

4. Lin RZ, Dreyzin A, Aamodt K, et al. Induction of erythropoiesis using human vascular networks genetically engineered for controlled erythropoietin release. *Blood* 2011;118:5420-8.
5. Bernhardt WM, Wiesener MS, Scigalla P, et al. Inhibition of prolyl hydroxylases increases erythropoietin production in ESRD. *J Am Soc Nephrol* 2010;21:2151-6.
6. Macdougall IC. New anemia therapies: translating novel strategies from bench to bedside. *Am J Kidney Dis* 2012;59:444-51.
7. Macdougall IC, Rossert J, Casadevall N, et al. A peptide-based erythropoietin-receptor agonist for pure red-cell aplasia. *N Engl J Med* 2009;361:1848-55.
8. Macdougall IC, Provenzano R, Sharma A, et al. Peginesatide for anemia in patients with chronic kidney disease not receiving dialysis. *N Engl J Med* 2013;368:320-32.
9. Fishbane S, Schiller B, Locatelli F, et al. Peginesatide in patients with anemia undergoing hemodialysis. *N Engl J Med* 2013;368:307-19.
10. Jelkmann W. Biosimilar recombinant human erythropoietins ("epoetins") and future erythropoiesis-stimulating treatments. *Expert Opin Biol Ther* 2012;12:581-92.

DOI: 10.1056/NEJMe1215043

Copyright © 2013 Massachusetts Medical Society.

New Evidence That Cigarette Smoking Remains the Most Important Health Hazard

Steven A. Schroeder, M.D.

Everyone knows cigarette smoking is bad for you. Most people in the United States assume that smoking is on its way out. But the grim reality is that smoking still exerts an enormous toll on the health of Americans, as documented in two articles in this issue of the *Journal*.^{1,2} Both articles review mortality trends over time for men and women according to smoking status, and both confirm that smoking remains a huge threat to the public's health.

Jha et al. review data from the U.S. National Health Interview Survey, which involved 113,752 women and 88,496 men 25 years of age or older who were interviewed between 1997 and 2004. The investigators examined the rates and causes of death by the end of 2006.¹ Within the age group 25 to 79 years, the mortality of current smokers of both sexes was three times that of participants who had never smoked. Diseases attributable to smoking accounted for about 60% of smokers' deaths. The benefits of quitting smoking were dramatic for all age groups, with substantial gains in life expectancy, as compared with participants who had continued to smoke. Those who quit between the ages of 25 and 34 years lived 10 years longer; those who quit between ages 35 and 44 gained 9 years, those who quit between ages 45 and 54 gained 6 years, and those who quit between ages 55 and 64 gained 4 years. These differences persisted after adjustment for such potentially confounding variables as educational level, alcohol use, and adiposity.

These investigators also found that the prevalence of smoking is much lower among persons older than 45 years of age than among younger persons, a finding that reflects both successful

efforts to quit and the earlier deaths among smokers. Those who continued to smoke rarely lived to the age of 85 years. It was surprising that many people began smoking after the age of 20 years, and 15% of women began smoking after age 25, which is later than is usually assumed and highlights the need to target young adults with appropriate nonsmoking messages. The hazard ratios for lung-cancer mortality were staggering: 17.8 for female smokers and 14.6 for male smokers. Also, the risk of death for women who smoke is 50% higher than the estimates reported in the 1980s.

Thun et al. analyzed seven U.S. population surveys to determine whether death rates among female smokers — previously documented to be lower than those among male smokers — were converging with those for men.² Indeed, women who smoke like men die like men who smoke. These investigators assessed mortality trends across three time periods in the United States (1959–1965, 1982–1988, and 2000–2010). During the 50-year survey span, mortality in the overall study population dropped by 50%, but female smokers received no benefit and male smokers showed only a 24% reduction. Relative risks for lung-cancer death among smokers were almost five times as high for men, as compared with women, in the 1959–1965 cohort, but in the 2000–2010 cohort the risks had equalized and had increased at 25 times as high for both men and women.

The study by Thun et al. spanned an era during which smoking habits were changing. Today, most smokers smoke filtered cigarettes that have less tar, and the habit of smoking is in-

creasingly concentrated among the less educated and the poor. Beginning in 1995, smokers smoked fewer cigarettes per day.³ Thun et al. speculate that increasing death rates from chronic obstructive pulmonary disease among male smokers over the three time periods reflect design changes in cigarettes that allow deeper inhaling. Similarly, there was an increased incidence in peripheral adenocarcinomas, offsetting declining rates of more central squamous-cell and small-cell lung cancers.

Population surveys accurately portray overall trends but omit nuances. Since frequency of smoking was not measured, we don't know whether less illness occurs among light smokers (an increasing proportion of the smoking population), as compared with heavy smokers. Overall, smoking prevalence in the study by Thun et al. was only 9.5% — half the 2011 prevalence of 19%⁴ — because the samples overrepresented people who were better educated. Population groups with high rates of smoking (e.g., incarcerated persons and those with mental illness or substance-abuse disorders) are probably under-sampled. Because both articles compared relative risks between smokers and nonsmokers, this omission would not alter the direction of the results. But because smokers in these populations smoke more cigarettes per day, the findings probably underestimate the overall mortality among smokers.⁵

Two important messages emerge from these articles. First, in terms of health benefits, it is never too late to quit. Clinicians in general, and especially those who care for patients with smoking-related illnesses (e.g., oncologists, cardiologists, pulmonologists, emergency physicians, psychiatrists, and primary care physicians),

should do more to stimulate quit attempts.^{6,7} Second, the importance of smoking as a health hazard needs to be elevated. More women die of lung cancer than of breast cancer. But there is no “race for the cure” for lung cancer, no brown ribbon, and no group analogous to the Susan G. Komen Breast Cancer Foundation. Because smoking has become a stigmatized behavior concentrated among persons of low social status, it risks becoming invisible to those who set health policies and research priorities. Yet, the need for greater attention to the policies known to reduce the prevalence of smoking remains urgent. As former Australian Health Minister Nicola Roxon has said, “We are killing people by not acting.”⁸

Disclosure forms provided by the author are available with the full text of this article at www.nejm.org.

From the Department of Medicine, University of California, San Francisco, San Francisco.

1. Jha P, Ramasundarahettige C, Landsman V, et al. 21st-Century hazards of smoking and benefits of cessation in the United States. *N Engl J Med* 2013;368:341-50.
2. Thun MJ, Carter BD, Feskanich D, et al. 50-Year trends in smoking-related mortality in the United States. *N Engl J Med* 2013;368:351-64.
3. Schroeder SA. How clinicians can help smokers to quit. *JAMA* 2012;308:1586-7.
4. Current cigarette smoking among adults — United States, 2011. *MMWR Morb Mortal Wkly Rep* 2012;61:889-94.
5. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: a population-based prevalence study. *JAMA* 2000;284:2606-10.
6. Fiore MC, Baker TB. Treating smokers in the health care setting. *N Engl J Med* 2011;365:1222-31.
7. Rigotti NA. Strategies to help a smoker who is struggling to quit. *JAMA* 2012;308:1573-80.
8. Australian Government Department of Health and Ageing. Launch of the Preventative Health Strategy: task force report, 2009 ([http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(09\)61647-0/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)61647-0/fulltext)).

DOI: 10.1056/NEJMe1213751

Copyright © 2013 Massachusetts Medical Society.

APPLY FOR JOBS AT THE NEJM CAREERCENTER

Physicians registered at the NEJM CareerCenter can apply for jobs electronically. A personal account created when you register allows you to apply for positions, using your own cover letter and CV, and keep track of your job-application history. Visit NEJMjobs.org for more information.