

Book Review

Smoking Kills: The Revolutionary Life of Richard Doll.

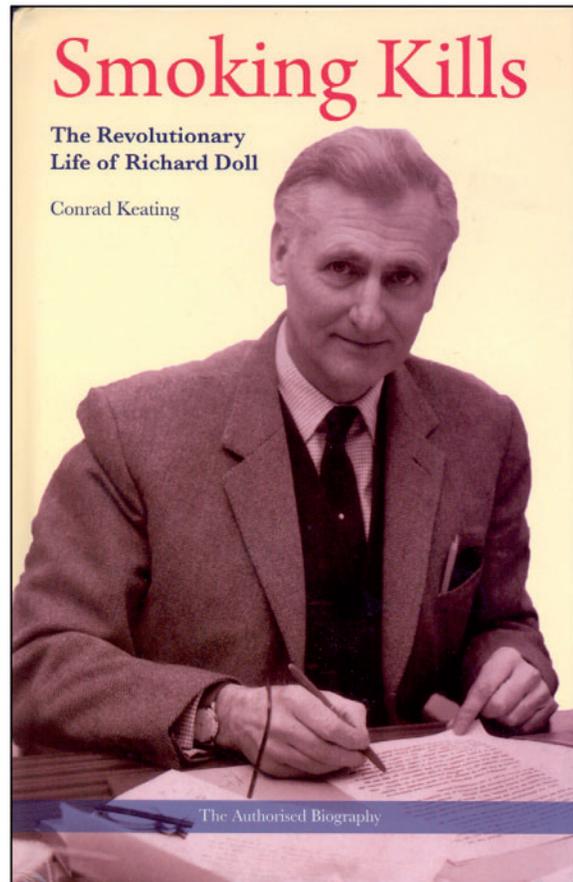
Conrad Keating. Oxford: Signal Books, 2009, pp. 495. £17.99 (hardback). ISBN 978-1-904955-63-4.

The unequivocal ‘Smoking Kills’ in this book’s main title is not the sort of statement that Richard Doll made readily. As this fascinating and fair-minded biography makes clear, while Doll’s political instincts were radical, he was nevertheless a conservative scientist, always cautious in causal inference. Even so, for Doll’s ‘signature research’ on smoking, cancer and overall mortality, his extensive epidemiological studies, conducted over half a century, certainly allowed the unadorned stark conclusion that smoking kills.

That conclusion (which faced hostility and disdain when first foreshadowed in the 1950s) is central to one of the four ‘revolutions’ that Conrad Keating constructs around the course and consequences of Doll’s life in medical science and epidemiology, a remarkable career that spanned eight decades until his death at age 93 in 2005.

Keating explores four ‘revolutions’ in the realms of politics, medical science, academia and public health. In approximate chronological order these refer to: (i) Doll’s active and deep commitment to socialist ideas and values, and his membership of the communist party during the 1930s to mid-50s; (ii) his generation of high-grade epidemiological evidence that smoking is a major cause of cancer—and the wider implications for studying non-communicable disease causation and preventability; (iii) his academic influence and institutional changes during the 1970s as Regius Professor of Medicine and founding head of the Cancer Epidemiology Research Group at Oxford University; and (iv) his subsequent tireless activities in ‘retirement’ in formal research and wider engagements with public policy and litigation cases relating to cancer causation.

Keating, a writer at the Wellcome Unit for the History of Medicine, was invited to write this authorized biography. He commenced during the last year or two of Richard Doll’s life, interviewing his subject many times, including during his terminal hospitalization in Oxford. He eventually tested the bed-bound patient’s gentlemanly demeanour to the limit, provoking Doll to protest: ‘What are you looking for now? You’re always digging around my life’. The biography is enriched by wide-ranging interviews with many of Doll’s colleagues and contemporaries and by extensive reference to historical documents, political context and scientific literature.



Keating clearly developed a fascinated, but not unqualified, admiration for his subject. His phraseology sometimes has hagiographic overtones. The word ‘revolutionary’, though, does not sit easily with the discipline of epidemiology, where one-off quantum-like discoveries are very rare. Indeed, in chapter 6 (titled, perhaps generously, ‘The Paradigm Shift’) Keating provides a thoughtful exploration of the painstaking and cautious approach that epidemiologists need in order to navigate the alternative explanations of chance (randomness), bias and true causation. That discussion, in turn, raises a question as to the book’s main intended readership. Keating’s overview, in that same chapter, of the methods used by Doll and Hill in their initial case-control study anticipates an audience that includes persons unfamiliar with epidemiological research. One hopes that there will be many such readers: Doll’s work and name deserves wider recognition - and conducting cohort studies (and talking ‘prevention’) does not

confer the glamour and celebrity status of doing heart or face transplants (and talking ‘miracle salvage’). Meanwhile, this book will almost certainly be read and enjoyed by very many epidemiologists and other health professionals who knew or knew of Richard Doll, particularly those in Britain.

Richard Doll was born in 1912 in late Edwardian London in well-to-do circumstances. His mother was a celebrated concert pianist, committed to keyboard practice and with little time for bonding with her firstborn. This emotionally constrained childhood presaged an adult of reserved nature, not given to easy, warm relationships. Doll, says Keating, was a private person, rather enigmatic, rarely emotional, and widely regarded by other than his few very close colleagues as cool and, often, rather daunting.

This is a big book, with many instructive and revealing narratives. There are early accounts of the young medical graduate’s engagement with communism (including a 1930s visit to Russia) and related tensions with the conservative medical establishment; his further radicalization following his voluntary medical assistance to the 200 destitute unemployed men who marched to London in the 1936 Jarrow Hunger March; Major Richard Doll’s war service in Cairo and at Dunkirk (where he contrived an escape path to and along the beach for the patients under his team’s care); and, post-war, his deepening affection for the redoubtable Joan Faulkner [a left-wing medical colleague and Medical Research Council (MRC) administrator] leading to their romantic relationship, then a minor scandal involving Doll as co-respondent in divorce proceedings, and finally marriage in 1949.

Soon after the war, encouraged by Joan, Richard Doll took a post in clinical epidemiological research in gastroenterology. Then, in 1947, the pre-eminent medical statistician Austin Bradford Hill, head of the MRC Medical Statistics Unit at the London School of Hygiene and Tropical Medicine (LSHTM), offered him a temporary research post that set the course of his future career. They embarked on a ground-breaking case-control study of lung cancer aetiology. The disease had increased 15-fold in British men since 1920, concern was growing and candidate theories abounded.

Hill’s unit, writes Keating, ideally suited Doll’s temperament and his flare for mathematics (his first love at Westminster School). A political Conservative, Hill was not bothered by Doll’s politics. He said of his young driven protégé: ‘Once you’ve got obsessive about research, you haven’t got time for communism or religion, or anything else at all’. In 1950, Doll joined Hill’s unit full time.

In that year, remarkably, five separate studies—the carefully executed Doll and Hill case-control study and four other studies from North America—were published, all implicating cigarette smoking in lung cancer. In the UK, the Doll–Hill findings encountered

widespread hostility and skepticism. Most of the male audience smoked, and, anyway, it seemed likely that the rise in urban-industrial air pollution was the cause of lung cancer. Less well known is that four very disparate studies, linking smoking with lung cancer, had previously been published. Two were from Germany, including the Schairer and Schoniger study (1943) which, as a product of war-time Nazism, was duly ignored. Subsequently, it was Doll and Hill who had the staying power on this topic front—realized particularly via Hill’s inspired suggestion to recruit a national cohort of doctors (most of whom smoked) and then follow them prospectively.

A battle royal emerged in the 1950s with the world’s most eminent geneticist-statistician, Sir Ronald Fisher, over the smoking-and-cancer evidence. Keating gives a lively account of this bitter gloves-off confrontation. Fisher, attuned to experimental studies of randomly assigned agricultural plots, argued that epidemiological studies without randomization were not ‘scientific’. To underscore the point, he hypothesized the existence of an underlying gene that caused both smoking behaviour and a disposition to lung cancer. He wrote abusive letters to Hill, and suggested publicly that he be stripped of his *FRS* for having perpetrated poor science. (Fisher partially recanted in the 1960s.)

The 1950s also saw Doll engaged on other fronts. At the LSHTM, he teamed with biostatistician Peter Armitage to develop their influential multistage model of cancer. Published in 1954, this seven-stage sequential model conformed with widespread evidence that the increase in cancer risk over time followed a power law. In the early 1950s, Doll was president of the newly formed Medical Association for the Prevention of War. Meanwhile, disillusioned, he left the communist party after the brutal Soviet suppression of the Hungarian uprising in 1956. In the late 1950s, he refused job offers from Harvard University so long as US Senator Joseph McCarthy’s crude witch-hunt for communist sympathizers persisted. On the home front, he and Joan went through the anguishing process of adopting two children. Being agnostics, they were shunned by the existing mainstream denominational adoption agencies. (Later, in the 1960s, the pair raised funds to establish the Agnostic Adoption Society, which, as the re-named ‘Independent Adoption Society’, had its 40-year anniversary in the year Doll died.)

Advances and changes occurred quickly in the 1960s. Doll took over the MRC Statistical Unit in 1961 when Hill retired. In 1962, the influential ‘Smoking and Health’ Report of the Royal College of Physicians was published, as counter-arguments by the tobacco industry and other conservative parties weakened. In 1965, Doll deferred to his wife’s career needs and turned down the invitation to become Director of the newly formed International Agency

for Research on Cancer in Lyon, France. That disappointment was offset, in 1996, by his election to fellowship of the prestigious Royal Society. In 1967, he appointed the young statistician Richard Peto to his MRC Unit (and appointed his younger brother Julian the following year). Over the ensuing three decades, and straddling a three-decade age gap, the two Richards collaborated in what Keating describes as a 'catalytic' and productive research programme, including the re-invigorated follow-up of the British Doctors Cohort.

Doll's appointment to the venerable Regius Chair of Medicine, Oxford University, in 1969—notwithstanding initial hostility to a left-wing appointee who lacked a stethoscope—led to an intensive decade of work at new frontiers, encompassing the rejuvenation and expansion of the Oxford Medical School, the development of his cancer epidemiology research unit, and the planning, fund-raising and establishment of Green College, Oxford, for medical students. Doll became the first Warden of Green College. Diverse political undercurrents flowed throughout.

In 1981, Doll and Richard Peto published a much-cited book *The Causes of Cancer*, based on their independent assessment for the US Government of the relative contributions to cancer incidence of a range of major risk factor categories. A prime stimulus for that assessment was the political argument over the cancer burden attributable to occupational exposures in the USA. In fact, Doll and Peto estimated that smoking and diet each accounted for around one-third of all cancers (the latter being a much more uncertain figure), and that occupational and environmental-chemical exposures accounted for around 4 and 2%, respectively.

Elucidating the role of diet in cancer has proven frustrating for epidemiologists. Bruce Armstrong and Doll published a much-cited paper in 1975, using international data and noting various clear-cut population-level associations between dietary components and cancer. Although not commented on by Keating, it was always going to be tempting for Doll and colleagues, given prevailing models and examples of chemical carcinogenesis, to anticipate that dietary risk (or protective) factors each acted independently, presumably by altering mutational probabilities. (In 1981, Peto, Doll and colleagues postulated, in a paper in *Nature*, that dietary β -carotene, as vitamin A precursor, may protect against cancer. Subsequent studies were inconclusive, even contradictory.)

Two major scientific controversies and the related political tensions, from the 1960s and 1970s, are explored in dedicated chapters. These were, first, the work by Doll and Julian Peto on asbestos carcinogenicity and the likely future incidence of mesotheliomas, and, secondly, the fraught professional relationship and disagreement between Doll and Alice Stewart (both at Oxford University) over the cancer risks of low-level ionizing radiation. Doll's public criticism of

Stewart's more recent research revealed him as a hard and uncompromising opponent.

Richard Doll officially 'retired' in 1983. He then became a mentor and active member of Richard Peto's thriving research unit at Oxford University. Retirement was a fiction.

In 1985 Doll submitted, uninvited, his written views to the Australian Government's Royal Commission on the cancer risks of Vietnam Veterans exposure to the phenoxy acids (contaminants of the herbicide Agent Orange). His influential criticism of herbicide exposure studies in Sweden conducted by two senior epidemiologists led to bitter recriminations, including the duo sending a protestation letter to Australia's Governor-General. This confrontation also reactivated darker subterranean allegations that Richard Doll was a 'friend of industry' and, as a well-paid consultant-on-retainer, was beholden to Monsanto, the herbicide manufacturer. In fact, says Keating, Doll was paid by Monsanto only for actual hours of work done. Doll, he says, always insisted that any fees, from Monsanto or others, be donated to Green College or to other nominated charities. (Elsewhere, Doll attested to this policy in court.)

In his later years, Doll appeared as a typically influential expert witness in several court cases to do with cancer risks—smoking, water fluoridation, nuclear power plant radiation exposures and others. Keating notes that at least some observers felt that Doll's performance as expert witness in the controversial 'Gardner Hypothesis' court case, in 1993, at age 81, was less stellar than in earlier cases. The excerpted transcripts of that case make gripping reading.

Keating refers to the 'Doll philosophy' of science, a philosophy of caution, thoroughness and social responsibility. Aware of the inherent uncertainty of statistics, Doll believed (in Keating's words) that 'if an investigation found something that was unexpected and which was going to be of social significance, then there was an obligation to make sure that the answer was right before publishing the results to the world'.

In describing Doll's philosophy and work, Keating's phraseology reflects the clinically based view of epidemiology that has long prevailed in Britain. The distinctly British phrase 'public health medicine' was duly reflected in a turn-of-the-century editorial in *The Lancet*, stating: 'Of all the branches of clinical medicine, public health is the most complex'. In that same vein, Keating writes that Doll 'ushered in a new era in medicine, shaped by the intellectual ascendancy of medical statistics' and achieved 'the greatest ever advance in the history of medical science'. (Well... Jenner, Snow, Virchow, Koch and others might have something to say about that.) Perhaps Keating took a partial cue from Doll himself, whose research rarely explored the wider (less measurable) horizons of public health and social policy in the way that his English contemporary Geoffrey Rose did.

Rose had a 'strategy of public health'; Doll had a 'philosophy of epidemiological research'.

Richard Doll lived long enough to see major changes in patterns of disease and in epidemiological research practice. These included the emergence of HIV/AIDS (he argued unsuccessfully with the UK Government for anonymous testing of pregnant women's blood, to monitor HIV prevalence) and other surprising emerging infectious diseases; the power of modern desktop computing (light years away from his 1950s hand-tabulating methods); the integration of molecular biology and genetics into epidemiology; widening concerns about environmental changes and their health risks; and increasingly stringent ethical guidelines. Keating comments that: 'The incremental advance of ethicists into the work of medical researchers had become so pervasive that by the end of the century it would have been impossible for Doll to undertake either his 1950s studies linking smoking to cancer, or his pioneering work on the cause of leukaemia in patients with ankylosing spondylitis'.

In 1954, Doll had published a paper in which he stated: 'The objective of science is to gain power to control nature in the interests of humanity'. (Keating uses this quote to introduce Chapter 9, *Man's Relationship with His Environment*.) In 2002, at the annual Florence Epidemiology Summer School, I chatted with Richard Doll one evening about human-induced changes to the natural

environment, the climate and the emerging risks to human health. This, he said, was an unwelcome price for us to pay for our egregious presumptions about environmental mastery and control. Perhaps, in 1954, he used the word 'nature' inclusively to encompass patterns of social relations and individual behaviour—both of which would perhaps have been better labeled 'nurture'.

Semantics aside, Doll, in 1954, was himself nurturing ideas and methods that would contribute hugely to developments in the practice of modern epidemiology that prevailed in the latter 20th century. This ever-evolving research discipline has extended greatly our understanding of the nature, causes and preventability of cancer and other non-communicable diseases.

Keating's impressive and engaging biography ends on a poignant note. He records that 'on 8 September 2005, Richard Doll's death certificate arrived from Southport in his own building [the newly-opened Richard Doll Building at Oxford University]. He was part of the fifty-year follow-up of British doctors. His death certificate—death due to heart failure—was his final contribution to its lasting testament.'

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