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William G. Cochran and the 1964 Surgeon General's Report

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By the late 1950's the causal connection between cigarette smoking and lung cancer was well established. Several excellent retrospective (case-control) and prospective (cohort) studies had been published that led the US Surgeon General to declare "excessive smoking is one of the causative factors of lung cancer" (Burney 1959). The next few years brought new evidence of this and other major health effects of smoking. Although "medical opinion had shifted significantly against smoking" (United States Surgeon General's Advisory Committee Report, 1964), no concerted action had yet been taken to alert the public to its dangers. The Federal Trade Commission (FTC) was clamoring for guidance on how to regulate the labeling and advertising of tobacco products.

Accordingly, in 1962, Surgeon General Luther Terry selected an advisory committee of ten members to revisit the scientific evidence and produce a technical report on the health hazards of smoking. Representatives of government, medicine and industry, including some from the Tobacco Institute Inc., submitted a list of over 150 candidates for possible appointment to the committee. Each organization reserved the right to veto, without explanation, any name on the list. People who had taken a position on the issue, which included all those who performed the studies under review, were excluded from consideration.

The committee on smoking and health ultimately comprised eight physicians, one chemist and one statistician, William Cochran. Reputed to be a "statistician you could talk to," Cochran was by then well known for prior service on several national advisory committees dealing with prominent science policy issues: the effectiveness of the battery additive ADX2; an evaluation of the Kinsey report on sexual behavior; and the planning of the Salk polio vaccine trial (Meier, 1984). His acceptability to all the organizations responsible for proposing candidates may have been helped by the fact that he was a heavy smoker (Colton, 1981). Indeed, smokers made up half the committee.

Cochran's influence on the report and its conclusions was enormous. Although none of its chapters were attributed to individual committee members, he was known in particular to have written Chapter 8, Mortality, and its appendices. This chapter reviewed seven large cohort studies of smoking and mortality in men. In his recent bestseller, Siddhartha Mukherjee (2010) stated:

The precise and meticulous Cochran devised a new mathematical insight to judge the trials [studies]. Rather than privilege any particular study, he reasoned, perhaps one could use a method to estimate the relative risk as a composite number through all the trials in the aggregate. (This method, termed meta-analysis, would deeply influence academic epidemiology in the future.)

Table 26 of Chapter 8 contained the key results. Its importance to the overall evaluation of the evidence was apparent from the fact that an abridged version appeared as Table 2 in Chapter 4, Summaries and Conclusions. For each of 25 specific causes of death, and for all causes, the table listed for each of the seven studies the observed numbers of deaths in smokers, the expected numbers and their ratio. Following principles of indirect standardization, the expected numbers were the sum over age categories of the age-specific death rates among non-smokers times the age-specific person-years of observation for smokers. Age adjustment was essential. Since smokers were younger than non-smokers, their crude death rates were less than those for non-smokers. Cochran's innovation was to present two summaries of the seven mortality ratios for each cause of death. The first was a summary mortality ratio, where the expected number was obtained by pooling the age-specific data over studies. The second was simply the median of the mortality ratios for the seven studies. These were remarkably consistent: 10.8 vs. 11.7, respectively, for lung cancer; 1.7 vs. 1.7 for coronary artery disease, the most common cause of death; and 1.68 vs. 1.65 for all causes.

In the parlance of modern meta-analysis, the first method, the summary mortality ratio, approximates the summary measure from a fixed effects model whereas the second, the median, corresponds more to a random effects model. In a 2014 letter to the editor of the *New England Journal of Medicine*, Schumacher et al. (2014) used modern software to produce a graphical "forest plot" of the 1964 results that shows study-specific and summary confidence intervals under both models.

In two appendices to Chapter 8, Cochran described the statistical methods he used to estimate the bias and uncertainty of results presented in the main report. The first appendix reports a sensitivity analysis of possible bias in the mortality ratios caused by non-response. The second appendix presents two approximate methods for obtaining a confidence interval for the mortality ratio. The first, derived under the admittedly false assumption that the age-specific ratios of person years of observation for smokers vs. non-smokers were constant over age, used the fact that the ratio of a Poisson variable to its sum with another, independent Poisson variable is binomial. The second method avoided the person-years assumption, but involved other assumptions including a normal approximation that "are shaky with small numbers of deaths" ((United States Surgeon General's Advisory Committee Report, 1964). Fortunately, the two methods produced comparable results, especially for the lower confidence limit.

Cochran's mortality ratio would be most compelling as a summary measure if the age-specific death rates for smokers vs. non-smokers were in constant ratio, in which case it consistently estimates the constant. A modern approach would be to fit the model assuming constant age-specific rate ratios using Poisson regression (Greenland and Robins, 1985). The "robust" standard error for the regression estimate of the (constant) log rate ratio, allowing for model misspecification, provides an alternative to the ad-hoc methods proposed by Cochran. The 1964 report makes clear, however, that the rate ratios declined with age, dropping by nearly half from ages 40-49 to 80-89. Accounting for this systematic decline in the model could clarify the interpretation of the summary measure as pertaining to a specific age, e.g., 65 years, with predictable changes for younger or older men. On the other hand, the simplicity of the observed/expected formulation was likely more persuasive to most readers of the report than a modeling approach would have been.

Many other aspects of Chapter 8, and of the 1964 report in general, reflect Cochran's philosophy regarding observational studies. Section 7.6 of his paper "Observational Studies" (reprinted in this volume), titled Judgment about Causality, expresses a common theme in his writing: "Given a specific causal hypothesis that is under investigation, the investigator should think of as many consequences of the hypothesis as he can and in the study try to include response measurements that will verify whether these consequences follow." He goes on to illustrate this point with examples drawn from Chapter 8 of the report. This contained sections that dealt with mortality ratios by amount smoked, by age at which smoking started, by duration of smoking, by inhalation of smoke, by current vs. ex smokers, by causes of death that one might expect to be related to smoking and by other causes one might not. There was a section on non-response and another on confounding ("disturbing") variables, which were measured and considered in some studies.

Needless to say, the 1964 report had enormous impact (Mukherjee, 2010). The morning after its release, on January 11, 1964, it was front-page news and the subject of widespread media coverage throughout the world. The tobacco industry initially took some refuge in the fact that public reaction was not as strong as feared, and for a time it appeared that they might escape significant regulation. The FTC proposed a strongly worded warning for cigarette packages, but this was watered down by congress. What eventually led to the voluntary withdrawal of tobacco advertising from radio and television, in 1971, was a 1968 court decision mandating that stations broadcasting tobacco ads had to give equal time to anti-tobacco advertising under the "fairness doctrine" that applied to controversial issues. While Cochran himself remained a heavy smoker until the end of his days, his work on the committee contributed to a dramatic decline in smoking in the US, to the easing of the burden of chronic disease and to demonstrably increased longevity.

References

- Burney, L.E. (1959). Smoking and lung cancer – a statement of the Public Health Service. *Journal of the American Medical Association*, 171, 1829-1837.
- Colton T. (1981). Cochran, Bill - his contributions to medicine and public-health and some personal recollections. *American Statistician*, 35, 167-170.
- Greenland S. and Robins, J.M. (1985). Estimation of a common effect parameter from sparse follow-up data. *Biometrics*, 41, 55-68.
- Meier P. (1984). William G. Cochran and public health. In: Rao, PSRS and Sedransk J., eds. *WG Cochran's Impact on Statistics*. Wiley, New York: 73-81.
- Mukherjee S. *The Emperor of all Maladies: A Biography of Cancer*. Scribner, New York.
- Schumacher, M., Rucker, G. and Schwarzer G. (2014). Meta-analysis and the Surgeon General's report on smoking and health. *New England Journal of Medicine*, 370, 186-188.
- United States Surgeon General's Advisory Committee Report (1964). *Smoking and Health*. U.S. Department of Health, Education and Welfare, Washington D.C.

A Personal Recollection

To my knowledge I met Bill Cochran only once. The occasion, during Spring of 1962, was a trip East to visit universities where I had applied to graduate school in mathematics. My father, a public health physician, was the principal investigator on two of the seven mortality studies summarized in the 1964 report and later testified before the committee. He knew and admired Cochran and arranged for me to have an interview at Harvard, undoubtedly hoping that I might become interested in statistics. I remember Cochran as a tall and, to me, somewhat formal figure who displayed little interest in my career choice. He may have known that Harvard's math faculty would reject my application. My experience at The Johns Hopkins University was different. After a disastrous interview with one of the senior math faculty, a meeting with Alan Kimball that had been similarly arranged by my father led me to withdraw my application on the spot and to re-apply to the statistics department that Kimball was attempting to resurrect. When I returned to my undergraduate college and told my professors what I had done, they said that if I was truly interested in statistics I should apply to UC Berkeley and to Stanford, from which I ultimately graduated. I always wondered how my career might have evolved had the interview with Cochran gone differently and I had applied (and been accepted) by Harvard statistics.