

Smoking Cessation Is Beneficial for All Smokers Despite Potential for Weight Gain

Clair C, Rigotti NA, Porneala B, et al. Association of smoking cessation and weight change with cardiovascular disease among adults with and without diabetes. JAMA 2013;309:1014–21.

Study Overview

Objective. To examine whether the weight gain associated with smoking cessation is associated with adverse cardiovascular disease (CVD) outcomes among adults with and without diabetes.

Design. Prospective cohort study.

Setting and participants. The study used the Offspring cohort from the Framingham Heart Study. The Framingham Offspring Cohort study began in 1971 and included the children and spouses of the original Framingham Heart Study cohort participants. Participants were followed prospectively every 4 to 6 years. The current study comprised 3251 adult participants who were free of CVD outcomes at the onset of examination 3. Follow-up time was defined by the time until the first CVD event or until censoring. Participants were followed for a total of 5 examinations (examination 3 [1984–1987] to examination 8 [December 2011]) over a 20-year period, and 73.6% of participants had at least 1 period of follow-up.

Main outcome measures. The primary outcome was total CVD events as a composite of coronary heart disease (CHD) (coronary death, myocardial infarction, coronary insufficiency, and angina), cerebrovascular events (ischemic stroke, hemorrhagic stroke, and transient ischemic attack), peripheral arterial disease (intermittent claudication), and congestive heart failure. The secondary outcome was a more restrictive outcome (“hard” CHD), and included only myocardial infarction and coronary death. Participants were considered to have diabetes if they had fasting plasma glucose levels of ≥ 126 mg/dL or if they were treated with a hypoglycemic agent or insulin. Current cigarette smokers were defined as those who smoked regularly in the past year. Recent quitters were those who reported not smoking during a follow-up examination but who were smoking in the examination 4 years prior

(ie, had quit for ≤ 4 years). Long-term quitters were those who reported not smoking for 2 or more consecutive examinations after an examination at which they had been a smoker (ie, had quit for > 4 years). Weight change was calculated at each visit as the weight in the current examination minus the weight at the previous examination.

The authors pooled the study visits so that they had 4 pools of a mean duration of 6 years. For each 6-year time period, smoking status was considered at the onset of the time interval, and CVD outcomes were considered during the 6-year follow-up. Age- and sex-adjusted 6-year incidence rates of CVD were calculated by smoking status. Using Cox proportional hazards, the authors examined the likelihood of a CVD event by smoking status. Separate analyses were conducted for people with and without diabetes, as the effect of weight change on CVD outcomes was hypothesized to be different depending on diabetes status. Hazard ratios (HRs) were reported for never smokers, recent quitters, and long-term quitters, compared with smokers. The authors ran minimally adjusted models, adjusting for age and sex, followed by fully adjusted models that included other cardiovascular risk factors such as alcohol consumption, self-reported family history of diabetes, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), triglyceride level, systolic blood pressure, baseline BMI, receipt of cholesterol lowering medications, and receipt of anti-hypertensive medications. Cox proportional hazards were used to examine the association of weight gain after smoking cessation and hard CHD outcomes (ie, myocardial infarction and coronary death).

Main results. Over the course of study follow-up, smoking prevalence decreased from 31% at the third examination to 13% at the eighth examination. Among participants without diabetes, recent quitters gained significantly more weight (median 2.7 kg) over 4 years than long-term quitters (median 0.9 kg), smokers (median 0.9 kg),

and nonsmokers (median 1.4 kg). A similar trend was observed among people with diabetes, with recent quitters gaining more weight (median 3.8 kg) than smokers (median 0.0 kg), long-term quitters (median 0.1 kg), and nonsmokers (median 0.5 kg). While there was no trend in weight change for recent quitters, weight gain decreased over time for long-term quitters with and without diabetes.

During study follow-up there were 631 CVD events, and of these, 337 (53.4%) were related to CHD. Age- and sex-adjusted incidence of CHD events for participants with and without diabetes were higher for smokers, followed by recent quitters, long-term quitters, and nonsmokers. In the CVD-adjusted models restricted to persons without diabetes, recent quitters (HR 0.47, 95% CI 0.24–0.93), long-term quitters (HR 0.46, 95% CI 0.34–0.63), and nonsmokers (HR 0.30, 95% CI 0.21–0.44) had lower HRs for CVD outcomes compared with smokers. Adding weight change to the model did not change the HRs for recent quitters and long-term quitters. The results among persons with diabetes were qualitatively similar, but did not reach statistical significance for recent quitters (HR 0.49, 95% CI 0.11–2.20) and long-term quitters (HR 0.56, 95% CI 0.28–1.14). In secondary analyses, restricting to hard CHD events ($n = 160$), the age- and sex-adjusted incidence of CHD events was much higher for smokers compared with recent quitters, long-term quitters, and nonsmokers with and without diabetes. The adjusted HRs for CHD events among persons without diabetes was lower among recent quitters (HR 0.58, 95% CI 0.20–1.68), long-term quitters (HR 0.29, 95% CI 0.16–0.52), and nonsmokers (HR 0.17, 95% CI 0.06–0.36), though the estimate among recent quitters did not reach statistical significance. Adjusting for weight change did not significantly change the results. The HRs for CHD events for persons with diabetes were similar to those without diabetes. In analyses stratified by the amount of weight gain, long-term quitters who lost weight or who gained 0 to 5 kg had lower HRs for CVD outcomes compared with smokers. Among participants who gained more than 5 kg, there was no statistically significant association by smoking or diabetes status.

Conclusion. Smoking cessation was associated with a lower risk of CVD events among participants without diabetes, and weight gain following smoking cessation did not modify this association. Among participants with

diabetes, a qualitatively similar but a statistically insignificant association was observed. These results suggest that smoking cessation may lead to a cardiovascular benefit despite subsequent weight gain.

Commentary

Many studies have shown the benefits of smoking cessation on decreasing CVD outcomes, but few studies have accounted for subsequent weight gain after smoking cessation and its potential effects on CVD events. In this study, the authors tested the hypothesis that weight gain after smoking cessation would not alter the beneficial effects of cessation on CVD outcomes. The study showed that among persons without diabetes, smoking cessation was associated with lower risk for CVD outcomes despite weight gain. While similar results were observed among persons with diabetes, the results did not attain statistical significance.

Smoking results in increased risk for CVD outcomes by increasing heart rate, myocardial contractility, arterial vasoconstriction, platelet aggregation, and endothelial dysfunction [1]. Many of these attributes are reversible after smoking cessation. The association of smoking and CVD outcomes may also be mediated by cardiac risk factors: an increase in LDL cholesterol or fasting plasma glucose may contribute to the increase in CVD risk among smokers. Many of these risk factors may improve after smoking cessation. Persons who stop smoking may adopt healthier lifestyles such as decreasing alcohol intake or changing their diet, which may contribute to the lowering of CVD risk after smoking cessation. While the current study adjusted for baseline cardiovascular risk factors including cholesterol levels, blood pressure, alcohol consumption, the role of these factors as mediators of the association of smoking cessation and CVD outcomes was not explored. This may merit further exploration in future studies.

The study did explore an important mediator of the association of smoking cessation and CVD outcomes—weight gain. Obesity has emerged as one of the leading causes of preventable morbidity and mortality in the United States, second only to smoking. The prevalence of obesity has increased to over 30% in most age and sex groups [2]. Obesity is linked with increased risk of hypertension, diabetes, CHD, and other chronic conditions [3]. Approximately 80% of recent quitters experience weight gain after smoking cessation, and some smokers may gain more than 10 kg to 15 kg after

smoking cessation [4]. This has led to the concern that the weight gain associated with smoking cessation could mitigate the beneficial effects of smoking cessation on CVD outcomes. However, the results of the current study refute these assertions by showing that the incidence of and the risk of CVD events were much higher for smokers compared with recent quitters, long-term quitters and nonsmokers. This association was independent of weight change associated with smoking cessation. The association of smoking cessation and CVD outcomes was similar among those with and without diabetes, although the latter finding did not attain statistical significance because of inadequate power. These results support a cardiovascular benefit from smoking cessation for all smokers, including quitters who have gained weight.

The study has several limitations. The authors conducted stratified analyses by weight. As 10% to 20% smokers gain more than 10 kg to 15 kg of weight after cessation, the current study may not have captured the full range of weight gain that is possible among persons with and without diabetes [5]. Thus, it is possible that these results may not apply to those who have gained a significant amount of weight, and this should be explored in future studies. The study used self-reported measures of smoking and the recall period was long, resulting in a potential for misclassification of smoking status. Because quitting was measured as point-prevalence abstinence in the last 4-year time period, relapse to smoking in between the measurement time points was not determined. The Framingham Offspring cohort is a predominantly white population, and therefore the results of this study may not be generalizable to populations with higher proportions of racial/ethnic minori-

ties. Despite these limitations, the study's strength are in the use of a large community-based cohort, with robust measures for smoking, diabetes, and other CVD risk factors over a 20-year time frame.

Applications for Clinical Practice

The results of the current study demonstrate the beneficial effects of smoking cessation for all smokers. Health care providers should encourage all smokers to quit smoking using currently available treatments. As the concern for weight gain may dissuade some smokers from making quit attempts, the results of the current study may be used to reassure these smokers that the weight gain may not mitigate the beneficial effects of cessation on subsequent CVD outcomes. Integrating exercise regimens with smoking cessation interventions may help counter the smoking cessation-related weight change.

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