with missing data ($n = 21{,}316$) (hazard ratio (HR) = 1.01, 95 percent confidence interval (CI): 0.73, 1.40).

Short height was associated ($p < 0.05$) with smoking (males only), low levels of alcohol intake, lower levels of education, being unmarried (males only), taking tranquilizers, and reporting symptoms related to common mental disorder. People with a low body mass index had a tendency ($p < 0.05$) to be smokers, to drink alcohol more frequently (females only), to be more educated, to be divorced, to use tranquilizers (females only), and to report symptoms related to common mental disorder. Education was the factor most strongly associated with differences in height and body mass index.

Association of height and body mass index with suicide

Among the 74,332 subjects with height and weight measures at baseline (1984–1986), there were 183 suicides, 143 males and 40 females, by the end of 2002. The age-adjusted annual suicide rate was 25.5 per 100,000 in males and 6.6 per 100,000 in females. Only three deaths were coded as of undetermined intent.

In age-adjusted analyses, greater height and body mass index were associated with a lower risk of suicide. The hazard ratio for suicide per standard deviation increase in height was 0.85 (95 percent CI: 0.71, 1.02) in males and 0.75 (95 percent CI: 0.53, 1.06) in females; the hazard ratio for suicide per standard deviation increase in body mass index was 0.86 (95 percent CI: 0.72, 1.03) in males and 0.75 (95 percent CI: 0.51, 1.12) in females.

These modest sex differences in the strength of associations must be interpreted cautiously, as there was no statistical evidence that the association of height or body mass index with suicide differed in males and females ($p_{\text{interaction}} = 0.98$ and 0.29, respectively). Likewise there was no evidence that associations of height differed in different age groups ($p_{\text{interaction}} = 0.53$). There was weak evidence that associations with body mass index were stronger in older compared with younger subjects ($p_{\text{interaction}} = 0.10$).

The associations of height and body mass index with suicide are shown in table 2. In age- and sex-adjusted models based on the full data set, greater height was associated with a lower suicide risk (HR per standard deviation (SD) increase in height = 0.83, 95 percent CI: 0.71, 0.97). Associations with height were somewhat weaker in the data set restricted to study members with information on all confounders (HR per SD increase in height = 0.91, 95 percent CI: 0.75, 1.10); this association was attenuated by more than 50 percent in the fully adjusted model (HR = 0.97, 95 percent CI: 0.80, 1.16). The factor that most strongly confounded the association of height with suicide was marital status.

Higher body mass index was associated with lower suicide risk. The hazard ratio per standard deviation increase in body mass index was 0.83 (95 percent CI: 0.71, 0.98). The hazard ratio per standard deviation increase in body mass index was 0.90 (95 percent CI: 0.72, 1.13) in those aged less than 50 years at baseline and 0.78 (95 percent CI: 0.62, 0.98) in those aged 50 years or more.

In the data set restricted to those with complete confounder information, associations with body mass index were slightly stronger than in the full data set (HR per SD increase in body mass index = 0.78, 95 percent CI: 0.64, 0.95). This association was only slightly attenuated in models controlling for the confounding factors (HR = 0.82, 95 percent CI: 0.68, 0.98).

In a sensitivity analysis, we excluded suicides in the first 2 years of follow-up to investigate whether the inverse associations of body mass index with suicide may have been due to weight loss preceding suicide in those with severe mental illness. The hazard ratio was little changed (HR = 0.80, 95 percent CI: 0.67, 0.96). We also investigated the association in nonsmokers ($n = 27{,}720$); the hazard ratio per standard deviation change in body mass index was 0.75 (95 percent CI: 0.54, 1.05). In a further sensitivity analysis, we investigated the association of body mass index with suicide in subjects who were in good mental health (Anxiety Depression Index negative) at the beginning of follow-up ($n = 54{,}805$). The association with body mass index was little changed (HR per SD increase in body mass index = 0.77, 95 percent CI: 0.63, 0.95). Similarly, we performed a multivariate analysis

TABLE 1. Characteristics of the total HUNT* 1 cohort (n = 74,332) and of the subsample (n = 53,016) with full confounder information in HUNT 1, Norway, 1984–1986

	Males	Females
Full sample (36,515 males and 37,817 females)		
Mean age (years)	48.8 (17.2)†	49.8 (17.7)
Mean height (cm)	176.2 (6.8)	162.8 (6.4)
Body mass index‡ (%)		
Underweight	0.6	2.1
Normal weight	50.2	54.7
Overweight	41.4	29.6
Obese	7.7	13.5
Subsample (26,755 males and 26,261 females)		
Marital status (%)		
Single	15.9	8.2
Married/cohabiting	79.4	79.3
Widower	2.9	10.3
Divorced	1.9	2.2
Education (%)		
<10 years	55.7	64.2
10–12 years	32.0	26.8
>12 years	12.3	9.1
Smoking habits (%)		
Never	34.2	51.2
Former	30.4	16.2
Current	35.5	32.5
Frequency of alcohol use (%)		
Less than monthly	43.1	66.9
1–4 times monthly	48.2	29.9
5 or more times monthly	8.7	3.2
Physical activity (%)		
No exercise	12.9	13.5
Exercise, less than weekly	29.4	27.7
Exercise, 1 or more times a week	57.7	58.8
Anxiety Depression Index		
Vitality (%)		
Very strong and fit	4.4	3.1
Strong and fit	22.9	17.8
Quite strong and fit	36.1	33.7
Neither fit nor exhausted	29.4	35.2
Tired and exhausted	7.1	10.2
Nervous (%)		
Never	58.1	44.3
Sometimes	36.4	46.0
Often	5.5	9.6
Calm (%)		
Most of the time	45.2	44.7
Often	32.9	31.4
Sometimes	20.1	22.2
Never	1.7	1.7
Mood (%)		
Very cheerful	40.1	41.4
A little cheerful	30.6	27.8
Neither cheerful nor depressed	27.0	28.3
Depressed	2.3	2.5
Use of tranquilizers (%)		
Daily	3.6	6.4
Weekly, but not every day	2.3	5.0
Not as often as weekly	4.6	8.5
Never	89.5	80.0

* HUNT, Nord-Trøndelag Health Study.
† Numbers in parentheses, standard deviation.
‡ World Health Organization criteria: underweight (≤18.4 kg/m^2), normal weight (18.5–24 kg/m^2), overweight (25–29 kg/m^2), obese (≥30 kg/m^2).

Table continues

excluding all participants who reported previous longstanding and/or other severe physical illnesses including diagnosis of any cancer in HUNT 1 (n = 5,348), but the results remained unchanged (HR per SD increase in body mass index = 0.82, 95 percent CI: 0.68, 0.99).

Associations of height with suicide were little changed when body mass index was included in models, as were associations of body mass index with suicide when height was included.

Association of body mass index and height with anxiety and depression

Higher body mass index was associated with increased risk of depression at follow-up (table 3). This association did not change in models controlling for possible confounding factors. Associations were similar in males and females. The fully adjusted odds ratio for depression per standard deviation increase in body mass index was 1.12 (95 percent CI: 1.06, 1.18) in males and 1.09 (95 percent CI: 1.03, 1.15) in females. Overall, there was no strong evidence of an association of body mass index with anxiety, but the relation differed in females and males (table 4). The fully adjusted odds ratio per standard deviation increase in body mass index was 1.00 (95 percent CI: 0.95, 1.05) among females and 1.07 (95 percent CI: 1.01, 1.14) among males ($p_{\text{gender interaction}} = 0.03$).

There was a weak inverse association between height and depression in age- and sex-adjusted models; this was abolished in the fully adjusted models (table 5). The p value for gender interaction was 0.53. The same was observed for the association of height with anxiety; here the p value for gender interaction was 0.93.

TABLE 2. Hazard ratio for suicide by body mass index (according to the WHO* categories and per standard deviation increase) and by height (in sex-specific quartiles and per standard deviation increase), HUNT* 1, Norway, 1984–1986

Covariates	Total cohort ($n = 74,332$)			Subsample with confounder information ($n = 53,016$)				
	Suicides (no.)	Adjusted for age and sex		Suicides (no.)	Adjusted for age and sex		Multivariable adjustment†	
		Hazard ratio	95% confidence interval		Hazard ratio	95% confidence interval	Hazard ratio	95% confidence interval
Height in quartiles								
Quartile 1	49	1.00	Referent	32	1.00	Referent	1.00	Referent
Quartile 2	50	1.01	0.68, 1.51	36	1.06	0.66, 1.72	1.17	0.72, 1.90
Quartile 3	41	0.65	0.43, 1.01	31	0.72	0.43, 1.19	0.84	0.50, 1.40
Quartile 4	43	0.69	0.45, 1.08	35	0.81	0.49, 1.36	0.94	0.56, 1.58
Height per SD* (sex specific‡)	183	0.83	0.71, 0.97	134	0.91	0.75, 1.10	0.97	0.80, 1.16
Body mass index (WHO criteria§)								
Underweight	1	0.58	0.08, 4.18	1	0.59	0.08, 4.27	0.59	0.08, 4.24
Normal weight	108	1.00	Referent	81	1.00	Referent	1.00	Referent
Overweight	61	0.72	0.52, 0.99	46	0.79	0.54, 1.15	0.79	0.50, 1.14
Obese	13	0.67	0.37, 1.21	6	0.42	0.18, 0.98	0.41	0.18, 0.96
Body mass index per SD (sex specific)	183	0.83	0.71, 0.98	134	0.78	0.64, 0.95	0.82	0.68, 0.98

* WHO, World Health Organization; HUNT, Nord-Trøndelag Health Study; SD, standard deviation.

† Multivariable adjustments for age, sex, education, marital status, smoking (never, former, current), frequency of alcohol use, physical activity, vigor, nervousness, calmness, cheerfulness, and frequency of using tranquilizers. Height and body mass index were not mutually adjusted for each other.

‡ Sex-specific quartiles of height: males (<172 cm, 172–175 cm, 176–180 cm, ≥181 cm) and females (<159 cm, 159–162 cm, 163–168 cm, ≥169 cm).

§ WHO criteria: underweight (≤18.4 kg/m^2), normal weight (18.5–24 kg/m^2), overweight (25–29 kg/m^2), obese (≥30 kg/m^2).

DISCUSSION

We found an inverse association between body mass index and suicide in both females and males. This effect was only minimally influenced by extensive adjustment for sociodemographic and lifestyle variables, including smoking, exercise, and alcohol intake. In contrast, the association of shorter height with suicide was largely confounded by participants' sociodemographic and psychological characteristics. In keeping with some previous studies, our study found a positive prospective association of body mass index with depression, but not anxiety. Because depression is a major risk factor for suicide (18), these results imply that the inverse association of body mass index with suicide is unlikely to be explained by the association of body mass index with common mental disorders.

Strengths and limitations

HUNT is a community-based study of adult males and females with a high baseline response rate (almost 90 percent). We were able to control for several potential confounders not examined in some earlier studies. Furthermore, weight and height were measured by trained nurses, thus avoiding reporting bias.

There are several limitations to our analysis. First, there was no baseline assessment of psychiatric morbidity by use of a validated instrument. Nevertheless, there was no indication that symptoms relating to common mental disorders confounded the body mass index–suicide association in our study. Second, we had only a one-off measure of body mass index. Of note, among participants measured in both HUNT 1 and HUNT 2, the correlation of body mass index across these two time points was high ($r = 0.83$). Third, it is possible that differential loss to follow-up may have biased the associations between body mass index and depression. This would occur if the relation between body mass index and depression differed in those attending follow-up and those not. Finally, we lacked detailed information on alcohol intake and had no data on diet—both possible confounders of the associations we observed. However, a recent analysis of the Health Professionals Follow-up Study, which controlled for confounding variables including diet, alcohol, incident disease, and social support, found little effect of these variables on body mass index–suicide associations (8).

Associations of height with suicide

The increased suicide risk associated with short stature observed in our study was largely explained by sociodemographic and psychological confounders. This is consistent with a cohort of almost 400,000 middle-aged South Korean men (7). The same effect was seen in relation to the inverse height–depression association. These findings

TABLE 3. Odds ratio for depression (HADS-D* score: ≥8) in HUNT* 2 (1995–1997) by body mass index measured in HUNT 1 (1984–1986) for all persons and separately for males and females, Norway

	All subjects participating in both HUNT 1 and HUNT 2 ($n = 44,396$)			Subsample participating in both HUNT 1 and HUNT 2 with full confounder information ($n = 34,378$)				
	No. of cases with a HADS-D score of ≥8	Adjusted for age		No. of cases with a HADS-D score of ≥8	Adjusted for age		Multivariable adjustment†	
		Odds ratio	95% confidence interval		Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
All persons								
Body mass index (WHO* criteria‡)								
Underweight	54	1.13	0.85, 1.50	42	1.14	0.82, 1.58	0.84	0.60, 1.20
Normal weight	2,789	1.00	Referent	2,150	1.00	Referent	1.00	Referent
Overweight	2,165	1.10	1.03, 1.17	1,617	1.09	1.02, 1.17	1.14	1.05, 1.23
Obese	646	1.25	1.13, 1.37	481	1.32	1.19, 1.48	1.29	1.14, 1.45
Body mass index per SD*	5,654	1.07	1.04, 1.11	4,290	1.09	1.05, 1.13	1.11	1.07, 1.15
Males								
Body mass index (WHO criteria)								
Underweight	7	0.97	0.44, 2.13	7	1.20	0.54, 2.68	0.91	0.39, 2.14
Normal weight	1,253	1.00	Referent	970	1.00	Referent	1.00	Referent
Overweight	1,211	1.08	0.99, 1.18	932	1.09	0.99, 1.20	1.15	1.03, 2.15
Obese	237	1.31	1.12, 1.53	191	1.43	1.20, 2.37	1.41	1.17, 1.70
Body mass index per SD	2,708	1.07	1.03, 1.12	2,100	1.09	1.04, 1.15	1.12	1.06, 1.18
Females								
Body mass index (WHO criteria)								
Underweight	47	1.15	0.84, 1.57	35	1.12	0.78, 1.60	0.80	0.55, 1.18
Normal weight	1,536	1.00	Referent	1,180	1.00	Referent	1.00	Referent
Overweight	954	1.11	1.01, 1.22	685	1.09	0.98, 1.21	1.11	0.99, 1.14
Obese	409	1.21	1.07, 1.37	290	1.25	1.08, 1.45	1.21	1.03, 1.41
Body mass index per SD	2,946	1.07	1.03, 1.12	2,190	1.08	1.02, 1.13	1.09	1.03, 1.15

* HADS-D, Hospital Anxiety and Depression Rating Scale consisting of seven items for depression; HUNT, Nord-Trøndelag Health Study; WHO, World Health Organization; SD, standard deviation.

† Multivariable adjustments for age, sex, education, marital status, smoking (never, former, current), frequency of alcohol use, physical activity, vigor, nervousness, calmness, cheerfulness, and frequency of using tranquilizers.

‡ WHO criteria: underweight (≤18.4 kg/m^2), normal weight (18.5–24 kg/m^2), overweight (25–29 kg/m^2), obese (≥30 kg/m^2).

contrast with those from a Swedish conscript study of more than one million young men (6), where the association was still evident after adjustment for socioeconomic confounders. Differences between the two cohorts (e.g., age, geographic setting) and the range of confounding factors controlled for are possible explanations for the divergent findings.

Body mass index and suicide

Our study adds to a growing body of evidence suggesting that adult body weight or factors influencing body weight affect the complex etiology of suicide. In keeping with recent studies of Swedish conscripts (6) and US health professionals (8), our study showed that adjustment for further factors known to increase the risk of suicide had little influence on the association that we observed. Furthermore, the association of body mass index with suicide persisted after suicides in the 2 first years of the study were excluded from the analysis and when the analysis was restricted to people without symptoms related to common mental disorder at baseline. As associations of body mass index with depression were in the opposite direction to those with suicide, it seems unlikely that our findings are confounded by mental illness at baseline.

In support of our findings, a population-based cohort study of hypertensive men and women (19) reported a lower suicide risk among overweight individuals. Nevertheless, in both studies, there were few suicides in the obese group, and the evidence of a linear association between body mass index and suicide can still not be firmly established. In

TABLE 4. Odds ratio for anxiety (HADS-A* score: ≥8) in HUNT* 2 (1995–1997) by body mass index measured in HUNT 1 (1984–1986) for all persons and separately for males and females, Norway

	All subjects participating in both HUNT 1 and HUNT 2 ($n = 43,372$)			Subsample participating in both HUNT 1 and HUNT 2 with full confounder information ($n = 33,777$)				
	No. of cases with a HADS-A score of ≥8	Adjusted for age		No. of cases with a HADS-A score of ≥8	Adjusted for age		Multivariable adjustment†	
		Odds ratio	95% confidence interval		Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
All persons								
Body mass index (WHO* criteria‡)								
Underweight	106	1.24	0.99, 1.54	83	1.25	0.97, 1.59	1.00	0.76, 1.31
Normal weight	3,870	1.00	Referent	2,995	1.00	Referent	1.00	Referent
Overweight	2,118	0.99	0.93, 1.05	1,613	0.99	0.93, 1.06	1.03	0.96, 1.11
Obese	624	1.11	1.00, 1.22	469	1.16	1.04, 1.30	1.16	1.03, 1.31
Body mass index per SD*	6,718	1.00	0.97, 1.03	5,160	1.00	0.98, 1.04	1.04	1.00, 1.08
Males								
Body mass index (WHO criteria)								
Underweight	13	1.70	0.92, 3.12	12	2.04	1.07, 3.89	1.90	0.96, 3.80
Normal weight	1,281	1.00	Referent	1,010	1.00	Referent	1.00	Referent
Overweight	960	0.99	0.90, 1.08	743	0.98	0.88, 1.08	1.03	0.93, 1.16
Obese	197	1.38	1.17, 1.62	160	1.49	1.24, 1.79	1.50	1.23, 1.83
Body mass index per SD	2,451	1.04	0.99, 1.09	1,925	1.05	0.99, 1.10	1.07	1.01, 1.14
Females								
Body mass index (WHO criteria)								
Underweight	93	1.21	0.96, 1.54	71	1.20	0.91, 1.57	0.93	0.69, 1.25
Normal weight	2,589	1.00	Referent	1,985	1.00	Referent	1.00	Referent
Overweight	1,158	0.98	0.90, 1.06	870	0.99	0.90, 1.09	1.01	0.92, 1.12
Obese	427	0.98	0.87, 1.10	309	1.00	0.87, 1.14	0.99	0.85, 1.15
Body mass index per SD	4,267	0.97	0.93, 1.01	3,235	0.97	0.92, 1.01	1.00	0.95, 1.05

* HADS-A, Hospital Anxiety and Depression Rating Scale consisting of seven items for anxiety; HUNT, Nord-Trøndelag Health Study; WHO, World Health Organization; SD, standard deviation.

† Multivariable adjustments for age, sex, education, marital status, smoking (never, former, current), frequency of alcohol use, physical activity, vigor, nervousness, calmness, cheerfulness, and frequency of using tranquilizers.

‡ WHO criteria: underweight (≤18.4 kg/m^2), normal weight (18.5–24 kg/m^2), overweight (25–29 kg/m^2), obese (≥30 kg/m^2).

contrast, several studies have demonstrated an increased risk of suicidal ideation and suicide attempts in the obese (9, 20, 21). Two of these studies suggested a *U*-shaped association with an increased risk of suicidal ideation and behavior in underweight and overweight subjects (20, 21). These findings indicate that the epidemiology and mechanisms of suicide ideation and suicide attempts differ from those leading to a completed suicide.

Two possible pathways may contribute to the increased risk of suicide associated with low body mass index. First, raised body mass index is a component of the insulin resistance syndrome and is associated with elevated levels of blood cholesterol and triglycerides, which in turn influence circulating tryptophan and brain serotonin levels (22, 23). Neuroendocrine challenge studies show that manipulation of dietary cholesterol in healthy subjects influences central serotonin function (24). A low body mass index, therefore, may result in low levels of tryptophan and serotonin, which are thought to be important in the neurobiology of suicidal behavior (25). This association appears to be independent of depressed mood (26). Postmortem studies have established a strong link between serotonergic hypofunction and suicide. In addition, clinical studies report that serotonergic function predicts the severity of suicidal behavior (27, 28), possibly through effects on impulsivity (29). Further, Ogden et al. (30) recently found that important candidate genes for affective disorder modulate food intake, metabolic functions, and adult body weight in ways that might well explain the inverse association between body weight and suicide risk.

TABLE 5. Odds ratio for anxiety (HADS-A* score: ≥8) and depression (HADS-D* score: ≥8) in HUNT* 2 (1995–1997) by height measured in HUNT 1 (1984–1986), Norway

	All subjects participating in both HUNT 1 and HUNT 2			Subsample participating in both HUNT 1 and HUNT 2 with full confounder information				
	No. of cases with a HADS score of ≥8	Adjusted for age and sex		No. of cases with a HADS score of ≥8	Adjusted for age and sex		Multivariable adjustment†	
		Odds ratio	95% confidence interval		Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
Depression (HADS-D)								
Height in quartiles								
Quartile 1	1,249	1.00	Referent	932	1.00	Referent	1.00	Referent
Quartile 2	1,277	0.91	0.84, 1.00	962	0.89	0.81, 0.98	0.92	0.83, 1.02
Quartile 3	1,571	0.96	0.88, 1.04	1,195	0.92	0.84, 1.01	0.99	0.89, 1.09
Quartile 4	1,557	0.93	0.85, 1.01	1,201	0.90	0.81, 0.99	0.98	0.88, 1.09
Height per SD* (sex specific‡)	5,654	0.97	0.94, 1.00	4,290	0.96	0.93, 1.00	1.00	0.96, 1.03
Anxiety (HADS-A)								
Height in quartiles								
Quartile 1	1,207	1.00	Referent	908	1.00	Referent	1.00	Referent
Quartile 2	1,537	0.98	0.90, 1.06	1,172	0.96	0.87, 1.06	0.98	0.89, 1.08
Quartile 3	1,842	0.89	0.82, 0.97	1,418	0.88	0.80, 0.97	0.90	0.82, 1.00
Quartile 4	2,132	0.88	0.81, 0.95	1,662	0.87	0.80, 0.96	0.93	0.84, 1.02
Height per SD (sex specific)	6,718	0.94	0.91, 0.97	5,160	0.95	0.91, 0.98	0.97	0.93, 1.00

* HADS-A, Hospital Anxiety and Depression Rating Scale consisting of seven items for anxiety; HADS-D, Hospital Anxiety and Depression Rating Scale consisting of seven items for depression; HUNT, Nord-Trøndelag Health Study; SD, standard deviation.

† Multivariable adjustments for age, sex, education, marital status, smoking (never, former, current), frequency of alcohol use, physical activity, vigor, nervousness, calmness, cheerfulness, and frequency of using tranquilizers.

‡ Sex-specific quartiles of height: males (<172 cm, 172–175 cm, 176–180 cm, ≥181 cm) and females (<159 cm, 159–162 cm, 163–168 cm, ≥169 cm).

Although low cholesterol levels have been associated with an increased suicide risk in numerous studies, the causal nature of this association is uncertain (9, 31–33).

The second possible pathway involves leptin, a hormone secreted from adipose tissue that regulates body weight. Leptin has a positive psychological effect on rats mediated by receptors in the limbic system (34). A clinical study showed significantly lower serum cholesterol and leptin levels in 24 suicide attempters compared with the healthy controls (35). In keeping with these findings, cholesterol and leptin were inversely associated with impulsivity and aggression in patients with borderline personality disorders, yet showed no association with comorbid depression (36). With regard to the metabolic syndrome, plasma leptin levels show a positive cross-sectional association with body mass index and triglycerides (37).

The association of body mass index with anxiety and depression

Depression can suppress or increase appetite, leading to a decline or increase in weight. Previous studies have reported inconsistent findings concerning the cross-sectional association of increased weight and factors associated with increased weight, such as insulin resistance, with depression (20, 38–43). However, prospective population studies from the Nordic countries (10) and the United States (11) have demonstrated a positive association between obesity (body mass index: ≥30) and subsequent depression in both genders. For the most part, previous studies have not investigated associations across the full range of body mass index values. Differences in the measurements used to assess weight might also account for some of these gender-specific findings, as several large population-based cohort studies have found that body mass index consistently predicts depression in women, while measures of central obesity may be more closely associated with depression in males (10, 20, 42). Several of the previous studies used self-report data on height and weight (10, 20, 39, 40) and therefore may have underestimated obesity in their samples. Our study confirmed the association of body mass index with increased long-term risk for depression in both males and females, and it indicates that this is a linear effect across the full body mass index range. The possible mechanisms underlying this association are unclear but may include the adverse psychological effects on body image of large body size or the effect of lower levels of physical activity on both mood and weight.

Interpretation of the conflicting findings of body mass index with depression and suicide

Our results suggest that the inverse body mass index–suicide association is likely to be mediated by mechanisms other than depression. Although depression and suicide are highly associated, their epidemiology shows important discrepancies. In industrialized nations, for example, depression and self-harm are more prevalent in females than males, yet the rate of completed suicide in men is 3–4 times that in women. Furthermore, depression is just one of a range of psychiatric disorders and social processes contributing to suicide; others include substance misuse and schizophrenia. Associations of weight with these disorders and with impulsivity may differ from those with depression. The biologic mechanisms underlying an impulsive suicide in a situation of acute stress may be different from those suicides occurring in the context of long-term mental disorder.

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