Letters

RESEARCH LETTER

Smoking Cessation, Weight Change, and Coronary Heart Disease Among Postmenopausal Women With and Without Diabetes

Cigarette smoking is an important cause of cardiovascular disease, and smoking cessation reduces the risk.[1,2] However, weight gain after smoking cessation may increase the risk of diabetes and weaken the benefit of quitting.[3] One study[4] found an association between smoking cessation and a lower risk of cardiovascular events among participants without diabetes that was not modified by weight gain. However, this study[4] had limited power for participants with diabetes and the more specific outcome of coronary heart disease (CHD). We used data from the Women's Health Initiative (WHI)[5] to assess the association between smoking cessation, weight gain, and subsequent CHD risk among postmenopausal women with and without diabetes.

Methods | In the WHI, 161 808 postmenopausal women aged 50 through 79 years were recruited from 40 sites between 1993 and 1998 and followed up every 6 to 12 months. Loss to follow-up was 3% to 5%. Smoking status was defined by self-report at baseline and year 3. Never smokers and former smokers did not smoke at either time point, current smokers smoked at both time points, and those who had newly quit smoked at baseline but not at year 3.

Women without known cancer or cardiovascular disease at baseline or CHD at year 3 were followed up until CHD diagnosis, date of death, loss to follow-up, or September 30, 2010, whichever occurred first. Cases of CHD were adjudicated by physicians and defined as the first occurrence of clinical myocardial infarction, silent myocardial infarction, or death due to CHD.

Diabetes was self-reported and defined as either having diabetes at baseline or year 3. Self-reported diabetes in the WHI has been validated as an indicator of diagnosed diabetes.[6] Cox proportional hazards regression models were used to estimate hazard ratios (HRs) for risk of CHD in relation to smoking status stratified by diabetes status and weight gain between baseline and year 3 (categorized as <5 kg, 5-<10 kg, or ≥10 kg), with and without additional adjustment for covariates.

Statistical analyses were performed using SAS version 9.3 (SAS Institute Inc). The WHI study was approved by institutional review boards at all participating centers. All participants gave written informed consent.

Results | Of 104 391 women followed up, 3381 developed CHD during a mean (SD) of 8.8 (2.8) years. Baseline characteristics appear in **Table 1**. The incidence rates of CHD per 1000 person-years were 3.3 in never smokers, 3.7 in former smokers, 7.6 in current smokers, and 5.3 in those who had newly quit. Among 98 053 women without diabetes, those who had newly quit had an adjusted HR for CHD of 0.74 (95% CI, 0.57-0.95) compared with current smokers; for former smokers, the adjusted HR was 0.39 (95% CI, 0.34-0.45). Among 6338 women with diabetes, those who had newly quit had a lower risk for CHD (HR, 0.36; 95% CI, 0.17-0.78), as did former smokers (HR, 0.41; 95% CI: 0.29-0.59) compared with current smokers. These associations were unchanged after further adjustment for weight change (**Table 2**).

Among women who gained less than 5 kg, the association between smoking status and CHD risk was similar to the overall results in both women with and without diabetes (Table 2). Among women without diabetes who gained 5 kg to less than 10 kg or 10 kg or more, former smokers had a lower CHD risk than current smokers. In women with diabetes who gained 5 kg to less than 10 kg, neither those who had newly quit nor former smokers had a statistically significantly lower CHD risk than current smokers. The number of women with diabetes and a weight gain of 10 kg or more was too small to allow modeling.

Discussion | In this study, smoking cessation was associated with a lower risk of CHD among postmenopausal women with and without diabetes. Weight gain following smoking cessation weakened this association, especially for women with diabetes who gained 5 kg or more, although power was limited in this subgroup due to the small number of cases. Other limitations of the study are that it included only postmenopausal women and did not account for further changes in smoking, weight, or diabetes status after year 3.

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Table 1. Characteristics of Women by Smoking Status Between Baseline and Year 3 of Follow-up (N = 104 391)

	Smoking Status			
	Never Smoked (n = 54 801)	Former Smoker (n = 42 912)	Current Smoker (n = 4787)	Newly Quit (n = 1891)
Age at baseline, mean (SD), y	63.1 (7.2)	62.7 (6.9)	60.8 (6.7)	61.0 (6.6)
White non-Hispanic, No. (%)	44 836 (81.8)	37 264 (86.8)	3787 (79.1)	1512 (80.8)
BMI at baseline[a]	27.7 (5.7)	27.9 (5.8)	26.7 (5.5)	27.3 (5.7)
Diabetes at year 3, No. (%)	3441 (6.3)	2495 (5.8)	252 (5.3)	150 (7.9)
Weight gain between baseline and year 3, mean (SD), kg	0.3 (9.8)	0.4 (9.8)	−0.04 (9.7)	3.0 (10.8)

[a] Body mass index (BMI) calculated as weight in kilograms divided by height in meters squared.

Table 2. Association Between Smoking Cessation and Coronary Heart Disease (CHD) Events (N=104 391)

	Overall				Weight Gain[a]								
					<5 kg			5-<10 kg			≥10 kg[b]		
		HR (95% CI)			HR (95% CI)			HR (95% CI)			HR (95% CI)		
Smoking Status	No. of CHD Cases	Model 1[c]	Model 2[d]	Model 3[e]	No. of CHD Cases	Model 1[c]	Model 2[d]	No. of CHD Cases	Model 1[c]	Model 2[d]	No. of CHD Cases	Model 1[c]	Model 2[d]
No diabetes by year 3													
Current smoker	260	1 [Reference]	1 [Reference]	1 [Reference]	210	1 [Reference]	1 [Reference]	19	1 [Reference]	1 [Reference]	6	1 [Reference]	1 [Reference]
Newly quit	76	0.73 (0.56-0.94)	0.74 (0.57-0.95)	0.74 (0.57-0.96)	48	0.73 (0.54-1.00)	0.75 (0.55-1.03)	16	0.95 (0.49-1.84)	0.95 (0.48-1.88)	7	0.65 (0.22-1.94)	0.79 (0.24-2.62)
Former smoker	1207	0.39 (0.34-0.45)	0.39 (0.34-0.45)	0.40 (0.35-0.46)	999	0.39 (0.34-0.45)	0.39 (0.34-0.46)	104	0.54 (0.33-0.89)	0.47 (0.28-0.79)	24	0.32 (0.13-0.78)	0.35 (0.13-0.98)
Never smoked	1346	0.33 (0.29-0.37)	0.32 (0.28-0.37)	0.33 (0.29-0.38)	1136	0.33 (0.28-0.38)	0.32 (0.28-0.38)	95	0.41 (0.25-0.68)	0.36 (0.21-0.61)	31	0.34 (0.14-0.83)	0.35 (0.13-0.97)
Diabetes by year 3													
Current smoker	39	1 [Reference]	1 [Reference]	1 [Reference]	35	1 [Reference]	1 [Reference]	3	1 [Reference]	1 [Reference]	1	1 [Reference]	1 [Reference]
Newly quit	8	0.37 (0.17-0.79)	0.36 (0.17-0.78)	0.36 (0.16-0.77)	5	0.34 (0.13-0.86)	0.33 (0.13-0.87)	3	0.66 (0.13-3.30)	0.26 (0.03-2.02)	0		
Former smoker	203	0.43 (0.30-0.60)	0.41 (0.29-0.59)	0.41 (0.29-0.59)	150	0.35 (0.24-0.51)	0.34 (0.23-0.50)	20	0.55 (0.16-1.86)	0.26 (0.06-1.03)	8	0.63 (0.08-5.17)	
Never smoked	242	0.36 (0.26-0.50)	0.33 (0.23-0.47)	0.33 (0.23-0.47)	197	0.32 (0.22-0.46)	0.30 (0.21-0.45)	20	0.41 (0.12-1.40)	0.17 (0.04-0.73)	11	0.75 (0.09-5.89)	

Abbreviation: HR, hazard ratio.

[a] The number of cases with weight gain (<5, 5-<10, or ≥10 kg) does not sum to total because of missing weight at baseline or year 3 in 233 cases.

[b] For women with diabetes and weight gain of 10 kg or more, adjusted HRs could not be calculated because of small sample size and unstable model fitting.

[c] Adjusted for age at enrollment (<55, 55-59, 60-64, 65-69, 70-74, or ≥75 y).

[d] Adjusted for age at enrollment (<55, 55-59, 60-64, 65-69, 70-74, or ≥75 y); race/ethnicity (American Indian or Native Alaskan, Asian or Pacific Islander, black, Hispanic or Latino, non-Hispanic white, or other); education (≤high school, some college or technical training, college degree or some postcollege, or ≥master's degree); body mass index (calculated as weight in kilograms divided by height in meters squared; <18.5, 18.5-24.9, 25.0-29.9, 30.0-34.9, 35.0-39.9, or ≥40); waist circumference (in continuous centimeters); physical activity (<5, 5-<10, 10-<20, 20-<30, or ≥30 metabolic equivalent tasks/wk); alcohol intake (nondrinker, past drinker, <1 drink/mo, 1 drink/mo-<1 drink/wk, 1-<7 drinks/wk, or ≥7 drinks/wk); hypertension (yes or no); high cholesterol level requiring pills (yes or no); and participation in other Women's Health Initiative subcohorts (observational study or clinical trials and different treatment assignments for all 4 clinical trials).

[e] Adjusted for all factors in footnote d plus weight change from baseline to year 3 (weight stayed within ±2.5 kg of original weight, weight gain of 2.5-<5 kg, weight gain of ≥5 kg, weight loss of 2.5-<5 kg, or weight loss of ≥5 kg).

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Study concept and design: Luo, Rossouw, Margolis.
Acquisition of data: Luo, Margolis.
Analysis and interpretation of data: Luo, Rossouw, Margolis.
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COMMENT & RESPONSE

Management Setting of Obstructive Sleep Apnea

To the Editor Dr Chai-Coetzer and colleagues[1] compared management models of obstructive sleep apnea (OSA) and found that primary care physicians and advanced practice nurses did not provide inferior screening and diagnosis of OSA vs physicians with specialized training in sleep medicine. I believe that several relevant issues suggest this conclusion is premature.

First, more than twice as many patients in the primary care group than in the sleep specialist group withdrew from the study. Second, the primary care pathway included a telephone call to the patient 2 weeks after starting continuous positive airway pressure (CPAP) and a total of 5 follow-up appointments. The follow-up with the sleep specialist group was unclear, which suggests the study methods may have been biased.

Third, at 6 months, there was a nonsignificant trend showing 0.6 hours greater use of CPAP per night in the specialist group, a difference meaningful in clinical practice. In addition, not everyone who seeks sleep medicine services is a patient with moderate to severe OSA. This is evident in the data in this study showing that 39% of referred cases were excluded for not meeting eligibility criteria.

Specialized training and comprehensive patient evaluation is the only way to ensure that all patients seeking sleep medicine services are well treated, and not just select cases as included in this trial. Both in-laboratory polysomnography and out-of-center sleep testing require the interpretation of a sleep specialist who has the training and expertise to make an accurate diagnosis of OSA, rule out common comorbid sleep disorders, and determine the most appropriate treatment plan. Studies have shown that both American Academy of Sleep Medicine accreditation and board certification in sleep medicine are associated with improved patient care, including increased CPAP adherence.[2,3]

Concerns about waiting lists are not valid in the United States where the number of accredited sleep disorders centers and certified sleep physicians is sufficient. The authors' attempt to generalize the results from Australia to the United States is misleading. The calculations for sleep center management only took into account in-laboratory polysomnography. However, an increasing number of centers are using portable monitors and autotitrating CPAP to evaluate and treat select patients, significantly reducing costs.[4]

I believe that it is unrealistic to expect an overburdened primary care system to take on the additional demands of OSA patients, and it is unnecessary when an extensive system of sleep centers is sufficiently meeting this need.

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To the Editor In patients screened for moderate to severe OSA, Dr Chai-Coetzer and colleagues[1] reported that management in a primary care setting was statistically noninferior to a specialist sleep center setting regarding change in subjective sleepiness measured by the Epworth Sleepiness Scale (ESS). There are several aspects of this study that we think should be highlighted.

Study withdrawal was 2- to 3-fold higher in the primary care vs sleep specialist groups, with almost half of the withdrawals in the primary care group due to CPAP intolerance. No patients in the sleep specialist group withdrew due to CPAP intolerance. The expertise of the sleep medicine specialist in improving CPAP adherence as well as adherence-related outcomes is well known.[2] Also unexplained in the article is how shifting management from the sleep specialist to the primary care clinician would "... improve patient access to sleep services" or result in care "... delivered at a lower cost."

Chai-Coetzer et al used an OSA screening method that they had previously developed and validated for their population.[3] Although such screening previously demonstrated a sensitivity of 97% and a specificity of 87% for severe OSA (apnea-hypopnea index ≥30 events per hour), it neither definitively diagnoses OSA nor assesses for other sleep-related breathing disorders and therefore may not be consistently applicable (despite the exclusion criteria used) to other patient populations.

Misclassifying or overlooking patients with nonsevere OSA, central sleep apnea syndromes, overlap syndromes, and chronic alveolar hypoventilation syndromes may potentially result in suboptimal application of available treatments for serious sleep-disordered breathing. The one noninferior outcome measure was change in ESS score, but previous studies have demonstrated that the ESS is highly variable during sequential scoring within patients,[4] as well as poorly correlated with objective measures of daytime sleepiness in patients with sleep-disordered breathing.[5]

These considerations suggest primary care may not be inferior to specialist sleep centers for management of serious sleep-related breathing disorders.

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