

Is there a role for health-effects research?

According to the US Surgeon General, "smoking represents the most extensively documented cause of disease ever investigated in the history of biomedical research."¹ Tens of thousands of studies on humans and animals have demonstrated how smoking affects myriad organs, tissues, and biological processes. Perusal of the Citations section of *Tobacco Control* (see p 312) would lead one to believe that health-effects research continues unabated.

Nevertheless the focus of tobacco-related research seems to have shifted in recent years, albeit slowly, towards studies of smoking behaviour and tobacco control. This journal aims to encourage that shift. A journal supplement, published simultaneously with the third issue, explores gaps in tobacco policy research and recommends priorities for future policy research.² An editorial by deputy editor Simon Chapman in the second issue addressed the need to upgrade the academic respectability of tobacco control advocacy studies.³

In the face of these currents, one might ask, Is there *any* role for continued health-effects research? Indeed, if tobacco control advocates were asked whether more research is needed on the health effects of smoking, most would probably respond with a quick and emphatic "no." But a case can be made on several grounds for more health-effects research.

In the first place, we must recognise that much, if not most, of today's research on the health effects of smoking does not come out of a tobacco control or tobacco research budget. Instead, studies are done to investigate cancer, heart disease, complications of pregnancy, and so on, and as part of those studies data are collected on smoking behaviour. This research is typically funded out of a categorical research budget targeted to a specific disease or organ system. Smoking data are often collected in these studies to allow investigators to "control" for smoking while pursuing other research questions. On other occasions, an assessment of smoking behaviour is built into study protocols to allow researchers to explore smoking-and-disease associations, although these analyses are usually not the primary reason for initiating the study.

As long as health-effects research does not divert funding from tobacco control or research on tobacco control, it should be encouraged. In fact, given the number and diversity of toxic chemicals in tobacco smoke, and the presence of many of those toxins in the bloodstream of smokers, one could argue that research on virtually all diseases should include an assessment of the possible role of smoking.

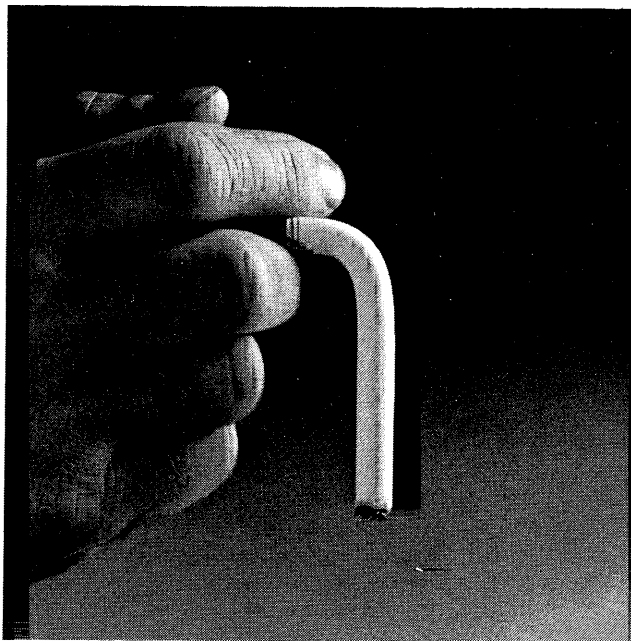
Tobacco control advocates may be more supportive of health-effects research if they appreciate how such research can have direct applications to tobacco control. I see at least four areas where health-effects research may enhance our ability to prevent and reduce tobacco use.

Acquiring new and powerful educational messages

Many smokers and potential smokers who are immune to warnings about lung cancer and heart disease may be susceptible to messages that hit "closer to home." Several studies, for example, have investigated the associations between smoking and impaired male sexual performance, low sperm density, and poor sperm quality. Overall

findings are inconclusive because of inconsistent results and methodological limitations in many of the studies.¹ If more and better research confirms a causal link between smoking and these effects, the impact on young and middle-aged men could be powerful. The advertisement reproduced in the figure and a 1988 cover story in *Reader's Digest* ("Warning: smoking endangers your sex life")⁴ illustrate the practical application of such research. The fact that some men give up life-saving anti-hypertension treatment because of its effect on sexual performance⁵ suggests that some would give up a life-taking behaviour such as smoking for the same reason.

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Eileen Korey

Halsey *et al* found an association between smoking and HIV infection in Haitian women after controlling for potential confounding.⁶ They postulated that several biological effects of smoking could increase the risk of HIV infection, including effects on the immune system, alteration of local immune factors in the genital tract, and hormonal effects. If research confirms that smoking increases the risk of HIV infection, it is likely that the widespread concern about HIV/AIDS in the community

will grow – with spin-off benefits to tobacco control, especially among populations at high risk of acquiring HIV infection.

Another example is the relation between smoking and athletic performance. A deleterious effect of smoking on athletic performance has been shown,⁷ but further information on the mechanisms and extent of this performance deficit should be collected. A highly innovative (but underutilised) educational campaign developed by the US Public Health Service – called “The Performance Edge” – teaches about the effects of smoking and alcohol on athletic performance and physical fitness.⁸ The target audience is physically active teenagers and pre-teenagers, among whom dire warnings about cancer, emphysema, and stroke may have little if any impact. If further research confirms a strong correlation between smoking and impaired athletic performance, programmes such as “The Performance Edge” might be developed and more widely disseminated and used.

Two other examples are especially pertinent to older populations: facial skin wrinkling and Alzheimer’s disease. Data from five studies show an association between smoking and facial skin wrinkling among whites; little information on this association is available, however, for blacks.⁹ A study published in the third issue of *Tobacco Control* showed an association between smoking and Alzheimer’s disease, although other studies have not found an association.¹⁰ Further research on the relation between smoking and premature aging (along with effective dissemination of the findings) might have a huge impact in discouraging smoking among middle-aged and older people. As Grady and Ernster point out, “For many smokers, the thought of facial wrinkles and the appearance of premature aging may be more loathsome than disability or death.”⁹ Interestingly, a postage stamp issued by Afghanistan in 1980 (reproduced on the cover of the second issue of *Tobacco Control*) portrays smoking as a cause of premature aging.

Health effects with relevance to public policy

Some health-effects research may have direct implications for public policy. An obvious example is passive smoking. Clearly, enough is already known about the health effects of passive smoking, particularly lung cancer,^{11–14} to justify a ban on smoking in public places and worksites. Nevertheless, more research documenting the full extent of the health effects of passive smoking – for example, the link with heart disease^{15–17} – may accelerate the passage of controls on smoking. Furthermore, research that isolates the health effects of passive smoking *in the workplace* will strengthen the already compelling case for workplace smoking bans.

Another example is research on the interactions between smoking and exposure to occupational toxins in the causation of disease.¹⁸ For instance, documentation of a new synergistic relation between smoking and exposure to a worksite chemical or fibre might affect hiring policies (smokers may be excluded), compensation benefits (smokers may receive less compensation than non-smokers), and assignment of liability (tobacco companies may have to share damages (this has been sought in asbestos litigation in the United States)).

Research on the toxicity of cigarette additives (and their combustion products) might lead to their regulation and public disclosure (for example, on package labelling). Research on the toxicity and health effects of new tobacco products – such as denicotined cigarettes (for example, Next), perfumed cigarettes (for example, Chelsea, Horizon), and cigarettes purported to yield less sidestream

smoke (for example, Premier, Vantage Excel, and Super-slims) – might provide support for regulations or bans on these specific products or more generally on all new, major product modifications.

Recruiting new allies

Research findings that indict smoking as a cause of disease in organs previously thought to be unaffected by smoking may recruit new health organisations to the cause and may encourage a new cadre of specialists to counsel their patients to stop smoking. For example, two studies published recently in the *Journal of the American Medical Association* documented an association between smoking and the risk of cataract in men and women.^{19,20} In an editorial commenting on these findings, Dr Sheila West estimated that approximately 20% of cataract cases in the United States may be attributable to smoking. “It appears that the litany of ills associated with smoking is growing,” she wrote, “as we add to it cataracts, the world’s leading cause of blindness.”²¹

There are more than 15 500 ophthalmologists involved in patient care in the United States,²² each of whom sees, on average, 120 patients each week.²³ If these specialists, as well as optometrists, began to routinely counsel their patients to stop smoking, the impact might be substantial.

Another example under this category is the relation between smoking and osteoporosis. Studies on the associations between smoking and (a) bone mass and (b) risk of osteoporotic fractures have yielded conflicting findings.¹ If future research confirms causal associations, perhaps orthopaedic surgeons, rheumatologists, and their professional associations will jump on the anti-tobacco bandwagon.

Estimating smoking-attributable disease in a population

Attributable-risk calculations used to determine smoking-attributable morbidity, mortality, and economic costs require knowledge of the relative risks of acquiring (or dying from) diseases among current and former smokers compared with the risks among never smokers.^{24,25} Estimates of relative risk are available for many developed countries but are unavailable for most developing countries. Consequently, studies of smoking-attributable disease in developing countries typically use estimates derived from other populations, despite the fact that smoking patterns – for example, duration and intensity of smoking – may differ between the two sites. Even though adjustments can be made – for instance, to account for the “maturity” of a country’s smoking epidemic²⁶ – the absence of country-specific estimates of relative risk reduces the precision of the attributable-risk estimates. Thus, health-effects research in developing countries would help define the *precise* risks of smoking-related diseases in those countries, permitting more accurate measures of the public health impact of smoking. *Domestic* research that allows precise estimates of smoking’s impact on a nation’s health may help build support for anti-tobacco programmes and policies.

This benefit of health-effects research is not confined to developing countries. It can also apply to developed countries, where the relative risks of smoking-related diseases may change as the smoking epidemic becomes more “mature,” as smoking patterns change, and as new tobacco products are introduced. For example, data from the American Cancer Society’s Cancer Prevention Study II (1982–6) showed substantial increases in relative risks, especially for women, compared with relative risks from

the Society's Cancer Prevention Study I (1959-65). The more current figures yielded much higher estimates of smoking-attributable mortality for the United States.²⁴ Those new estimates quickly became a prominent feature of media alerts, legal briefs, and other documents put out by pro-health agencies and organisations.

* * *

As seen above, health-effects research can still yield important dividends for tobacco control. Beyond those benefits, however, such research provides information of intrinsic scientific and medical interest. That information may eventually open up new avenues for the prevention and treatment of disease – avenues which will have nothing to do with avoiding tobacco use. As Dr Jonathan Samet has noted,

Cigarette smoking represents an unfortunate but scientifically important research opportunity. It is being used to understand carcinogenesis, biomarkers of injury, and chemoprevention. Some important scientific lessons have been learned already from smoking, and the scientific community continues to heavily utilize the research opportunities afforded by smoking (written communication, 14 September 1992).

Research on smoking is of particular interest in the case of diseases whose aetiologies are incompletely understood. Included are diseases for which smokers are at higher risk – for example, cervical, hepatocellular, penile, and anal cancers¹ – as well as diseases for which smoking seems to provide a protective effect (endometrial cancer,¹ Parkinson's disease,²⁷ and ulcerative colitis²⁸). With respect to endometrial cancer, for example, the 1990 Surgeon General's report¹ (noted on page 172) that

...further investigation of the mechanisms for the protective effect of smoking on endometrial cancer is of scientific interest to better understand the effects of smoking on hormones *and of hormones on endometrial cancer risk*.... [my italics]

(The report hastened to add that "this inverse association with smoking has no public health relevance as the well-substantiated risks to other organ systems from continued smoking far outweigh any potential benefits to the endometrium.")

* * *

In summary, continued health-effects research will provide important benefits to tobacco control, and will enhance our ability to understand, to prevent, and to treat a variety of diseases. My argument that health-effects research should be encouraged hinges on the premise that such research will not drain resources from tobacco control and research on tobacco control. If, however, a health-effects study would consume resources that would otherwise be available for research on smoking behaviour or anti-tobacco interventions, then the former should proceed only if the potential benefits of the investigation are sizable.

To illustrate this point, let's consider a hypothetical example. A developing country would like more precise estimates of smoking-attributable mortality and is considering funding an epidemiological study to generate its own relative risk estimates for smoking-related diseases. This country has little or no information on the prevalence of smoking among youth, on public awareness of the dangers of smoking, on the degree to which the hazards of smoking are taught in school curricula, or on the

prevalence of workplace smoking restrictions. If all tobacco-and-health research in this country competes for the same pot of money, studies to investigate tobacco use and tobacco-related programmes and policies should be funded in preference to a study on the relative risks of smoking-related disease.

RONALD M DAVIS

Editor

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- 1 US Department of Health and Human Services. *The health benefits of smoking cessation: a report of the Surgeon General, 1990*. Atlanta, Georgia: Centers for Disease Control, Office on Smoking and Health, 1990. (DHHS Publication No (CDC) 90-8416.)
- 2 Policy research: strategic directions. *Tobacco Control* 1992; 1 (suppl): S1-S6.
- 3 Chapman S. Upgrading the academic respectability of advocacy studies. *Tobacco Control* 1992; 1: 81-3.
- 4 Reuben D. Warning: smoking endangers your sex life. *Reader's Digest* 1988 April: 98-100.
- 5 Delaney P. When medication affects sex, some men risk hypertension. *New York Times* 1992 July 8: B8(N).
- 6 Halsey NA, Coberly JS, Holt E, Coreil J, Kissinger P, Moulton LH, et al. Sexual behavior, smoking, and HIV-1 infection in Haitian women. *JAMA* 1992; 267: 2062-6.
- 7 Royal College of Physicians of London. *Smoking and the young: a report of a working party of the Royal College of Physicians*. London: Royal College of Physicians of London, 1992: 35-6.
- 8 Surgeon General announces new campaign against tobacco and alcohol. *Chronic Disease Notes & Reports* 1990 Sept; 3 (3): 7-8. (Atlanta, Georgia: Centers for Disease Control.)
- 9 Grady D, Ernster V. Does cigarette smoking make you ugly and old? *Am J Epidemiol* 1992; 135: 839-42.
- 10 Hirayama T. Large cohort study on the relation between cigarette smoking and senile dementia without cerebrovascular lesions. *Tobacco Control* 1992; 1: 176-9.
- 11 US Department of Health and Human Services. *The health consequences of involuntary smoking. A report of the Surgeon General*. Washington, DC: US Department of Health and Human Services, Public Health Service, Centers for Disease Control, 1986. (DHHS Publication No (CDC) 87-8398.)
- 12 National Research Council. *Environmental tobacco smoke. Measuring exposures and assessing health effects*. Washington, DC: National Academy Press, 1986.
- 13 International Agency for Research on Cancer. *Tobacco smoking*. Lyons: International Agency for Research on Cancer, 1986: 303-8, 314. (IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans, vol 38.)
- 14 US Environmental Protection Agency. *Respiratory health effects of passive smoking: lung cancer and other disorders* (preliminary draft). Washington, DC: US Environmental Protection Agency, Office of Health and Environmental Assessment, Office of Research and Development, May 1992. (EPA draft report EPA/600/6-90/006B.)
- 15 Wells AJ. An estimate of adult mortality in the United States from passive smoking. *Environment International* 1988; 14: 249-65.
- 16 Glantz S, Parnley W. Passive smoking and heart disease: epidemiology, physiology, and biochemistry. *Circulation* 1991; 83: 1-12.
- 17 Steenland K. Passive smoking and the risk of heart disease. *JAMA* 1992; 267: 94-9.
- 18 US Department of Health and Human Services. *The health consequences of smoking: cancer and chronic lung disease in the workplace. A report of the Surgeon General, 1985*. Rockville, Maryland: Public Health Service, Office on Smoking and Health, 1985. (DHHS Publication No (PHS) 85-50207.)
- 19 Christen WG, Manson JE, Seddon JM, Glynn RJ, Buring JE, Rosner B, et al. A prospective study of cigarette smoking and risk of cataract in men. *JAMA* 1992; 268: 989-93.
- 20 Hankinson SE, Willett WC, Colditz GA, Seddon JM, Rosner B, Speizer FE, et al. A prospective study of cigarette smoking and risk of cataract in women. *JAMA* 1992; 268: 994-8.
- 21 West S. Does smoke get in your eyes? *JAMA* 1992; 268: 1025-6.
- 22 Roback G, Randolph L, Seidman B. *Physician characteristics and distribution in the U.S.* Chicago: American Medical Association, 1992: 95.
- 23 Gonzalez ML. *Physician marketplace statistics 1991*. Chicago: American Medical Association, 1991: 28.
- 24 US Department of Health and Human Services. *Reducing the health consequences of smoking: 25 years of progress. A report of the Surgeon General, 1989*. Atlanta, Georgia: Centers for Disease Control, Office on Smoking and Health, 1989: chapter 3. (DHHS Publication No (CDC) 89-8411.)
- 25 Shultz JM, Novotny TE, Rice DP. Quantifying the disease impact of cigarette smoking with SAMMEC II software. *Pub Health Rep* 1991; 106: 326-33.
- 26 US Department of Health and Human Services. *Smoking and health in the Americas: A 1992 report of the Surgeon General, in collaboration with the Pan American Health Organization*. Atlanta, Georgia: Centers for Disease Control, Office on Smoking and Health, 1992: chapter 3. (DHHS Publication No (CDC) 92-8419.)
- 27 Sasco AJ, Paffenbarger RS. Smoking and Parkinson's disease. *Epidemiology* 1990; 1: 460-5.
- 28 Sandler RS, Sandler DP, McDonnell CW, Wurzelmann JI. Childhood exposure to environmental tobacco smoke and the risk of ulcerative colitis. *Am J Epidemiol* 1992; 135: 603-8.