



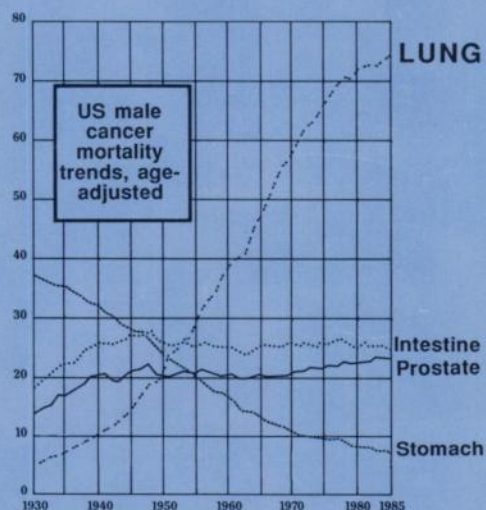
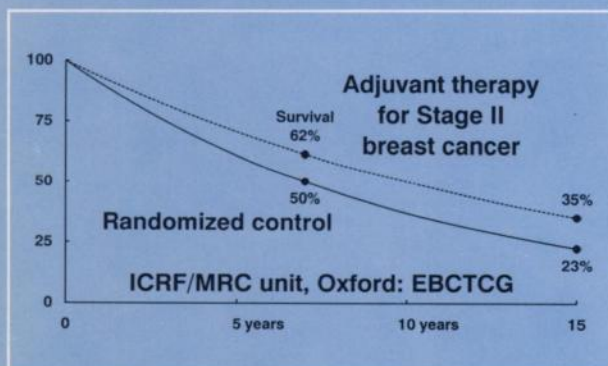
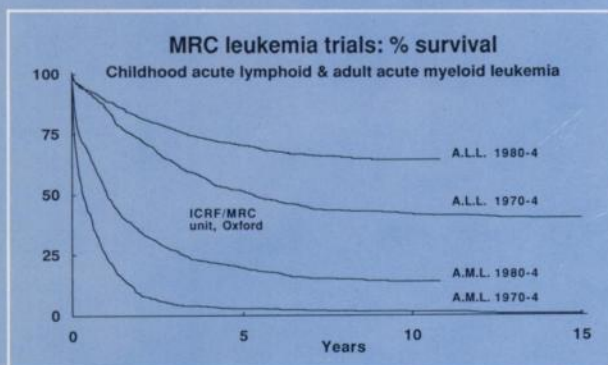
# Supplement to Cancer Research

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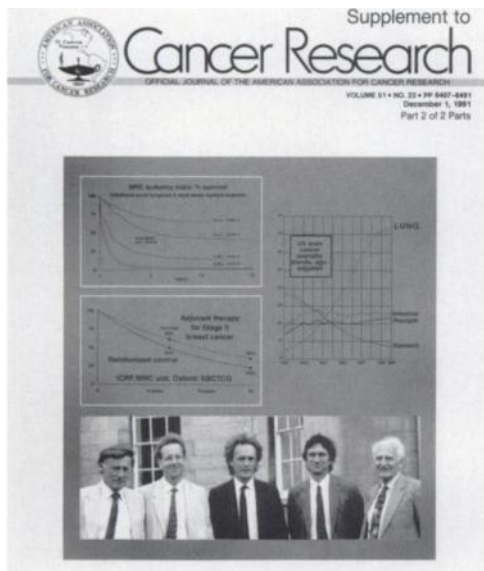
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Part 2 of 2 Parts



# COVER LEGEND



In 1990, about 1 million Americans developed cancer. Of those cured, most were cured by surgery; smaller numbers were cured by other treatments. Of the half million who died of cancer, about one-third developed the disease because they smoked; far smaller numbers were attributable to other factors. Other causes that have been identified, including alcohol consumption, obesity, and asbestos exposure, among others, account for only small percentages of the cancer deaths in the United States, and, although there is much evidence that some dietary factors are of substantial importance, there is no wholly reliable evidence as to their exact nature. Since good surgical services already exist, current cancer control strategies can expect to reduce cancer mortality in the United States considerably only if they substantially reduce death from cancers caused by tobacco use. The effects of tobacco have been shown in United States cancer mortality trends for decades [see illustration on cover, *right* (redrawn from CA-A Cancer Journal for Clinicians, 39: 9, 1989 and reprinted with permission from J. B. Lippincott Co., Phila., PA)]. Along with essential laboratory-based studies on the mechanisms of cancer, given the magnitude of the problem worldwide, there should be a dominant epidemiologically based perspective on the avoidable causes of cancer due to tobacco use.

Although the analyses by Peto *et al.* and Gray *et al.* detailed in this Part 2 issue of *Cancer Research* (December 1, 1991) deal with vast nitrosamine dose-response studies from BIBRA, the chief aim of the ICRF/MRC unit at the University of Oxford (NDM) at which they work is to generate and analyze *human* data on the causes and treatment of disease. Pictured, *right to left*, are half of the senior scientists at the ICRF/MRC unit: Richard Doll, Richard Gray, Richard Peto (codirector), Rory Collins (codirector), and, newly arrived, John Cairns. They have been awarded

various prizes for their outstanding accomplishments, including three Fellowships of the Royal Society, the MacArthur award, the General Motors award, and, most recently, the 1991 Helmut Horten award for their studies of the prevention and treatment of chronic disease. The two main themes of the unit, epidemiology and clinical trials, are connected by a common emphasis on human studies of unusual size.

After his early studies of tobacco, Richard Doll has remained at the forefront of cancer epidemiology for 40 years, and the influential report by Doll and Peto to the United States Congressional OTA on The Causes of Cancer (JNCI, 66: 1191-1308, 1981) led to wider realization that tobacco is the most important cause of cancer in developed countries. More recently, estimates by Peto in China (Lancet, 2: 1038, 1986) and in Eastern Europe (World Smoking & Health, 16: 4-6, 1991) have emphasized that tobacco will become a major cause of premature death throughout the world (WHO Tobacco Alert, January 1991), and the ICRF unit is now helping to establish large prospective and case-control studies, particularly in China, to monitor the growth of this epidemic.

Turning to treatment, those now at the ICRF/MRC Oxford unit were responsible for developing the standard "log-rank" test and for helping to achieve a consensus among statisticians on the Design and Analysis of Randomized Trials (Peto, Pike, Armitage, & 7 others, Br. J. Cancer, 34: 585-611, 1976; 35: 1-39, 1977). The unit has used these methods for over 15 years in running the many nationwide Medical Research Council leukemia trials. Those trials now randomize the large majority of all children or young adults with this disease in the United Kingdom and show significant survival improvements both between (see illustration on cover, *top left*) and within trials. More recently, the unit has developed the principles and the practice of worldwide collaboration among investigators in several systematic "overviews" or "meta-analyses" of trial results. The Early Breast Cancer Trialists' Collaborative Group (N. Engl. J. Med., 319: 1681-1692, 1988; Lancet, in press, 1992) now involves 100,000 women in 200 randomized trials and shows that hormonal and cytotoxic adjuvant treatment of 1,000 women with stage II disease can eventually avoid over 100 deaths (see illustration on cover, *bottom left*). Because breast cancer is so common, such adjuvant therapy is expected to save many lives. Systematic overviews have been completed, or planned, by Collins, Gray, Peto, and others in the ICRF/MRC unit in many neoplastic and nonneoplastic diseases. Several small but definite improvements in survival are being demonstrated [*e.g.*, avoiding pulmonary embolus after cancer surgery (Collins *et al.*, N. Engl. J. Med., 318: 1162-1173, 1988)] that will collectively prevent a few thousand deaths a year in America, and a few tens of thousands worldwide.

Meanwhile, tobacco continues to be responsible for the death of about 3 million people a year worldwide, a figure which could potentially escalate threefold within a few decades if improved cancer control strategies are not implemented to curtail tobacco use.