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Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study

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ABSTRACT

Objective To examine the relation between body mass index (kg/m²) and cancer incidence and mortality.

Design Prospective cohort study.

Participants 1.2 million UK women recruited into the Million Women Study, aged 50-64 during 1996-2001, and followed up, on average, for 5.4 years for cancer incidence and 7.0 years for cancer mortality.

Main outcome measures Relative risks of incidence and mortality for all cancers, and for 17 specific types of cancer, according to body mass index, adjusted for age, geographical region, socioeconomic status, age at first birth, parity, smoking status, alcohol intake, physical activity, years since menopause, and use of hormone replacement therapy.

Results 45 037 incident cancers and 17 203 deaths from cancer occurred over the follow-up period. Increasing body mass index was associated with an increased incidence of endometrial cancer (trend in relative risk per 10 units=2.89, 95% confidence interval 2.62 to 3.18), adenocarcinoma of the oesophagus (2.38, 1.59 to 3.56), kidney cancer (1.53, 1.27 to 1.84), leukaemia (1.50, 1.23 to 1.83), multiple myeloma (1.31, 1.04 to 1.65), pancreatic cancer (1.24, 1.03 to 1.48), non-Hodgkin's lymphoma (1.17, 1.03 to 1.34), ovarian cancer (1.14, 1.03 to 1.27), all cancers combined (1.12, 1.09 to 1.14), breast cancer in postmenopausal women (1.40, 1.31 to 1.49) and colorectal cancer in premenopausal women (1.61, 1.05 to 2.48). In general, the relation between body mass index and mortality was similar to that for incidence. For colorectal cancer, malignant melanoma, breast cancer, and endometrial cancer, the effect of body mass index on risk differed significantly according to menopausal status.

Conclusions Increasing body mass index is associated with a significant increase in the risk of cancer for 10 out of 17 specific types examined. Among postmenopausal women in the UK, 5% of all cancers (about 6000 annually) are attributable to being overweight or obese. For endometrial cancer and adenocarcinoma of the oesophagus, body mass index represents a major modifiable risk factor; about half of all cases in postmenopausal women are attributable to overweight or obesity.

INTRODUCTION

Obesity is known to be associated with excess mortality from all causes combined,¹⁻³ but less is known about its effects on cancer. Although it is widely accepted that body mass index (BMI) is positively associated with cancers of the colon, endometrium, and kidney, adenocarcinoma of the oesophagus, and postmenopausal breast cancer,⁴ the magnitudes of such effects and the role of BMI in the development of other, rarer, cancers are less certain. Body mass index may affect not only the development of certain cancers but also the subsequent risk of death.⁵ Examining the effect of BMI on both incidence and mortality within the same population is therefore important. We report here on the risk of incident and fatal cancer for a wide range of malignancies according to BMI among women in the Million Women Study, a large cohort study of women in the UK.

METHODS

Data collection, follow-up, and definitions—In 1996-2001 a total of 1.3 million women aged 50-64 who had been invited for screening for breast cancer throughout England and Scotland completed the first study questionnaire. The cohort was resurveyed three years after recruitment. Study participants have been flagged on the National Health Service central registers, so that cancer registrations and deaths are routinely notified to the study investigators. At recruitment, we asked women for their current weight and height to derive body mass index (weight (kg)/height (m)²), which we categorised as less than 22.5, 22.5-24.9, 25.0-27.4, 27.5-29.9, and 30 or more. We chose the BMI category of 22.5-24.9 as the reference group. We defined women with a BMI of 25-29.9 as “overweight” and women with a BMI of 30 or more as “obese”.⁶ We examined incidence of and mortality from cancer in relation to BMI for all cancers combined and for 17 of the most common cancer sites or types of cancer.

Statistical analysis—We excluded women diagnosed before recruitment as having cancer, or for whom height, weight, or both were unknown. In analyses of cancer

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incidence, eligible women contributed person years from the date of recruitment until the date of registration with the cancer of interest, date of death, or end of follow-up, whichever was the earliest. The end of follow-up for cancer incidence was the end of 2004 for all registries except Trent and North Yorkshire, Northwest, and Scotland, for which the corresponding dates were 30 June 2004, 31 December 2003, and 31 December 1999. For analyses of cancer mortality, eligible women contributed person years from recruitment until death from the cancer of interest, death from some other cause, or end of 2005, whichever was the earliest. We considered each of the cancer sites of interest as an endpoint in a proportional hazards model with body mass index included as a categorical variable and attained age as the underlying time variable. We summarised the relation between BMI

and incidence for each cancer site or type in the form of a log-linear trend in risk per 10 unit increase in BMI. We also did a range of sensitivity analyses to assess the extent to which the summary estimates changed under various restrictions and after allowing for potential regression dilution with respect to self reported BMI.

RESULTS

In total, 1 222 630 women were eligible for analysis. The average age at recruitment was 55.9 years. During an average follow-up period of 5.4 years for cancer incidence and 7.0 years for cancer mortality, 45 037 incident cancers and 17 203 deaths from cancer occurred. We found that BMI was strongly associated with almost all of the sociodemographic and lifestyle characteristics examined (see bmj.com).

Relative risk* of cancer incidence for individual cancer sites or types according to body mass index

Site (ICD-10 code)	No of cases	FAR (95% FCI) for incidence in women with body mass index (kg/m ²)					Trend (95% CI) per 10 units
		<22.5	22.5-24.9 (reference group)	25-27.4	27.5-29.5	≥30	
Adenocarcinoma of oesophagus† (C15)	150	1.06 (0.70 to 1.62) (n=22)	1.00 (0.68 to 1.46) (n=27)	1.28 (0.90 to 1.83) (n=30)	1.57 (1.04 to 2.36) (n=23)	2.54 (1.89 to 3.41) (n=48)	2.38 (1.59 to 3.56)
Squamous cell carcinoma of oesophagus‡ (C15)	263	2.04 (1.67 to 2.48) (n=106)	1.00 (0.78 to 1.28) (n=63)	0.96 (0.73 to 1.26) (n=52)	0.61 (0.40 to 0.94) (n=21)	0.47 (0.31 to 0.73) (n=21)	0.26 (0.18 to 0.38)
Stomach (C16)	521	1.26 (1.05 to 1.51) (n=117)	1.00 (0.84 to 1.20) (n=121)	1.04 (0.86 to 1.25) (n=111)	1.10 (0.88 to 1.38) (n=76)	1.04 (0.84 to 1.27) (n=96)	0.90 (0.72 to 1.13)
Colorectum (C18-C20)	4008	1.02 (0.95 to 1.10) (n=789)	1.00 (0.94 to 1.06) (n=1034)	1.04 (0.97 to 1.11) (n=913)	1.01 (0.93 to 1.10) (n=555)	1.01 (0.94 to 1.09) (n=717)	1.00 (0.92 to 1.08)
Pancreas (C25)	795	1.15 (0.98 to 1.34) (n=166)	1.00 (0.86 to 1.16) (n=184)	1.02 (0.88 to 1.19) (n=160)	1.20 (1.00 to 1.44) (n=116)	1.37 (1.18 to 1.60) (n=169)	1.24 (1.03 to 1.48)
Lung (C34)	3171	1.17 (1.09 to 1.25) (n=828)	1.00 (0.93 to 1.07) (n=823)	0.91 (0.85 to 0.99) (n=653)	0.83 (0.75 to 0.91) (n=376)	0.84 (0.77 to 0.92) (n=491)	0.74 (0.67 to 0.82)
Malignant melanoma (C43)	1635	1.00 (0.90 to 1.11) (n=346)	1.00 (0.91 to 1.10) (n=456)	1.05 (0.95 to 1.16) (n=384)	0.91 (0.79 to 1.05) (n=198)	0.94 (0.83 to 1.07) (n=251)	0.94 (0.82 to 1.07)
Premenopausal breast (C50)	1179	0.96 (0.85 to 1.08) (n=271)	1.00 (0.90 to 1.11) (n=352)	0.93 (0.82 to 1.05) (n=239)	0.99 (0.84 to 1.16) (n=151)	0.79 (0.68 to 0.92) (n=166)	0.86 (0.73 to 1.00)
Postmenopausal breast§ (C50)	5629	0.85 (0.80 to 0.91) (n=879)	1.00 (0.95 to 1.06) (n=1336)	1.10 (1.04 to 1.16) (n=1262)	1.21 (1.13 to 1.29) (n=878)	1.29 (1.22 to 1.36) (n=1274)	1.40 (1.31 to 1.49)
Cervix (C53)	330	0.90 (0.70 to 1.15) (n=66)	1.00 (0.81 to 1.23) (n=90)	0.94 (0.75 to 1.19) (n=71)	0.79 (0.57 to 1.10) (n=37)	1.02 (0.80 to 1.31) (n=66)	1.04 (0.79 to 1.38)
Endometrium (C54)	2657	0.84 (0.75 to 0.93) (n=340)	1.00 (0.92 to 1.09) (n=524)	1.21 (1.11 to 1.32) (n=516)	1.43 (1.29 to 1.58) (n=366)	2.73 (2.55 to 2.92) (n=911)	2.89 (2.62 to 3.18)
Ovary (C56)	2406	0.98 (0.89 to 1.07) (n=478)	1.00 (0.92 to 1.08) (n=631)	0.99 (0.91 to 1.08) (n=510)	1.13 (1.02 to 1.25) (n=349)	1.12 (1.02 to 1.23) (n=438)	1.14 (1.03 to 1.27)
Kidney (C64)	723	0.95 (0.79 to 1.14) (n=119)	1.00 (0.86 to 1.17) (n=165)	1.10 (0.94 to 1.28) (n=155)	1.19 (0.99 to 1.44) (n=106)	1.52 (1.31 to 1.77) (n=178)	1.53 (1.27 to 1.84)
Bladder (C67)	615	0.99 (0.83 to 1.19) (n=117)	1.00 (0.85 to 1.18) (n=149)	1.14 (0.97 to 1.34) (n=147)	1.15 (0.93 to 1.41) (n=92)	1.07 (0.88 to 1.30) (n=110)	1.09 (0.89 to 1.34)
Non-Hodgkin's lymphoma (C82-C85)	1509	0.99 (0.88 to 1.12) (n=283)	1.00 (0.90 to 1.11) (n=376)	1.07 (0.96 to 1.19) (n=339)	1.03 (0.90 to 1.19) (n=204)	1.19 (1.06 to 1.34) (n=307)	1.17 (1.03 to 1.34)
Multiple myeloma (C90)	491	0.80 (0.64 to 1.00) (n=76)	1.00 (0.84 to 1.19) (n=127)	1.11 (0.92 to 1.32) (n=118)	1.11 (0.88 to 1.40) (n=73)	1.16 (0.95 to 1.42) (n=97)	1.31 (1.04 to 1.65)
Leukaemia (C91-C95)	635	0.71 (0.57 to 0.87) (n=91)	1.00 (0.86 to 1.16) (n=169)	0.97 (0.82 to 1.14) (n=137)	1.14 (0.93 to 1.38) (n=99)	1.25 (1.05 to 1.48) (n=139)	1.50 (1.23 to 1.83)
Brain (C71)	571	1.14 (0.95 to 1.38) (n=113)	1.00 (0.84 to 1.19) (n=133)	1.27 (1.08 to 1.50) (n=143)	1.19 (0.96 to 1.47) (n=83)	1.08 (0.88 to 1.32) (n=99)	1.01 (0.81 to 1.26)
All cancers (C00-C97, excluding C44)	45 037	0.99 (0.97 to 1.01) (n=8952)	1.00 (0.98 to 1.02) (n=11 648)	1.01 (0.99 to 1.03) (n=9757)	1.04 (1.01 to 1.06) (n=6141)	1.12 (1.10 to 1.15) (n=8539)	1.12 (1.09 to 1.14)

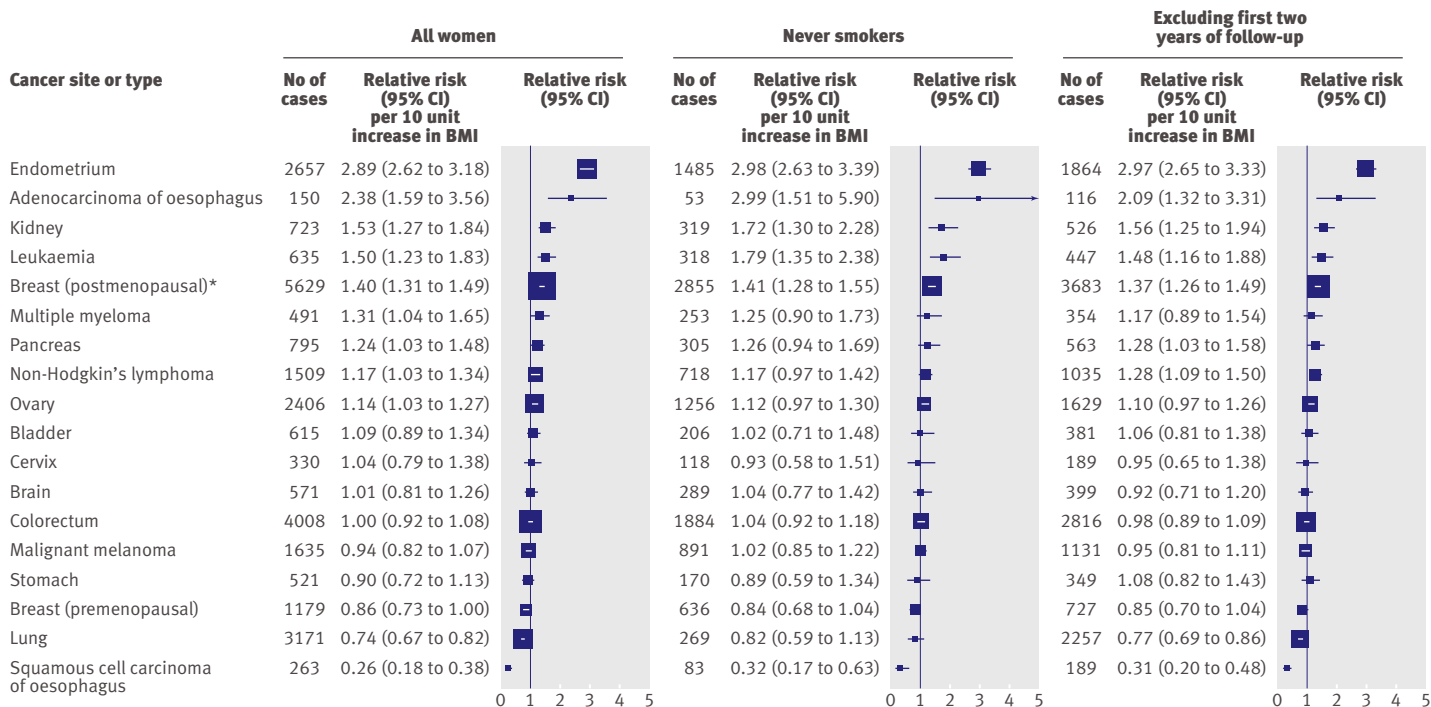
FAR=floating absolute risk; FCI=floated confidence interval.

*Adjusted for age, geographical region, socioeconomic status, reproductive history, smoking status, alcohol intake, physical activity, and, where appropriate, time since menopause and use of hormone replacement therapy.

†ICD-0 morphology codes 8140/3, 8144/3, 8145/3, 8260/3, 8480/3, 8481/3, 8490/3.

‡ICD-0 morphology codes 8070/3, 8071/3, 8072/3, 8074/3.

§Restricted to never users of hormone replacement therapy.



Estimated trend in the relative risk of cancer incidence by site or type per 10 unit increase in body mass index (BMI). Adjusted for age, geographical region, socioeconomic status, age at first birth, parity, smoking status, alcohol intake, physical activity, and, where appropriate, time since menopause and use of hormone replacement therapy. *Restricted to never users of hormone replacement therapy

The table shows the relative risk of cancer incidence for all cancers and for each of the 17 specific sites or types considered, according to BMI, adjusted for age, geographical region, socioeconomic status, age at first birth, parity, smoking status, alcohol intake, physical activity, and, where appropriate, years since menopause and use of hormone replacement therapy.

Significant heterogeneity existed in the relative risk of cancer incidence across BMI categories for all cancers ($P<0.0001$), adenocarcinoma of the oesophagus ($P=0.0009$), squamous cell carcinoma of the oesophagus ($P<0.0001$), pancreatic cancer ($P=0.03$), lung cancer ($P<0.0001$), postmenopausal breast cancer ($P<0.0001$), endometrial cancer ($P<0.0001$), kidney cancer ($P=0.0005$), and leukaemia ($P=0.0007$). Although a general test for heterogeneity across the five categories of BMI was not statistically significant for ovarian cancer ($P=0.1$), non-Hodgkin's lymphoma ($P=0.2$), or multiple myeloma ($P=0.1$), a more directed test of linear trend in the log relative risks with increasing BMI was significant for each of these cancers ($P=0.02$ for each type of cancer).

For most of the sites that showed significant heterogeneity in risk according to BMI, the relative risk of cancer increased with increasing BMI. The exceptions to this pattern were squamous cell carcinoma of the oesophagus and lung cancer, for which we found trends of decreasing risk with increasing BMI ($P<0.0001$ in both cases).

The patterns for cancer mortality according to BMI were broadly similar to those for cancer incidence, and

most cancer sites that showed a significant trend in the relative risk of incidence with increasing BMI also showed a similar trend in the risk of mortality with increasing BMI (see bmj.com). For stomach cancer, colorectal cancer, malignant melanoma, cervix cancer, bladder cancer, and brain cancer, we found no significant evidence of any variation in the overall risk of incidence or mortality according to BMI.

The figure presents, in order of decreasing magnitude, the estimated relative risk of cancer incidence associated with an increase of 10 units in BMI for each individual cancer site or type for all women and within certain subgroups. Based on all women, sites for which we found a significant positive trend in the relative risk of incidence with BMI were endometrial cancer (relative risk per 10 unit increase in BMI=2.89, 95% confidence interval 2.62 to 3.18), adenocarcinoma of the oesophagus (2.38, 1.59 to 3.56), kidney cancer (1.53, 1.27 to 1.84), leukaemia (1.50, 1.23 to 1.83), postmenopausal breast cancer (1.40, 1.31 to 1.49), multiple myeloma (1.31, 1.04 to 1.65), pancreatic cancer (1.24, 1.03 to 1.48), non-Hodgkin's lymphoma (1.17, 1.03 to 1.34), and ovarian cancer (1.14, 1.03 to 1.27). The only cancers for which a significant inverse association existed between BMI and cancer incidence were squamous cell carcinoma of the oesophagus (0.26, 0.18 to 0.38) and lung cancer (0.74, 0.67 to 0.82). We also found evidence of a decrease in the risk of premenopausal breast cancer with increasing BMI (0.86, 0.73 to 1.00), although this was of borderline statistical significance ($P=0.05$). The trend in the risk of all

cancers combined associated with a 10 unit increase in BMI was 1.12 (1.09 to 1.14).

Most sites that showed a significant association with BMI among all women also showed a similar magnitude of association in never smokers, although the trend estimate in never smokers did not always achieve statistical significance. For lung cancer, the trend among never smokers was non-significant (0.82, 0.59 to 1.13) and somewhat attenuated compared with that in all women (0.74, 0.67 to 0.82). For other smoking related cancers (namely, kidney cancer and adenocarcinoma of the oesophagus) and for leukaemia, the trend in risk with increasing body mass index became greater in magnitude after restriction to never smokers. The trend in risk per 10 unit increase in BMI for all cancers combined was also slightly greater in never smokers (1.20, 1.15 to 1.24) than in all women (1.12, 1.09 to 1.14). Excluding the first two years of follow-up from the analysis had little effect on the trend estimates.

We found significant differences in the trend estimates between premenopausal women and postmenopausal women who had never used hormone replacement therapy for breast cancer ($P < 0.0001$), endometrial cancer ($P = 0.0001$), colorectal cancer ($P = 0.03$), and malignant melanoma ($P = 0.05$). For colorectal cancer and malignant melanoma, we found positive trends in risk with BMI in premenopausal women (relative risk per 10 unit increase 1.61 and 1.62) but no evidence of any association in postmenopausal never users of hormone replacement therapy (0.99 and 0.92). By contrast, increased BMI was associated with a decreased risk of breast cancer in premenopausal women (relative risk 0.86) and an increased risk in postmenopausal women (1.40). For endometrial cancer, we found a significant increase in risk with increasing BMI for both groups, but the magnitude of the trend was substantially greater in postmenopausal women than in premenopausal women (relative risk 3.98 compared with 1.77).

The estimated proportion of all cancers attributable to being overweight or obese among postmenopausal women was 5%. For endometrial cancer and adenocarcinoma of the oesophagus, about a half of cases (51% and 48%) were attributable to being overweight or obese. By comparison, the estimated proportion of cancers attributable to being overweight or obese was between 10% and 20% for multiple myeloma, kidney cancer, leukaemia, and pancreatic cancer and below 10% for all other specific sites or types.

DISCUSSION

We found increasing body mass index to be associated with an increased risk of incident cancer for all cancers combined and for 10 out of the 17 specific sites or types of cancer considered, including eight sites in which a positive association existed in all women and two sites in which it was confined to either premenopausal women (colorectal cancer) or postmenopausal women (breast cancer). Patterns of cancer mortality in relation to BMI were broadly similar to those for

incidence. The findings suggest that menopausal status is a key factor in the relation between BMI and risk of cancer, not only for those cancers that are known to be hormonally related, such as breast and endometrial cancer, but also for other common cancers not generally thought to be mediated by hormones.

Female reproductive cancers

The relation between BMI and breast cancer is complicated by the fact that BMI has a different effect on breast cancer risk among premenopausal and postmenopausal women.⁴ Our data confirm this observation, in that the risk of breast cancer among premenopausal women decreases with increasing BMI whereas the risk increases with BMI among postmenopausal women who have never used hormone replacement therapy. The increase in the risk of breast cancer with increasing BMI among postmenopausal women is likely to be due to increased concentrations of circulating sex hormones,⁷ but the opposite relation among premenopausal women is less well understood.

The increased risk of endometrial cancer with increasing adiposity is also thought to be mediated by concentrations of endogenous sex hormones.⁸ The substantially greater increase in risk with increasing BMI found here for women who reported being postmenopausal at recruitment is a novel finding. Whereas the effect of obesity on postmenopausal endometrial cancer is thought to be due to increased concentrations of unopposed oestrogens, any effect in premenopausal women may be due to progesterone deficiency rather than an excess of oestrogen.⁸

Few individual studies have reported a significant effect of adiposity on risk of ovarian cancer. The small increase in ovarian cancer risk with increasing BMI found here is consistent with the conclusions of a review of the published evidence.⁹

Other cancers

Colorectal cancer has been consistently associated with increased adiposity among men.⁶ However, results in women have been less consistent.^{5,10-15} Our data show no overall association between BMI and the overall risk of incidence of or mortality from colorectal cancer but do suggest that this relation differs between premenopausal and postmenopausal women, with a significant increase in risk with increasing BMI among premenopausal women but not among postmenopausal women. This apparent interaction between adiposity and menopausal status may explain, at least in part, the variability in published results on the relation between BMI and colorectal cancer in women.

Relatively few studies have reported on the relation between BMI and haematopoietic cancers, and findings have been equivocal regarding BMI in relation to non-Hodgkin's lymphoma,^{5,10,11,16,17} multiple myeloma,^{5,10} and leukaemia.^{5,10,11,18} Our findings show significant trends of increasing risk with increasing BMI for each type of cancer. Data on the risk of malignant melanoma in relation to BMI have also been

WHAT IS ALREADY KNOWN ON THIS TOPIC

Increased body mass index is known to increase the risk of adenocarcinoma of the oesophagus, endometrial cancer, kidney cancer, and postmenopausal breast cancer in women

Body mass index has also been associated with the risk of other, rarer, cancers, but the findings are not yet conclusive

WHAT THIS STUDY ADDS

High body mass index in women may increase the risk of multiple myeloma, leukaemia, pancreatic cancer, non-Hodgkin's lymphoma, and ovarian cancer

Menopausal status seems to affect the relation between body mass index and risk of breast cancer, endometrial cancer, and colorectal cancer

Among postmenopausal women in the UK, 5% of all cancers (about 6000 annually) are attributable to women being overweight or obese

Around half of all cases of endometrial cancer and adenocarcinoma of the oesophagus in postmenopausal UK women are attributable to women being overweight or obese

inconsistent.^{5 10 11 19-23} Although we found no overall association between BMI and malignant melanoma, some evidence suggested that the effect of BMI on risk is greater in premenopausal women than in postmenopausal women.

Previous studies of the risk of adenocarcinoma of the oesophagus, pancreatic cancer, and kidney cancer in relation to BMI have consistently reported a material increase in risk with increasing BMI,^{4 5 10 11 24-26} and our findings provide further support for these associations.

Two sites for which we found a significant inverse relation between BMI and incidence were lung cancer and squamous cell carcinoma of the oesophagus. The inverse association between BMI and lung cancer was considerably attenuated when we restricted analyses to never smokers; however, the small number of cases of lung cancer among never smokers means that we had insufficient power to exclude an association. By contrast, the substantial inverse association between BMI and squamous cell carcinoma of the oesophagus remained significant after restriction to never smokers, after exclusion of the first two years of follow-up (0.31, 0.20 to 0.48), and after allowance for a possible interaction between smoking status and alcohol intake. Thus, although we cannot rule out residual bias in the relation between BMI and squamous cell carcinoma of the oesophagus, the association seems to be remarkably robust.

Strengths and weaknesses

The Million Women Study includes one in four UK women who were aged 50-64 during the period of recruitment, making it the largest ever study of women's health. To our knowledge, no previous study has examined the role of BMI in both incidence of and mortality from cancer within the same cohort.

As with most large epidemiological studies, BMI in our cohort was based on self reported height and weight, and is likely to be subject to both random and systematic errors. However, a validation study of 2500 UK women of a similar age found that a close numerical agreement existed between self reported BMI and measured BMI.²⁷

For many cancers, weight loss often precedes clinical recognition of the disease and, in affected patients, BMI recorded before diagnosis is an underestimate of their usual BMI. This potential bias can give rise to spuriously increased risks at low levels of BMI. Although exclusion of the first two years of follow-up within these data did not materially affect the findings, the fact that the relatively short follow-up period precludes exclusion of longer periods is a limitation of the study.

Previous publications have suggested a non-linear relation between BMI and mortality, with an increased risk at very low levels of BMI as well as at high levels.² In our data, the numbers of cancers in women with a BMI below 18.5 were extremely small and exclusion of the substantial period of follow-up needed to minimise any effect of reverse causality was not yet feasible. Thus, we cannot rule out the possibility of an adverse effect on risk of cancer at extremely low BMI.

In the case of smoking related cancers, residual confounding with smoking history is a key potential source of bias. A large study of mortality from cancer found evidence of a greater adverse effect of BMI in never smokers compared with all women for oesophageal cancer, pancreatic cancer, and all cancers.⁵ However, exclusion of smokers from the analyses presented here did not materially alter the findings.

Attributable risks

In these data, the great majority (81%) of cancers occurred in postmenopausal women, and we therefore confined estimates of attributable risk to postmenopausal women. We estimate that 5% of all cancers among postmenopausal women in the UK are attributable to being overweight or obese (BMI ≥ 25) and that 4% are attributable to obesity (BMI ≥ 30). For endometrial cancer and adenocarcinoma of the oesophagus, BMI represents a major modifiable risk factor; as many as about half of all cases of these cancers in postmenopausal women are attributed to being overweight or obese. These findings imply that 6000 new cancers annually in postmenopausal women in the UK are due to being overweight or obese, of which 4800 are due to obesity.

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Million Women Study Steering Committee, Coordinating Centre staff, and collaborating UK NHS breast screening centres: See bmj.com.

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Detection of prostate cancer in unselected young men: prospective cohort nested within a randomised controlled trial

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ABSTRACT

Objective To investigate the feasibility of testing for prostate cancer and the prevalence and characteristics of the disease in unselected young men.

Design Prospective cohort nested within a randomised controlled trial, with two years of follow-up.

Setting Eight general practices in a UK city.

Participants 1299 unselected men aged 45-49.

Intervention Prostate biopsies for participants with a prostate specific antigen level of 1.5 ng/ml or more and the possibility of randomisation to three treatments for those with localised prostate cancer.

Main outcome measures Uptake of testing for prostate specific antigen; positive predictive value of prostate specific antigen; and prevalence of prostate cancer, TNM disease stage, and histological grade (Gleason score 6-10).

Results 442 of 1299 men agreed to be tested for prostate specific antigen (34%) and 54 (12%) had a raised level.

The positive predictive value for prostate specific antigen was 21.3%. Ten cases of prostate cancer were detected (2.3%) with eight having at least two positive results in biopsy cores and three showing perineural invasion. One tumour was of high volume (cT2c), Gleason score 7, with a positive result on digital rectal examination; nine tumours were cT1c, Gleason score 6, and eight had a negative result on digital rectal examination. Five of the nine eligible participants (55%) agreed to be randomised. No biochemical disease progression occurred in two years of follow-up.

Conclusions Men younger than 50 will accept testing for prostate cancer but at a much lower rate than older men. Using an age based threshold of 1.5 ng/ml, the prevalence of prostate cancer was similar to that in older men (3.0 ng/ml threshold) and some cancers of potential clinical significance were found.

Trial registration Current Controlled Trials ISRCTN20141297