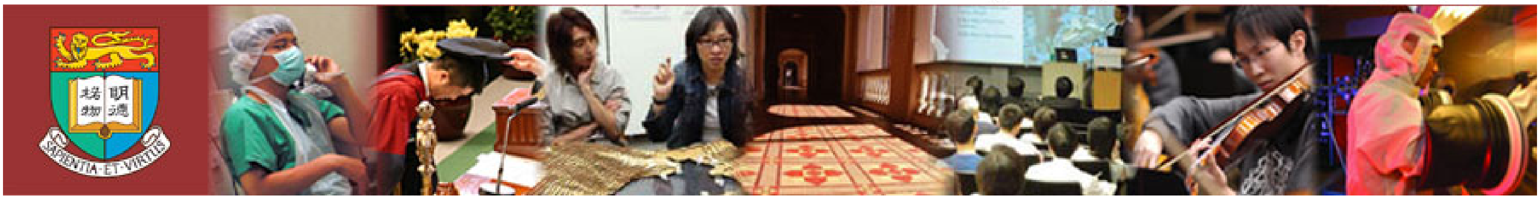

Title	Adiposity, its related biologic risk factors, and suicide: a cohort study of 542,088 Taiwanese adults
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ADIPOSITY, ITS RELATED BIOLOGICAL RISK FACTORS AND SUICIDE MORTALITY: A COHORT STUDY OF 542,088 TAIWANESE ADULTS

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ABSTRACT

Recent studies in Western nations have found inverse associations of body mass index (BMI) with suicide. However, it is uncertain whether the association is similar in non-Western settings and biological pathways underlying the association are unclear. We investigated these issues in a cohort of 542,088 Taiwanese aged 20 years or above (1994-2008) who participated in a health check-up program; there were 573 suicides over a mean 8.1 years follow-up. There was a J-shaped association of BMI with suicide risk (*P* for the quadratic term=0.033) but little evidence for a linear association; compared with individuals whose BMI was 18.5-22.9 kg/m^2, adjusted hazard ratios for those with a BMI < 18.5 kg/m^2 and >= 35 kg/m^2 were 1.56 (95% confidence interval [CI]: 1.07, 2.28) and 3.62 (95% CI: 1.59, 8.22) respectively. High waist-hip ratio was associated with increased risk of suicide. There was some evidence for a reverse J-shaped association of systolic blood pressure and high-density lipoprotein cholesterol with suicide and an association of higher triglyceride level with increased suicide risk; these associations did not appear to mediate the associations of BMI and waist-hip ratio with suicide. There was little evidence for associations with fasting glucose, total cholesterol or low-density lipoprotein cholesterol.

body mass index; cholesterol; cohort studies; suicide; systolic blood pressure; Taiwan;

triglyceride; waist-hip ratio

Abbreviations: BMI, body mass index; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; PUFA, polyunsaturated fatty acid; SD, standard deviation

An emerging body of research indicates that body mass index (BMI, a measure of adiposity) is inversely associated with suicide risk. Greater BMI has been found to be related to a stepwise decreased risk of completed suicide in several large cohorts from Western nations including the UK (1), Sweden (2), Norway (3, 4) and the US (5-8). Similar associations with attempted suicide are also reported (9, 10). These associations are found across the whole range of BMI and persist after controlling for potential confounding factors such as socioeconomic position, smoking and alcohol use. Such findings are intriguing as obesity has been associated with stigma (11) and increased risk of depression (12), and depression is a well-established risk factor for suicide (13). With the exception of one recent Chinese study (14), analysis of the adiposity-suicide relationship has generally been restricted to Western settings.

Biological mechanisms underlying the association of low BMI with suicide may involve metabolic consequences of adiposity such as insulin resistance, a syndrome associated with high BMI and raised levels of insulin and fatty acids. Increased blood levels of fatty acids may raise levels of circulating tryptophan, which may in turn increase brain serotonin (15), an important neurotransmitter associated with reduced impulsivity and suicidality (16). Suicide risk was found to decrease with increasing numbers of markers of insulin resistance such as high BMI, high systolic blood pressure and low high-density lipoprotein cholesterol in one Finnish study (17). It is also postulated that lower circulating cholesterol levels, resulting from lower BMI, may reduce cerebral serotonin (18) and thus predispose to suicidal behaviours (19). While a number of studies have found an association of suicide risk with low blood cholesterol level, findings are inconsistent (20).

To assess whether the association of adiposity with suicide is similar in non-Western settings and possible biological pathways underlying the association, we have investigated the risk of suicide in relation to a range of adiposity measures (BMI, waist circumstance and waist-hip ratio) and related physiological or biochemical changes (systolic blood pressure, fasting glucose, cholesterol and triglyceride) in a large sample of Taiwanese adults.

MATERIALS AND METHODS

Participants

The study cohort consists of 542,088 Taiwanese adults aged 20 years or above who participated in a large health check-up program run by a private company (MJ Health Management Institution, Taiwan; https://www.mjclinic.com.tw) from 1994. Program participants undergo a series of physical examinations and biochemical tests using standardized procedures, as described elsewhere (21). Figure 1 shows a flow chart of the participants included in the study. The final numbers of the subsamples that had complete information on potential confounders and were included in the multivariable analyses for i) BMI, ii) waist circumference and waist-hip ratio, iii) systolic blood pressure, fasting glucose, total cholesterol and triglyceride, and iv) high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were 408,075 (75.3% of the total cohort), 345,357 (63.7%), 406,610 (75.0%) and 377,056 (69.6%) respectively.

Measurements of adiposity and related biological factors

Participants were measured barefoot and wearing light clothes. Weight (to the nearest 0.1 kg) and height (to the nearest mm) were measured using an auto-anthropometer, Nakamura KN-5000A (Nakamura, Tokyo, Japan). Waist circumference (to the nearest mm) was measured at the midpoint between the lower end of rib cage and the crest of the ilium. Hip circumference (to the nearest mm) was measured around the pelvis at the point of maximal protrusion of the buttocks. Blood pressure on the right arm was measured twice at 10 min intervals, with the participants seated after a 5-min rest, using a computerized auto-mercury-sphygmomanometer, Citizen CH-5000 (Citizen, Tokyo, Japan); the mean of two measurements was used for the analysis. Fasting (overnight) blood was collected for the measurement of glucose, total cholesterol, HDL-C, LDL-C and triglyceride using the Hitachi 7150 auto-analyser (Hitachi, Tokyo, Japan). Study participants had given written consent after complete description of the use of data collected from the health check-up for research. The study was approved by the National Health Research Institutes, Taiwan, and the MJ Health Management Institution.

Ascertainment of suicide mortality

Suicide deaths up to December 31, 2008 were obtained through linkage with Taiwan’s national cause-of-death register, using the International Classification of Diseases Ninth Revision codes E950-E959. Previous research indicates that, in keeping with findings seen in Western nations, many Taiwanese deaths coded as undetermined intent (E980-E989), accidental pesticide poisoning (E863) and accidental suffocation (E913) are likely to be misclassified suicides (22). We therefore included these deaths in our definition of suicide. In a sensitivity analysis we included certified suicides coded as E950-E959 only.

Statistical analysis

Sex-specific *z* scores for adiposity measures (BMI, waist circumstance and waist-hip ratio), systolic blood pressure and biochemical levels (fasting glucose, total cholesterol, HDL-C, LDL-C and triglyceride) were calculated as the number of standard deviations above (positive values) or below (negative values) the mean. BMI was also categorized into seven groups according to the World Health Organization criteria (23), with additional cut-off points proposed for Asian populations (24) (underweight: <18.5; normal weight: 18.5-22.9 and 23.0-24.9; overweight: 25.0-26.9 and 27.0-29.9; grade I obesity: 30.0-34.9; and grade II and III obesity: >=35), and other risk factors into quintiles.

Cox proportional hazards models were used to investigate the association of adiposity and associated risk factors with suicide. Time at entry was the date of recruitment; time of exit was December 31, 2008 or the date of death if earlier. The proportional hazards assumption was assessed by plotting Schoenfeld residuals versus time and examining their correlation.

We initially controlled for sex and age using the full sample. To test whether the associations differ by sex or age, we included interaction terms in the models. To investigate evidence for non-linear associations we performed likelihood ratio tests comparing models with and without the quadratic terms for *z* scores of variables investigated. We used multivariable models to investigate the effect on the association of simultaneously controlling for sex, age, marital status (single, married, divorced or separated, widowed), education (middle school or below, high school, junior college, college or higher), smoking (never, former, current), alcohol use (no or occasional use, former drinking, regular drinking), physical activity (inactive, low, moderate or high), history of diabetes and history of cancer. Information on these potential confounders was obtained from the baseline questionnaire completed by participants.

Severe mental illness and use of psychotropic drugs are associated with both suicide risk and weight loss/gain or metabolic abnormalities (e.g. high lipid levels) (25). To assess their possible impact on the associations of our exposures with suicide, we conducted two sensitivity analyses. First, in the subset of participants with data on medicine use we controlled for the use of psychotropic drugs in multivariable models. Second, in keeping with previous studies (2, 3) we excluded all suicides occurring in the first two years of follow-up as BMI in these participants was more likely to be influenced by any severe mental illness at baseline. All analyses in this study were conducted using SAS software, version 9.1 (SAS Institute).

RESULTS

Participant characteristics

Among the total cohort of 542,088 participants we identified 573 certified or possible suicides (455 [79.4%] certified suicides, 104 [18.2%] deaths of undetermined intent, 9 [1.6%] accidental deaths by pesticide poisoning and 5 [0.9%] accidental deaths by suffocation) over an average 8.1-year follow-up period. The crude suicide rates were 16.2 and 10.4 per 100,000 person-years for males and females respectively. The mean age at baseline was 41.2 years for males and 41.1 years for females.

At baseline, mean BMI was 23.9 (standard deviation [SD] 3.4) kg/m^2 for males and 22.1 (SD 3.6) kg/m^2 for females; corresponding figures for waist circumference and waist-hip ratio were 82.3 (SD 9.2) cm and 0.86 (SD 0.07) for males and 71.6 (SD 8.9) cm and 0.77 (SD 0.06) for females respectively. Overweight and obesity were more common in men than women – the proportions of males who were underweight, normal, overweight and obese were 4.1%, 61.9%, 29.8% and 4.3%; the corresponding figures for females were 12.0%, 66.7%, 17.7% and 3.6%.

Compared with participants without information on socio-demographic and health-related factors, the 408,075 participants (356 certified or possible suicides) with these data were slightly younger (40.3 versus 43.3 years) and more likely to be male (49.4% versus 42.2%). Characteristics of the 408,075 participants are shown in Table 1. Underweight subjects and very obese males were younger than those in other BMI categories. Individuals with a high BMI were more likely to have lower educational levels (females) and diabetes than those with a lower BMI. The proportions of individuals who were current smokers, unmarried or physically inactive were highest at the high and low extremes of the BMI distributions. The prevalence of current smoking was high in male participants (40.6%) but low in females (6.7%). High BMI was associated with higher blood pressure, fasting glucose, total cholesterol, LDL-C and triglyceride but lower HDL-C.

Body mass index and suicide

In sex- and age-adjusted models based on data for the total cohort, there was little evidence for a linear association of BMI *z* score with suicide risk (hazard ratio [HR]=0.94 per one SD increase, 95% confidence interval [CI]: 0.86, 1.02) (Table 2). There was evidence for a quadratic relationship (*P* for likelihood ratio test=0.033), in keeping with the finding of increased suicide risk in both underweight and extremely obese subjects (Table 2). There was no evidence for sex or age differences in associations of BMI with suicide (both *P* values for interaction > 0.10); in age-adjusted models HRs for suicide per one SD increase in BMI were 0.98 (95% CI: 0.87, 1.10) for males and 0.88 (95% CI: 0.77, 1.03) for females.

Associations were very similar in the subsample with information on confounders (Table 2). In separate sex- and age-adjusted analyses both current smoking (HR=2.16, 95% CI: 1.69, 2.76) and regular drinking (HR=1.78, 95% CI: 1.30, 2.43) were associated with increased risk of suicide, but there was no strong evidence for interactions with BMI in relation to suicide risk (both *P* values for interaction > 0.10). Stratified analyses (fully adjusted) by smoking or drinking status showed somewhat weak evidence for an inverse association of BMI with suicide among smokers (HR=0.87, 95% CI: 0.73, 1.04) but not in non-/former smokers (HR=1.01, 95% CI: 0.87, 1.17); there was no strong evidence for a linear association in regular drinkers (HR=0.94, 95% CI: 0.69, 1.27) or non-/occasional/former drinkers (HR=0.94, 95% CI: 0.84, 1.06).

In the subsample with information on psychotropic drug use, sex- and age-adjusted analyses showed a strong association of this variable with suicide risk (HR=13.79, 95% CI: 8.43, 22.55); when further controlling for the use of psychotropic drugs, there was still limited evidence for a linear association of BMI with suicide (HR=0.92, 95% CI: 0.78, 1.07). Results were similar when excluding all suicides occurring in the first two years after baseline measurements or restricting analyses to certified suicides only (data not shown).

Waist circumference, waist-hip ratio and suicide

Waist circumference was not associated with risk of suicide; there was no evidence for an association in the total sample or the subsample with full information on socio-demographic and health-related variables (Table 2). Greater waist-hip ratio was associated with a higher suicide risk. In sex- and age-adjusted models based on the total cohort, HR per SD increase in waist-hip ratio was 1.04 (95% CI: 1.01, 1.07). This association did not differ by sex, age, smoking or drinking status (all *P* values for interaction > 0.10). When we examined associations using quintiles, there appeared to be a threshold effect, with increased suicide risk only clearly increasing in those in the top two quintiles and statistical evidence for a curvilinear association (*P* for likelihood ratio test comparing the model with a quadratic term to that without=0.018). Results were similar in the subset of participants with full information on confounders. Results remained unchanged in sensitivity analyses further adjusting for psychotropic drug use or excluding all suicides occurring in the first two years of follow-up, as well as in analyses based on certified suicides only (data not shown).

Biological factors related to adiposity and suicide

There was no evidence for a linear association of suicide risk with systolic blood pressure (Table 3), although there was evidence for a quadratic relationship (*P* for likelihood ratio test=0.005), with increased risk towards the extremes of systolic blood pressure distributions (a reverse J-shaped association). Fasting glucose was not associated with suicide risk in the total sample when adjusting for sex and age; in the subsample with information on confounders there was weak evidence for an association of higher glucose with lower suicide risk (fully adjusted HR per SD increase=0.90, 95% CI: 0.80, 1.03). There was no evidence for an association of suicide risk with total cholesterol, while there was some evidence for a quadratic relationship between HDL-C and suicide, with increased suicide risk towards the two ends of the HDL-C distribution (*P* for likelihood ratio test=0.039). There was limited evidence for an association of LDL-C with suicide risk.

In the sex- and age-adjusted model for the total sample, higher triglyceride was associated with greater suicide risk (HR per SD increase=1.08, 95% CI: 1.03, 1.13). When restricting to participants with information on potential confounders, this association was similar in the sex- and age-adjusted model but somewhat attenuated after adjusting for potential confounders (HR=1.06, 95% CI: 0.99, 1.13). In a sensitivity analysis further controlling for psychotropic drug use, the association was similar (HR=1.07, 95% CI: 0.98, 1.17). Individuals in the highest quintile of triglyceride had 28-44% increased risk of suicide compared to those in the lowest quintile.

When assessing the impact of controlling for systolic blood pressure, HDL-C and triglyceride, given the evidence for their associations with suicide, we found similar associations of BMI/waist-hip ratio with suicide when controlling for each of the three biological markers respectively (data not shown).

DISCUSSION

In contrast to the linear inverse association of BMI with suicide in several Western cohorts (1-8), we found only limited evidence of such a relationship in this Taiwanese study. Suicide risks were increased in both underweight and extremely obese individuals. There was also evidence for quadratic relationships of waist-hip ratio, systolic blood pressure and HDL-C with suicide. Greater triglyceride levels were associated with a higher risk of suicide. The associations of systolic blood pressure, HDL-C and triglycerides with suicide did not appear to mediate the associations of BMI and waist-hip ratio with suicide. We found limited evidence that waist circumference, fasting glucose, total cholesterol or LDL-C were associated with suicide.

Strengths and limitations

This study, to the best of our knowledge, is the first large cohort study to investigate the association of a range of adiposity measures and related biological markers with risk of suicide in a non-Western setting. Anthropometric data were measured using standardized procedures as part of a comprehensive health check. The study has several limitations. First, associations could be confounded by unmeasured factors; for example, we had no detailed information on psychiatric morbidity (e.g. depression), although associations were similar in models controlling for a proxy indicator of psychiatric disorders (i.e. psychotropic drug use). Second, adiposity and related biological markers were measured once only at the baseline assessment – repeated measures of these factors and psychiatric morbidity may provide further information on their relationships with suicide. Third, the cohort was derived from a privately run health check-up program. However, the prevalence of obesity and other characteristics such as smoking in this cohort was similar to that shown in a national survey in 2000-2001 (26, 27), although suicide rates in this cohort were slightly lower than those for Taiwan's population (8.4 versus 11.9 per 100,000, age-standardized rates) (28).

Association of adiposity with suicide

We found an increased risk of suicide in both underweight and extremely obese individuals. A recent study of British male government employees also showed increased suicide risk in obese men (BMI>=30) (29), although evidence for increased suicide risk in individuals with obesity/extreme obesity remains to be firmly established because there were few suicides in the obese in the British study (n=6) or the very obese group in our study (n=6). Unlike findings from several large cohort studies in Western countries (1-8), we did not find that suicide risk decreased linearly from low to high BMI, although the 95% confidence interval estimates of the association with BMI from our study overlapped those reported in previous research - in one Norwegian cohort the hazard ratio for suicide was estimated to be 0.82 (95% CI: 0.68, 0.98) per one SD increase in BMI (3) while our estimate based on the total cohort was 0.94 (95% CI: 0.86, 1.02).

It is possible that the obesity-suicide association differs in Western and non-Western settings, although a recent cohort study of 170,000 Chinese adults found some evidence of an inverse association of BMI with suicide (14). If our study findings do signal a difference in associations between Asian and Western settings possible explanations include differing cultural attitudes towards body size and dietary differences. In traditional Chinese culture thinness is associated with poverty, misfortune and poor health, while a certain degree of 'fullness' symbolizes prosperity and longevity (30), in contrast to the Western pattern of attitudes towards body size. One dietary factor, the polyunsaturated fatty acids (PUFAs), has been linked to decreased risk of depression and suicidal ideation (31), and a recent study showed that the Taiwanese population had the highest percentage (% of total dietary energy intake) of PUFAs among 28 countries investigated (32). However, one US study found that the inverse association of BMI with suicide persisted after controlling for dietary omega-3 fatty acids, an important type of PUFAs (7).

Our finding that greater waist-hip ratio is associated with greater suicide risk differs from one previous US study that found weak evidence for higher suicide risk in men with lower values of self-reported waist-hip ratios (7). In the absence of other studies of this association it remains unclear what the true association of waist-hip ratio is with suicide risk.

Association of biological markers of adiposity with suicide

In general, beyond studies of the associations of BMI/cholesterol with suicide there are few studies investigating other markers of adiposity, or adiposity related mediators, in relation to suicide risk. Of the range of potential mediators that we examined only three related to suicide risk – systolic blood pressure and HDL-C with a reverse J-shaped association and triglyceride with a positive association – but controlling for these factors in multivariable models indicated that they did not mediate associations of adiposity with suicide. Findings from previous studies of the relationship between blood pressure and suicide are inconsistent (17, 33-35). To our knowledge no previous study has investigated the association of triglyceride with risk of completed suicide; the small number of studies that have examined its association with suicide attempts have produced inconsistent findings (36-40).

Our finding of no evidence for an association of total cholesterol with suicide risk is consistent with a meta-analysis of 19 randomized control trials, which reported no relation of cholesterol lowering treatments and non-illness mortality (including suicide and accident) (41). Our finding that fasting glucose is not associated with suicide risk is also consistent with one previous study (33).

Possible explanations for associations

This association of underweight with suicide risk may be confounded by psychopathology such as anorexia nervosa that is related to both low body weight and increased risk of suicide (42). As discussed earlier, it is also possible that physiological changes associated with low body weight, including low circulating fatty acids, may influence neurotransmitter level which in turn affects impulsivity and suicide risk (17), but we found no evidence that lower levels of fasting glucose, cholesterol or triglyceride were associated with increased risk. Indeed higher triglyceride levels were associated with increased risk.

Increased abdominal fat, indicated by high waist-hip ratios, has been found to be associated with heightened cortisol elevations in response to stress (43) and depressive symptoms (44) and may lead to increased suicide risk. Alternatively, use of certain psychotropic drugs (e.g. some antipsychotics) may result in greater waist-hip ratios (45) and explain an association with suicide. However, our results remained unchanged when controlling for psychotropic drug use.

One biological factor that may contribute to the association of high triglyceride with increased suicide risk, as mentioned earlier, is dietary PUFAs, which have been found to be associated with both reduced triglyceride level (46) and reduced risk of having suicidal ideation (31). Another possible underlying mechanism is hyperactivity of the hypothalamic-pituitary-adrenocortical axis; increased circulating cortisol level has been linked to both hypertriglyceridemia (47) and depression (48), although its other related physiological effects such as hypercholesterolemia and hypertension were not found to be associated with suicide risk in our study.

Implications

Our study indicates that associations of adiposity with suicide risk may differ in Asian populations from those observed in the West. A better understanding of the complex interactions between adiposity, its related biological factors and suicide may pave the way to new findings about the causes of suicide and, possibly, novel targets for intervention and drug development.

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FIGURES

Figure 1. Flow chart of participants of the MJ health check-up program, Taiwan, 1994-2008 (N = 542,088). From 1996 the program included a self-completed questionnaire to collect baseline information on socio-demographic and health-related factors. From 1998 the questionnaire added in questions on the use of medications, including psychotropic drugs. Subsamples of the participants were used in the sex and age-adjusted analyses (A), main multivariable analyses (B) and sensitivity analyses additionally controlling for psychotropic drug use (C).

TABLES

Table 1. Characteristics of the Participants With Socio-demographic and Health-related Information, According to Body Mass Index Categories (n = 408,075), MJ Health Check-up Program, Taiwan, 1994-2008.

	Body mass index categories (kg/m^2)														All participants	
Characteristic	<18.5		18.5-22.9		23.0-24.9		25.0-26.9		27.0-29.9		30.0-34.9		>=35.0		(by sex)	
Males	(n = 8,062)		(n = 74,604)		(n = 50,631)		(n = 36,191)		(n = 23,449)		(n = 7,612)		(n = 1,101)		(n = 201,650)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	36.8	14.7	38.7	13.7	41.5	13.3	42.7	13.1	42.3	12.9	39.5	12.4	35.0	10.6	40.5	13.5
Systolic blood pressure (mmHg)[a]	114.9	15.3	119.5	15.9	123.2	16.5	126.1	17.1	129.0	17.2	132.3	17.5	136.7	17.7	123.1	17.0
Fasting glucose (mg/dl)[a]	95.0	19.6	98.1	21.5	101.0	22.2	103.3	24.3	105.3	25.9	107.8	29.7	108.9	28.6	100.9	23.3
Total cholesterol (mg/dl)[a]	177.5	34.1	188.5	35.8	198.2	36.4	202.5	37.2	205.1	37.8	206.1	39.3	203.9	37.3	195.7	37.3
HDL cholesterol (mg/dl)[a]	55.0	14.5	49.5	13.2	45.6	12.1	43.7	11.4	42.4	10.9	41.6	10.5	40.9	10.1	46.5	12.7
LDL cholesterol (mg/dl)[a]	107.0	30.5	118.5	32.0	125.9	32.1	128.3	32.6	128.7	33.1	127.2	33.1	125.9	31.5	123.2	32.7
Triglyceride (mg/dl)[a]	79.9	49.8	106.1	81.1	141.0	111.3	164.7	138.5	187.0	153.2	206.4	190.2	204.5	172.3	138.1	120.3
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Married	4,263	52.9	46,461	62.3	37,363	73.8	28,146	77.8	18,031	76.9	5,268	69.2	588	53.4	140,120	69.5
College or higher education	2,496	31.0	27,711	37.1	18,967	37.5	12,722	35.2	7,830	33.4	2,614	34.3	405	36.8	72,745	36.1
Current smoker	3,746	46.5	30,016	40.2	19,694	38.9	14,493	40.0	9,744	41.6	3,322	43.6	510	46.3	81,525	40.4
Regular alcohol use	707	8.8	7,483	10.0	5,539	10.9	4,285	11.8	2,861	12.2	793	10.4	80	7.3	21,748	10.8
Physically inactive	4,488	55.7	34,091	45.7	22,251	43.9	16,289	45.0	11,209	47.8	3,841	50.5	624	56.7	92,793	46.0
History of diabetes	154	1.9	2,453	3.3	2,488	4.9	2,509	6.9	2,100	9.0	881	11.6	152	13.8	10,737	5.3
History of cancer	77	1.0	472	0.6	252	0.5	203	0.6	100	0.4	30	0.4	5	0.5	1,139	0.6
Use of psychotropic drugs[b]	58	1.0	397	0.7	217	0.6	151	0.6	105	0.6	39	0.6	5	0.5	972	0.6
Females	(n = 27,239)		(n = 107,774)		(n = 31,437)		(n = 19,413)		(n = 13,868)		(n = 5,767)		(n = 927)		(n = 206,425)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	31.2	9.3	37.4	12.0	45.9	13.6	48.8	13.5	50.0	13.3	48.8	13.9	44.3	14.1	40.1	13.6
Systolic blood pressure (mmHg)[a]	107.1	13.4	112.0	16.6	122.3	21.1	127.6	21.9	131.7	22.1	135.1	22.1	137.7	21.3	116.4	19.9
Fasting glucose (mg/dl)[a]	90.8	11.4	94.1	17.0	100.2	24.7	103.3	28.3	106.9	31.8	110.1	34.7	112.6	35.4	96.8	21.7
Total cholesterol (mg/dl)[a]	178.3	31.7	187.1	34.9	199.8	39.0	204.8	39.5	207.4	39.5	208.1	39.1	207.5	40.9	191.6	37.3
HDL cholesterol (mg/dl)[a]	63.8	15.3	59.0	15.1	54.0	14.5	51.7	13.9	50.4	13.4	49.2	12.9	48.0	12.2	57.2	15.3
LDL cholesterol (mg/dl)[a]	101.2	28.1	112.0	31.0	123.6	33.9	127.7	34.5	129.2	34.1	129.6	34.2	129.1	35.4	115.7	33.0
Triglyceride (mg/dl)[a]	66.1	28.5	82.7	54.0	116.2	91.2	132.7	97.7	146.7	105.8	153.8	104.8	160.1	106.0	96.9	74.7
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Married	12,107	44.4	67,021	62.2	22,650	72.0	14,171	73.0	10,058	72.5	3,974	68.9	538	58.0	130,519	63.2
College or higher education	10,712	39.3	33,685	31.3	5,428	17.3	2,443	12.6	1,386	10.0	521	9.0	117	12.6	54,292	26.3
Current smoker	2,712	10.0	7,377	6.8	1,628	5.2	892	4.6	695	5.0	356	6.2	78	8.4	13,738	6.7
Regular alcohol use	475	1.7	1,814	1.7	545	1.7	341	1.8	210	1.5	96	1.7	13	1.4	3,494	1.7
Physically inactive	18,593	68.3	63,093	58.5	16,619	52.9	10,333	53.2	7,783	56.1	3,419	59.3	629	67.9	120,469	58.4
History of diabetes	179	0.7	2,216	2.1	1,926	6.1	1,663	8.6	1,663	12.0	909	15.8	178	19.2	8,734	4.2
History of cancer	198	0.7	1,455	1.4	677	2.2	492	2.5	393	2.8	139	2.4	19	2.0	3,373	1.6
Use of psychotropic drugs[b]	139	0.6	614	0.7	255	1.1	150	1.1	116	1.2	50	1.2	11	1.6	1,335	0.9

Abbreviation: SD, standard deviation.

[a]In the subsample with information on biochemical tests (n = 200,915 for males and 205,695 for females, except n = 184,2824 for males and 192,774 for females for HDL-C and LDL-C).

[b]In the subsample with information of the use of psychotropic drugs (n = 150,515 for males and 155,326 for females).

Table 2. Hazard Ratio for Suicide by Body Mass Index (According to the WHO Classification and per SD Increase), Waist Circumference and Waist-hip Ratio (in Sex-specific Quintiles and per SD Increase), MJ Health Check-up Program, Taiwan, 1994-2008.

	Total cohort[a]					Subsample with confounder information[a]							
			Adjusted for sex and age					Adjusted for sex and age			Multivariable adjustment[b]		
Covariates	Number of participants	Number of suicides	Hazard ratio	95% CI	*P* value	Number of participants	Number of suicides	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
Body mass index[c]													
<18.5	44,545	47	1.40	1.02 , 1.93		35,301	35	1.62	1.11 , 2.36		1.56	1.07 , 2.28	
18.5-22.9	239,050	229	1.00	Reference		182,378	139	1.00	Reference		1.00	Reference	
23.0-24.9	110,022	127	0.99	0.80 , 1.24		82,068	86	1.14	0.87 , 1.51		1.18	0.89 , 1.55	
25.0-26.9	75,733	90	0.97	0.76 , 1.25		55,604	48	0.90	0.65 , 1.26		0.91	0.65 , 1.28	
27.0-29.9	51,406	55	0.88	0.66 , 1.19		37,317	31	0.88	0.59 , 1.31		0.87	0.58 , 1.29	
30.0-34.9	18,581	19	0.94	0.59 , 1.50		13,379	11	0.97	0.52 , 1.79		0.91	0.49 , 1.70	
>=35.0	2,751	6	2.42	1.08 , 5.43		2,028	6	4.15	1.83 , 9.39		3.62	1.59 , 8.22	
Per standard deviation (sex-specific)			0.94	0.86 , 1.02	0.14[f]			0.95	0.85 , 1.06	0.35[f]	0.95	0.85 , 1.06	0.35[f]
			P for quadratic term		0.033[g]					0.013[g]			0.050[g]
Waist circumference in quintiles[d]													
Quintile 1	70,637	61	1.00	Reference		63,448	50	1.00	Reference		1.00	Reference	
Quintile 2	67,721	43	1.58	1.07 , 2.35		60,294	35	1.33	0.88 , 2.02		1.25	0.82 , 1.89	
Quintile 3	81,761	46	1.24	0.82 , 1.89		72,199	44	1.05	0.67 , 1.63		1.03	0.66 , 1.61	
Quintile 4	81,580	62	1.24	0.84 , 1.82		71,015	50	1.06	0.71 , 1.60		1.04	0.70 , 1.57	
Quintile 5	91,187	93	1.42	0.99 , 2.04		78,401	83	1.37	0.94 , 2.00		1.30	0.89 , 1.89	
Per standard deviation (sex-specific)			1.02	0.91 , 1.15	0.74[f]			1.09	0.96 , 1.23	0.20[f]	1.08	0.95 ,1.22	0.25[f]
			P for quadratic term		0.063[g]					0.11[g]			0.24[g]
Waist-hip ratio in quintiles[e]													
Quintile 1	56,203	32	1.00	Reference		50,634	27	1.00	Reference		1.00	Reference	
Quintile 2	76,484	45	1.03	0.65 , 1.63		68,407	38	1.03	0.63 , 1.70		1.01	0.62 , 1.67	
Quintile 3	77,819	47	1.02	0.64 , 1.62		68,757	39	1.02	0.62 , 1.69		1.00	0.60 , 1.65	
Quintile 4	88,478	77	1.34	0.86 , 2.07		77,307	67	1.43	0.89 , 2.30		1.36	0.85 , 2.19	
Quintile 5	93,902	104	1.40	0.89 , 2.18		80,252	91	1.55	0.96 , 2.51		1.37	0.84 , 2.23	
Per standard deviation (sex-specific)			1.04	1.01 , 1.07	0.022[f]			1.04	1.01 , 1.07	0.013[f]	1.04	1.00 ,1.07	0.045[f]
			P for quadratic term		0.018[g]					0.008[g]			0.041[g]

Abbreviation: SD, standard deviation; WHO, World Health Organization.

[a]N = 542,088 for total cohort and n = 408,075 for subsample (body mass index) and n = 392,886 for total cohort and 345,357 for subsample (waist-hip ratio and waist circumference).

[b]Multivariable adjustments for sex, age, education, marital status, smoking, frequency of alcohol use, physical activity, diabetes history and cancer history.

[c]Sex-specific quintiles of body mass index (kg/m^2): males (<21.1, 21.1-22.9, 23.0-24.7, 24.8-26.6, >=26.7) and females (<19.3, 19.3-21.3, 21.4-23.2, 23.3-25.4, >=25.5).

[d]Sex-specific quintiles of waist circumference (cm): males (<74.8, 74.8-78.9, 79.0-83.9, 84.0-88.9, >=89.0) and females (<64.0, 64.0-67.9, 68.0-71.9, 72.0-77.9, >=78.0).

[e]Sex-specific quintiles of waist-hip ratio: males (<0.80, 0.80-0.83, 0.84-0.86, 0.87-0.90, >=0.91) and females (<0.71, 0.71-0.73, 0.74-0.76, 0.77-0.80, >=0.81).

[f]*P* value for the linear associations of adiposity measures (body mass index, waist circumference and waist-hip ratio) with suicide (i.e. tests of linear trends), derived by including these adiposity measures as continuous variables (i.e. using their z scores) in the models.

[g]*P* value of likelihood ratio test comparing the goodness of fit of models with and without the quadratic term of the continuous z score. Small *P* value indicates quadratic relationship.

Table 3. Hazard Ratio for Suicide by Systolic Blood Pressure, Fasting Glucose, Total Cholesterol, Triglyceride, High-density Lipoprotein Cholesterol and Low-density Lipoprotein Cholesterol (in Quintiles and per Standard Deviation Increase), MJ Health Check-up Program, Taiwan, 1994-2008.

	Total cohort (n = 537,620)					Subsample with confounder information (n = 406,610)							
			Adjusted for sex and age					Adjusted for sex and age			Multivariable adjustment[a]		
Covariates	Number of participants	Number of suicides	Hazard ratio	95% CI	*P* value	Number of participants	Number of suicides	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
Systolic blood pressure in quintiles[b]													
Quintile 1	110,524	139	1.00	Reference		84,218	87	1.00	Reference		1.00	Reference	
Quintile 2	108,582	109	0.85	0.66 , 1.09		84,672	68	0.81	0.59 , 1.12		0.84	0.61 , 1.16	
Quintile 3	109,380	84	0.61	0.47 , 0.80		84,689	56	0.63	0.45 , 0.89		0.66	0.47 , 0.92	
Quintile 4	99,384	89	0.65	0.50 , 0.86		75,514	51	0.60	0.42 , 0.85		0.62	0.43 , 0.88	
Quintile 5	109,750	151	0.75	0.58 , 0.98		77,517	94	0.81	0.59 , 1.13		0.83	0.60 , 1.16	
Per standard deviation (sex-specific)			0.95	0.87 , 1.04	0.25[f]			1.00	0.90 , 1.12	0.96[f]	1.01	0.90 , 1.13	0.87[f]
			P for quadratic term		0.005[g]					0.001[g]			0.002[g]
Fasting glucose in quintiles[c]													
Quintile 1	116,391	151	1.00	Reference		85,291	91	1.00	Reference		1.00	Reference	
Quintile 2	99,942	96	0.78	0.60 , 1.00		76,377	57	0.71	0.51 , 0.99		0.74	0.53 , 1.03	
Quintile 3	115,161	118	0.82	0.64 , 1.04		89,623	79	0.82	0.61 , 1.11		0.87	0.64 , 1.18	
Quintile 4	104,168	92	0.71	0.55 , 0.93		80,151	62	0.72	0.52 , 1.00		0.77	0.55 , 1.06	
Quintile 5	101,958	115	0.78	0.60 , 1.01		75,168	67	0.70	0.50 , 0.98		0.73	0.52 , 1.02	
Per standard deviation (sex-specific)			0.97	0.89 , 1.05	0.46[f]			0.90	0.79 , 1.03	0.14[f]	0.90	0.80 , 1.03	0.12[f]
			P for quadratic term		0.42[g]					0.41[g]			0.33[g]
Total cholesterol in quintiles[d]													
Quintile 1	110,888	127	1.00	Reference		78,603	69	1.00	Reference		1.00	Reference	
Quintile 2	105,503	111	0.92	0.71 , 1.19		79,566	63	0.86	0.61 , 1.21		0.88	0.62 , 1.24	
Quintile 3	107,906	93	0.73	0.56 , 0.96		82,890	66	0.82	0.59 , 1.16		0.84	0.59 , 1.18	
Quintile 4	108,063	129	0.98	0.76 , 1.25		83,582	77	0.89	0.64 , 1.25		0.91	0.65 , 1.27	
Quintile 5	105,260	112	0.80	0.61 , 1.04		81,969	81	0.85	0.60 , 1.19		0.85	0.61 , 1.19	
Per standard deviation (sex-specific)			0.97	0.89 , 1.05	0.41[f]			0.97	0.87 , 1.08	0.59[f]	0.97	0.87 , 1.08	0.54[f]
			P for quadratic term		0.15[g]					0.40[g]			0.54[g]
Triglyceride in quintiles[e]													
Quintile 1	107,842	91	1.00	Reference		84,060	55	1.00	Reference		1.00	Reference	
Quintile 2	109,128	104	1.03	0.78 , 1.36		83,657	68	1.12	0.79 , 1.60		1.10	0.77 , 1.57	
Quintile 3	105,924	93	0.90	0.67 , 1.20		80,408	62	1.01	0.70 , 1.45		0.97	0.67 , 1.40	
Quintile 4	107,122	128	1.17	0.89 , 1.54		79,968	74	1.15	0.81 , 1.65		1.09	0.76 , 1.57	
Quintile 5	107,604	156	1.33	1.01 , 1.74		78,517	97	1.44	1.02 , 2.03		1.28	0.90 , 1.81	
Per standard deviation (sex-specific)			1.08	1.03 , 1.13	0.001[f]			1.08	1.02 , 1.15	0.007[f]	1.06	0.99 , 1.13	0.087[f]
			P for quadratic term		0.15[g]					0.25[g]			0.47[g]

[a]Multivariable adjustments for sex, age, education, marital status, smoking, frequency of alcohol use, physical activity, diabetes history and cancer history.
[b]Sex-specific quintiles of systolic blood pressure (mmHg): males (<=109, 110-117, 118-126, 127-136, >136) and females (<=100, 101-109, 110-118, 119-132, >132).
[c]Sex-specific quintiles of fasting glucose (mg/dl): males (<=90, 91-94, 95-99, 100-105, >105) and females (<=87, 88-91, 92-95, 96-101, >101).
[d]Sex-specific quintiles of total cholesterol (mg/dl): males (<=163, 164-182, 183-200, 201-223, >223) and females (<=160, 161-178, 179-196, 197-220, >220).
[e]Sex-specific quintiles of triglyceride (mg/dl): males (<=71, 72-95, 96-126, 127-179, >179) and females (<=54, 55-70, 71-90, 91-128, >128).
[f]*P* value for the linear associations of biological markers (systolic blood pressure, fasting glucose, total cholesterol, triglyceride, HDL cholesterol and LDL cholesterol) with suicide (i.e. tests of linear trends), derived by including these biological markers as continuous variables (i.e. using their z scores) in the models.
[g]*P* value of likelihood ratio test comparing the goodness of fit of models with and without the quadratic term of the continuous z score. Small *P* value indicates quadratic relationship.

Table 3. Continued

	Total cohort (n = 437,368)					Subsample with confounder information (n = 377,056)							
			Adjusted for sex and age					Adjusted for sex and age			Multivariable adjustment[a]		
	Number of participants	Number of suicides	Hazard ratio	95% CI	*P* value	Number of participants	Number of suicides	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
HDL cholesterol in quintiles[h]													
Quintile 1	89,880	120	1.00	Reference		75,003	100	1.00	Reference		1.00	Reference	
Quintile 2	86,642	89	0.97	0.74 , 1.28		74,160	73	0.94	0.69 , 1.27		0.97	0.72 , 1.32	
Quintile 3	89,872	66	0.78	0.58 , 1.06		77,853	52	0.72	0.51 , 1.00		0.75	0.53 , 1.05	
Quintile 4	86,902	69	0.93	0.69 , 1.25		75,893	59	0.92	0.66 , 1.27		0.97	0.70 , 1.34	
Quintile 5	84,072	63	0.93	0.68 , 1.26		74,147	52	0.88	0.63 , 1.23		0.91	0.64 , 1.27	
Per standard deviation (sex-specific)			0.97	0.88 , 1.07	0.56[f]			0.94	0.84 , 1.06	0.31[f]	0.96	0.86 , 1.07	0.42[f]
			P for quadratic term		0.039[g]					0.022[g]			0.034[g]
LDL cholesterol in quintiles[i]													
Quintile 1	89,423	81	1.00	Reference		78,594	66	1.00	Reference		1.00	Reference	
Quintile 2	86,647	75	0.84	0.61 , 1.15		75,524	66	0.91	0.65 , 1.28		0.94	0.67 , 1.32	
Quintile 3	88,313	69	0.69	0.50 , 0.95		76,289	58	0.72	0.51 , 1.03		0.76	0.53 , 1.08	
Quintile 4	87,577	92	0.84	0.62 , 1.14		74,768	74	0.86	0.61 , 1.21		0.90	0.64 , 1.26	
Quintile 5	85,440	90	0.74	0.54 , 1.01		71,909	72	0.76	0.54 , 1.08		0.80	0.56 , 1.13	
Per standard deviation (sex-specific)			0.91	0.83 , 1.01	0.080[d]			0.94	0.84 , 1.05	0.24[f]	0.95	0.85 , 1.06	0.33[f]
			P for quadratic term		0.26[g]					0.36[g]			0.54[g]

Abbreviation: HDL, high-density lipoprotein; LDL, low-density lipoprotein.

[h]Sex-specific quintiles of HDL cholesterol (mg/dl): males (<=36, >36-<=42, >42-<=48, >48-<=56, >56) and females (<=43, >43-<=51, >51-<=59, >59-<=69, >69).

[i]Sex-specific quintiles of LDL cholesterol (mg/dl): males (<=96, >96-<=113, >113-<=129, >129-<=149, >149) and females (<=89, >89-<=105, >105-<=121, >121-<=142, >142).