The state of knowledge regarding tobacco harm, 1920-1964: industry and public health service perspectives

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Abstract

Referencing once-confidential tobacco industry documents, we compare reviews of the epidemiological literature concerning tobacco harm that were carried out by the U.S. Tobacco Industry Research Committee (T.I.R.C.) and the U.S. Public Health Service and related groups during the 1950s and early 1960s. Results show that the T.I.R.C. operated an unbiased and reasonably comprehensive literature review operation which, from 1956 onwards, was providing summaries of published epidemiological studies to its members within an average of 2.3 months of date of publication. Although the epidemiological evidence reviewed by the T.I.R.C. was similar to that reviewed by the U.S. Public Health Service and related groups, public statements assessing the evidence made by the organisations differ significantly. We discuss our results in the light of present-day academic and legal debates concerning the ‘controversy’ surrounding tobacco harm in the mid-twentieth century.
1 Introduction

Faced with a health scare concerning the consumption or use of a particular product or technology, the evaluation of the state of scientific knowledge concerning its potential to harm is as important for the industry producing the product as it is for a state institution faced with regulating it. If, over time, harm becomes ‘proven’, the ability of a legal system retrospectively to assess the evolution of such knowledge is a key element in the success or failure of negligence claims made against the industry. Few stories illustrate these points more vividly than the ‘controversy’ surrounding harm caused by tobacco use in the mid- to late-twentieth century.

This paper uses once-confidential tobacco industry documents to present a unique picture of the evolution of epidemiological knowledge concerning tobacco harm as possessed by the tobacco companies and public health and related organisations in mid-twentieth century America. It compares reviews of the epidemiological literature concerning tobacco harm that were carried out by the Tobacco Industry Research Committee (T.I.R.C., renamed the Council for Tobacco Research, U.S.A., Inc. (C.T.R.) in 1964) with those of the U.S. Public Health Service and related groups during the 1950s and early 1960s. It addresses the following issues:

1. the quality of the T.I.R.C.’s literature retrieval and review process, including its comprehensiveness (how much of the total body of epidemiological literature it collected), responsiveness (how quickly it collected the literature and made summaries available to its sponsors) and bias (whether it appears to have selected or reviewed literature in a biased manner);

2. in the light of the knowledge possessed by the T.I.R.C., the U.S. Public Health Service and related groups:
   (a) the degree to which their public statements assessing the evidence reflected that knowledge;
   (b) the degree to which the T.I.R.C.’s public statements, through the annual reports of its Scientific Director, were faithful to its stated aims of making factual information on the tobacco-health question available to the public.

The work contributes to contemporary academic debate on the legitimacy of the ‘controversy’ surrounding tobacco harm in the 1950s and 1960s that has witnessed contributions from, amongst others, Talley et al. (2004), Stolley (1991), Kluger (1997), Glantz et al. (1996) and Parascandola (2004). However, it does so, not by reevaluating the role of epidemiology in making judgments about causal relationships, but by comparing and contrasting the private literature collection activities and public statements of the T.I.R.C.
with those of the U.S. Public Health Service and related groups. It also
passes comment on the legal argument used by tobacco companies which
says that the ‘passing of time’ between the mid-twentieth century and to-
day is sufficient to dismiss claims of negligence brought by plaintiffs with
tobacco-related illnesses. For example, in the High Court of Ireland in 2004,
Justice F. Geoghegan dismissed three claims for negligence, one of which was
against Benson and Hedges Ltd., a founding member of the T.I.R.C., on a
number of grounds, including this one:

‘the claims would require the court to decide issues of fact per-
taining to the state of scientific knowledge [regarding tobacco
harm] which they either were aware of or ought to have been
aware of and the precise decision taken by the defendants not
only in relation to the manufacturing but including detailed de-
cisions effecting such matters as the level of nicotine over much
of the twentieth century . . . For a court to be asked in the years
2006 or 2008 or later to determine issues of fact of the nature
which would be required by these claims . . . “puts justice to the
hazard” ’ (Manning vs. Benson and Hedges Ltd., 2004).

This paper is one of a series of three to result from our resear-
ch. The other two present a Bayesian model of the ‘weight of evidence’ concerning
tobacco harm (Forster et al., 2006), and a review of the inner-workings of the
T.I.R.C. between 1954 and 1964, especially the role of the academics who
served on its Scientific Advisory Board (Bowden et al., 2006).

The rest of this paper is organised as follows. In section 2 we discuss the
background to the work. We then outline our methods (section 3), present
results (section 4) and discuss them (section 5). Section 6 concludes.

2 Background

The invention of the ‘Bonsack’ machine in the 1880s allowed
cigarettes to be produced at a fraction of the unit cost prevailing at the
time, heralding an era in which the smoking habit became accessible to the
whole of society rather than just those in elite circles (Hilton, 2000). By
1955 in the U.S.A., around 65% of men and 35% of women were thought to
be regular cigarette smokers (Haenszel et al., 1956).

It was concern with the increasing incidence of cancer, especially of the
lung and bronchus, during the first half of the twentieth century, which led
researchers to investigate whether tobacco use played a causal role. Evidence
supporting such concerns came from a number of scientific disciplines. Clinical
reports suggested that particular methods of consuming tobacco were
associated with cancers of particular sites;\(^1\) chemical studies attempted to

\(^1\)For example, betel nut chewers who mixed tobacco into the quid were thought to
identify harmful constituents of tobacco and its smoke and experimental work attempted to induce tumours in laboratory animals using tobacco tars and smoke. Epidemiological studies of a retrospective nature can be traced back to the early 1920s (Broders, 1920).

By the end of 1950, the results of at least fourteen separate retrospective studies investigating the link between tobacco use and cancer at various sites of the body had been published in the medical literature, the overwhelming majority of which reported significant statistical associations between the two. By the 1950s investigators had also started to research the relationship between tobacco use and cardiovascular disease. Research continued throughout that decade, during which time growing public concern prompted both the U.S. Public Health Service and the U.S. tobacco industry to review the literature on tobacco and health and release statements to the public.

2.1 Activities of the U.S. Public Health Service and Related Groups

In 1957, a scientific study group comprising members of the National Cancer Institute, the National Heart Institute, the American Cancer Society and the American Heart Association reported on the tobacco-health question. Examining the content of 18 independent epidemiological studies into the relationship between smoking and lung cancer, together with experimental, pathological and other evidence, the group concluded that ‘[t]he sum total of scientific evidence establishes beyond reasonable doubt that cigarette smoking is a causative factor in the rapidly increasing incidence of human epidermoid cancer of the lung’ (Study Group on Smoking and Health, 1957). In responding to the report, the Surgeon General stated ‘it is clear that there is an increasing and consistent body of evidence that excessive cigarette smoking is one of the causative factors in lung cancer.’ Two years later, reviewing additional evidence, Surgeon General Burney concluded that ‘the weight of evidence at present implicates smoking as the principal factor in the increased incidence of lung cancer . . . cigarette smoking particularly is associated with an increased chance of developing lung cancer’ (Burney, 1959).  

In 1962, the Surgeon General established the ‘Advisory Committee on Smoking and Health’ and charged it with examining again the Public Health Service’s statement of 1959. The work program of the committee was defined

be more prone to oral cancer (Davidson, 1923); Haberer (cited by Lickint (1930) and Ebenius (1943)) reported women pipe smokers in Alpine regions to have an unusually high prevalence of lip cancer and Redi (1954) reporting observations made in late 1940s Sardinia, suggested that cancer of the palate was more common amongst ex-soldiers of the ‘Sassari Brigade’ who, during the first world war, acquired the habit of smoking cigars with the lit end inside their mouths while on night duty in the trenches, to avoid being shot by sniper fire.

2The main change between Burney’s 1957 statement and that of 1959 appears to have been the dropping of the adjective ‘excessive’ in describing the nature of the smoking.
in two phases: the first involved making ‘an objective assessment of the nature and magnitude of the health hazard, to be made by an expert scientific advisory committee which would review critically all available data but would not conduct new research.’ Recommendations for the second phase were only to be made upon completion of the first.

The Committee set out to investigate whether or not the use of tobacco was bad, good or devoid of effects on health. It was to give ‘particular attention’ to the effect of cigarette smoking on health from the perspective of overall mortality and disease categories. The Committee examined three main types of scientific evidence: animal studies, clinical and autopsy studies and population/epidemiological studies. In so doing, it stressed in its report the importance of epidemiology and statistics in contributing to the evidence-base:

‘the main evidence of the effects of smoking and other uses of tobacco upon the health of human beings has been secured through clinical and pathological observations of conditions occurring in men, women and children in the course of their lives, and by the application of epidemiological and statistical methods by which a vast array of information has been assembled and analysed . . . ’

In reviewing the literature for its report, the Committee used the bibliographic service of the National Library of Medicine, together with a T.I.R.C.-funded review of the tobacco literature published by Larson, Haag and Silvette (Larson et al., 1961). The cigarette manufacturers were also invited to make submissions. Between November 1962 and December 1963, the full committee held nine sessions lasting from between two and four days, during which the report was drafted and written.

The report was published on January 11th, 1964. It found that cigarette smoking was associated with a 70% increase in the age-specific death rates of males and an increased death rate of females. It concluded that cigarette smoking ‘contributes substantially to mortality from certain specific diseases and to the overall death rate’ and that it ‘is a health hazard of sufficient importance in the United States to warrant appropriate remedial action.’ With regard to the relationship between smoking and lung cancer, it concluded that ‘[c]igarette smoking is causally related to lung cancer in men; the magnitude of the effect of cigarette smoking far outweighs all other factors. The data for women, though less extensive, point in the same direction’

Further on, the Committee noted that ‘the epidemiological evidence was used extensively in the assessment of causal factors in the relationship of smoking to health among human beings upon whom direct experimentation could not be imposed’. Among the epidemiological studies, it was the prospective and retrospective studies, which form the focus of this paper, that were described by the Committee as furnishing information ‘of the greatest value’.

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2.2 The Tobacco Industry Research Committee

In December 1953, the U.S. tobacco companies, warehouse and growers’ associations responded to the adverse publicity surrounding tobacco by forming the Tobacco Industry Research Committee. This held its first formal meeting on 18th January, 1954. A statement concerning the origins, purpose and proposed functions of the T.I.R.C. was tendered to the Attorney General of the United States by Paul M. Hahn, President of the American Tobacco Company, Inc.. It outlined the T.I.R.C.’s purpose as being to ‘aid and assist research into tobacco use and health, and particularly into the alleged relationship between tobacco use and lung cancer, and to make available to the public factual information on this subject.’ A public relations firm, Hill and Knowlton, Inc., was to assist the Committee (C.T.R., not dated). Funding for the T.I.R.C. came from the contributions of the individual members, based on volume of business. The formation of the Committee was made public on 4th January, 1954, in a full-page newspaper advertisement entitled ‘A Frank Statement to Cigarette Smokers’, published in 448 newspapers across the United States (T.I.R.C., 1954). In it, the T.I.R.C. stated that an interest in people’s health was ‘a basic responsibility, paramount to every other consideration in our business’. Reference was made to the fact that statistical studies linking cigarette smoking with lung cancer had been questioned by ‘numerous scientists’, that the members of the Committee believed that ‘the products we make are not injurious to health’ and that they would cooperate closely with those whose task it is to safeguard the public health.’ The statement went on to describe the formation of the T.I.R.C. and announced that funding would be made available for research into tobacco and health (T.I.R.C., 1954).

In an attempt to split the research and public relations aspects of its work, the Committee created what it called the ‘Scientific Advisory Board’ (hereafter S.A.B.) and charged it with promoting and funding scientific research. The board’s membership included seven ‘prominent scientists and doctors’

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5By the end of 1956, grants awarded by the T.I.R.C. totalled over $1,200,000 (Little, 1956).
and was chaired, in the early years, by the T.I.R.C.’s Scientific Director, Clarence Cook Little. Also formed were a Law Committee, which provided advice on legal matters, and an Industry Technical Committee, which comprised the Research Directors of the member companies (C.T.R., not dated).

Hill and Knowlton, Inc., the public relations company, was responsible for T.I.R.C. publications. The quarterly ‘Tobacco News’, with a circulation of about 70,000 news desks, editors, publishers, columnists etc., aimed to promote the economic benefits of tobacco to the U.S.A. as well as ‘the comforts and relief of tensions of this nation and the world’ (T.I.R.C., 1959). The annual ‘Report of the Scientific Director’, first published in 1956, aimed to summarise progress on tobacco-related research and discuss research activities (C.T.R., not dated). ‘Tobacco and Health’, first published in 1956, was designed for public consumption and referred principally to articles on tobacco appearing in medical and scientific journals. Its first issue had a print run of 350,000, the bulk of which was sent to doctors and dentists (T.I.R.C., 1957). By April 1959, the print run had increased to approximately 536,000 (T.I.R.C., 1959). Finally, the confidential ‘Current Digest of Scientific Papers Relating to Tobacco Use’, a central focus of this paper, excerpted the latest publications, letters, opinion pieces and annual reports relating to the tobacco/health question.

T.I.R.C. sources used for our review

The T.I.R.C. recognised from the outset the importance of collecting together the scientific literature investigating the tobacco-health question, which it described as being ‘basic to research, public relations and related activities’ (C.T.R., not dated). As a result, it organised a library to screen, catalogue and file relevant scientific articles in the public domain. The library served the Committee and its sponsors, its scientific staff and the S.A.B., but not the general public.

Kenneth Austin, librarian to the T.I.R.C., directed the literature search, retrieval and reporting. This involved the screening of press reports and scientific literature and the checking of the programmes of scientific and

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6These were: Professor McKeen Cattell, Head of Department of Pharmacology, Cornell University Medical College; Dr. Leon O. Jacobson, Professor of Medicine, University of Chicago; Dr. Paul Kotin, Assistant Professor of Pathology, University of Southern California; Dr. Stanley P. Reimann, Director, The Institute for Cancer Research and the Lankenau Hospital Research Institute; Dr. William F. Reinhoff, Jr., Associate Professor of Surgery, Johns Hopkins School of Medicine; Dr. Clarence Cook Little, Director, Roscoe B. Jackson Memorial Laboratory and Dr. Kenneth Merrill Lynch, Professor of Pathology, Medical College of South Carolina. A lung physiologist, Dr. Julius Comroe, Professor, Department of Physiology and Pharmacology, University of Pennsylvania Graduate School of Medicine, was appointed during 1954 (C.T.R., not dated). Although initially no statistician or epidemiologist was present, Dr. Edwin B. Wilson, Professor Emeritus of Vital Statistics, Harvard University, was appointed to the Board soon after its inception.
medical meetings in which papers discussing tobacco use and health and related areas were presented.

Two publications from the T.I.R.C. library form the major sources for this research. One is entitled ‘A working reference catalog’ (hereafter ‘the Catalog’), which listed scientific literature published prior to 1st August 1955; the other is the ‘Current Digest of Scientific Papers Relating to Tobacco Use’ (hereafter ‘Current Digest’), published monthly from July 1956.

The content of the Catalog is described in detail in the trial deposition of William D. Jenkins (Almquist et al. v. American Brands, Inc., et al., 1986). Jenkins was Austin’s successor, appointed as librarian to the T.I.R.C. in 1971. In pages 39 to 44 of the deposition, Jenkins explains that Austin, as well as collecting scientific literature as it was published, had reviewed literature published prior to August 1955 and published the results in the Catalog.

Scientific articles listed in the Catalog are collected under a range of headings relating to the tobacco/health question. For example, the first section, entitled ‘Technical Papers on Lung Cancer’, contains major subsections on individuals’ opinions on the lung cancer question, statistical work and experiments. Within these major subsections, published works are listed within further subsections, alphabetically by author, author’s location and/or affiliation, the nature of the paper (e.g. ‘review’ or ‘statistical’), the date of publication, whether or not the author had published more than one article in that year and, finally, a code letter A to E. In the introduction to the Catalog, the letters A to C are described as denoting that ‘[s]pecial excerpts or abstracts of these papers have been prepared. Full paper is on file at T.I.R.C. offices.’ D denotes ‘[n]either paper nor excerpt is on file, but copies . . . can be obtained from medical libraries or publishers.’ E denotes ‘[c]opies of full paper on file but no excerpt or abstract available.’

Although not alluded to in the Catalog, the letters A to C hold further meaning. Jenkins’s deposition refers to a separate document entitled ‘Some hints on use of catalog’ (T.I.R.C., not dated (b)), which explains that these three letters were used to rate each article as taking a ‘favorable’ (A), ‘neutral or unrelated’ (B) or ‘unfavorable’ (C) position on the effects of tobacco. Jenkins’s deposition goes on to explain that he interpreted the letters A to

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7The full title is ‘A working reference catalog of selected scientific papers relating to: technical papers on lung cancer, cancer of the larynx and buccal cavity, technical papers on cardiovascular disease, psychology and physiology of smoking, air pollution - general, general papers and textbooks’. The Catalog was obtained from a collection of documents donated by Ness Motley, attorneys in the State of Mississippi’s case against the tobacco industry, to the site tobaccodocuments.org, where it had been located in a collection of papers donated to the State Historical Society of Wisconsin by the late John W. Hill, founder of Hill and Knowlton (see http://tobaccodocuments.org/ness/5305.html). Only one other copy was subsequently located by us in on-line tobacco company archives, in the Lorillard collection of the Legacy tobacco documents site, at http://legacy.library.ucsf.edu/tid/ejx71e00.
C as follows: A means ‘not harmful . . . tobacco is not harmful’; B means ‘neutral’ and C means ‘tobacco is harmful’ (page 42, deposition of Jenkins, Almquist et al. v. American Brands, Inc., et al., 1986).

Although it appears that the Catalog was updated by the T.I.R.C. librarians from time to time, we were not able to locate any versions other than the one dated 1st August, 1955, in the on-line archives. To identify the literature reviewed by the T.I.R.C. after this date, we therefore used the Current Digest. Austin scanned the scientific publications to which the T.I.R.C. subscribed, as well as abstracts of the world literature and, together with his staff, checked the scientific publications at the New York Academy of Medicine. Articles of interest were then ordered and ‘pertinent’ ones were selected and used to compile the Current Digest. By 1968 it was claimed that the library received 129 scientific publications, ten publications abstracting the literature, and information on the monitoring of 2,500 U.S. and foreign journals carried out by the Philadelphia College of Physicians (page 1, Austin (1968)).

Current Digest volume I, number 1, dated July 1956, ran to nine pages and contained summaries of twenty-one published papers, letters and editorial pieces relating to tobacco use and health. The summaries were collected under eight sections: ‘Smoking and the lungs’, ‘Statistics’, ‘Chemical and physical properties of tobacco smoke’, ‘Editorials in medical and scientific journals’, ‘Views of physicians and scientists’, ‘Experiments with tobacco tar’, ‘Heart and circulation’ and ‘Grants for tobacco research’. By the end of our review period, Current Digest volume VIII, number 12, dated December 1963, ran to 52 pages and contained 102 summaries. In contrast to the Catalog, the Current Digest did not rate articles according to whether or not they concluded that tobacco was harmful.

Over the period in question, the subject matter covered by the Current Digest - roughly represented by the sections into which summaries were divided - changed, reflecting the evolution of the science and the debate in wider society. For example, a section on the psychology of smoking made its first appearance in December 1956, a section on medical society activities in April 1963, a section on smoking in schools in May 1963 and a section on teenage smoking in June 1963.

The Current Digest was described by Hill and Knowlton as being ‘useful to research development, to research departments of company members, and to legal departments in the conduct of their affairs.’ It provided ‘the fundamental source of information for story ideas for the lay press, when desirable, and for supplying specific information to writers working on stories relating to tobacco and health or T.I.R.C.’ (Hill and Knowlton, Inc., 1956). Such was...
the sensitivity of the publication that, in 1956, a note was sent to T.I.R.C.
members reminding them that ‘[t]he CURRENT DIGEST is prepared for
use only by members of the T.I.R.C., their authorized personnel and the
Scientific Advisory Board. Because of possible misinterpretation by others
of the purpose of this DIGEST, no wider distribution is advised’ (T.I.R.C.,
1956).

It is important to note that neither the Catalog nor the Current Digest
were made generally available to the public (we found no evidence to suggest
that the Catalog was made publicly available; the Current Digest is described
in one document as going to ‘T.I.R.C. members, their authorized personnel,
and the Scientific Advisory Board’ (Hill and Knowlton, Inc., 1956)). To ad-
dress the need for public information, the S.A.B. awarded a grant to Drs.
Haag and Larson of the Medical College of Virginia, who had collected to-
gether articles and abstracts dealing with tobacco and health. Their work
resulted in the publication of ‘Tobacco, Experimental and Clinical Studies’
in 1961 (Larson et al., 1961) and was to be used as one of the sources of
reference by the Surgeon General’s Advisory Committee two years later.

Documents from the T.I.R.C. archives that are used in this paper have
been made available courtesy of the ‘Master Settlement Agreement’ of 1998,
an agreement signed by the Attorneys General of 46 U.S. states and the four
largest U.S. tobacco companies (National Association of Attorneys General,
1998). The agreement introduced major restrictions on the advertising, mar-
keting and promotion of cigarettes, dissolved the C.T.R. and required the
tobacco companies to open, at their own expense, websites holding all ‘non-
privileged’ documents requested in relevant state and other smoking-related
lawsuits (non-privileged documents being those documents for which the
tobacco companies did not make a claim of attorney-client privilege, trade-
secret protection etc.). These documents are collected together in a number
of websites9 and we believe they are comprehensive enough to present a rich,
historical, insight into an industry’s literature retrieval and review operation
in the presence of a major health scare concerning its sole product.

Images of the Catalog and Current Digest are shown in figure 1. The
main sources of literature which we review are summarised in figure 2.

3 Methods for our review

We set out to identify, for the organisations listed in figure 2, their sum-
maries and reviews of primary epidemiological studies (both retrospective
and prospective) published in the medical literature prior to 1964 which in-
vestigated the link between tobacco use and six cancer sites and between

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9Essential for our research was the Legacy Tobacco Documents Library at the Uni-
versity of California, San Francisco (http://legacy.library.ucsf.edu/) and the site
‘tobaccodocuments.org’ (http://tobaccodocuments.org/).
Figure 1: Left: a page from the T.I.R.C.’s ‘Catalog’, summarising retrospective studies on lung cancer. The T.I.R.C.’s classifications regarding whether or not each paper listed took a ‘favourable’ (A), ‘neutral or unrelated’ (B) or ‘unfavourable’ (C) position towards tobacco can be seen in the final column. Right: Current Digest volume I, number 1, page 1.
tobacco use and cardiovascular disease. In addition, we searched for studies which were not included in the reviews of any of the organisations, but which were available at the time, using our own review of the literature for 1950-59 and our own review of citations from relevant articles.

In identifying studies within the organisations’ reviews, we applied the following inclusion criteria:

1. studies had to be on humans and investigate harm to the user thought to be associated with tobacco use. ‘Tobacco use’ includes the smoking of cigarettes, pipes, cigars and other products (such as the Indian ‘bidi’), the use of snuff and chewing tobacco. Our disease categories of interest were cancer of the lung, oral cavity, larynx, oesophagus, urinary bladder and stomach, together with cardiovascular disease. In vitro and animal studies were excluded, as were any studies relating to the effects of passive smoking;

2. studies had to be prospective or retrospective in nature, investigate the association between tobacco use and the diseases defined above and reported in primary sources prior to 1964. ‘Primary sources’ include medical and scientific journals as well as major annual reports of appropriate organisations (such as the British Empire Cancer Campaign). They exclude editorials, letters and opinion pieces. Autopsy studies were excluded, as were cohort studies which used as a study group a sample already ill at baseline. Reports of work presented at meetings, symposia, congresses etc. were excluded. However, where it was possible to identify a summary of a published ‘final version’ of a
conference paper, this was included. Retrospective studies needed to reference a control group without the disease of interest, and we were flexible in our definition of controls, to reflect the fact that the choice of control groups varied widely across studies (for example, some studies chose matched control groups of hospital patients with diseases not suspected of being associated with tobacco consumption, while others took non-diseased controls from a local population).\textsuperscript{10}

The ideal approach to this research would have been to view the organisations’ summaries in the light of a true systematic review of the literature. This approach meets virtually insurmountable problems. Firstly, the electronic version of MEDLINE goes back as far as 1966 and OLDMEDLINE covers the period from 1965 to 1950, yet retrospective studies meeting our inclusion criteria go back much further in time. Secondly, OLDMEDLINE records do not contain any abstracts. As a result, the identification of those studies meeting our inclusion criteria could only have been done by obtaining and reading each article thought to be of relevance. Thirdly, the process of scientific discovery in any study of disease causality inevitably involves attempting to ‘narrow down’ a field of potential causal factors, and many studies would not explicitly have mentioned words such as ‘smoking’, ‘cigarettes’ and ‘tobacco’ in their titles, even though tobacco was studied as a potential causative factor for the disease under investigation. As a result, to be truly comprehensive, searches would have had to have been incredibly broad to encompass all possible studies of interest to us.\textsuperscript{11}

We therefore adopted a different approach to our research. In the first stage, two reviewers (M.F. and M.W.) read each summary in Current Digest volumes I-VIII (covering the period July 1956 to December 1963) independently and without conferring. Each summary was classified independently by each reviewer as either meeting or not meeting the inclusion criteria outlined above. In a series of meetings, the reviewers then compared their classifications to agree on a final ‘include/exclude’ classification for each study.

\textsuperscript{10}The Surgeon General’s Advisory Committee did not treat these latter studies as true case-control studies. The T.I.R.C., in its summaries presented in the Current Digest, was not always clear in reporting how the control groups were chosen. We include these types of studies in our listings for two reasons. Firstly, during the period in question, epidemiology was in its infancy and there appears to have been much debate about the appropriate methodology to be applied in study design. Secondly, by including them, we illustrate how the organisations themselves chose to report the studies, with the U.S. Surgeon General’s Advisory Committee appearing to have chosen a more rigorous definition of a control group than the T.I.R.C.. It is our hope that the resulting lists of articles identified by our review can be thought of as ‘inclusive’ rather than exclusive, and that researchers referencing them can apply their own inclusion criteria to narrow the lists down as they see fit.

\textsuperscript{11}The Surgeon General’s Advisory Committee encountered exactly this problem, as it recounts when describing its failed attempt to take an ‘encyclopedic approach’ to ‘all aspects of the use of tobacco and the resulting effects’.
Studies which met the inclusion criteria were then classified according to whether or not the summary contained in the Current Digest suggested that tobacco use was harmful.\textsuperscript{12} Details were then entered on to a database.\textsuperscript{13}

In the second stage, one reviewer (M.F.) identified studies meeting the inclusion criteria from statements and reports of the U.S. Public Health Service and related groups during the 1950s and the tables of the Surgeon General’s Advisory Committee’s report of 1964. Studies not already identified from our review of the Current Digest were then added to the database. For studies which had also been summarised in the Current Digest, we recorded the content of the relevant organisation’s summary and conclusions so that we could contrast them.

In the third stage, we used our own search of the literature for 1950-59 and a review of the literature cited in other relevant articles to identify any studies which appeared to have been ‘missed’ by the organisations listed in figure 2. We were aware that our own searches could not come close to competing with those carried out by these organisations, which would have had access to books, reports, unpublished data and conference proceedings from that era which were rarely indexed anywhere and so are almost impossible to identify today. However, we felt that the review was of some value, in that a negative result would not contradict our belief that, taken together, the organisations’ reviews were comprehensive in their coverage of the literature.

After these three stages were complete, we obtained as many as possible of the articles meeting our inclusion criteria.

In the final stage, we used the results of stages two and three to identify in the Catalog studies that the T.I.R.C. had reviewed prior to August 1955. We used the Catalog’s ‘A’ to ‘C’ classifications (no studies received a ‘D’ or ‘E’ classification) to record the T.I.R.C.’s view regarding whether or not each study suggested that tobacco use was harmful. Since there exists a gap of about a year in our coverage of T.I.R.C. records (between August 1955 and July 1956), we were careful to check whether the T.I.R.C. appears to have missed any studies published during this period.\textsuperscript{14}

For each article meeting our inclusion criteria, the database recorded information relating to the study itself (for example, the journal in which the article was published, the authors, authors’ affiliations etc.) and the adverse

\textsuperscript{12}When the reviewers disagreed (as to whether or not the study should be included or on its conclusion), the summary was referred to M.R. for a final decision.

\textsuperscript{13}The reviewers considered firstly the volumes of the Digest published between July 1956 and the end of 1959 and results were entered on to the database. This process was then repeated for the volumes published between 1960 and the end of 1963. The 1964 volume was also scanned to locate any papers published in 1963, which were also entered on to the database.

\textsuperscript{14}This was not a serious problem: only one study published between August 1955 (the date of publication of the Catalog) and July 1956 (the date of publication of Current Digest I(1)) appears to have been ‘missed’ by both the Catalog and Current Digest (Blümlein (1955) (laryngeal cancer)).
health outcomes investigated (a number of studies considered more than one adverse health outcome). In addition, separate sections for the Current Digest and the Surgeon General’s Advisory Committee recorded whether the organisation summarised the study and, if it did, what information was reported in its summary. This section included the summary’s reporting of: 1. population characteristics; 2. outcomes investigated; 3. (a) whether the summary suggested that the results of the study appeared to support an association between tobacco use and each health outcome studied; (b) the statistical data used in reaching this conclusion; (c) whether the summary suggested that the conclusions of the study supported an association between tobacco use and each health outcome studied. Based on this information, and for each relevant health outcome, the reviewers then agreed an overall classification of ‘tobacco harmful’, ‘tobacco not harmful’ or ‘unclear’ for the summary. It should be noted that this process did not judge the content of the article itself, rather, we were interested in the organisations’ judgments regarding whether or not the article suggested that tobacco was harmful to health.

Once completed, we used the results to assess the quality of the T.I.R.C.’s review process, including its comprehensiveness, responsiveness and bias. Comprehensiveness was considered for the six cancer sites only and was measured by calculating, for each cancer site, the proportion of the studies identified by the Surgeon General’s Advisory Committee that were also classified/summarised by the T.I.R.C.\textsuperscript{15} Responsiveness was assessed by calculating the average time, in months, between the month of publication of an article meeting our inclusion criteria and the month in which a summary of the article was published in the Current Digest (responsiveness could only be assessed using the studies appearing in the Current Digest, since the Catalog contained a summary of all literature in existence as of August 1955). Bias was assessed by considering whether or not the T.I.R.C. appeared selective in the studies it chose to review (for example, whether or not it only reviewed studies whose findings suggested that tobacco was not harmful) and whether its classifications and summaries appeared to misrepresent the findings of the articles themselves.

It should be noted that the fact that a paper did not appear in the Catalog or the Current Digest does not mean that the T.I.R.C. or its members were unaware of its existence. Since T.I.R.C. sponsors included most of the major U.S. tobacco companies, each with its own literature retrieval operations, other sources of articles and literature reviews can be located in the on-line archives. We focus here on the Catalog and the Current Digest because they are two of the major outputs of the T.I.R.C. and because the content of the

\textsuperscript{15} We used the Advisory Committee’s studies as a ‘gold standard’ list of publications. The Advisory Committee was not comprehensive in assessing the literature for cardiovascular disease, which is why we limited our focus to the six cancer sites.
Current Digest allows us to pinpoint, month by month over seven years, the epidemiological evidence which the T.I.R.C. had within its possession.

4 Results

Table 1 presents the annual page length of the Current Digest, together with the number of summaries contained within each volume. Table 1 shows how the size of the T.I.R.C.'s literature review operation grew during the late 1950s and early 1960s: the annual page length rose from 105 in 1957 to 416 in 1963. By October 1960, it appears that the T.I.R.C. was struggling to keep up with the volume of scientific articles in circulation since, from this volume onwards, some articles were noted as being received by the T.I.R.C. but not excerpted in the Current Digest. The annual number of such articles is reported in the final column of table 1: the October 1960 volume contained eleven such articles; by December 1963, the figure had risen to 49.

In general, for stage one of our review, it was straightforward to classify the summaries of articles contained within the Current Digest; few were referred to M.R. for a ‘third opinion’. Our biggest problem came with identifying, from the summaries themselves, the precise statistical methods used by the studies’ authors in reaching their conclusions. The Current Digest summaries often reported point estimates, but reporting of test statistics, p values and confidence intervals was rarer. For the period in question, table 1 shows that the number of pages of the Current Digest reviewed by us totalled 1715 and the number of summaries reviewed totalled 3274.

Stage two of our review, the reviews of the reports of the U.S. Public Health Service and related groups, was also straightforward. The reports of 1957 and 1959 concentrated mainly on lung cancer, with the Study Group on Smoking and Health referencing 16 retrospective and two prospective studies. Surgeon General Burney’s statement of 1959 added the results of five retrospective studies and one prospective study. The report of the Surgeon

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16 Table 1 does not include summaries included as supplements to the Current Digest, which normally included conference, congress and annual reports and which were excluded from our review (unless they concerned annual reports from major organisations).  
17 In isolated cases (Segi et al., 1957 and Wynder et al., 1957b), the Current Digest summaries did not make the retrospective nature of the study clear. These studies were ‘missed’ by both reviewers when reviewing the Digest. Another study, Staszewski (1960a), was cited in the Current Digest as having been received by the T.I.R.C. but not excerpted. These are noted in tables 2 to 11.  
18 One other difficulty was that not all of the summaries in the Current Digest made the study design clear (this was the case for Segi et al., 1957 and Wynder et al., 1957b). These studies were ‘missed’ by both reviewers when reviewing the Digest. Another study, Staszewski (1960a), was cited in the Current Digest as having been received by the T.I.R.C. but not excerpted. These cases are noted in our tables of results.  
19 Surgeon General Burney’s statement of 1957 (Burney, 1958) referred to the results of the Study Group’s report.
Table 1: Current Digest: page length, summaries and articles received but not excerpted, volumes I - VIII, 1956 - 1963.

Notes

\(^a\) July to December 1956.

General's Advisory Committee added further retrospective and prospective studies and included analysis of cancer of the other five sites considered in this paper, as well as cardiovascular disease.

For stage three, our own review of the literature between 1950 and 1959, we consulted approximately 641 papers out of the 1638 titles identified in the search of the databases described in the appendix to this paper. Where possible, we obtained translations of papers not written in English.\(^{20}\) This yielded only one paper - the Japanese retrospective study by Hirayama and Hamano (1955) - which did not appear in the reviews of the organisations listed in figure 2. Another article by Hoffman (1931) was identified in our review of other relevant articles. It reports the results of what appears to be a very early case-control study examining the relationship between smoking and cancer at a number of sites, including the lungs, oral cavity, larynx and oesophagus. The study is of note because it pre-dates what generally appears to be accepted as the first case-control study of lung cancer (Müller, 1939) by eight years.\(^{21}\)

Finally, stage four, the review of the Catalog, was again straightforward. The classifications regarding tobacco harm (the letters ‘A’ to ‘E’) are already

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\(^{20}\) We used a number of translations that had been commissioned by the tobacco companies themselves and which we found in the on-line archives. In addition, we translated the relevant sections of papers written in French, German, Italian, Japanese, Spanish, Norwegian and Polish. At the time of writing, we are still awaiting receipt of translations of a small number of articles.

\(^{21}\) Hoffman found that the percentage of heavy smokers in his group of lung cancer patients was 67% compared with 42.3% in the control group. However, his analysis concentrates on pooling the percentage of heavy smokers for cancers at all sites which, at 45.6%, is similar to the percentage of heavy smokers in the controls.
provided in this document, so we simply had to use the results of stages two
and three of our review to identify the relevant studies published prior to
August 1955 which were listed in the Catalog.

The articles that were identified by our review are summarised in tables
2 to 11. The final columns of these tables contain the T.I.R.C.’s and the
Surgeon General’s Advisory Committee’s classifications regarding tobacco
harm. These classifications are either the letters ‘A’ to ‘C’ (for studies listed
in the Catalog) or our reviewers’ classifications (‘N’- tobacco not harmful; ‘U’
unclear, given the summary; ‘Y’- tobacco harmful), for studies appearing in
the Current Digest or in the Surgeon General’s Advisory Committee’s report.
In addition, the lung cancer articles included in the Study Group on Smoking
and Health’s report of 1957 and Surgeon General Burney’s statement of 1959
are noted in tables 2 to 4.

Table 2 lists the seven major prospective studies identified by the Advi-
sory Committee. Tables 3 to 9 list the retrospective studies for cancer at the
six sites of interest. Table 10 lists other prospective studies reviewed by the
organisations and table 11 lists the retrospective studies for cardiovascular
disease that were identified in the Current Digest (the Advisory Committee
does not appear to have attempted a comprehensive review of these studies).
<table>
<thead>
<tr>
<th>Study</th>
<th>Published</th>
<th>Country</th>
<th>Source</th>
<th>Date</th>
<th>T.I.R.C. Classification</th>
<th>Surgeon General’s Advisory Committee Classification</th>
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<tr>
<td><strong>British doctors</strong></td>
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<td>Doll and Hill</td>
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<td>Catalog</td>
<td>08/1955</td>
<td>C</td>
<td>Y</td>
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<td>Doll and Hill</td>
<td>10/11/1956</td>
<td>United Kingdom</td>
<td>C.D. I(6)</td>
<td>12/1956</td>
<td>Y</td>
<td></td>
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<tr>
<td><strong>Nine U.S. States</strong></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>Hammond and Horn</td>
<td>07/08/1954</td>
<td>U.S.A.</td>
<td>Catalog</td>
<td>08/1955</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Hammond and Horn (1958a)</td>
<td>08/03/1958</td>
<td>U.S.A.</td>
<td>C.D. III(4)</td>
<td>04/1958</td>
<td>-</td>
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</tr>
<tr>
<td>Hammond and Horn (1958b)</td>
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<td>Dorn (1958)</td>
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<td>U.S.A.</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Dorn (1959)</td>
<td>07/1959</td>
<td>U.S.A.</td>
<td>C.D. IV(8)</td>
<td>08/1959</td>
<td>Y</td>
<td>Y</td>
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<tr>
<td><strong>California occupational groups</strong></td>
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<td>Dunn et al.</td>
<td>1963</td>
<td>U.S.A.</td>
<td>Special report for Surgeon General’s Advisory Committee</td>
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<td>-</td>
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<td><strong>Canadian pensioners</strong></td>
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<tr>
<td>Best et al.</td>
<td>03/1961</td>
<td>Canada</td>
<td>C.D. VI(4)</td>
<td>04/1961</td>
<td>Y</td>
<td>Y</td>
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<tr>
<td><strong>Men in 25 U.S. states</strong></td>
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<td></td>
<td></td>
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</tr>
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<td>C.D. VII(9)</td>
<td>09/1962</td>
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<td>Y</td>
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<tr>
<td>Hammond</td>
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<td>U.S.A.</td>
<td>Special report for Surgeon General’s Advisory Committee</td>
<td>Y</td>
<td>Y</td>
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</tbody>
</table>

Table 2: The seven ‘large prospective studies’ reviewed by the Surgeon General’s Advisory Committee: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications for lung cancer and cardiovascular disease (based on the sources used in this review).

**Notes**

Classifications for studies contained in the Catalog (pre-August 1955): A (tobacco not harmful), B (‘neutral’ regarding effects of tobacco), C (tobacco harmful); for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful).

1Study cited by the Study Group on Smoking and Health (1957).

2Study added to those reviewed by the Study Group on Smoking and Health (1957) by Surgeon General Burney’s statement of 1959 (Burney, 1959). Entries in the final two columns refer to the main articles referenced in the Surgeon General’s Advisory Committee report’s chapters on cancer and cardiovascular disease. The Advisory Committee, as well as referring to these articles, also obtained the latest results from the prospective studies (all but the ‘Nine U.S. States’ study, which was not ongoing at the time the Committee was preparing its report) and reported ‘pooled’ results.

"Report in two parts: Hammond (1958a) considers ‘total mortality’; Hammond (1958b) considers ‘death rates by cause’.

"Also referenced are Dorn (1958) (previous entry in table).
Table 3: Lung cancer retrospective studies, pre-July 1956: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications (based on the sources used in this review).

### Notes
Classifications for studies contained in the Catalog (pre-August 1955): A (tobacco not harmful), B (‘neutral’ regarding effects of tobacco), C (tobacco harmful); for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful).

†Study cited by the Study Group on Smoking and Health (1957).

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### Study		Published	Country	Tobacco Industry Research Committee Source	Date	Classification	Surgeon General’s Advisory Committee Classification
Müller	1939	Germany	Catalog	08/1955	C	Y†
Schairer and Schöniger	1943	Germany	-	-	-	Y†
Potter and Tully	05/1945	U.S.A.	Catalog	08/1955	C	Y
Wassink	13/11/1948	Netherlands	-	-	-	Y†
Schrek et al.	01/1950	U.S.A.	Catalog	08/1955	C	Y†
Levin et al.	27/05/1950	U.S.A.	Catalog	08/1955	C	Y†
Wynder and Graham	27/05/1950	U.S.A.	Catalog	08/1955	C	Y†
Watson a	20/06/1950	U.S.A.	Catalog	08/1955	B	-
Doll and Hill	30/09/1950	England	Catalog	08/1955	C	-
Mills and Porter	09/1950	U.S.A.	Catalog	08/1955	C	Y†
McConnell et al.	04/10/1952	England	Catalog	08/1955	C	Y†
Doll and Hill b	13/12/1952	England	Catalog	08/1955	C	Y†
Wynder and Cornfield	12/03/1953	U.S.A.	-	-	-	Y†
Koulimies	03/1953	Finland	-	-	-	Y†
Sadowsky et al.	04/1953	U.S.A.	Catalog	08/1955	C	Y†
Lickint	1953	Germany	-	-	-	Y†
Breslow et al.	02/1954	U.S.A.	Catalog	08/1955	C	Y†
Levin c	15/03/1954	U.S.A.	Catalog	08/1955	C	Y†
Watson and Conte	03/1954	U.S.A.	Catalog	08/1955	C	Y†
Gsell	1954	Switzerland	Catalog	08/1955	C	Y
Randig	12/1954	Germany	-	-	-	Y

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*Reanalysis of half of the cases from Wynder and Graham (1950).
*Updating Doll and Hill (1950).
*Updating Levin et al. (1950).
<table>
<thead>
<tr>
<th>Study</th>
<th>Published</th>
<th>Country</th>
<th>Tobacco Industry Research Committee</th>
<th>Surgeon General’s Advisory Committee</th>
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<tr>
<td>Kreyberg</td>
<td>01/02/1956</td>
<td>Norway</td>
<td>C.D. I(1) 07/1956  Y</td>
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<tr>
<td>Fuchs</td>
<td>15/03/1956</td>
<td>Germany</td>
<td>C.D. I(4) 10/1956 Y</td>
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<td>Wynder et al. (1956b)</td>
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<td>U.S.A.</td>
<td>C.D. II(1) 01/1957 Y</td>
<td>Y†</td>
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<td>Segi et al.</td>
<td>04/1957</td>
<td>Japan</td>
<td>C.D. II(12) 12/1957 Y</td>
<td>Y†</td>
</tr>
<tr>
<td>Schwartz and Denoix</td>
<td>30/10/1957</td>
<td>France</td>
<td>-</td>
<td>Y‡</td>
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<tr>
<td>Mills and Porter</td>
<td>11/1957</td>
<td>U.S.A.</td>
<td>C.D. III(1) 01/1958 Y</td>
<td>Y‡</td>
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<td>Denoix et al.</td>
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<td>C.D. III(8) 08/1958 Y</td>
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<td>Wynder et al.</td>
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<td>Cuba</td>
<td>C.D. III(6) 06/1958 Y</td>
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<tr>
<td>Stocks (1957)</td>
<td>01/07/1958</td>
<td>England and Wales</td>
<td>C.D. III(8) 08/1958 Y</td>
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</tr>
<tr>
<td>Haenszel et al.</td>
<td>11/1958</td>
<td>U.S.A.</td>
<td>C.D. IV(1) 01/1959 Y</td>
<td>Y‡</td>
</tr>
<tr>
<td>Lombard and Snegireff</td>
<td>03-04/1959</td>
<td>U.S.A.</td>
<td>C.D. IV(4) 04/1959 Y</td>
<td>Y‡</td>
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<tr>
<td>Pernu</td>
<td>1960</td>
<td>Finland</td>
<td>C.D. V(12) 12/1960 Y</td>
<td>Y</td>
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<tr>
<td>Conti and Negro</td>
<td>21/02/1961</td>
<td>Italy</td>
<td>C.D. VI(7) 07/1961 Y</td>
<td>-</td>
</tr>
<tr>
<td>Schwartz et al. (1961b)</td>
<td>05/1961</td>
<td>France</td>
<td>C.D. VI(7) 07/1961 Y</td>
<td>-</td>
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<td>Dean</td>
<td>16/12/1961</td>
<td>South Africa</td>
<td>C.D. VII(1) 01/1962 Y</td>
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<td>Wynder et al.</td>
<td>16/12/1961</td>
<td>Italy</td>
<td>C.D. VII(1) 01/1962 Y</td>
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<td>Haenszel et al.</td>
<td>04/1962</td>
<td>U.S.A.</td>
<td>C.D. VII(6) 06/1962 Y</td>
<td>Y</td>
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<td>Kissen</td>
<td>03-04/1962</td>
<td>Scotland</td>
<td>C.D. VII(6) 06/1962 Y</td>
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<td>Lancaster</td>
<td>30/06/1962</td>
<td>Australia</td>
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<td>Levin</td>
<td>05/1963</td>
<td>U.S.A.</td>
<td>C.D. VIII(7) 07/1963 Y</td>
<td>-</td>
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<td>Milicevic</td>
<td>1963</td>
<td>Yugoslavia</td>
<td>C.D. IX(12) 12/1964 Y</td>
<td>-</td>
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<tr>
<td>Haenszel and Taeuber</td>
<td>1963</td>
<td>U.S.A.</td>
<td>Special report for Surgeon General’s Advisory Committee</td>
<td>Y</td>
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</table>

**Table 4:** Lung cancer retrospective studies, post-July 1956: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications (based on the sources used in this review).

**Notes:**
Classifications for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful).

†Study cited by the Study Group on Smoking and Health (1957).
‡Study added to those reviewed by the Study Group on Smoking and Health (1957) by Surgeon General Burney’s statement of 1959 (Burney, 1959).

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*a* Noted in Current Digest as being from ‘Foreign Letters’, JAMA, 05/1956.

*b* Noted in Current Digest as being from an abstract in Excerpta Medica - Cancer 08/1956.

*c* Not clear retrospective study based on the Current Digest’s summary.

*d* Updating Schwartz and Denoix (1957).


*f* Noted in Current Digest as being from abstract in JAMA, 06/1961.

*g* Updating Schwartz and Denoix (1957) and Denoix et al. (1958).

*h* Updating Levin et al. (1950) and Levin (1954).
<table>
<thead>
<tr>
<th>Study</th>
<th>Published</th>
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<th>Tobacco Industry Research Committee Source</th>
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<td>Broders</td>
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<td>Lombard and Doering</td>
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<td>08/1955</td>
<td>C</td>
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<td>Bigelow and Lombard</td>
<td>1933</td>
<td>U.S.A.</td>
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<td>Ebenius</td>
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<td>Levin et al.</td>
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<td>Sadowsky et al.</td>
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<td>Moore et al.</td>
<td>07/1953</td>
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<td>09/1957</td>
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<td>U.S.A.</td>
<td>C.D. III</td>
<td>01/1958</td>
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<td>Y</td>
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<tr>
<td>Wynder et al.</td>
<td>04/1958</td>
<td>Cuba</td>
<td>C.D. III</td>
<td>06/1958</td>
<td>Y</td>
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<td>Peacock et al.</td>
<td>04/1960</td>
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<td>C.D. V</td>
<td>05/1960</td>
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<td>Y</td>
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<tr>
<td>Staszewski (1960c)</td>
<td>1960</td>
<td>Poland</td>
<td></td>
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<tr>
<td>Pernu</td>
<td>1960</td>
<td>Finland</td>
<td>C.D. V</td>
<td>12/1960</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Schwartz et al. (1961b)</td>
<td>05/1961</td>
<td>France</td>
<td>C.D. VI</td>
<td>07/1961</td>
<td>Y</td>
<td></td>
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<tr>
<td>Vogler et al.</td>
<td>03-04/1962</td>
<td>U.S.A.</td>
<td>C.D. VIII</td>
<td>05/1962</td>
<td>Y</td>
<td></td>
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<td>Shanta and Krishnamurthi</td>
<td>03/1963</td>
<td>India</td>
<td>C.D. VIII</td>
<td>07/1963</td>
<td>Y</td>
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<tr>
<td>Levin (a)</td>
<td>05/1963</td>
<td>U.S.A.</td>
<td>C.D. VIII</td>
<td>07/1963</td>
<td>Y</td>
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</tbody>
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**Table 5:** Oral cancer retrospective studies: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications (based on the sources used in this review).

**Notes:**
Classifications for studies contained in the Catalog (pre-August 1955): A (tobacco not harmful), B ('neutral' regarding effects of tobacco), C (tobacco harmful); for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful).

- **a** Not clear retrospective study based on the Current Digest's summary.
- **b** Reporting results of Wynder and Bross (1957).
- **c** Updating Schwartz et al. (1957).
- **d** Updating Levin et al. (1950).
<table>
<thead>
<tr>
<th>Study</th>
<th>Published</th>
<th>Country</th>
<th>Tobacco Industry Research Committee</th>
<th>Surgeon General’s Advisory Committee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schrek et al.</td>
<td>01/1950</td>
<td>USA</td>
<td>Catalog 08/1955 C</td>
<td>U</td>
</tr>
<tr>
<td>Valko</td>
<td>1952</td>
<td>Czechoslovakia</td>
<td>-</td>
<td>U</td>
</tr>
<tr>
<td>Sadowsky et al.</td>
<td>04/1953</td>
<td>U.S.A.</td>
<td>Catalog 08/1955 C</td>
<td>Y</td>
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<tr>
<td>Blümlein</td>
<td>10/1955</td>
<td>Germany</td>
<td>-</td>
<td>Y</td>
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<tr>
<td>Wynder et al. (1956c)</td>
<td>01-02/1956</td>
<td>U.S.A. and India</td>
<td>-</td>
<td>Y</td>
</tr>
<tr>
<td>Wynder et al. (1956a)</td>
<td>21/04/1956</td>
<td>U.S.A., India and Sweden</td>
<td>C.D. I(1) 07/1956 Y</td>
<td>-</td>
</tr>
<tr>
<td>Schwartz et al.</td>
<td>04-06/1957</td>
<td>France</td>
<td>-</td>
<td>Y</td>
</tr>
<tr>
<td>Wynder et al. (1957b)</td>
<td>05-06/1957</td>
<td>Sweden</td>
<td>C.D. II(9) 09/1957 U</td>
<td>Y</td>
</tr>
<tr>
<td>Stocks (1957)</td>
<td>01/07/1958</td>
<td>England and Wales</td>
<td>C.D. III(8) 08/1958 Y</td>
<td>Y</td>
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<tr>
<td>Dutta-Choudhuri et al.</td>
<td>01/05/1959</td>
<td>India</td>
<td>C.D. IV(8) 08/1959 Y</td>
<td>-</td>
</tr>
<tr>
<td>Ruppmann</td>
<td>20/05/1960</td>
<td>Germany</td>
<td>C.D. V(12) 12/1960 Y</td>
<td>-</td>
</tr>
<tr>
<td>Permu</td>
<td>1960</td>
<td>Finland</td>
<td>C.D. V(12) 12/1960 Y</td>
<td>-</td>
</tr>
<tr>
<td>Staszewski (1960c)</td>
<td>1960</td>
<td>Poland</td>
<td>-</td>
<td>Y</td>
</tr>
<tr>
<td>Schwartz et al. (1961b)</td>
<td>05/1961</td>
<td>France</td>
<td>C.D. VI(7) 07/1961 Y</td>
<td>-</td>
</tr>
<tr>
<td>Levin</td>
<td>05/1963</td>
<td>U.S.A.</td>
<td>C.D. VIII(7) 07/1963 Y</td>
<td>-</td>
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</table>

Table 6: Laryngeal cancer retrospective studies: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications (based on the sources used in this review).

Notes:
Classifications for studies contained in the Catalog (pre-August 1955): A (tobacco not harmful), B (‘neutral’ regarding effects of tobacco), C (tobacco harmful); for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful).

*a* Reporting the same study as Wynder et al. (1956c).

*b* Not clear retrospective study and not clear study of laryngeal cancer based on the Current Digest’s summary. This accounts for ‘U’ classification for T.I.R.C..


*d* Updating Schwartz et al. (1957).
### Table 7: Oesophageal cancer retrospective studies: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications (based on the sources used in this review).

**Notes**
- Classifications for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful), N.E. (received by T.I.R.C. but not excerpted).
- a) Not clear retrospective study and not clear study of oesophageal cancer based on the Current Digest’s summary. This accounts for ‘U’ classification for T.I.R.C..
- c) Also referenced by Surgeon General’s Advisory Committee is Staszewski (1960b) which does not appear to have investigated oesophageal cancer and so is omitted from tables.

<table>
<thead>
<tr>
<th>Study</th>
<th>Published</th>
<th>Country</th>
<th>Tobacco Industry Research Committee</th>
<th>Surgeon General’s Advisory Committee</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Source</td>
<td>Date</td>
</tr>
<tr>
<td>Sadowsky et al.</td>
<td>04/1953</td>
<td>U.S.A.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sanghvi et al.</td>
<td>07/05/1955</td>
<td>India</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Wynder et al. (1957b)</td>
<td>05-06/1957</td>
<td>Sweden</td>
<td>C.D. II(9)</td>
<td>09/1957</td>
</tr>
<tr>
<td>Stocks (1957)</td>
<td>01/07/1958</td>
<td>England and Wales</td>
<td>C.D. III(8)</td>
<td>08/1958</td>
</tr>
<tr>
<td>Staszewski (1960a)</td>
<td>1960</td>
<td>Poland</td>
<td>C.D. VII(4)</td>
<td>04/1962</td>
</tr>
<tr>
<td>Pernu</td>
<td>1960</td>
<td>Finland</td>
<td>C.D. V(12)</td>
<td>12/1960</td>
</tr>
<tr>
<td>Wynder and Bross</td>
<td>03-04/1961</td>
<td>U.S.A.</td>
<td>C.D. VI(4)</td>
<td>04/1961</td>
</tr>
<tr>
<td>Schwartz et al. (1961b)</td>
<td>05/1961</td>
<td>France</td>
<td>C.D. VI(7)</td>
<td>07/1961</td>
</tr>
<tr>
<td>Shanta and Krishnamurthi</td>
<td>03/1963</td>
<td>India</td>
<td>C.D. VIII(7)</td>
<td>07/1963</td>
</tr>
<tr>
<td>Levin</td>
<td>05/1963</td>
<td>U.S.A.</td>
<td>C.D. VIII(7)</td>
<td>07/1963</td>
</tr>
<tr>
<td>Study</td>
<td>Published</td>
<td>Country</td>
<td>Tobacco Industry Research Committee</td>
<td>Surgeon General's Advisory Committee</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------</td>
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<td>-------------------------------------</td>
<td>-------------------------------------</td>
</tr>
<tr>
<td>Lilienfeld et al.</td>
<td>08/1956</td>
<td>U.S.A.</td>
<td>C.D. I(5) 11/1956 Y</td>
<td>Y</td>
</tr>
<tr>
<td>Schwartz et al. (1961b)</td>
<td>05/1961</td>
<td>France</td>
<td>C.D. VI(7) 07/1961 Y</td>
<td>Y</td>
</tr>
<tr>
<td>Lockwood</td>
<td>07/1961</td>
<td>Denmark</td>
<td>C.D. VI(8) 08/1961 Y</td>
<td>Y</td>
</tr>
<tr>
<td>Levin</td>
<td>05/1963</td>
<td>U.S.A.</td>
<td>C.D. VIII(7) 07/1963 Y</td>
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</tr>
</tbody>
</table>

Table 8: Urinary bladder cancer retrospective studies: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications (based on the sources used in this review).

Notes
Classifications for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful).

"Noted in Surgeon General’s Advisory Committee’s report as ‘to be published’.
### Table 9: Stomach cancer retrospective studies: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications (based on the sources used in this review).

**Notes**
Classifications for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful), N.E. (received by T.I.R.C. but not excerpted).


<table>
<thead>
<tr>
<th>Study</th>
<th>Published</th>
<th>Country</th>
<th>Tobacco Industry Research Committee</th>
<th>Surgeon General’s Advisory Committee</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Source</td>
<td>Date</td>
</tr>
<tr>
<td>Dunham and Brunschwig</td>
<td>1946</td>
<td>U.S.A.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Kraus et al.</td>
<td>08/1957</td>
<td>U.S.A.</td>
<td>C.D. II(9)</td>
<td>09/1957</td>
</tr>
<tr>
<td>Stocks (1957)*</td>
<td>01/07/1958</td>
<td>England and Wales</td>
<td>C.D. III(8)</td>
<td>08/1958</td>
</tr>
<tr>
<td>Pernu</td>
<td>1960</td>
<td>Finland</td>
<td>C.D. V(12)</td>
<td>12/1960</td>
</tr>
<tr>
<td>Staszewski (1960a)</td>
<td>1960</td>
<td>Poland</td>
<td>C.D. VII(4)</td>
<td>04/1962</td>
</tr>
<tr>
<td>Schwartz et al. (1961b)</td>
<td>05/1961</td>
<td>France</td>
<td>C.D. VI(7)</td>
<td>07/1961</td>
</tr>
<tr>
<td>Wynder et al. (1963a)</td>
<td>11/1963</td>
<td>Various</td>
<td>C.D. IX(1)</td>
<td>01/1964</td>
</tr>
<tr>
<td>Study</td>
<td>Published</td>
<td>Country</td>
<td>Source</td>
<td>Date</td>
</tr>
<tr>
<td>-----------------------------------</td>
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</tr>
<tr>
<td>Philadelphia Pulmonary Neoplasm Research Project</td>
<td>Boucot and Cooper&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10/1957</td>
<td>U.S.A.</td>
<td>C.D. II(11)</td>
</tr>
<tr>
<td></td>
<td>Boucot et al.</td>
<td>03/1961</td>
<td>U.S.A.</td>
<td>C.D. VI(5)</td>
</tr>
<tr>
<td>Canadian asbestos miners</td>
<td>Braun and Truan</td>
<td>06/1958</td>
<td>Canada</td>
<td>C.D. III(7)</td>
</tr>
<tr>
<td></td>
<td>Borhani et al.</td>
<td>12/1963</td>
<td>U.S.A.</td>
<td>C.D. IX(1)</td>
</tr>
<tr>
<td>Framingham and Albany studies</td>
<td>Dawber et al.&lt;sup&gt;c&lt;/sup&gt; (Framingham)</td>
<td>10/1959</td>
<td>U.S.A.</td>
<td>C.D. IV(11)</td>
</tr>
<tr>
<td></td>
<td>Doyle et al. (Albany)</td>
<td>26/11/1959</td>
<td>U.S.A.</td>
<td>C.D. V(1)</td>
</tr>
<tr>
<td></td>
<td>Doyle et al. (studies combined)</td>
<td>19/04/1962</td>
<td>U.S.A.</td>
<td>C.D. VII(5)</td>
</tr>
<tr>
<td>Massachusetts physicians</td>
<td>Snegireff and Lombard</td>
<td>02/1963</td>
<td>U.S.A.</td>
<td>C.D. VIII(3)</td>
</tr>
<tr>
<td>Industrial population</td>
<td>Paul et al.</td>
<td>07/1963</td>
<td>U.S.A.</td>
<td>C.D. VIII(8)</td>
</tr>
</tbody>
</table>

Table 10: Classifications of other prospective studies reviewed by the T.I.R.C. and whether they were referred to by the Surgeon General’s Advisory Committee’s report (based on the sources used in this review).

Notes:
Classifications for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful), N.C. - study referenced in Surgeon General’s Advisory Committee’s report, but no comment made on findings. None of these articles were referred to in the Advisory Committee’s discussion of lung cancer.

<sup>a</sup>Proceedings, but not noted as so in Current Digest.
<sup>b</sup>Panel discussion at annual session of the California Medical Association, 1958. Surgeon General’s Advisory Committee refers to Buechley et al. (1958).
<sup>c</sup>Conference report, American Public Health Association, 1958.
Table 11: Cardiovascular disease retrospective studies: T.I.R.C.’s and Surgeon General’s Advisory Committee’s classifications (based on the sources used in this review).

Notes
Classifications for summaries reviewed in the Current Digest (C.D., July 1956 - December 1963) and by the Surgeon General’s Advisory Committee and related groups: N (tobacco not harmful), U (unclear, given the summary), Y (tobacco harmful).

Reporting the same study as Russek and Zohman (1958).

<table>
<thead>
<tr>
<th>Study</th>
<th>Published</th>
<th>Country</th>
<th>Tobacco Industry Research Committee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russek and Zohman</td>
<td>03/1958</td>
<td>U.S.A.</td>
<td>C.D. III(4) 04/1958 U</td>
</tr>
<tr>
<td>Feiks</td>
<td>09/1959</td>
<td>Austria</td>
<td>C.D. V(4) 04/1960 N</td>
</tr>
<tr>
<td>Russek</td>
<td>03/10/1959</td>
<td>U.S.A.</td>
<td>C.D. IV(11) 11/1959 U</td>
</tr>
<tr>
<td>Zukel et al.</td>
<td>12/1959</td>
<td>U.S.A.</td>
<td>C.D. V(2) 02/1960 Y</td>
</tr>
<tr>
<td>Ustvedt</td>
<td>02/03/1961</td>
<td>Norway</td>
<td>C.D. VI(5) 05/1961 U</td>
</tr>
<tr>
<td>Schwartz et al. (1961a)</td>
<td>08-09/1961</td>
<td>France</td>
<td>C.D. VI(11) 11/1961 Y</td>
</tr>
<tr>
<td>Jouve et al.</td>
<td>10/02/1962</td>
<td>France</td>
<td>C.D. VII(5) 05/1962 Y</td>
</tr>
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<td>Rigner</td>
<td>06/12/1962</td>
<td>Sweden</td>
<td>C.D. VIII(3) 03/1963 Y</td>
</tr>
<tr>
<td>Kasanen et al.</td>
<td>1963</td>
<td>Finland</td>
<td>C.D. IX(2) 02/1964 U</td>
</tr>
</tbody>
</table>
4.1 Evaluation of the quality of the T.I.R.C.’s literature review process

Comprehensiveness

Table 2, which summarises the seven large prospective studies considered by the Surgeon General’s Advisory Committee, shows that the T.I.R.C. had obtained and classified six of the seven as ‘tobacco harmful’ by 1964 (the study of Dunn et al. (1963) was a special report to the Surgeon General’s Advisory Committee and therefore was not available to the T.I.R.C. prior to the publication of the Committee’s report). In their reports to the Surgeon General’s Advisory Committee, researchers in all of the on-going prospective studies provided their most up-to-date data,\(^ {22}\) which gave a far more comprehensive summary of mortality ratios by cause of death. As far as we are aware, this information was not available to the T.I.R.C. until the Advisory Committee’s report was published.

Turning to the retrospective studies, tables 12 and 13 present cross-tabulations showing, for each of the six cancer sites, the number of studies which had been summarised by the T.I.R.C. and/or the Surgeon General’s Advisory Committee. In compiling the tables we note that, in some cases, essentially the same study had been reported in more than one article (for example, Wynder et al. (1956c,a)) and also that some authors published updated results of the same study from time to time (for example, Levin (1963) appears to have updated the results of Levin et al. (1950) and Levin (1954)). As long as an organisation had summarised at least one of the articles relating to a particular study, we deemed it to have had ‘knowledge’ of that study (although it would have been possible for a study’s updated results to change authors’ conclusions, we found no evidence to suggest that an updated study contradicted, in a significant manner, previously reported results).

For lung cancer, table 12 shows that, of the 18 studies referenced by ‘Smoking and Health’ and published prior to July 1956, the T.I.R.C. had listed in the Catalog twelve (67%). The six missing studies originated from Germany (3), Finland (1), the Netherlands (1) and the U.S.A. (1).\(^ {23}\) Two of these eighteen studies were reported in more than one paper with updated results: Doll and Hill (1950, 1952) and Levin et al. (1950), Levin (1954, 1963). In both cases the Advisory Committee reported one article for each study. Only ten of the eleven studies referenced by ‘Smoking and Health’

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\(^{22}\)The exception being the ‘Nine U.S. States’ study, which was not ongoing at the time the Advisory Committee prepared its report.

\(^{23}\)It is worth mentioning that the T.I.R.C. was aware of the majority of these missing studies, since its records contain a review of the literature by Dorn (1954) which lists them (Schairer and Schöniger (1943), Wassink (1948), Wynder and Cornfield (1953), Koulumies (1953) and Lickint (1953)) (T.I.R.C., not dated (a)). It is not clear why these studies were not summarised in the Catalog.
### Table 12: Retrospective studies for lung, oral and laryngeal cancer: cross-tabulations of studies listed by the Surgeon General’s Advisory Committee’s report ‘Smoking and Health’ and reviewed/appearing as summaries in the T.I.R.C.’s ‘Catalog’ (pre-July 1956) and Current Digest (post-July 1956).

#### Notes

Numbers in parentheses refer to the studies summarised by the T.I.R.C. as a percentage of the total listed in ‘Smoking and Health’.


b Percentages calculated on the basis of articles available to the T.I.R.C., that is, excluding the special report for the Surgeon General’s Advisory Committee by Haenszel and Tauber (1963).

c Wynder et al. (1956c) (in ‘Smoking and Health’) and Wynder et al. (1956a) (in the Current Digest) report the same study and are included here as one, pre-1956 study. Percentages calculated on the basis of articles available for summarising in either the Catalog or Current Digest, that is, excluding Blümllein (1955), which was published after the Catalog but well before the first issue of the Current Digest.

post-July 1956 were in the public domain prior to the report’s publication (Haenszel and Tauber (1963) was a special report for the Advisory Committee). The T.I.R.C. had reviewed nine of these, the omitted one being the Australian study of Lancaster (1962). Post-July 1956, table 12 shows that

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Surgeon General’s Advisory Committee</th>
<th>T.I.R.C.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Included (%)</td>
<td>Not included (%)</td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catalog</td>
<td>Included</td>
<td>12 (67)</td>
<td>18</td>
</tr>
<tr>
<td>(Pre-July 1956)</td>
<td>Not included</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Current Digest</td>
<td>Included</td>
<td>9 (90)</td>
<td>11</td>
</tr>
<tr>
<td>(Post-July 1956)</td>
<td>Not included</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Oral cancer</td>
<td>Included</td>
<td>4 (40)</td>
<td>10</td>
</tr>
<tr>
<td>Catalog</td>
<td></td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>(Pre-July 1956)</td>
<td>Not included</td>
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</tr>
<tr>
<td>Total</td>
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<tr>
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<td>7</td>
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</tr>
<tr>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
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</tr>
<tr>
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<td>T.I.R.C.</td>
<td></td>
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<tr>
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</tr>
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</tr>
<tr>
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<td>-</td>
</tr>
<tr>
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<td>2</td>
</tr>
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<td>4</td>
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<tr>
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<td>-</td>
</tr>
<tr>
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<td>7</td>
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</tr>
<tr>
<td>(Post-July 1956)</td>
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<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
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<td>5</td>
</tr>
<tr>
<td><strong>Stomach cancer</strong></td>
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<td></td>
</tr>
<tr>
<td>Catalog</td>
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<td>1 (100)</td>
<td>1</td>
</tr>
<tr>
<td>(Pre-July 1956)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
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<td>1</td>
</tr>
<tr>
<td>Current Digest</td>
<td>2 (67)</td>
<td>1 (33)</td>
<td>3</td>
</tr>
<tr>
<td>(Post-July 1956)</td>
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<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>1</td>
<td>6</td>
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Table 13: Retrospective studies for oesophageal, urinary bladder and stomach cancer: cross-tabulations of studies listed by the Surgeon General’s Advisory Committee’s report ‘Smoking and Health’ and reviewed/appearing as summaries in the T.I.R.C.’s ‘Catalog’ (pre-July 1956) and Current Digest (post-July 1956).

**Notes**

Numbers in parentheses refer to the studies summarised by the T.I.R.C. as a percentage of the total listed in ‘Smoking and Health’.

A further seven retrospective studies examining lung cancer had been summarised by the T.I.R.C. but were not reported in the Advisory Committee’s tables.\textsuperscript{24}

Details concerning cancer at the other five sites can also be found in tables 12 and 13. We believe that the general message from these tables is that the T.I.R.C. was operating a reasonably comprehensive review process, especially for epidemiological studies relating to lung cancer, throughout the period under review. Overall, the Current Digest appears to have been picking up a higher proportion of the literature than does the Catalog. The T.I.R.C.’s review process appears especially impressive if one bears in mind that no electronic resources (on-line databases, electronic journals etc.) would have been available to the organisation to assist it in its work during the period.

\textsuperscript{24}Excluding repeated studies (Denoix et al. (1958), Schwartz et al. (1961b), Levin (1963)) and that of Milicevic (1963), which was only summarised in the Current Digest in late 1964.
the 1950s and 60s. We also note that the tables show that the T.I.R.C. summarised many studies which, we felt, met the inclusion criteria for our review, but which were not included by the Advisory Committee in its report.

**Responsiveness**

Of the 55 unique articles listed in tables 2 to 11, the mean delay between the month of publication of an article and the month in which a summary was published in the Current Digest equals 2.3 months (the median being two months). A histogram of the delay is shown in figure 3. For only five articles was the delay equal to or greater than six months and all of these were published in non-U.S./U.K. journals: the longest delay was eight months (the Japanese study by Segi et al., 1957), followed by two papers published in German journals (Fuchs, 1956 and Ruppmann, 1960) and one in an Austrian journal (Feiks, 1959), with a delay of seven months.

**Bias**

In our assessment of bias, we firstly considered whether or not the T.I.R.C.’s classifications and summaries of the articles appear to have misrepresented the findings of the articles themselves. The first thing to note, for those studies reviewed by both the T.I.R.C. and the Surgeon General’s Advisory Committee, is the strong agreement between the classifications that are shown in the final columns of tables 2 to 10. For all of the major prospective study articles which were reviewed by both organisations, classifications were consistent in suggesting that tobacco use was harmful. Of the 43 retrospective studies reviewed by both the T.I.R.C. and the Advisory Committee, disagreement in classifications only appeared twice.

For those studies which were reviewed by the T.I.R.C. but not the Advisory Committee, we compared the classification/summary in the Catalog or Current Digest to the content of the paper itself. We found very little

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25 The histogram was drawn using all articles listed in tables 2 to 11 which were summarised in the Current Digest between July 1956 and December 1963 inclusive. Duplicate articles - those which investigated more than one cancer site of interest and hence which appear in more than one table - were included once only. Articles for which only the year of publication was available were excluded. For dates spanning more than two months, we used the middle month (e.g. 01-03/1958 was taken to be 02/1958). For dates spanning two months, we used the first month (e.g. 03-04/1959 was taken to be 03/1959).

26 For Schrek et al. (1950), reporting on the relationship between tobacco use and laryngeal cancer, the Advisory Committee reported ‘evidence not firm’ and the Catalog recorded ‘C’ (tobacco harmful). For Wynder et al. (1957b), reporting on the relationship between tobacco use and laryngeal cancer, the Advisory Committee reported ‘tobacco not harmful’ and the reviewers classified the Current Digest summary as ‘unclear’, mainly because the cancer sites investigated were not clearly specified in the summary, nor was the retrospective nature of the study made clear.

27 This we did for the papers written in English only.
Figure 3: T.I.R.C.’s ‘responsiveness’ post-July 1956: histogram of the delay (in months) between publication month of an article and the month in which it was summarised in the Current Digest.

to suggest that the T.I.R.C. summarised the papers in a biased manner, although isolated cases which appear to misinterpret the original article were found. For example, the Current Digest’s summary of Kreyberg (1956) states that ‘one out of five appear to have acquired cancer as a reaction to smoking’, whereas Kreyberg wrote that ‘one out of five cases arises from causes unrelated to tobacco smoking.’

4.2 The Surgeon General’s Advisory Committee’s assessment of the evidence

We have seen on page 4 how the statements of the Study Group on Smoking and Health and the Surgeon General during the 1950s alluded to the growing weight of evidence implicating cigarette smoking as a causative factor in lung cancer. In this section we review the Surgeon General’s Advisory Committee’s assessments of the evidence regarding the disease categories which form the focus of this paper.

Chapter 3 of the report explains, in general terms, the methodology used by the Advisory Committee to make assessments of causal relationships. The Committee judged the validity of all reports and publications it reviewed (not solely epidemiological ones) individually, taking into account such factors as
the competence of the investigators, the quality of study design and the conclusions of the study. Epidemiological evidence was used to establish whether or not an association existed between tobacco use and a disease and, if an association was established, that evidence was then combined with evidence from other sources to make judgments about causality. The criteria used to judge causality included the consistency, strength, specificity, temporal relationship and coherence of the association (we discuss these in more detail below).

Chapter 8 of ‘Smoking and Health’ focuses on the seven major prospective studies of tobacco use and disease in men which are listed in table 2 of this paper. The chapter notes that results of these studies show the all-cause mortality rate to be higher for smokers of cigarettes than non-smokers, ranging from 44% higher in the ‘British doctors’ study, to 83% higher in the ‘men from the 25 states’ study. Further, the mortality ratio increases with the quantity of cigarettes smoked in all studies but one (California occupational groups).

The report’s analysis of mortality ratios by cause combines the results of the seven studies by summing the expected and observed deaths across them. Median mortality ratios for the seven studies are also reported. Ordering causes of death according to the size of the resulting mortality ratios, the report notes that, in every one of the prospective studies considered, lung cancer occupies first place (combined ratio of 10.8). Although coronary artery disease appears lower down the table, with a mortality ratio of 1.7, the report notes that, when analysed according to the percentage contribution to the total number of excess deaths of cigarette smokers due to different causes, coronary artery disease is ‘the prime contributor to excess mortality, with lung cancer in second place.’

Chapter 9 of the report presents detailed analyses for cancer at the six sites considered in this paper. Cancer of the lung, larynx, oral cavity, oesophagus and urinary bladder were chosen by the Committee because the combined results of the seven prospective studies showed that cigarette smokers had a ‘substantially higher’ cancer risk than non-smokers. Stomach cancer was added because the Committee believed that the results showed some consistency across the prospective studies and some additional evidence was available from retrospective studies. For each of these six sites, to the results of the seven prospective studies is added evidence from the studies reviewed by the Advisory Committee that are listed in tables 3 to 9 of this paper.

The report reserves the most space for lung cancer. Noting that the retrospective studies vary widely in terms of design, it comments: ‘[i]t is indeed striking that every one of the retrospective studies of male lung cancer

\[28\] The report cites differences in approach with respect to subject selection (men only, men and women etc.), choice of control group, method of interviewing, history of tobacco use and sub-group analyses (such as urban versus rural effects, occupational effects and so on).
cases showed an association between smoking and lung cancer. All have shown that proportionately more heavy smokers are found among the lung cancer patients than in the control populations and proportionately fewer non-smokers among the cases than among the controls. Sections reporting the results of animal and pathological studies are then presented.

Having referred to both indirect and direct measures of association (aggregate-level and epidemiological data on smoking and lung cancer respectively), the report states that ‘it would appear that an association between cigarette smoking and lung cancer does indeed exist.’ It then considers whether or not the association has causal significance by evaluating:

1. the consistency of the association, that is, whether or not the diverse methods adopted by the epidemiological studies reach similar conclusions in terms of association. It comments that the consistent association observed between smoking and lung cancer would exist if the relationship were causal or if some unmeasured factor - such as a genetic factor - were instead responsible;

2. the strength of the association. Here the report notes that the results of the retrospective and prospective studies show similar-sized effects. It concludes that ‘it would appear that the strength of the association between cigarette smoking and lung cancer must be judged to be high’;

3. the specificity of the association, defined as the degree to which the presence of lung cancer can predict the presence of smoking. Noting that the relative risk ratios for lung cancer are around the 9 to 10 mark, the report states that ‘it is reasonable to conclude that the association between cigarette smoking and lung cancer has a high degree of specificity’;

4. the temporal relationship of the association, which simply concerns which came first - the smoking or the lung cancer. The report comments that no evidence was available to suggest that lung cancer pre-dates smoking;

5. the coherence of the association, which concerns whether the results agree with the natural history and biology of the disease. None of the considerations discussed in this section - they range from the rise in lung cancer mortality through to the dose-response relationship - are thought by the report to ‘detract from’ the coherence of the association between cigarette smoking and lung cancer.

Finally, the report assesses the histopathological evidence, the constitutional hypothesis, which suggests that some common factor is responsible both for making a person a smoker and prone to lung cancer, other etiological factors and confounding variables. It concludes by evaluating the evidence available to it as follows:
Disease Surgeon General’s Advisory Committee’s assessment of the evidence

**Oral cancer**
‘The causal relationship of the smoking of pipes to the development of cancer of the lip appears to be established. Although there are suggestions of relationships between cancer of other specific sites of the oral cavity and the several forms of tobacco use, their causal implications cannot at present be stated.’

**Laryngeal cancer**
‘Evaluation of the evidence leads to the judgment that cigarette smoking is a significant factor in the causation of laryngeal cancer in the male.’

**Oesophageal cancer**
‘The evidence on the tobacco-esophageal relationship supports the belief that an association exists. However, the data are not adequate to decide whether the relationship is causal.’

**Urinary bladder cancer**
‘Available data suggest an association between cigarette smoking and urinary bladder cancer in the male but are not sufficient to support a judgment on the causal significance of this association.’

**Stomach cancer**
‘No relationship has been established between tobacco use and stomach cancer.’

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<th>Disease</th>
<th>Surgeon General’s Advisory Committee’s assessment of the evidence</th>
</tr>
</thead>
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<td>Oral cancer</td>
<td>‘The causal relationship of the smoking of pipes to the development of cancer of the lip appears to be established. Although there are suggestions of relationships between cancer of other specific sites of the oral cavity and the several forms of tobacco use, their causal implications cannot at present be stated.’</td>
</tr>
<tr>
<td>Laryngeal cancer</td>
<td>‘Evaluation of the evidence leads to the judgment that cigarette smoking is a significant factor in the causation of laryngeal cancer in the male.’</td>
</tr>
<tr>
<td>Oesophageal cancer</td>
<td>‘The evidence on the tobacco-esophageal relationship supports the belief that an association exists. However, the data are not adequate to decide whether the relationship is causal.’</td>
</tr>
<tr>
<td>Urinary bladder cancer</td>
<td>‘Available data suggest an association between cigarette smoking and urinary bladder cancer in the male but are not sufficient to support a judgment on the causal significance of this association.’</td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>‘No relationship has been established between tobacco use and stomach cancer.’</td>
</tr>
</tbody>
</table>

Table 14: Assessment of the evidence concerning tobacco use and cancer at five sites made by the U.S. Surgeon General’s Advisory Committee.

1. Cigarette smoking is causally related to lung cancer in men; the magnitude of the effect of cigarette smoking far outweighs all other factors. The data for women, though less extensive, point in the same direction. 2. The risk of developing lung cancer increases with duration of smoking and the number of cigarettes smoked per day, and is diminished by discontinuing smoking. 3. The risk of developing cancer of the lung for the combined group of pipe smokers, cigar smokers and pipe and cigar smokers is greater than for non-smokers, but much less than for cigarette smokers. The data are insufficient to warrant a conclusion for each group individually.’

The conclusions reached by the Advisory Committee for cancer at each of the other five sites are summarised in table 14. They show that the Committee felt that the evidence available to it was strong enough to declare relationships causal for cancer of the lip and larynx. For cancer of the oesophagus and urinary bladder, the Committee judged that an association existed, but it did not declare the relationship causal. For stomach cancer, it judged that no evidence of a relationship had been established.

Chapter 11 of the Advisory Committee’s report reviews the evidence on
cardiovascular diseases. The report devotes only eleven pages to this subject, in contrast to the 109 pages spent discussing cancer in Chapter 9. The chapter deals principally with coronary artery disease and the results of studies of ‘large population groups’. It observes that a ‘considerable number’ of epidemiological studies on different populations had been published in the two decades prior to 1964 and these had reported, with ‘remarkable consistency’, significant relationships between cigarette smoking and increased death rates from coronary heart disease in males, particularly during middle life. It is of note that the Committee’s report does not deal with retrospective studies of cardiovascular disease in detail and no table reporting such studies is presented in its report (in contrast to the report’s coverage of the six cancer sites). It is possible that this is due to the wide variation in findings of such studies (see table 11 of this paper, which lists the ones we identified in the Current Digest, together with the T.I.R.C.’s classifications), a consequence perhaps of the fact that many of them were carried out on small samples, meaning that the studies lacked the power to detect a true effect for a disease which was multicausal in nature.

In citing the epidemiological evidence, the report notes that the prospective studies of Doll and Hill (1956), Hammond and Horn (1958) and Dorn (1959), all show an association between cigarette smoking and coronary disease. Confirmation of this relationship is obtained by reference to the median mortality ratio of 1.7 in the seven large prospective studies and studies carried out on special groups of men, including Buechley et al. (1958), Spain and Nathan (1961) and Paul et al. (1963). The Framingham (Dawber et al., 1959) and Albany (Doyle et al., 1959) studies are also mentioned, but their results are only discussed in terms of a paper which pooled the results of the two studies (Doyle et al., 1962) and which showed a strong association between heavy cigarette smoking, mortality from coronary disease and the incidence of myocardial infarction.29

In its assessment of the evidence, the report concludes that ‘male cigarette smokers have a higher death rate from coronary artery disease than non-smoking males, but it is not clear that the association has causal significance.’

4.3 The T.I.R.C.’s annual reports of the Scientific Director

The annual reports of the Scientific Director were written by C. C. Little. Each report contains a general assessment of the evidence concerning tobacco harm and then presents detailed information on the research program and projects funded by the T.I.R.C.. The reports run from around 25 to 70

29 Updated results for the Framingham study are referred to in a special report to the Surgeon General’s Advisory Committee (Kannel, 1963). It is of note that both Dawber et al.’s (1959) and Doyle et al.’s (1959) individual studies did not find significant associations between tobacco use and heart disease.
pages, so we have had to be selective about what we cover in this section of the paper; we try to focus on Little’s comments regarding the overall state of knowledge regarding tobacco harm and the role played by epidemiological and statistical evidence in informing assessments about causal relationships. Unlike the Surgeon General’s Advisory Committee’s report, we were unable to find a statement about how Little went about assessing the evidence that was in the possession of the T.I.R.C..

In the 1956 report, Little comments that the Scientific Advisory Board of the T.I.R.C. realised ‘[a]t the outset’ that the scientific knowledge concerning tobacco smoking and health was ‘uncertain and spotty.’ The report comments that ‘[t]he need for further study is, if anything, more compelling than it was two years ago … perhaps the most important thing we have learned is how much more must be done before definitive answers can be given’ (Little, 1956).

In the 1957 report, Little writes that progress in medical research is ‘slow and painstaking . . . Advances are made by difficult stages, somewhat as one would cut his way through jungle undergrowth.’ In a section listing statistical relationships between heavy cigarette smoking and twenty three causes of death (including all of the ones considered in this paper), Little comments that ‘such data would provide clear evidence of the fact that the outward and visible habit of heavy smoking is a reflection of such a wide and varied gamut of internal disturbances and unbalances that its possible specific, causative value becomes reduced almost to an absurdity’ (Little, 1957).

In the 1958 report, Little expresses his concern about the ‘proponents of the tobacco theory’, who have ‘generated increasingly intensive and extensive propaganda by selecting evidence for and asserting an acceptance of this theory. As a result, a non-scientific atmosphere, conducive to prematurity, unbalance, and inadequacy of public judgment has pervaded the whole field.’ He highlights a number of areas of controversy in statistical work, including whether or not inhalation of tobacco smoke is an important factor, whether a ‘threshold effect’ exists for tobacco use, and the variations in the estimates of a ‘latency period’ associated with tobacco consumption and disease. Commenting on the smoking-lung cancer question, Little highlights the fact that non-smokers develop lung cancer and the overwhelming majority of smokers do not and suggests that genetic characteristics may play a role. He concludes by stating ‘[w]e thus find ourselves in 1958 with differences, doubts and conflicting claims of statistical evidence still unreconciled . . . the exponents of the tobacco theory have failed since the first public propaganda for that theory in 1953 to produce any new evidence that provides any quantitatively different support beyond the original type of statistical association’ (Little, 1958).

In the 1959 report, Little comments that the divergence of opinion among doctors and scientists in regard to tobacco and health has become ‘more
marked’ since 1954. The situation indicates ‘unequivocally’ the need for further research, proving ‘the wisdom of the attitude of scientific conservatism.’ Commenting on the statistical studies linking tobacco use to lung cancer, Little states that there is ‘growing support for the point of view that the statistical association claimed by various studies has an explanation or explanations that may still not be apparent from our present knowledge.’ The accumulation of circumstantial or inferential data, he argues, ‘is not a substitute for experimental and clinical evidence based on direct observation.’ To support his views, he quotes a JAMA editorial in December of that year, which stated that neither side has enough evidence to assume an ‘all or none’ authoritative position on the matter (Little, 1959).

In the 1960 report, Little writes that ‘the tobacco theory is rapidly losing much of the unique importance claimed by its adherents at its original announcement. It has not received definitive support in the clinic and laboratory.’ A subsequent section is entitled: ‘One Hard Fact: Much More Must be Found Out.’ Little argues that epidemiological data should be obtained by ‘direct clinical observation rather than by questionnaires and hearsay opinion’ and in longitudinal studies ‘factors and habits other than smoking should also be included.’

The preface to the 1961 report quotes a monograph on cancer morbidity published by the U.S. Public Health Service: ‘[i]n the study of cancer . . . one cannot realistically expect to do more than identify factors that appear to be frequently associated with cancer. The proof of an etiological relationship must then be sought through more intensive clinical or experimental studies.’ Little states that this was the position adopted by the S.A.B. in 1954 and it remains unchanged in 1961. On epidemiological studies, he comments: ‘data derived solely from epidemiological studies leave much to be desired as a foundation on which to pose sweeping and dogmatic hypotheses of cancer causation. Scientists, physicians, and the public are recognising that fact in ever increasing numbers, and are admitting the need for far more understanding than we now possess before this complex problem is fully understood and the answers to its many challenges can be expected.’ The need for further research is again stressed: ‘[w]hile the answers we seek are still not within our grasp, we now have a far better understanding of the questions’ (Little, 1961).

In the 1962 report, Little comments that ‘it is a matter of scientific fact that, in our present state of knowledge, no one knows the answers.’ He concludes by writing ‘[a]s the tobacco industry continues its support of the search for truth and knowledge, it must recognise, as is always the case in true scientific research, there can be no promise of a quick answer. The important thing is to keep on adding to knowledge until the accumulative facts provide the basis for a sound conclusion’ (Little, 1962).

By the 1963-4 report, the T.I.R.C. had been renamed the Council for Tobacco Research - U.S.A., Inc.. Little reviews the results of the first decade
of research conducted by the organisation:

‘[a]s is often the case in basic scientific exploration, intensive research has raised more new questions than it has answered; the task before us is, if anything, larger and more complex than it appeared a decade ago, and the major research problems underlying the relationships of smoking to health, though somewhat better defined, remain formidable . . . After ten years, the fact remains that knowledge is insufficient either to provide adequate proof of any hypothesis or to define the basic mechanisms of health and disease with which we are concerned. It is true now as it was in 1954 that continued research in all areas where knowledge is deficient offers the best hope for the future.’

Little explains that the C.T.R. is ‘especially concerned’ to support research under four broad categories, including ‘epidemiological and statistical analysis of morbidity and mortality data.’ We note, for the first time, some praise for epidemiological evidence: ‘[i]f the limitations of epidemiological research as well as its suggestive and stimulating value are kept in mind, increased activity in such studies will be an important contributor to increase in knowledge’ (Little, 1963).

Finally, we consider the report for 1964-5 (which refers to 1964, the year of the Surgeon General’s Advisory Committee’s report). On page six Little comments:

‘[t]he research program of The Council received impetus from the publication of several epidemiological studies that reported mortality from a score of diverse diseases to be higher among cigarette smokers than among non-smokers; reports which have been and still are the subject of much debate among statisticians on technical grounds.’

Epidemiological studies are described as being ‘helpful’, contributing ‘hints and leads’ for clinical and experimental researchers. In a rare citation of a published epidemiological study, Little mentions a result from the Framingham Study: ‘cigarette smokers have no greater incidence of angina pectoris than non-smokers. Since this syndrome is regarded as most often being a chronic manifestation of coronary artery sclerosis, this finding suggests that smoking does not cause or accelerate such sclerosis’. He concludes: ‘[a]t the present time therefore, the weight of evidence is against the concept that either nicotine or smoking influences the atherosclerotic process.’

In summary, Little (1964) comments:

‘[o]ver the years . . . evidence to support the thesis that cigarettes exercise a direct carcinogenic effect on man has not been forthcoming.’
What is clear from the results, we believe, is that, by the mid-1950s, the T.I.R.C. was running an unbiased and reasonably comprehensive literature retrieval and review operation. This was yielding, on a monthly basis, the majority of the epidemiological studies that were considered by the U.S. Public Health Service and related groups in their assessments of the evidence-base for lung cancer in 1957 and 1959 and for a wide range of diseases in 1964. Noteworthy is the high degree of consistency in the classifications of ‘harm’ made by these organisations: for all cancer sites except stomach cancer, the organisations classified almost every article as showing tobacco to be harmful.

In contrast, for the six cancer sites considered, the content of the annual reports of the Scientific Director of the T.I.R.C. and the statements of the Study Group on Smoking and Health (1957), the Surgeon General (1958, 1959) and the Surgeon General’s Advisory Committee (1964), could hardly be more different. The annual reports of the T.I.R.C.’s Scientific Director failed to make any significant reference to the evidence relating to five of the six cancer sites (oral cavity, larynx, oesophagus, urinary bladder and stomach), despite the fact that the T.I.R.C. had collected together evidence from epidemiological studies in the Catalog and Current Digest. The T.I.R.C.’s evaluation of the evidence for lung cancer contrasts starkly with the evaluations published by the U.S. Public Health Service and related organisations.

Clearly, our research has focused only on the epidemiological evidence-base and not the experimental, pharmacological and biochemical research which was also being carried out into the tobacco-health problem during the 1950s and 1960s (and which was also summarised by the T.I.R.C. in the Catalog and the Current Digest). Further, we do not focus on the views of the ‘experts’ of the day, whose opinions, as expressed in the pages of the medical and wider scientific press, will clearly have had an impact on the thinking of the time. This makes it difficult for the paper to contribute directly to the work by the likes of Talley et al. (2004), Stolley (1991), Kluger (1997) and Glantz et al. (1996), who have debated the legitimacy of the duration of the ‘controversy’ regarding whether or not tobacco was harmful during the mid-twentieth century. Nevertheless, what this paper does offer these debates is a detailed analysis - month-by-month from 1956 - of exactly what epidemiological knowledge was possessed by the T.I.R.C. in private and what it was saying in public.

One of the T.I.R.C.’s stated aims, described on page 6 of this paper, was ‘to make available to the public factual information on the [alleged relationship between tobacco use and lung cancer]’. In our opinion, the annual reports written by Little were not faithful - in an objective manner at least - to this aim. That this was the case could reasonably be explained by the T.I.R.C.’s ‘line’ that statistical association did not imply causation and that
the value of epidemiological evidence was therefore limited. But, as we have seen, Little did cite a limited amount of epidemiological evidence in his annual reports. His reference to the Framingham study in his 1964-5 annual report was used to argue that ‘the weight of evidence is against the concept that either nicotine or smoking influences the atherosclerotic process.’ Results of a paper combining data from the Framingham and Albany studies (Doyle et al. (1962)) were available to Little at the time he wrote this passage, having been reviewed in Current Digest VII(5), 1962. The Current Digest summary of this paper includes the following section: ‘[h]eavy cigarette smokers experience a threefold increase in the incidence of myocardial infarction and in death from all causes as compared to non-smokers, pipe and cigar smokers, and former cigarette smokers, the authors say . . . ’. This finding is not referred to by Little in any annual report that we read. Such selective use of epidemiological evidence - citing it explicitly in a rare case when results were favourable towards tobacco - reduces, in our eyes at least, the credibility of the T.I.R.C.’s ‘line’ that statistical association does not imply causation.

What is also of interest is that the Surgeon General’s Advisory Committee’s report devoted so little space to the discussion of the evidence relating to cardiovascular disease. It is possible that this is because the epidemiological and other evidence relating to cardiovascular disease was weaker in the 1950s and early 1960s, perhaps a result of the multicausal nature of the disease, meaning that studies had to be large if they were to be sufficiently powered to detect differences as being significant. This could account for the fact that the Committee failed to summarise comprehensively retrospective studies investigating this disease (we have already seen, from table 11, that the evidence from retrospective studies was far from consistent) and also that the Committee’s reference to results from the Framingham and Albany studies was restricted to Doyle et al. (1962), which combined data from the two studies. Table 10 of this paper shows that the findings of earlier reports for each study - Dawber et al. (1959) (Framingham) and Doyle et al. (1959) (Albany) - had been cited without reference to their findings by the Advisory Committee (they had been classified as ‘U’ and ‘N’ respectively in our review of the Current Digest summaries).

Before concluding, we comment on the grounds for defence submitted by tobacco companies involved in the case of Manning vs. Benson and Hedges Ltd. (2004) in the High Court of Ireland, to which we referred in section 1 of this paper. The defendants (Benson and Hedges Ltd. - one of the founding members of the T.I.R.C. - John Player and Sons Ltd. and P. J. Carroll and Company Ltd.) proposed three major grounds for dismissing the claims for negligence, one of which was that the lapse of time between the alleged wrongful acts and the trial date put a fair trial at risk. A crucial part of this argument related to the availability of evidence concerning what the tobacco companies knew regarding the harmful effects of their product
around the time that the three plaintiffs were starting to smoke (the years being 1948, 1942 (or 1945) and 1968). In dismissing the claims, Justice Geoghegan commented that attempting retrospectively to assess the state of scientific knowledge possessed by the tobacco companies during the twentieth century, together with their decisions relating to manufacturing, would put justice ‘to the hazard’. In his decision, he commented:

‘[c]ounsel for the plaintiffs sought to submit that significant issues might be determined on documentary evidence. I do not accept this, the primary factual issues in relation to what was done; the scientific information available to or which ought to have been available to the defendants and the decisions taken in light of same would have to be decided on oral evidence.’

Considering the specific point about assessing the state of the scientific evidence, we believe that the content of this paper contradicts this conclusion. We develop some of these themes further in our sister paper (Forster et al., 2006), in which we use the listings in tables 2 to 9 as inputs to a simple Bayesian model of the accumulation of the ‘weight’ of epidemiological evidence concerning tobacco harm. The elements to this model, such as the strength of prior beliefs and the weight placed on epidemiological evidence in making an assessment of the full evidence-base, are used to explore the possible reasons for Little to have written what he did in his annual reports.

6 Conclusion

The main point of this paper has been to demonstrate that it is possible to document and date, to a reasonably high degree of accuracy, what epidemiological knowledge the T.I.R.C. (and, by implication, the American tobacco companies) had within their possession from mid-1955 onwards. Further, we have shown that the T.I.R.C.’s literature retrieval and review process was, in our opinion, unbiased, reasonably comprehensive and responsive. We believe the annual reports of the Scientific Director do not fully reflect the evidence within the T.I.R.C.’s possession and that this cannot be explained entirely by the T.I.R.C.’s aversion to using epidemiological methods in making assessments about causal relationships, given that its Scientific Director did reference epidemiological evidence when results suggested that tobacco use was not harmful. We are not convinced that the annual reports of the Scientific Director were faithful - in an objective manner at least - to the T.I.R.C.’s stated aim of making factual information on the tobacco-health question available to the public.

Finally, we note that the Catalog and Current Digest also reviewed the results of experimental, biochemical, pharmacological work and so on. In fact, our research is based on approximately 60 summaries of articles out
of around 3,270 that were published by the T.I.R.C. in the Current Digest between 1956 and the end of 1963. Since the C.T.R. continued to publish the Current Digest well into the 1990s, there is much scope for extending our methods to consider: (a) the T.I.R.C.’s summaries of evidence from other scientific disciplines prior to 1964 and (b) evidence relating to all scientific disciplines after 1964. This, we believe, would yield an even richer picture of the state of scientific knowledge of the American tobacco industry during the mid- to late-twentieth century.

A Our own review of the epidemiological literature for 1950-59

The search was carried out by S.D..

Only a limited number of databases going back to the 1950s were available: ‘OLDMEDLINE’, created by the U.S. National Library of Medicine (which supplied both the Surgeon General’s Advisory Committee and the T.I.R.C. with references), ‘Science Citation Index’ (S.C.I.), ‘Social Science Citation Index’ (S.S.C.I.), ‘PsycINFO’ and the International Bibliography of the Social Sciences (I.B.S.S.). Since initial searches of OLDMEDLINE indicated that there may have been problems making the citations for 1950-51 available electronically, supplementary searches of the print copies of Index Medicus for these early years were also undertaken.

The search strategy had to be kept relatively simple to take into account the poor quality of reference citations available for 1950-59. No abstracts are available in OLDMEDLINE and subject heading indexing is very limited. Consequently, the search strategies were reliant primarily on the title field, using the terms ‘smoking’, ‘tobacco’, ‘cigarettes’, and ‘nicotine’. This meant that potentially useful articles about cancer or cardiovascular disease and smoking, but with no mention of the search terms (tobacco, smoking, etc.) in the title or indexing, were not identified. Due to the simplicity of the search strategy, a large proportion of the articles identified were irrelevant and were removed from the final set of results.

Since the electronic sources searched consisted almost entirely of journal articles, supplementary searches were undertaken using the British Library, U.S. Library of Congress and U.S. National Library of Medicine catalogues to try to identify book/report publications for the same time period.

As a number of databases were searched, some degree of duplication resulted. In order to manage this issue, the results were imported into the Endnote bibliographic software and duplicate records removed. Those references deemed obviously irrelevant were also removed.

30 These included tobacco leaf diseases, agricultural methods of production, chemical experiments with nicotine, air pollution, and so on.
Once the list of studies from the search was available, two reviewers (M.W. and M.F.) independently read through the list of titles and eliminated ones which did not appear to meet the inclusion criteria. 675 studies remained after this stage and we tried, as far as possible, to consult all of them. Translations of foreign articles were obtained where possible. It was not possible to obtain 34 of these articles.

One reviewer (M.F.) then selected those articles which appeared to meet our inclusion criteria and which had not already been identified in stages 1 and 2 of our review process. M.W. received these articles to double-check the classifications.

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