

## Smoking Kills: Experimental Proof from the Lung Health Study

In 1938, Raymond Pearl reported in *Science* that tobacco smoking shortened the life span (1). In a study of determinants of longevity in East Baltimore families, he developed life tables for smokers and nonsmokers, using data from 6813 men, most of whom were smokers. Pearl showed that life span after age 30 years for white men was reduced by about 10 years in “heavy smokers” compared with nonsmokers (Figure). Longevity was also lower for “moderate smokers.” In retrospect, this powerful observation received surprisingly little attention, even though an effect of this magnitude on total mortality, a crude but integrating measure of population health, must have come from strong increments in risk for death from specific diseases. George Seldes, an investigative reporter who championed tobacco control, attributed the limited media coverage of the finding to the influence of the tobacco industry (2).

Further studies of smoking and overall mortality were not reported until the 1950s, when early findings of cohort studies initiated to prospectively investigate the risks of lung cancer and other diseases associated with smoking were published. By 1964, the first U.S. Surgeon General’s Report on smoking and health (3) had reviewed the results of 7 cohort studies, including the study of British physicians for which 50-year findings were recently reported (4). All of the studies showed increased risk for dying in smokers compared with nonsmokers, and some studies showed that the risk increased with the number of cigarettes smoked. The 1964 report carefully discussed the possibility that either biased selection of participants or failure to control for the effects of confounding factors accounted for the negative association of smoking with longevity. The report evaluated these possibilities qualitatively and quantitatively and set them aside. The Surgeon General’s Advisory Committee concluded that “cigarette smoking contributes substantially to mortality from certain specific diseases and to the overall death rate.”

Even after publication of this report, however, the tobacco industry and its consultants continued to argue that smoking had not been established as a “cause” of lung cancer and other diseases (5). These critics characterized epidemiologic evidence as insufficient to infer causality and as subject to selection bias and confounding; they insisted that experimental evidence was the accepted standard for establishing causation. In principle, a randomized clinical trial of active smoking would exclude the possibility of selection bias and confounding, since the smoking status of individuals would depend on random assignment rather than on personal characteristics that could determine the risk for disease and death. A randomized trial of smoking is neither feasible nor ethical. An alternative strategy is to study the effect of stopping smoking by conducting a randomized trial of smoking cessation. Such trials have in-

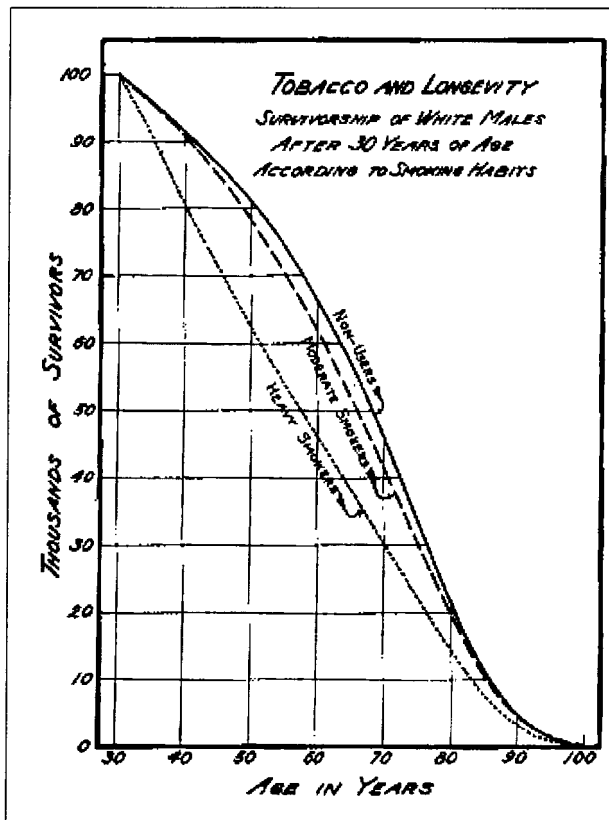
involved random assignment of smokers to an intensive intervention group or to a control group of “usual” management. Lower mortality rates in the intervention group would provide strong and incontrovertible evidence that smoking caused increased mortality, since removing the causal factor at a greater rate from 1 of 2 comparable groups resulted in lower mortality. This result would also prove that smoking cessation decreases mortality rates. Among the trials of smoking cessation, few have had enough participants or long enough follow-up to accurately measure the risks for disease and death.

In this issue, Anthonisen and colleagues (6) describe their findings from more than 14 years of follow-up of participants in the Lung Health Study, which was of sufficient size and duration to test whether smoking cessation reduces mortality. This randomized trial tested the hypothesis that smoking cessation and inhaled bronchodilator therapy improved the early natural history of chronic obstructive pulmonary disease (7). After 5 years of follow-up, the rate of smoking cessation was higher for those randomly assigned to the special intervention group (21.7%) than for those assigned to the usual care group (5.4%). With continued follow-up to 14.5 years, mortality rates from all causes, lung cancer, and cardiovascular disease were higher in the usual care group. The characteristics of the 2 groups were similar at baseline (7), and the findings support the inference that reduction of smoking *caused* a reduction in mortality. In fact, the reductions were substantial for causes of death that have long been linked to smoking: lung cancer, respiratory disease, and coronary heart disease.

The Lung Health Study is not the first trial to measure the effect of smoking cessation on mortality. The Multiple Risk Factor Intervention Trial (MRFIT) was a randomized trial of risk factor reduction strategies in 12 866 middle-aged men at high risk for cardiovascular disease (8). The intervention arm included counseling for smoking cessation, and more men in the intervention group stopped smoking compared with the usual care group. However, the intervention did not reduce either coronary heart disease deaths or total deaths. The authors attributed this “negative” finding to an unexpectedly high level of risk factor reduction in the usual care group, which reduced the effect of the MRFIT interventions. The R.J. Reynolds Tobacco Company used this “negative” finding in a 1985 advertisement but agreed to desist after the Federal Trade Commission cited it for making false and misleading statements (9).

Beyond the findings of the clinical trials, observational studies provide massive and incontrovertible evidence that smoking is linked to death from all causes and from specific causes (10–13). In general, mortality risks of smoking increase with numbers of cigarettes smoked and decrease

Figure. The survivorship lines of life tables for white males falling into three categories relative to the usage of tobacco.



A. Non-users (solid line); B. Moderate smokers (dash line); C. Heavy smokers (dot line). Originally published in Science. 1938;87:216-7.

progressively with increasing number of years after stopping smoking (10, 12). Cessation has benefits at all ages (12). The risks for cardiovascular diseases drop more quickly after cessation than do risks for cancer, but nonetheless lung cancer mortality rates were lower in the Lung Health Study’s intervention group with 14.5 years of follow-up. In many countries, declining mortality rates from coronary heart disease and from lung cancer in men reflect trends of smoking cessation, providing population-level evidence of its benefit.

Given the extensive evidence available and the long-accepted conclusion that smoking causes increased mortality rates, why are the new findings from the Lung Health Study noteworthy? From a historical perspective, they provide further “proof,” based on experiment rather than observation, that smoking is causally responsible for the increased risk for death in smokers. No one can make a serious claim to the contrary in light of this randomized trial evidence. The Lung Health Study findings also offer a reminder that smoking kills middle-aged people; persons who die in middle age lose over 23 years of life on average (14). In fact, if we are to begin to control the rising numbers of smoking-related deaths soon, we must increase rates of smoking cessation now, since we won’t see the benefits

for decades. The new results from the Lung Health Study confirm again that smoking cessation prolongs life.

These findings have clinical as well as public health implications. For clinicians, they offer a reminder of the benefits of smoking cessation. The clinical toolbox includes few interventions that are certain to have immediate benefits for life span. Interventions by clinicians do increase the rates of successful quitting, and clinicians should follow recommended guidelines by obtaining a smoking history from all patients and assisting smokers in quitting (15). Mentioning the powerful new findings from the Lung Health Study may motivate some smokers to stop.

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References

1. Pearl R. Tobacco smoking and longevity. *Science*. 1938;87:216-7.
2. Seldes G. The suppressed story of tobacco. *IN FACT*. 1942;VI:10.
3. U.S. Department of Health, Education and Welfare (DHEW). Smoking and health. Report of the Advisory Committee to the Surgeon General. DHEW Publication No. [PHS] 1103. Washington, DC: U.S. Government Printing Office; 1964.
4. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years’ observations on male British doctors. *BMJ*. 2004;328:1519-27. [PMID: 15213107]
5. Kluger R. Ashes to Ashes: America’s Hundred-Year Cigarette War, the Public Health, and the Unabashed Triumph of Philip Morris. New York: Alfred A. Knopf; 1996.
6. Anthonisen NR, Skeans MA, Wise RA, Manfreda J, Kanner RE, Connett JE. The effects of a smoking cessation intervention on 14.5-year mortality. A randomized clinical trial. *Ann Intern Med*. 2005;142:233-9.
7. Anthonisen NR, Connett JE, Kiley JP, Altose MD, Bailey WC, Buist AS, et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The Lung Health Study. *JAMA*. 1994;272:1497-505. [PMID: 7966841]
8. Ockene JK, Hymowitz N, Sexton M, Broste SK. Comparison of patterns of smoking behavior change among smokers in the Multiple Risk Factor Intervention Trial (MRFIT). *Prev Med*. 1982;11:621-38. [PMID: 6761682]
9. Heads butt over an ad. *Time*. 30 June 1986.
10. U.S. Department of Health and Human Services, Public Health Service, National Cancer Institute. Changes in Cigarette-Related Disease Risks and Their Implication for Prevention and Control. Smoking and Tobacco Control Monograph. Burns DM, Garfinkel L, Samet JM, eds. Bethesda, MD: U.S. Government Printing Office; 1997. NIH publication no. 97-4213.
11. U.S. Department of Health and Human Services. Reducing the Health Consequences of Smoking. 25 Years of Progress. A Report of the Surgeon General. Washington, DC: U.S. Government Printing Office; 1989.
12. U.S. Department of Health and Human Services. The Health Benefits of Smoking Cessation. A Report of the Surgeon General. Washington, DC: U.S. Government Printing Office; 1990. DHHS publication no. 90-8416.
13. U.S. Department of Health and Human Services. The Health Effects of

Active Smoking. A Report of the Surgeon General. Washington, DC: U.S. Government Printing Office; 2004.

14. **Peto R, Lopez AD, Boreham J, Thun M, Heath C Jr.** Mortality from tobacco in developed countries: indirect estimation from national vital statistics. *Lancet*. 1992;339:1268-78. [PMID: 1349675]

15. **Fiore M, Bailey W, Cohen S.** Treating Tobacco Use and Dependence: Clinical Practice Guidelines. Rockville, MD: U.S. Department of Health and Human Services, U.S. Public Health Service; 2000.

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