

This section looks back to some of the ground-breaking public health papers of the twentieth century, reproducing them in their original form and adding a commentary on their significance from a modern-day perspective. This month, Alan Lopez reviews the importance of Doll & Hill's 1950 paper on the potential link between smoking and lung cancer. The original paper is reproduced by permission of the *British medical journal*.

## Measuring the health hazards of tobacco: Commentary

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"We therefore conclude that smoking is a factor, and an important factor, in the production of carcinoma of the lung". With this cautious statement, and an equally prudent remark on the evidence for a dose-response relationship, which while "admittedly speculative", none the less suggested that "... the risk of developing the disease increases in simple proportion with the amount smoked", the case was launched against tobacco as a leading cause of disease (1). Almost five decades and thousands of scientific studies later, the extraordinary individual risks of smoking are now well established in populations where the habit is widespread, and are no longer a question of substantial scientific uncertainty.

But this has not always been the case, and certainly was far from accepted wisdom in 1950 when Doll & Hill published their study. Indeed, not long after its introduction into Europe at the end of the fifteenth century, tobacco was thought to have medicinal value! While some undoubtedly found the smoking of tobacco disagreeable, such was its social acceptability that when King James I of England published a vigorous attack on the habit in 1603 (*Misocapnus sive de abusu tobacci lusur regius*), it was "read widely, dutifully praised, and generally ignored" (see ref. 2, page 98).

The evidence that tobacco was harmful began to accumulate during the 19th century, much of it relating to cancer and the use of clay pipes. As the incidence of lung cancer among men began to rise in the first decades of the 20th century, several epidemiological (case-control) studies were carried out in Britain, Germany, and the USA to explore the reasons for the observed increase. For various reasons, these studies failed to establish unequivocally the role of tobacco in producing lung cancer. Even the laboratory evidence was far from convincing, and "in 1950 ... was still not thought to support a significant role for smoking in cancer in either Britain

or the USA" (see ref. 2, page 91). Indeed, at that time "general atmospheric pollution from the exhaust fumes of cars, from the surface dust of tarred roads, and from gas-works, industrial plants, and coal fires" was suspected as being the major cause, along with tobacco (see ref. 1, page 739).

The situation changed dramatically in 1950 with the publication of five major case-control studies (four carried out in the USA (Schrek et al. (3), Levin et al. (4), Mills & Porter (5), and Wynder & Graham (6)) and one in the United Kingdom (Doll & Hill (1)), all of which revealed a close association between smoking and lung cancer. These studies were methodologically more rigorous than previous case-control investigations, and two studies in particular (those by Doll & Hill and by Wynder & Graham) were particularly noteworthy in view of the numbers of cases they studied (over 600 in each instance), their differentiation of risk by amount and duration of smoking, the exclusion of ex-smokers (whose risks of lung cancer are intermediate between current and life-long nonsmokers), and the careful consideration of possible selection bias and sources of confounding.<sup>a</sup>

While Doll & Hill's findings about the strength and nature of the association between smoking and carcinoma of the lung were widely accepted when they were published by the medical and scientific community, their conclusions as to cause and effect were not. The significance of the study was, as Doll himself remarked almost 50 years later, that the "... idea that smoking might be an important cause of disease had, however, been raised as a serious possibility and a great deal of research into its effects was initiated in many countries" (see ref. 2, page 97).

<sup>a</sup> Although the study by Doll & Hill is the focus of this commentary, the significance of Wynder & Graham's contribution should not be underestimated. Their conclusions, based on equally rigorous methods, were similar to those of Doll & Hill's; namely, that the "excessive and prolonged use of tobacco, especially of cigarettes, seems to be an important factor in the induction of bronchogenic cancer" (see ref. 6, page 336).

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Doll & Hill immediately followed up their retrospective study with a large prospective study of over 40 000 doctors registered in Britain, who were contacted in October 1951 about their smoking habits and other possible causes of disease. This study eventually became a landmark in the production of evidence on the hazards of tobacco, and, by 1954 had confirmed their earlier findings from the case-control study. It is a testament to the careful scientific method and ingenuity of Richard Doll's work that today, nearly 50 years after this classic cohort study commenced, many of the doctors can still be traced and the relative mortality of the smokers and nonsmokers among them carefully and reliably monitored. The results, after 40 years of follow-up, have described, perhaps better than any other research, the extreme hazards of persistent smoking, with the all-cause death rates of smokers being twice as high as those of nonsmokers, and, conforming to

their prediction made almost half a century earlier, 20 times higher for deaths from lung cancer (7).

The rigour, plausibility and timeliness of Doll & Hill's retrospective study, and the vast amount of scientific inquiry into the health hazards of tobacco that it generated, have laid the foundations for the massive global public health response to tobacco use that is gaining momentum, and success, as the 20th century draws to a close. The challenge remains, however, to accelerate public health action to reduce cigarette consumption everywhere, but particularly in the developing world. As the evidence on the hazards of tobacco continues to accumulate in developing countries, the need for more effective tobacco control programmes will become increasingly urgent. If appropriate policy and programme responses are not implemented today, the prediction of 10 million deaths a year from tobacco consumption worldwide by 2030 (8) will, tragically, become a reality. ■

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## References

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