The Mortality Risk of Smoking and Obesity Combined

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Background: Both smoking and obesity have been linked to increased mortality, but evaluating the joint effect has been limited. This nationwide, prospective mortality study of U.S. radiologic technologists was designed to evaluate the combined mortality risks of obesity and smoking.

Methods: Mortality risk was investigated in 64,120 women and 18,760 men who completed a baseline questionnaire (1983 to 1989). Body mass index (BMI) (weight adjusted for height, or kilograms divided by meters squared) was calculated from self-reported weight and height at baseline, with five categories: less than 18.5 (underweight), 18.5 to 24.9 (normal), 25.0 to 29.9 (overweight), 30.0 to 34.9 (moderately obese), and 35.0 and higher (very obese). Participants were followed from the questionnaire until the date of death or through 2002, whichever occurred first. The combined association among BMI and smoking and all-cause, cancer, and circulatory disease mortality by gender and attained age (less than 65 years, 65 years and older) was examined using Cox proportional hazards regression analyses (conducted in 2005). Person-years at risk averaged 16 years (women aged less than 65), 6 years (women aged 65 and older), 15 years (men aged less than 65), and 7 years (men aged 65 and older), totaling 1.35 million person-years.

Results: In all gender/age groups, both obesity and smoking, particularly current smoking, contributed substantially to all-cause mortality, with 3.5- to 5-fold risks for very obese, current smokers compared to normal weight, never smokers. Current smoking was the predominant risk factor for cancer mortality. Combining obesity with current smoking increased circulatory disease mortality by 6- to 11-fold for people aged less than 65 years, compared to normal weight, never smokers. Obese former smokers (less than 65 years) had notably lower risks.

Conclusions: Obese smokers (aged less than 65 years) had strikingly high mortality risks, particularly from circulatory disease mortality.

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Introduction

Obesity and smoking have each been linked to many serious illnesses, including coronary heart disease, cerebrovascular disease, and cancer.[1–5] Recent National Health and Nutrition Examination Surveys (NHANES)[6] estimate that more than one quarter of the population of the United States smoke, and more than 35% are obese.[7,8] Several studies have examined the mortality risks associated with body mass index (BMI) in nonsmokers,[9,10] and in separate groups of never smokers and smokers.[11–13]

There are, however, only limited data on the magnitude of the mortality risks faced by individuals of excess weight who are also current or former smokers. To the authors' knowledge, no large prospective study of women and men has examined the combined mortality impact of a high BMI and smoking compared to being normal weight and never smoking. It is important to investigate the combined effects of obesity and smoking because NHANE surveys suggest that about 20% of obese adults smoke,[6] which corresponds to about 7% of the U.S. population. This study reports a prospective examination (1983 to 2002) of the risk of BMI and smoking combined on all-cause, cancer, and circulatory disease mortality in a nationwide cohort of 18,760 men and 64,120 women.

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Methods

The U.S. Radiologic Technologists (USRT) Study, an ongoing collaboration of the U.S. National Cancer Institute, the University of Minnesota, and the American Registry of Radiologic Technologists (ARRT), has been following a nationwide

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cohort of radiologic technologists residing in the U.S. and certified by ARRT for at least 2 years between 1926 and 1980. Detailed information on the methods is provided elsewhere.[14,15] The current study was approved by the Institutional Review Boards of the National Cancer Institute and the University of Minnesota.

Mortality risk was investigated in technologists who completed a self-administered baseline questionnaire (1983 to 1989), were cancer-free (except for non-melanoma skin cancer); and reported no history of myocardial infarction (MI) at baseline, in order to limit confounding due to illness (n=85,940 remained, after excluding 4218 with prior cancer/MI). Participants who reported insufficient information to calculate BMI (n=2315) or smoking status (n=745) were also excluded. The final study population included a total of 82,880 subjects, who completed the questionnaire at ages 22 to 92 years, and were followed through December 31, 2002. The questionnaire collected information on birth date, height, weight, smoking behavior (including duration, intensity, current status), alcohol use, and reproductive/hormonal factors, as well as work history and other factors.

Cases included those who died on or before December 31, 2002, as determined by linkage with the Social Security Death Mortality File or the National Death Index. Deaths were classified by the underlying cause of death coded according to the International Classification of Diseases (ICD-8–10).

The BMI (weight adjusted for height, kg/m^2)[16] was calculated from self-reported weight and height, with five categories: <18.5 (underweight), 18.5 to 24.9 (normal), 25.0 to 29.9 (overweight), 30.0 to 34.9 (moderately obese), and ≥35.0 (very obese). Where the number of deaths in the obesity categories was small, mortality risks were calculated for a single obesity category. Smoking status was categorized as never, former, or current. Both BMI and smoking status were reported at baseline.

Participants were stratified into two age groups—<65 years and ≥65 years by 2002. The age boundary, 65 years, was selected to ensure a similar numbers of deaths in each group and because it has been used in other mortality studies.[11] Participants in the younger group were followed from the return date of the questionnaire until death, age 65, or December 31, 2002, whichever occurred first; those in the older group were followed from age 65 (or the age at questionnaire return for those aged >65 at that time) until death or December 31, 2002. There were a total of 1351 deaths in women aged <65 years, 1370 in women aged ≥65 years, 871 in men <65 years, and 887 in men aged ≥65 years. Person-years at risk averaged 16, 6, 15, and 7 years, respectively, for a total of 1.35 million person-years.

Cox proportional hazards regression was used to compute relative risks (RRs) with 95% confidence intervals (CIs), using age (beginning at the baseline questionnaire) as the timescale,[17] and stratifying at baseline for birth cohort in 5-year intervals to control for secular trends. SAS software, version 8.2 (SAS Institute, Cary NC, 2001), was used for all analyses, which were conducted in 2005. The referent group was composed of never smokers with a normal BMI (18.5 to 24.9).

Multivariate models incorporated established factors related to mortality risk, including education, race/ethnicity, and alcohol use, as reported at baseline. The year (decade) that the radiation technologist first worked as a radiation technologist, which crudely corresponds to levels of occupational radiation dose, was also included as a potential confounder. Models were run with and without pack-years (<20 years and ≥20 years) to reflect dose and duration of smoking. For the most part, higher pack-years increased risk within smoking status categories (former/current). Generally, however, even when pack-years were included in the models, the risk relationship between former and current smokers remained. In the interest of clarity, results are presented by smoking status and BMI, rather than in more numerous categories (combining pack-years with smoking status).

Although the full range of BMI levels was included in the models, the study does not report results for those considered underweight (BMI <18.5) because a very low BMI is sometimes due to pre-existing illness and the small number of deaths in this category in many of the analyses made risk estimates unstable. Point estimates and 95% confidence intervals are provided in tabular form and accompanying figures provide a visual presentation of the relative magnitude of the point estimates. Interaction on a multiplicative scale was tested in each of the models using the chi square statistic.

Results

Selected demographic and other characteristics of the four gender/age groups are presented in Table 1. More than 90% of each gender/age group was white. Participants resided in all geographic regions of the country. Except for the group of men aged <65, a minority of each of the other gender/age groups had attended college.

In all four gender/age groups, both obesity and smoking, particularly current smoking, increased all-cause mortality risk (Figures 1 and 2, Tables 2 and 3). In fact, in those aged <65, being a normal weight, current smoker, posed higher mortality risks than being a very obese, never smoker. Current smokers who were very obese (BMI ≥35) had especially high risks (3.5- to 5-fold) in comparison to normal weight, never smokers. In contrast, the all-cause mortality risks for those who were very obese (BMI ≥35) and had stopped smoking were notably lower (RRs of 1.4 to 2.5). Generally, never and former smokers in any BMI category had substantially lower risks than current smokers.

In general, being a current smoker was a far stronger risk factor for cancer mortality than obesity. In both women and men aged <65 years, who were never or former smokers, increasing BMI had little effect on cancer mortality risk. However, cancer mortality risk was somewhat higher in current smokers who were obese than in current smokers who were not, when both groups were compared to never smokers of normal weight. In contrast, in men and women who were aged ≥65 years, the relationship between obesity and cancer mortality was more apparent in never smokers than in current or former smokers, although few cancer deaths among obese current smokers limits interpretation.

Table 1. Baseline demographic and other characteristics in the U.S. Radiologic Technologists Study cohort by gender and attained age groups[a,b]

	Women <65 years		Women ≥65 years		Men <65 years		Men ≥65 years	
Characteristics	***n* = 62,781**	**%**	***n* = 7819**	**%**	***n* = 18,108**	**%**	***n* = 3467**	**%**
Race/ethnicity								
White	60,409	96.2	7,443	95.2	16,348	90.3	3,141	90.6
Black	1,417	2.3	243	3.1	702	3.9	159	4.6
Other/unknown	955	1.5	133	1.7	1058	5.8	167	4.8
Education[c]								
Radiation technology program (2 years)/high school	37,992	60.5	4,129	52.8	5,963	32.9	1,366	39.4
1 year college/graduate school	21,738	34.6	2,916	37.3	10,950	60.5	1,660	47.9
Other/unknown	3,051	4.9	774	9.9	1195	6.6	441	12.7
Residence at baseline								
Northeast	16,503	26.3	1,694	21.7	3,822	21.1	699	20.2
Midwest	20,190	32.2		30.7	4,882	27.0	862	24.9
South	15,699	25.0	1,835	23.5	5,183	28.6	978	28.2
West	10,378	16.5	1,890	24.2	4,220	23.3	926	26.7
Unknown	11	0.0	1	0.0	1	0.0	2	0.1
Body mass index								
<18.5	2,714	4.3	209	2.7	106	0.6	21	0.6
18.5–24.9	45,708	72.84	4,886	62.5	8,286	45.8	1,439	41.5
25–29.9	10,024	16.0	1914	24.5	7,779	43.0	1,619	46.7
30–34.9	3,047	4.9	598	7.7	1,569	8.7	318	9.2
≥35	1,288	2.1	212	2.7	368	2.0	70	2.0
Smoking duration (years)								
Never smoker	31,779	50.6	3,525	45.1	7,006	38.7	1,047	30.2
<10	9,406	15.0	507	6.5	2,470	13.6	233	6.7
10–19	12,907	20.6	676	8.7	4,392	24.3	387	11.2
20–29	6,046	9.6	946	12.1	2,587	14.3	488	14.1
≥30	2,216	3.5	2,060	26.4	1,386	7.7	1228	35.4
Unknown (smoking status or years)	427	0.7	105	1.3	267	1.5	84	2.4
Alcohol intake (drinks/week)								
0	10,682	17.0	1,902	24.3	3,331	18.4	883	25.5
<1–6	46,423	73.9	4,824	61.7	11,340	62.6	1,877	54.1
7–14	4,688	7.5	891	11.4	2,484	13.7	1502	14.5
>14	640	1.0	127	1.6	836	4.6	178	5.1
Unknown	348	0.6	75	1.0	117	0.7	27	0.8

[a]Restricted to respondents in first baseline survey who at that time were cancer-free (other than nonmelanoma skin cancer) and reported never having had a myocardial infarction.
[b]Numbers for the four groups exceed the total number of participants because some individuals are followed in the younger age group until they reached age 65, and then followed in the separate analysis for those aged ≥65 until they died or follow-up ended.
[c]Subjects were placed in the "highest" educational category applicable, with college ranked after radiological training.

In all four gender/age groups, risk of circulatory disease mortality generally increased with additional increments in BMI category and with increases in smoking status severity. Thus, for example, compared to overweight never smokers, risk was greater in overweight former smokers, greater still in overweight current smokers, and greatest in obese current smokers. Risks were strikingly high in men and women aged <65 years who were obese and current smokers (6- to 11-fold). In all four gender/age groups, there was a notably lower mortality risk in obese former smokers than in obese current smokers, which was especially pronounced in women aged <65 years.

Multiplicative interaction was assessed between smoking status and BMI in each of the gender/age groups for each of the mortality outcomes. The only significant interaction was the joint effect on circulatory disease mortality of smoking and BMI in women aged <65 years (p=0.03).

Discussion

This nationwide prospective study of more than 80,000 U.S. radiologic technologists provides one of the first reports on the association between all-cause, cancer, and circulatory disease mortality risk and the combination of BMI and smoking status. Obesity and current smoking both contributed substantially to all-cause and circulatory disease mortality in the four gender/age groups examined, whereas current smoking was the predominant risk factor for cancer mortality. Combining obesity with current smoking posed especially large risks for circulatory disease mortality in people aged less than 65 years, with 6- to

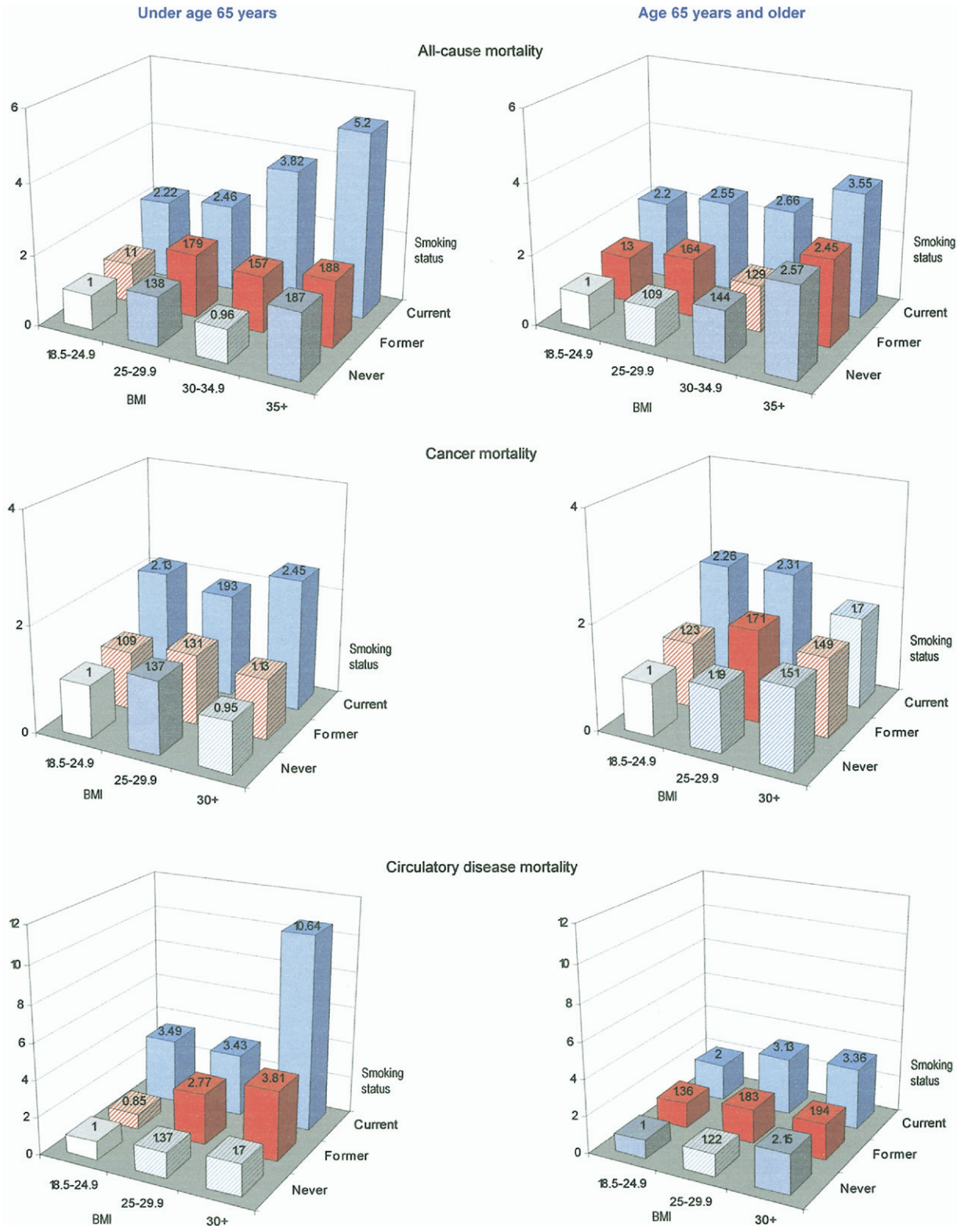

Figure 1. Relative risks for all-cause, cancer, and circulatory disease mortality by BMI and cigarette smoking categories in women aged <65 and ≥65 years. The magnitude of RR for each BMI/smoking category is identified on each bar. Solid bars denote a statistically significant RR, with a lower 95% CI of >1. Striped bars denote a nonstatistically significant RR, with a lower 95% CI of ≤1. White bars denote reference group (normal BMI/never smoker), with RR=1.0.
BMI, body mass index; CI, confidence interval; RR, relative risk.

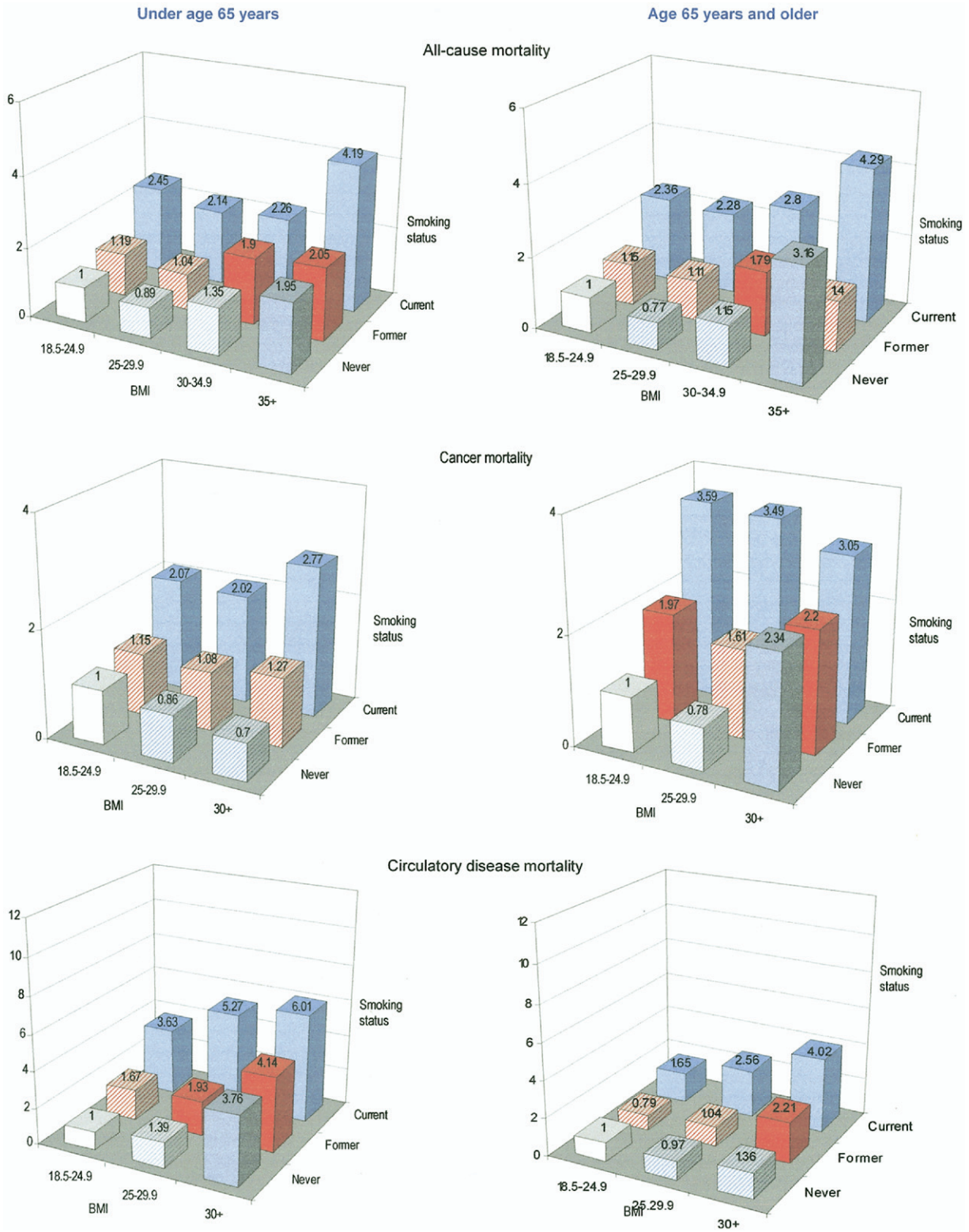

Figure 2. Relative risks for all-cause, cancer, and circulatory disease mortality by BMI and cigarette smoking categories in men aged <65 and ≥65 years. The magnitude of RR for each BMI/smoking category is identified on each bar. Solid bars denote a statistically significant RR, with a lower 95% CI of >1. Striped bars denote a nonstatistically significant RR, with a lower 95% CI of ≤1. White bars denote reference group (normal BMI/never smoker), with RR=1.0.
BMI, body mass index; CI, confidence interval; RR, relative risk.

Table 2. RR for all-cause, cancer, and circulatory disease mortality, in women aged <65 and ≥65 years by BMI and smoking status[a]

	Attained age <65 years				Attained age ≥65 years			
	All-cause mortality							
BMI	**18.5–24.9**	**25.0–29.9**	**30.0–34.9**	**≥35.0**	**18–24.9**	**25.0–29.9**	**30.0–34.9**	**≥35.0**
Never smoker								
Deaths (*n*)	287	109	27	20	317	141	56	23
RR	1.0 (ref)	1.38	0.96	1.87	1.0 (ref)	1.09	1.44	2.57
95% CI	—	1.10–1.72	0.65–1.43	1.19–2.95	—	0.89–1.33	1.08–1.92	1.68–3.95
Former smoker								
Deaths (*n*)	186	86	23	14	223	115	30	16
RR	1.10	1.79	1.57	1.88	1.30	1.64	1.29	2.45
95% CI	0.91–1.33	1.40–2.29	1.02–2.40	1.10–3.22	1.09–1.55	1.32–2.04	0.88–1.89	1.48–4.06
Current smoker								
Deaths (*n*)	362	100	40	20	260	84	17	6
RR	2.22	2.46	3.82	5.20	2.20	2.55	2.66	3.55
95% CI	1.90–2.60	1.96–3.10	2.74–5.32	3.30–8.20	1.86–2.62	1.99–3.25	1.63–4.36	1.57–8.02
	Cancer mortality							
BMI	**18.5–24.9**	**25.0–29.9**	**≥30.0**		**18–24.9**	**25.0–29.9**	**≥30.0**	
Never smoker								
No. deaths	160	62	21	—	79	39	20	
RR	1.0 (ref)	1.37	0.95	—	1.0 (ref)	1.19	1.51	
95% CI	—	1.02–1.83	0.60–1.50	—	—	0.81–1.76	0.92–2.48	
Former smoker								
Deaths (*n*)	108	38	15		61	36	13	
RR	1.09	1.31	1.13		1.23	1.71	1.49	
95% CI	0.85–1.40	0.92–1.88	0.66–1.92		0.87–1.73	1.15–2.56	0.83–2.70	
Current smoker								
Deaths (*n*)	201	46	20		86	25	5	
RR	2.13	1.93	2.45		2.26	2.31	1.70	
95% CI	1.73–2.64	1.38–2.68	1.54–3.91		1.64–3.10	1.47–3.64	0.69–4.22	
	Circulatory disease mortality							
BMI	**18.5–24.9**	**25.0–29.9**	**≥30.0**		**18–24.9**	**25.0–29.9**	**≥30.0**	
Never smoker								
Deaths (*n*)	34	13	8		116	58	34	
RR	1.0 (ref)	1.37	1.70		1.0 (ref)	1.22	2.15	
95% CI	—	0.72–2.60	0.78–3.68		—	0.89–1.69	1.46–3.17	
Former smoker								
Deaths (*n*)	17	16	10		81	42	18	
RR	0.85	2.77	3.81		1.36	1.83	1.94	
95% CI	0.47–1.53	1.52–5.05	1.87–7.76		1.02–1.83	1.28–2.64	1.17–3.22	
Current smoker								
Deaths (*n*)	68	17	19		72	30	7	
RR	3.49	3.43	10.64		2.00	3.13	3.36	
95% CI	2.29–5.31	1.91–6.18	6.03–18.77		1.47–2.71	2.07–4.72	1.55–7.29	

[a]Relative risks are adjusted for race/ethnicity, education, alcohol behavior, and year first worked as a radiologic technologist by decade.
BMI, body mass index; CI, confidence interval; ref, referent category; RR, relative risk.

11-fold risks compared to never smokers of normal weight.

Limitations of this study include reliance on self-reported values for height and weight. Other studies that have validated self-reported weight or height, however, have found strong correlations with measured values.[10,18] Nonetheless, it is probable that heavy participants underreported their weight, which likely underestimated BMI,[18] and thus may have exaggerated the magnitude of risks associated with being overweight and moderately obese. Other limitations include the unavailability of data on physical activity or abdominal obesity, which could affect the risks associated with BMI, and the restriction of BMI/smoking information to the 1983–1989 questionnaire, although it may have changed subsequently. Lacking information on changes in BMI, one cannot confidently infer how weight loss affects mortality. Moreover, risks associated with former smoking may have been inflated, if some former smokers resumed smoking after completing the survey. Small numbers of deaths charac-

Table 3. RR for all-cause, cancer, and circulatory disease mortality, in men aged <65 and ≥65 years by BMI and smoking status[a]

	Attained age <65 years				Attained age ≥65 years			
	All-cause mortality							
BMI	**18.5–24.9**	**25.0–29.9**	**30.0–34.9**	**≥35.0**	**18–24.9**	**25.0–29.9**	**30.0–34.9**	**≥35.0**
Never smoker								
Deaths (*n*)	97	83	26	10	103	79	19	5
RR	1.0 (ref)	0.89	1.35	1.95	1.0 (ref)	0.77	1.15	3.16
95% CI	—	0.67–1.20	0.87–2.08	1.02–3.74	—	0.57–1.03	0.70–1.89	1.27–7.84
Former smoker								
Deaths (*n*)	101	115	45	10	193	182	48	6
RR	1.19	1.04	1.90	2.05	1.15	1.11	1.79	1.40
95% CI	0.90–1.58	0.79–1.37	1.33–2.72	1.07–3.95	0.90–1.48	0.86–1.42	1.26–2.55	0.59–3.30
Current smoker								
Deaths (*n*)	188	144	29	14	140	86	12	5
RR	2.45	2.14	2.26	4.19	2.36	2.28	2.80	4.29
95% CI	1.91–3.15	1.64–2.79	1.49–3.44	2.38–7.37	1.81–3.09	1.69–3.08	1.52–5.16	1.73–10.64
	Cancer mortality							
BMI	**18.5–24.9**	**25.0–29.9**	**≥30.0**		**18–24.9**	**25.0–29.9**	**≥30.0**	
Never smoker								
Deaths (*n*)	26	23	5		21	16	9	
RR	1.0 (ref)	0.86	0.70		1.0 (ref)	0.78	2.34	
95% CI	—	0.49–1.51	0.27–1.83		—	0.41–1.51	1.06–5.16	
Former smoker								
Deaths (*n*)	29	38	12		59	55	15	
RR	1.15	1.08	1.27		1.97	1.61	2.20	
95% CI	0.67–1.96	0.65–1.80	0.63–2.53		1.17–3.29	0.96–2.71	1.12–4.34	
Current smoker								
No. deaths	47	42	14		45	29	4	
RR	2.07	2.02	2.77		3.59	3.49	3.05	
95% CI	1.27–3.38	1.22–3.33	1.43–5.34		2.09–6.17	1.94–6.27	1.03–9.06	
	Circulatory disease mortality							
BMI	**18.5–24.9**	**25.0–29.9**	**≥30.0**		**18–24.9**	**25.0–29.9**	**≥30.0**	
Never smoker								
Deaths (*n*)	15	21	15		42	41	10	
RR	1.0 (ref)	1.39	3.76		1.0 (ref)	0.97	1.36	
95% CI	—	0.72–2.70	1.83–7.72		—	0.62–1.50	0.68–2.75	
Former smoker								
Deaths (*n*)	23	37	21		57	67	25	
RR	1.67	1.93	4.14		0.79	1.04	2.21	
95% CI	0.87–3.21	1.05–3.55	2.12–8.11		0.52–1.20	0.69–1.56	1.32–3.71	
Current smoker								
Deaths (*n*)	44	56	16		37	35	7	
RR	3.63	5.27	6.01		1.65	2.56	4.02	
95% CI	2.00–6.57	2.95–9.41	2.95–12.25		1.04–2.64	1.59–4.12	1.76–9.18	

[a]Relative risks are adjusted for race/ethnicity, education, alcohol behavior, and year first worked as a radiologic technologists by decade.
BMI, body mass index; CI, confidence interval; ref, referent category; RR, relative risk.

terize some subgroups and may contribute to uncertainty about the magnitude of the risks.

There are few published findings with which to compare these results. A study that assessed the combined risk of smoking and BMI on all-cause mortality was limited to Japanese-American men in Hawaii and used three relatively low BMI categories (less than 21.21, 21.21 to 26.3, and more than 26.31).[19] Like the current study, it reported that smokers faced greater risks regardless of BMI level in comparison to a reference group of never smokers who were comparable to the normal weight category (BMI of 18.5 to 24.9). The American Cancer Society study used a weight index (rather than BMI) and a reference group of average weight smokers and nonsmokers, making comparisons to our study difficult.[20] Although a few prospective mortality studies have assessed the relationship between mortality and BMI, they used separate reference groups for each group of nonsmokers and smokers,[11,12,21] rather than a single reference group of normal-weight never smokers.

These data suggest that combining smoking with obesity poses high mortality risks, especially from circulatory disease deaths for women aged less than 65. It would be useful for other large cohort studies to clarify the relationship among excess weight, smoking, and mortality, and particularly, to examine whether the combined risk is especially elevated in younger women.

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