cambridge.org/psm

Original Article

*These authors contributed equally to this work.

†Collaborators are listed at the end of paper.

Cite this article: Geulayov G, Ferrey A, Hawton K, Hermon C, Reeves GK, Green J, Beral V, Floud S, for the Million Women Study Collaborators (2019). Body mass index in midlife and risk of attempted suicide and suicide: prospective study of 1 million UK women. *Psychological Medicine* **49**, 2279–2286. https://doi.org/10.1017/S0033291718003239

Received: 30 April 2018 Revised: 20 July 2018 Accepted: 9 October 2018 First published online: 29 November 2018

Key words:

Body mass index; prospective; self-harm; suicide; weight; women

Author for correspondence: Sarah Floud, E-mail: sarah.floud@ndph.ox.ac.uk

Body mass index in midlife and risk of attempted suicide and suicide: prospective study of 1 million UK women

Galit Geulayov^{1,*}, Anne Ferrey^{2,*}, Keith Hawton¹, Carol Hermon³,

Gillian K. Reeves³, Jane Green³, Valerie Beral³, Sarah Floud³ for the Million

Women Study Collaborators[†]

¹Department of Psychiatry, University of Oxford, Oxford, UK; ²Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK and ³Nuffield Department of Population Health, University of Oxford, Oxford, UK

Abstract

Background. High body mass index (BMI) has been associated with lower risks of suicidal behaviour and being underweight with increased risks. However, evidence is inconsistent and sparse, particularly for women. We aim to study this relationship in a large cohort of UK women.

Methods. In total 1.2 million women, mean age 56 (s.D. 5) years, without prior suicide attempts or other major illness, recruited in 1996–2001 were followed by record linkage to national hospital admission and death databases. Cox regression yielded relative risks (RRs) and 95% confidence intervals (CIs) for attempted suicide and suicide by BMI, adjusted for baseline lifestyle factors and self-reported treatment for depression or anxiety.

Results. After 16 (s.D. 3) years of follow-up, 4930 women attempted suicide and 642 died by suicide. The small proportion (4%) with BMI <20 kg/m² were at clearly greater risk of attempted suicide (RR = 1.38, 95% CI 1.23–1.56) and suicide (RR = 2.10, 1.59–2.78) than women of BMI 20–24.9 kg/m²; p < 0.0001 for both comparisons. Small body size at 10 and 20 years old was also associated with increased risks. Half the cohort had BMIs >25 kg/m² and, while risks were somewhat lower than for BMI 20–24.9 kg/m² (attempted suicide RR = 0.91, 0.86–0.96; p = 0.001; suicide RR = 0.79, 0.67–0.93; p = 0.006), the reductions in risk were not strongly related to level of BMI.

Conclusions. Being underweight is associated with a definite increase in the risk of suicidal behaviour, particularly death by suicide. Residual confounding cannot be excluded for the small and inconsistent decreased risk of suicidal behaviour associated with being overweight or obese.

Introduction

Abnormal body weight has been associated with poor mental health and poor quality of life (McLaren et al., 2008; Audureau et al., 2016). Obesity has also been associated with a high level of stigma (Wang et al., 2004; Seacat et al., 2016), which is a risk factor for poor mental health (Lillis et al., 2011). Therefore a higher risk of suicidal behaviour for those with higher than normal body mass index (BMI) might be expected. However, evidence from prospective cohort studies is inconsistent with this hypothesis, with a lower risk of suicide or attempted suicide found for people who are overweight or obese in most (Magnusson et al., 2006; Kaplan et al., 2007; Mukamal et al., 2007; Bjerkeset et al., 2008; Batty et al., 2010; Mukamal and Miller, 2010; Jee et al., 2011; Gao et al., 2013; McCarthy et al., 2014; Sorberg et al., 2014) but not all studies (Elovainio et al., 2009; Chang et al., 2012; Schneider et al., 2014). Evidence from cohort studies on the risks of suicide or attempted suicide for underweight people suggests that they have a higher risk relative to individuals who have a healthy weight (Magnusson et al., 2006; Kaplan et al., 2007; Batty et al., 2010; Jee et al., 2011; Chang et al., 2012; Gao et al., 2013; McCarthy et al., 2014; Sorberg et al., 2014). However, there have only been three studies that have separately estimated the risks of suicide or attempted suicide in women, and these studies have been underpowered to look at death by suicide (Kaplan et al., 2007; Jee et al., 2011; Gao et al., 2013).

It is possible that the association between BMI and suicidal behaviour is confounded by psychiatric disorders such as depression, which is associated with weight loss and is implicated in suicidal behaviour (Mukamal and Miller, 2010). An examination of the association with body size in early life, before the onset of most psychiatric disorders, could throw some light on this hypothesis, but to our knowledge no other study has used measures of body size at different stages of the lifecourse. The association could also be confounded by factors

© Cambridge University Press 2018



that may raise the risk of suicidal behaviour, such as deprivation and alcohol misuse, as well as by factors that may lower the risk, such as having a partner. Most previous studies have adjusted for these factors. However, having had children could also lower the risk of suicide (Kjaer *et al.*, 2011) and this has not been adjusted for in studies of individuals who are older at baseline. It has also been proposed that the lower risk of suicide or suicide attempt for overweight individuals could be due to their choice of less lethal methods of suicide, either because a highly lethal method such as hanging requires more physical exertion, or because a larger body mass would reduce the likelihood of dying from selfpoisoning (Mukamal and Miller, 2010; McCarthy *et al.*, 2014; Perera *et al.*, 2016). However, few studies have been able to test this hypothesis.

We investigated the association between BMI in midlife and suicidal behaviour separately for attempted suicide and suicide, after excluding major prior illnesses and adjusting for many potential confounders, in a large prospective cohort of women in the UK. This study has accrued about double the number of cases of attempted suicide and of suicide in women than any other prospective study. We were therefore also able to compare the method of suicide employed by women of different BMI and to examine the long-term association between BMI and attempted suicide using reported body size at younger ages.

Methods

Study population and definitions

In total, 1.3 million women, aged 50-64 years old, were recruited to the Million Women Study in 1996-2001 in England and Scotland at the time that they were invited for routine NHS breast screening. At that time, the NHS Breast Screening Programme routinely invited women aged 50-64 years for their mammographic screen, by sending each individual a letter offering them a date and time at a specific screening centre. In 66 (about half) of the screening programme's centres, Million Women Study questionnaires were included in the invitation letter, and approximately 50% of eligible women returned a questionnaire. Thus, the Million Women Study recruited one in four of UK women aged 50-64 years in 1996-2001, with most born between 1935 and 1950. The recruitment questionnaire contained questions on health conditions and socio-demographic, lifestyle and reproductive factors and forms the baseline for the main analysis in the current study. Participants were sent a re-survey questionnaire approximately 3 years later, with a response rate of 65%; this included questions on birth weight, relative body size at 10 years old and 20 years old, recent change in diet, happiness, self-rated health and marital status. The respondents gave written consent to follow-up and the study has ethical approval from the Multi-Centre Research Ethics Committee for Anglia and Oxford (REC 97/5/001). Questionnaires and further details of the data access policies can be viewed online at http://www.millionwomenstudy.org.

The records of study participants were linked electronically using their unique National Health Service (NHS) number and date of birth to routinely collected NHS databases for causespecific deaths, emigrations, cancer registrations and hospital admissions. Information provided to the investigators included the date of each event, with diagnoses coded to the 9th and 10th Revisions of the World Health Organisation's International Classification of Diseases (ICD).

The outcomes for these analyses were: (i) attempted suicide: first hospital admission after baseline coded as 'intentional selfharm' (ICD-10 code X60-X84); and (ii) suicide: death with the underlying cause coded as 'intentional self-harm' (ICD-10 code X60-X84) or as 'undetermined intent' (ICD-10 code Y10-Y34). It is customary in the UK to combine deaths recorded as intentional self-harm and those of undetermined intent as suicides because it is recognised that the majority of deaths of undetermined intent are probable suicides (Office for National Statistics, 2017). ICD-9 codes (E950-59) were used to identify hospital admissions for attempted suicide prior to the study baseline for exclusion purposes, as participants were not asked about prior suicide attempts in the recruitment questionnaire. However hospital admission data were only available from 1st April 1997 for participants in England (Hospital Episode Statistics) and from 1st January 1981 for participants in Scotland (Scottish Morbidity Records).

At recruitment, women were asked for their current weight and height, and these were used to derive BMI in kg/m², categorised as: <20, 20–24.9, 25–29.9, ≥ 30 kg/m². In a validation study where weight and height were measured in a sample of the cohort about 9 years after recruitment, the regression dilution ratio between BMI based on self-reported and measured weight was 0.95 (Wright *et al.*, 2015). In order to minimise regression dilution bias, we adjusted for measurement error in analyses by taking the average BMI in each category as that measured nine years later, using data from 3564 women (MacMahon *et al.*, 1990).

Statistical analysis

Cox regression models, using time since recruitment as the underlying time variable, were used to estimate hazard ratios, described here as relative risks (RRs), of first suicide attempt and of suicide by categories of BMI at recruitment. Women with unknown BMI (n = 62610) and women with a hospital record of prior suicide attempt (n = 2335) were excluded from the analyses. We also excluded women who had reported previous heart disease, stroke or cancer at recruitment (n = 98818) as these conditions may affect weight. The remaining participants were followed from recruitment until 31st March 2015. For attempted suicide, personyears were calculated until the date of first hospital admission for attempted suicide, death, emigration or end of follow-up, whichever came first. For suicide, person-years were calculated until death, emigration or end of follow-up, whichever came first. Follow-up for this cohort is virtually complete: only 1% of participants has been lost to follow-up, mainly through migration, and those participants contributed person-years up to the date of loss.

The BMI category $20-24.9 \text{ kg/m}^2$ was used as the reference group, and 95% group-specific confidence intervals (g-s CIs) were calculated using Plummer's method and presented in figures and tables (Plummer, 2004). This allows confidence intervals (CIs) to be estimated for each group, including the reference group, so that any two groups can be compared. Conventional 95% CIs are described in the text when comparisons are made only with the reference group.

The Cox models were stratified by single year of birth (\leq 1930, 1931, 1932,...,1949, \geq 1950) and single year of recruitment, and adjusted for the following variables all reported at recruitment: geographical region (London and Southeast, South West, Midlands, Northern England, Scotland); area deprivation (tertiles, based on the Townsend index, a score incorporating census area data for employment, car ownership, home ownership and household

Table 1. Characteristics of Million Women Study participants by BMI, and follow-up information

		BMI (kg/m ²)			
	<20	20-24.9	25-29.9	≥30	
	n = 44 010 3.8%	n = 503 160 43.5%	n = 410 094 35.5%	n = 198 387 17.2%	
Characteristics					
Age (mean, s.d.)	55.9 (5.0)	55.8 (4.8)	56.2 (4.8)	56.0 (4.7)	
Most deprived tertile (%)	32.3	28.0	32.6	40.1	
No educational qualifications (%)	37.1	37.2	45.1	51.7	
Nulliparous (%)	17.4	11.6	9.7	10.0	
≥7 alcoholic drinks/week (%)	26.0	28.0	23.2	16.1	
Current smoker (%)	32.2	21.3	18.8	16.1	
No strenuous exercise (%)	57.8	54.3	61.9	71.5	
Reported being treated for depression/anxiety (%)	9.3	7.2	8.3	10.2	
Fair or poor self-rated health ^a (%)	21.9	16.1	22.3	35.6	
Rarely, never or sometimes happy ^a (%)	22.1	16.5	16.4	18.2	
Not currently married or living with a partner ^a (%)	24.6	18.6	18.1	21.2	
Changed diet in past five years ^a (%)	27.3	33.7	43.7	53.6	
Follow-up					
No. of attempted suicides	300	2162	1592	876	
Person years of follow-up	670 715.5	7 907 218.7	6 420 953.3	3 070 769.9	
No. of suicides	61	297	195	89	
Person years of follow-up	672 986.6	7 923 292.9	6 432 760.7	3 077 194.9	

Percentages are calculated based on women with information for that specific variable.

^aDenotes information collected 3.3 years after baseline.

overcrowding) (Townsend *et al.*, 1988); educational attainment [in three categories: tertiary qualifications (college or university), secondary qualifications (A levels or O levels usually obtained at 18 or 16 years of age, respectively) or technical qualifications (nursing, teaching, clerical or commercial), no educational qualifications] (Floud *et al.*, 2016); parity (nulliparous, parous); smoking status (never, past, current); alcohol intake (<2, 2–6, \geq 7 drinks/week); strenuous exercise (rarely/never, once per week, 2– 7 times per week); self-reported treatment for depression or anxiety (yes, no). Missing data for each adjustment variable (<6% for each variable) were assigned to a separate category.

Using χ^2 tests, heterogeneity was examined across subgroups defined by length of follow-up, self-reported treatment for depression or anxiety, happiness, self-rated health, change of diet in past 5 years and marital status. The latter four variables were reported for the first time at the 3 year re-survey on average 3.3 (s.d. 1.1) years after recruitment.

We investigated whether BMI was related to method of suicide, by comparing the distribution of cases of attempted suicide and of suicide across BMI categories according to three types of methods: either (i) self-poisoning (ICD-10 X60–X69 and Y10–Y19), or (ii) self-injury using low lethality methods (ICD-10 self-cutting by sharp or blunt object X78, X79, Y28, Y29), or (iii) self-injury using high lethality methods (ICD-10 hanging/asphyxiation X70, Y20; drowning X71, Y21; firearms X72–X74, Y22–Y24; explosives X75, Y25; smoke, fire, flames X76, Y26; steam, hot vapours, hot objects X77, Y27; jumping X80, X81, Y30, Y31; crashing motor vehicle X82, Y32). Diagnoses codes X83–X84 and Y33–Y34 were excluded from this analysis because the method is not specified.

Using Cox regression, we also estimated RRs of attempted suicide and suicide in relation to birth weight and body size in childhood and early adulthood (10 years old and 20 years old) reported by participants at the 3-year re-survey, adjusted for the other variables reported at recruitment and with and without adjustment for BMI in midlife. Birth weight had two categories: <2.5 kg, ≥ 2.5 kg. Relative body size at age 10 years had two categories: thinner than peers and plumper/average compared with peers. Clothes size at age 20 years used smallest UK clothes size reported among 8 or less, 10, 12, 14, 16 and 18+ to make two categories: small (size < 12), medium/large (size 12 or larger). These self-reported measures were found to be strongly correlated with birth weight and with BMI which had been measured at age 10 and at age 20 in a subgroup of women (n = 541) who also participated in the National Survey of Health and Development (1946 birth cohort) study (Cairns et al., 2011).

Three sensitivity analyses were conducted: using the WHO categories for BMI (<18.5, 18.5–24.9, 25–29.9, $30 + \text{kg/m}^2$), using finer categories for BMI (<20, 20–22.4, 22.5–24.9, 25–27.4, 27.5–29.9, 30-32.4, 32.5-34.9, 35+) and excluding deaths of undetermined intent (ICD-10 code Y10–Y34).

All analyses used Stata 14.1 (StataCorp, College Station, TX, USA) and figures were drawn in R (R Core Team, 2013).



*Adjusted for geographical region, deprivation index, parity, education, strenuous exercise, alcohol, smoking and treatment for depression or anxiety. Stratified by year of birth and year of recruitment.

Fig. 1. RR of attempted suicide and suicide by BMI.

Results

In total, 1155651 women with known BMI and without known prior suicide attempt, cancer, heart disease or stroke were eligible for analysis. Among these women, the average age at baseline was 56.0 (s.D. 4.8) years. The proportion with low BMI (<20 kg/m²) at baseline was 4% and the proportions of overweight (25–29.9 kg/m²) and obese (\geq 30 kg/m²) women were 36% and 17%, respectively (Table 1). During a follow-up of 15.7 (s.D. 2.6) years on average, 4930 women attempted suicide and 642 died by suicide, at mean ages 63.4 (s.D. 7.0) years and 64.0 (s.D. 6.7) years, respectively.

Low weight women

Compared with women with BMI of $20-24.9 \text{ kg/m}^2$, women with lower BMI at baseline were more likely to live in less affluent areas, be current smokers, be nulliparous and do no strenuous exercise (Table 1). They were also more likely to report being treated for depression or anxiety and, 3 years after baseline, they were more likely to rate their health as fair or poor and to report being unhappy (Table 1).

In prospective analyses, women with BMI lower than 20 kg/m² had a higher RR of attempted suicide (adjusted RR = 1.38, 95% CI 1.23–1.56, p < 0.0001) and a higher RR of suicide (adjusted RR = 2.10, 95% CI 1.59–2.78, p < 0.0001) than women with a BMI of 20–24.9 kg/m² (Fig. 1). The RR for suicide was significantly greater than for attempted suicide (test for heterogeneity between the two RRs p = 0.007). Adjustment for parity, deprivation, education, strenuous exercise and alcohol made little impact on the risk estimates, whereas there was some evidence of confounding by treatment for depression/anxiety and by smoking (online Supplementary Table S1). The excess risk either of attempted suicide or of suicide in women with a low BMI did not differ by duration of follow-up, self-reported treatment for depression or anxiety at recruitment, reported happiness, self-rated health, change of diet in past 5 years or marital status (Fig. 2).

Having a smaller body size at 10 and 20 years old was associated with an increased risk of attempted suicide in middle age (adjusted RR = 1.20, 95% CI 1.10–1.30, p < 0.0001 and adjusted RR = 1.15, 95% CI 1.05–1.25, p = 0.002 respectively) compared

	Number of cases	RR* (95% g-sCl)	Number of cases	RR* (95% g-sCl)
Length of follow-up <10 years >=10 years	213 87	- ■ - 1.45 (1.27, 1.67) ■ - 1.23 (1.00, 1.52)	38 — 23 —	2 .02 (1.46, 2.78) 2 .27 (1.51, 3.43)
Being treated for depression /anxiety Yes No	113 - 187	■ 1.29 (1.07, 1.55) ■ 1.47 (1.27, 1.70)	13 48	1.33 (0.77, 2.31) 2.51 (1.89, 3.34)
<i>Happy</i> [†] Rarely, never or sometimes Usually or most of the time	65 - 76 -	■ 1.42 (1.11, 1.82) ■ 1.34 (1.07, 1.68)	12 16 ———	→ 3.10 (1.75, 5.51) 1.98 (1.21, 3.25)
Self-rated health[†] Fair or poor Excellent or good	68 70	—■ 1.48 (1.17, 1.88) ■ 1.21 (0.96, 1.53)	12 14	→ 3.30 (1.86, 5.85) 1.78 (1.05, 3.01)
Changed diet in last 5 years[†] Yes No	45 96	■ 1.53 (1.14, 2.06) ■ 1.41 (1.15, 1.72)	5	1.38 (0.57, 3.33) → 2.89 (1.93, 4.33)
Married or living with a partner[†] Yes No	99 44 0.5 1.0	1.43 (1.17, 1.74) 1.30 (0.97, 1.75)	17 9 0.5 1.0 1.5	2.21 (1.37, 3.57) 1.98 (1.02, 3.83) 2.0 2.5 3.0 3.5 4.0

Attempted suicide Relative risk* for BMI <20 versus BMI 20-24.9 kg/m²

Suicide Relative risk* for BMI <20 versus BMI 20-24.9 kg/m²

†Data from re-survey 3 years after baseline. *Adjusted for geographical region, deprivation index, parity, education, strenuous exercise, alcohol, smoking and treatment for depression or anxiety as appropriate. Stratified by year of birth and year of recruitment.

Fig. 2. RRs of attempted suicide and suicide in various subgroups; in low weight women compared with women of BMI 20-24.9 kg/m².

with being larger at those ages; lower birth weight was also associated with an increased risk but the association was not statistically significant (adjusted RR = 1.14, 95% CI 0.99-1.31, p = 0.07; Table 2). Adjustment for BMI in midlife did not affect the estimates for the relation between smaller body size at younger ages and risk of attempted suicide. Numbers of deaths by suicide by body size in early life were too small for a reliable estimation of risk.

Where information about the methods of suicide or attempted suicide was available, 95% of women who attempted suicide used self-poisoning methods, and this did not vary greatly across categories of BMI (online Supplementary Table S2). For suicide, however, women with lower BMI were more likely to use self-poisoning as the method of suicide (53%, 28 out of 53) compared with women with BMI of $20-24.9 \text{ kg/m}^2$ (37%, 100 out of 271; p = 0.03), and less likely to use methods of high lethality (43%, 23 out of 53, v. 61%, 164 out of 271, respectively; p = 0.02).

Overweight and obese women

Overweight and obese women were more likely to live in less affluent areas and do no strenuous exercise than women with BMI of $20-24.9 \text{ kg/m}^2$, and were also more likely to report being treated for depression or anxiety (Table 1). Three years after baseline, they were more likely to rate their health as fair or poor and to have changed their diet in the past 5 years (Table 1).

In prospective analyses, women who were overweight or obese had lower RRs of attempted suicide and suicide compared with women with BMI of 24-24.9 kg/m², but effect estimates were smaller in comparison with the increase in risk of suicide found for women with low BMI <20 kg/m² (Fig. 1). For suicide, women who were overweight had an adjusted RR of 0.81 95% CI (0.68-0.98) and women who were obese had an adjusted RR of 0.74 (95% CI 0.58-0.95), with a statistically significant trend (test for trend p = 0.006). However the RRs of attempted suicide did not decrease with increasing BMI (test for trend p = 0.09): overweight women had an adjusted RR of 0.89 (95% CI 0.83-0.94) whereas obese women had an adjusted RR of 0.96 (95% CI 0.88-1.04). Adjustment for treatment for depression/anxiety had the greatest impact on the risk estimates (online Supplementary Table S1).

We combined overweight and obese women into one category and compared them with women with BMI 20-24.9 kg/m² to examine differences in the associations in certain subgroups (Fig. 3). The RRs in women who were overweight and obese did not vary significantly by subgroup except that there was a lower risk of attempted suicide largely restricted to those who had not reported being treated for depression or anxiety at baseline (p = 0.005 for difference between those who reported and did not report being treated for depression or anxiety).

To enable comparison with other cohorts, we used the WHO classification of BMI in a sensitivity analysis (online Supplementary Table S3) and the results were similar to the main results except that the estimated risks for suicide attempt in the underweight group (<18.5 v. 18.5–24.9 kg/m²) were slightly higher than in the main analyses (where we used <20 v. $20-24.9 \text{ kg/m}^2$). We also conducted a sensitivity analysis using finer categories of BMI to investigate the shape of the associations (online Supplementary Table S4). This analysis showed that the higher risks of attempted suicide and suicide were apparent in women with BMI of 20-22.4 kg/m², and also showed that the lower risks for overweight and obese women were not consistently below the null as BMI increased. The results from the sensitivity analysis excluding deaths of undetermined intent did not differ markedly from the main results except that the estimated RR in the obese group was slightly lower than in the main results (online Supplementary Table S5).

Table 2. RR of attempted suicide by birth weight and body size at age 10 and 20 years

	Attempted suicide			
	No. of women	No. of cases	RR ^a	RR ^b (95% CIs)
Birth weight (kg)				
<2.5	55 910	231	1.14	1.14 (0.99–1.31)
≥2.5	367 105	1273	1.00	1.00
Relative body size at 10 years old				
Thinner than average	228 594	914	1.21	1.20 (1.10-1.30)
Average/plumper	511 802	1639	1.00	1.00
Clothes size at 20 years old				
Small	218 412	864	1.16	1.15 (1.05–1.25)
Medium/large	517 980	1679	1.00	1.00

^aRRs and 95% Cls adjusted for geographical region, deprivation index, parity, education, strenuous exercise, alcohol, smoking, treatment for depression or anxiety. Stratified by year of birth and year of recruitment.

^bRRs adjusted as in RR^a with additional adjustment for BMI in midlife.

	Attempted suicide Relative risk* for BMI >=25 versus BMI 20-24.9 kg/m ²		Suicide Relative risk* for BMI >=25 versus BMI 20-24.9 kg/m ²			
	Number of cases		RR* (95% g-sCl)	Number of cases		RR* (95% g-sCl)
Length of follow-up <10 years >=10 years	1623 845	-	0.91 (0.87, 0.96) 0.90 (0.84, 0.96)	191 93 —		0.83 (0.71, 0.96) 0.73 (0.59, 0.90)
Being treated for depression /anxiety Yes No	1062 1406	• +	1.01 (0.95, 1.08) 0.85 (0.80, 0.89)	96 188		0.83 (0.67, 1.02) 0.78 (0.67, 0.90)
<i>Happy</i> [†] Rarely, never or sometimes Usually or most of the time	489 745		1.09 (0.99, 1.19) 0.94 (0.87, 1.02)	48 76 —		+ 1.20 (0.89, 1.62) 0.71 (0.57, 0.90)
Self-rated health[†] Fair or poor Excellent or good	588 642		0.89 (0.81, 0.96) 0.95 (0.88, 1.03)	49 66 ——	<u> </u>	0.94 (0.70, 1.26) 0.69 (0.54, 0.89)
Changed diet in last 5 years[†] Yes No	640 585	_	1.03 (0.95, 1.12) 0.98 (0.90, 1.06)	61 64		0.87 (0.67, 1.13) 0.87 (0.67, 1.12)
<i>Married or living with a partner</i> [†] Yes No	903 362 0.5	 1.0	0.94 (0.88, 1.01) 1.12 (1.00, 1.24) 1.5	83 38 0.5	1.0	0.81 (0.65, 1.02) 0.80 (0.58, 1.12) 1.5

†Data from re-survey 3 years after baseline.
*Adjusted for geographical region, deprivation index, parity, education, strenuous exercise, alcohol, smoking and treatment for depression or anxiety as appropriate.
Stratified by year of birth and year of recruitment.

Fig. 3. RRs of attempted suicide and suicide in various subgroups; in overweight or obese women compared with women of BMI 20-24.9 kg/m².

Discussion

In this large prospective study of women in the UK, the small proportion (4%) who were of low BMI ($<20 \text{ kg/m}^2$) at baseline had a two-fold greater risk of suicide over the next 16 years than women with a BMI of 20–24.9 kg/m² and a 38% greater risk of attempting suicide. Evidence suggests little, if any, bias due to reverse causation, as the higher risks did not differ by length of follow-up. There appeared to be some confounding by depression and smoking but not by any other factor adjusted for. Small body sizes at age 10 and at age 20 were also associated with increased risks of attempted suicide in later life, suggesting that this association was not a recent effect. The age at onset of eating disorders is 18 years old on average and therefore the effect of eating disorders, which are known to be risk factors for suicidal behaviour,

could account for the higher risk of suicide in women who are of low weight in midlife (Kostro *et al.*, 2014; Volpe *et al.*, 2016). Unfortunately, we did not have information on eating disorders, although the association with body size at age 10 and, possibly with low birth weight, both before the onset of most eating disorders, suggest that other factors may be important.

We have compared our results with those of other studies that have reported results separately for women. Our finding that attempted suicide was associated with low BMI in adulthood agrees broadly with a study in the UK using The Health Improvement Network (THIN) database involving women aged 18 and over, of whom 782 had attempted suicide over a 7 year period (Gao *et al.*, 2013). The THIN study did not report the risk of suicide separately for women, but two other prospective studies, the US National Health Interview Survey (NHIS) and the Korean Cancer Prevention Study (KCPS) reported higher risks of death by suicide for women who were underweight, as we found (Kaplan *et al.*, 2007; Jee *et al.*, 2011). However both studies were underpowered, with only 261 and 83 suicides in women in the NHIS and KCPS, respectively, and the estimates from these studies were not statistically significant. We found a significant difference between the risk for low weight women of suicide and the risk of attempted suicide. Evidence from previous studies does not aid interpretation about the reason for this difference.

When we examined the method of suicide, women of low weight were more likely to die by self-poisoning than women in other BMI categories, suggesting that the excess risk in these women might perhaps be due to similar doses of drugs being more fatal in women of lower body mass (Perera *et al.*, 2016). There was no support for the hypothesis that women of low weight were choosing more lethal methods, such as hanging or jumping, which require more physical exertion (McCarthy *et al.*, 2014; Perera *et al.*, 2016). The finding regarding self-poisoning may have implications for clinical decision-making with respect to the dose of potentially toxic medications prescribed for women of low BMI, in whom self-poisoning may be particularly dangerous.

The large proportion of women (53%) who were overweight or obese was at a somewhat lower risk of attempting or dying from suicide than women with BMI of $20-24.9 \text{ kg/m}^2$. This finding is difficult to interpret as the risk did not decrease consistently with increasing BMI, as could be seen when finer categories of BMI were used in the sensitivity analysis. The THIN study also reported that risk of attempted suicide did not decrease with increasing BMI but that for men and women combined the risk of suicide decreased with increasing BMI (Gao et al., 2013), and both the NHIS and KCPS studies reported risk of suicide decreasing with increasing BMI. It is not clear why the effect of BMI should differ between attempted suicide and suicide. It is also not clear why the lower risks of attempted suicide were strongest in overweight and obese women who were not being treated for depression or anxiety, although this was also found by the THIN study (Gao et al., 2013). Given our findings and the inconsistent results from studies of mixed and men-only cohorts (Magnusson et al., 2006; Kaplan et al., 2007; Mukamal et al., 2007; Bjerkeset et al., 2008; Elovainio et al., 2009; Batty et al., 2010; Mukamal et al., 2010; Chang et al., 2012; Gao et al., 2013; McCarthy et al., 2014; Schneider et al., 2014), it remains possible that residual confounding by unmeasured factors may explain the somewhat lower risks associated with being overweight and obese.

The strength of the current study is that it includes one in four of all UK women born in 1935-1950, making it the largest ever study of women's health. Other strengths are the prospective design, the long and virtually complete follow-up, and the ability to adjust for many potential confounding factors. The large number of events of both attempted suicide and of suicide has allowed an examination of the association within categories of BMI, rather than treating BMI as a continuous variable which can distort any non-linear associations. The size of the study also meant that we were able to exclude women with pre-existing diseases which may have affected weight. However, there are some limitations. Firstly, the measures of psychiatric morbidity available to us were selfreported treatment for depression or anxiety at baseline and selfrated health and happiness at the 3 year resurvey, and so not all forms of psychiatric morbidity would have been captured. Secondly, the self-reported body size variables at younger ages

(birth weight, relative body size at age 10 years, and clothes size at age 20) were retrospective rather than prospective. However, they were validated against prospectively collected measurements of BMI in a subsample of the cohort, and so misclassification is unlikely (Cairns *et al.*, 2011). Thirdly, use of hospital admission records for attempted suicide would have missed some cases since not all women who self-harm are admitted to hospital (Clements *et al.*, 2016), but any misclassification would tend to dilute estimates of RRs. Lastly, within accidental deaths there could be some 'hidden suicides' and therefore some suicides may have been missed, but analyses of confirmed suicides with and without the inclusion of deaths of undetermined intent suggests that any misclassification of cases would not have had much effect on the results.

In conclusion, low weight is associated with a substantial increased risk of suicidal behaviour, particularly death by suicide, for women in their 50s and 60s. Smallbody size in childhood and early adulthood is also associated with increased risk of suicide attempt. For women who are overweight or obese, the risks of suicidal behaviour are somewhat reduced and inconsistently related to level of BMI and so residual confounding by unmeasured factors cannot be excluded.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S003291718003239.

Acknowledgements. The authors thank the women recruited to the Million Women Study and the staff of collaborating NHS Breast Screening Centres and General Practices. We also thank NHS Digital in England (http://www.digital. nhs.uk) and the Information Services Division in Scotland (http://www.isdscotland.org) for linked health data.

Million Women Study Collaborators. The Million Women Study Advisory Committee are: Emily Banks, Valerie Beral, Lucy Carpenter, Carol Dezateux, Jane Green, Julietta Patnick, Richard Peto and Cathie Sudlow.

The Million Women Study Co-ordinating Centre staff are as follows: Hayley Abbiss, Simon Abbott, Rupert Alison, Krys Baker, Angela Balkwill, Isobel Barnes, Valerie Beral, Judith Black, Roger Blanks, Kathryn Bradbury, Anna Brown, Benjamin Cairns, Andrew Chadwick, Dave Ewart, Sarah Floud, Kezia Gaitskell, Toral Gathani, Laura Gerrard, Adrian Goodill, Jane Green, Lynden Guiver, Carol Hermon, Darren Hogg, Isobel Lingard, Sau Wan Kan, Nicky Langston, Kirstin Pirie, Alison Price, Gillian Reeves, Keith Shaw, Emma Sherman, Rachel Simpson, Helena Strange, Sian Sweetland, Ruth Travis, Lyndsey Trickett, Anthony Webster, Clare Wotton, Lucy Wright, Owen Yang and Heather Young.

The following NHS breast screening centres took part in the recruitment and breast screening follow-up for the Million Women Study: Avon, Aylesbury, Barnsley, Basingstoke, Bedfordshire & Hertfordshire, Cambridge & Huntingdon, Chelmsford & Colchester, Chester, Cornwall, Crewe, Cumbria, Doncaster, Dorset, East Berkshire, East Cheshire, East Devon, East of Scotland, East Suffolk, East Sussex, Gateshead, Gloucestershire, Great Yarmouth, Hereford & Worcester, Kent (Canterbury, Rochester, Maidstone), Kings Lynn, Leicestershire, Liverpool, Manchester, Milton Keynes, Newcastle, North Birmingham, North East Scotland, North Lancashire, North Middlesex, North Nottingham, North of Scotland, North Tees, North Yorkshire, Nottingham, Oxford, Portsmouth, Rotherham, Sheffield, Shropshire, Somerset, South Birmingham, South East Scotland, South East Staffordshire, South Derbyshire, South Essex, South Lancashire, South West Scotland, Surrey, Warrington Halton St Helens & Knowsley, Warwickshire Solihull & Coventry, West Berkshire, West Devon, West London, West Suffolk, West Sussex, Wiltshire, Winchester, Wirral and Wycombe.

Financial support. The Million Women Study is funded by the UK Medical Research Council (grant no. MR/K02700X/1) and by Cancer Research UK (grant no. C570/A16491). GG is funded by the Department of Health. AF was funded by the National Institute for Health Research (NIHR), Programme

Grant for Applied Research Programme (Grant Reference Number RP-PG-0610-10026). KH is an NIHR Senior Investigator and is funded by Oxford Health NHS Foundation Trust. Funders had no role in study design, data collection, analysis or interpretation, manuscript preparation, or the decision to publish. The corresponding author confirms that she had full access to the data in the study and had final responsibility for the decision to submit for publication.

Conflict of interest. The authors declare no competing interests.

References

- Audureau E, Pouchot J and Coste J (2016) Gender-related differential effects of obesity on health-related quality of life via obesity-related comorbidities: a mediation analysis of a French Nationwide Survey. *Circulation: Cardiovascular Quality and Outcomes* 9, 246–256.
- Batty GD, Whitley E, Kivimaki M, Tynelius P and Rasmussen F (2010) Body mass index and attempted suicide: cohort study of 1133019 Swedish men. *American Journal of Epidemiology* **172**, 890–899.
- Bjerkeset O, Romundstad P, Evans J and Gunnell D (2008) Association of adult body mass index and height with anxiety, depression, and suicide in the general population: the HUNT study. *American Journal of Epidemiology* 167, 193–202.
- Cairns BJ, Liu B, Clennell S, Cooper R, Reeves GK, Beral V and Kuh D (2011) Lifetime body size and reproductive factors: comparisons of data recorded prospectively with self reports in middle age. *BMC Medical Research Methodology* 11, 7.
- Chang SS, Wen CP, Tsai MK, Lawlor DA, Yang YC and Gunnell D (2012) Adiposity, its related biologic risk factors, and suicide: a cohort study of 542 088 Taiwanese adults. *American Journal of Epidemiology* 175, 804–815.
- Clements C, Turnbull P, Hawton K, Geulayov G, Waters K, Ness J, Townsend E, Khundakar K and Kapur N (2016) Rates of self-harm presenting to general hospitals: a comparison of data from the multicentre study of self-harm in England and hospital episode statistics. *BMJ Open* 6, e009749.
- Elovainio M, Shipley MJ, Ferrie JE, Gimeno D, Vahtera J, Marmot MG and Kivimaki M (2009) Obesity, unexplained weight loss and suicide: the original Whitehall study. *Journal of Affective Disorders* **116**, 218–221.
- Floud S, Balkwill A, Moser K, Reeves GK, Green J, Beral V, Cairns BJ and Million Women Study C (2016) The role of health-related behavioural factors in accounting for inequalities in coronary heart disease risk by education and area deprivation: prospective study of 1.2 million UK women. BMC Medicine 14, 145.
- Gao S, Juhaeri J, Reshef S and Dai WS (2013) Association between body mass index and suicide, and suicide attempt among British adults: the health improvement network database. *Obesity (Silver Spring)* 21, E334–E342.
- Jee SH, Kivimaki M, Kang HC, Park IS, Samet JM and Batty GD (2011) Cardiovascular disease risk factors in relation to suicide mortality in Asia: prospective cohort study of over one million Korean men and women. *European Heart Journal* **32**, 2773–2780.
- Kaplan MS, McFarland BH and Huguet N (2007) The relationship of body weight to suicide risk among men and women: results from the US National Health Interview Survey Linked Mortality File. *Journal of Nervous and Mental Disease* 195, 948–951.
- Kjaer TK, Jensen A, Dalton SO, Johansen C, Schmiedel S and Kjaer SK (2011) Suicide in Danish women evaluated for fertility problems. *Human Reproduction* **26**, 2401–2407.
- Kostro K, Lerman JB and Attia E (2014) The current status of suicide and self-injury in eating disorders: a narrative review. *Journal of Eating Disorders* 2, 19.

- Lillis J, Levin ME and Hayes SC (2011) Exploring the relationship between body mass index and health-related quality of life: a pilot study of the impact of weight self-stigma and experiential avoidance. *Journal of Health Psychology* 16, 722–727.
- MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, Abbott R, Godwin J, Dyer A and Stamler J (1990) Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *Lancet* 335, 765–774.
- Magnusson PK, Rasmussen F, Lawlor DA, Tynelius P and Gunnell D (2006) Association of body mass index with suicide mortality: a prospective cohort study of more than one million men. *American Journal of Epidemiology* **163**, 1–8.
- McCarthy JF, Ilgen MA, Austin K, Blow FC and Katz IR (2014) Associations between body mass index and suicide in the veterans affairs health system. *Obesity (Silver Spring)* **22**, 269–276.
- McLaren L, Beck CA, Patten SB, Fick GH and Adair CE (2008) The relationship between body mass index and mental health. *Social Psychiatry and Psychiatric Epidemiology* **43**, 63–71.
- Mukamal KJ and Miller M (2010) Invited commentary: body mass index and suicide – untangling an unlikely association. *American Journal of Epidemiology* 172, 900–904, discussion 905–906.
- Mukamal KJ, Kawachi I, Miller M and Rimm EB (2007) Body mass index and risk of suicide among men. Archives of Internal Medicine 167, 468–475.
- Mukamal KJ, Rimm EB, Kawachi I, O'Reilly EJ, Calle EE and Miller M (2010) Body mass index and risk of suicide among one million US adults. *Epidemiology* **21**, 82–86.
- Office for National Statistics (2017) Suicides in Great Britain: 2016 registrations [Online]. Available at https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/suicidesintheunitedkingdom/2016registration (Accessed 25 October 2017).
- Perera S, Eisen RB, Dennis BB, Bawor M, Bhatt M, Bhatnagar N, Thabane L, de Souza R and Samaan Z (2016) Body mass index is an important predictor for suicide: results from a systematic review and meta-analysis. Suicide and Life-Threatening Behavior 46, 697–736.
- Plummer M (2004) Improved estimates of floating absolute risk. Statistics in Medicine 23, 93–104.
- R Core Team (2013) R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Available at http:// www.R-project.org/.
- Schneider B, Lukaschek K, Baumert J, Meisinger C, Erazo N and Ladwig KH (2014) Living alone, obesity, and smoking increase risk for suicide independently of depressive mood findings from the population-based MONICA/KORA Augsburg cohort study. *Journal of Affective Disorders* 152–154, 416–421.
- Seacat JD, Dougal SC and Roy D (2016) A daily diary assessment of female weight stigmatization. *Journal of Health Psychology* **21**, 228–240.
- Sorberg A, Gunnell D, Falkstedt D, Allebeck P, Aberg M and Hemmingsson T (2014) Body mass index in young adulthood and suicidal behavior up to age 59 in a cohort of Swedish men. *PLoS One* 9, e101213.
- Townsend P, Beattie A and Phillimore P (1988) Health and Deprivation: Inequality and the North. London: Croom Helm.
- Volpe U, Tortorella A, Manchia M, Monteleone AM, Albert U and Monteleone P (2016) Eating disorders: what age at onset? *Psychiatry Research* 238, 225–227.
- Wang SS, Brownell KD and Wadden TA (2004) The influence of the stigma of obesity on overweight individuals. *International Journal of Obesity and Related Metabolic Disorders* 28, 1333–1337.
- Wright FL, Green J, Reeves G, Beral V, Cairns BJ and Million Women Study C (2015) Validity over time of self-reported anthropometric variables during follow-up of a large cohort of UK women. *BMC Medical Research Methodology* 15, 81.