

[SIGN UP]

Home

Collections

Profiles

Email

Password

(Forgot Password?)

More

Recent Searches

Philip Morris

the Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today

<http://tobaccodocuments.org/pm/2025030544-0660.html>

snapshot_pm 2025030544-2025030660

Date:

19810600/P

Length:

117 pages

2025030544-

2025030660

[Jump To](#)

[Images](#)

Fields

Author

Doll, R.
Peto, R.

Area

LEGAL DEPT/CARLSTADT

Type

PSCI, PUBLICATION SCIENTIFIC
ABST, ABSTRACT
BIBL, BIBLIOGRAPHY
CHAR, CHART, GRAPH, TABLE, MAPS

Site

N28

Request

Stmn/R1-004

Named Organization

Ny Tumor Registry
Office of Technology Assessment
Oxford Univ Press
Populations Division
Surveillance Epidemiology End Results Se
US Congress
Biometry Branch
Bureau of the Census
Ct Tumor Registry
Natl Heart Lung + Blood Inst
NCI, Natl Cancer Inst

Named Person

Fensterheim, R.
Godwin, V.
Gray, R.
Harwood, C.
Peto, R.
Rogot, E.
Stratton, I.

Document File

2025030516/2025030772/Doll & Hill

Litigation

Stmn/Produced

Author (Organization)

Green College Oxford

Imperial Cancer Research Fund
Jnci
Radcliffe Infirmary
Univ of Oxford

Master ID

2025030542/0660

Related Documents:

- o [2025030542 Doll and Peto Study](#)
- o [2025030543](#)

Characteristic

MARG, MARGINALIA

Date Loaded

05 Jun 1998

UCSF Legacy ID

[dbe35e00](#)

Document Images

Text Control

Hide Citation

(above)

Highlight Text:

OCR Text Alignment:

Image Control

Image Rotation:

Image Size:

Document Navigation

View of

Range: **117**

[NEXT »](#)

Page 1: [dbe35e00](#) [Log in](#) for more options!

'jNC1 t' : 11qz- i3op j!.A-,,, e- c9b'I The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today icine, Uni erial Cancer Research Fund Reader in Cancer Studies, Nuffield rsity of Oxford, Radcliffe Infirmary, Oxford OX2 6HE, United Kingdom~ Received~ November 6, 1980; accepted January 21, 1981.. Reprints are not available, as the article will be republished: by permission of the Editor in Chief of the JNCI, as an Oxford University Press paperback. Doll, onorary Director, Imperial Cancer Research Fund Cancer Epidemiology and M oe n of Green College, Oxford, United Kingdom Peto, In;

JNCI 66/6 : 1192-1308
June 1981



The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today

Richard Doll, Honorary Director, Imperial Cancer Research Fund Cancer Epidemiology and Clinical Trials Unit, and Warden of Green College, Oxford, United Kingdom

and **Richard Peto**, Imperial Cancer Research Fund Reader in Cancer Studies, Nuffield Department of Clinical Medicine, University of Oxford, Radcliffe Infirmary, Oxford OX2 6HE, United Kingdom

Received November 6, 1980; accepted January 21, 1981.
Reprints are not available, as the article will be republished, by permission of the Editor in Chief of the JNCI, as an Oxford University Press paperback.

2025030544

't Avoidable Risks of Cancer In the U.S. 1193 This article was commissioned as a report to the Office of Technology Assessment, U.S. Congress, to provide background material for their assessment of "Technologies for Determining Cancer Risks From the Environment " (OTA, 1981). It will be republished, by permission of the Editor in Chief of the JNCI, as an Oxford University Press paperback. Acknowledgments First and foremost, we wish to thank Mrs. Virginia Godwin for her assistance in preparing this report, and we are particularly indebted to Eugene Rogot, of the National Heart, Lung, and Blood Institute, for making available to us the data from the study of a quarter of a million U.S. veterans. Robert Fensterheim abstracted the cancer mortality data from 1933-78 from Government publications, and a tape of these data is available from R. Peto. The staff of the Populations Division of the Bureau of the Census provided corrected U.S. population estimates from 1950; Irene Stratton and Richard Gray analyzed the mortality data, and Cathy Harwood drew the figures. The Surveillance, Epidemiology, and End Results section of the Biometry Branch of the National Cancer Institute and the New York and Connecticut tumor registries kindly provided us with access to cancer incidence data. Finally, we wish to thank the dozens of known or anonymous scientists who, through us or through the Office of Technology Assessment, scrutinized and offered helpful criticism of previous versions of this report. ABBREVIATIONS used: ACS=American Cancer Society; AF2=2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide; CPEAP=Committee on Prototype Explicit Analyses for Pesticides; DAB=p-dimethylaminoazobenzene; DES=diethylstilbestrol; DMBA=7,12-dimethylbenz[a]anthracene; EPA=Environmental Protection Agency; GESAMP=Group of Experts on the Scientific Aspects of Marine Pollution; IARC=International Agency for Research on Cancer; ICD=International Classification of Diseases; NAS=National Academy of Sciences; NCI=National Cancer Institute; NIOSH=National Institute of Occupational Safety and Health; NIEHS=National Institute of Environmental Health Sciences; OSHA=Occupational Safety, and Health Administration; PVC=polyvinyl chloride; SEER=Surveillance, Epidemiology, and End Results program of NCI; SNCS=Second National Cancer Survey; TNCS=Third National Cancer Survey; TSSC=Toxic Substances Strategy Committee; WHO=World Health Organization. JNCI, vol. 71, no. 11, 1981

Avoidable Risks of Cancer in the U.S. 1193

This article was commissioned as a report to the Office of Technology Assessment, U.S. Congress, to provide background material for their assessment of "Technologies for Determining Cancer Risks From the Environment" (OTA, 1981). It will be republished, by permission of the Editor in Chief of the JNCI, as an Oxford University Press paperback.

Acknowledgments

First and foremost, we wish to thank Mrs. Virginia Godwin for her assistance in preparing this report, and we are particularly indebted to Eugene Rogot, of the National Heart, Lung, and Blood Institute, for making available to us the data from the study of a quarter of a million U.S. veterans. Robert Fensterheim abstracted the cancer mortality data from 1933-78 from Government publications, and a tape of these data is available from R. Peto. The staff of the Populations Division of the Bureau of the Census provided corrected U.S. population estimates from 1950, Irene Stratton and Richard Gray analyzed the mortality data, and Cathy Harwood drew the figures. The Surveillance, Epidemiology, and End Results section of the Biometry Branch of the National Cancer Institute and the New York and Connecticut tumor registries kindly provided us with access to cancer incidence data. Finally, we wish to thank the dozens of known or anonymous scientists who, through us or through the Office of Technology Assessment, scrutinized and offered helpful criticism of previous versions of this report.

ABBREVIATIONS USED: ACS = American Cancer Society; AF2 = 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide; CPEAP = Committee on Prototype Explicit Analyses for Pesticides; DAB = p-dimethylaminoazobenzene; DES = diethylstilbestrol; DMBA = 7,12-dimethylbenz[a]anthracene; EPA = Environmental Protection Agency; GESAMP = Group of Experts on the Scientific Aspects of Marine Pollution; IARC = International Agency for Research on Cancer; ICD = International Classification of Diseases; NAS = National Academy of Sciences; NCI = National Cancer Institute; NIOSH = National Institute of Occupational Safety and Health; NIEHS = National Institute of Environmental Health Sciences; OSHA = Occupational Safety and Health Administration; PVC = polyvinyl chloride; SEER = Surveillance, Epidemiology, and End Results program of NCI; SNCS = Second National Cancer Survey; TNCS = Third National Cancer Survey; TSSC = Toxic Substances Strategy Committee; WHO = World Health Organization.

Health Sciences; OSHA=Occupational Safety and Health Administration; PVC=polyvinyl chloride; SEER=Surveillance, Epidemiology, and End Results program of NCI; SNCS=Second National Cancer Survey; TNCS=Third National Cancer Survey; TSSC=Toxic Substances Strategy Committee; WHO=World Health Organization.

2025030545

JNCI, VOL. 66, NO. 6, JUNE 1981

Page 3: dbe35e00 [Log in](#) for more options!

1194 Doll and Peto ABSTRACT-Evidence that the various common types of cancer are largely avoidable diseases is reviewed: Life-style and other environmental factors are divided into a dozen categories, and for each category the evidence relating those particular factors to cancer onset rates is summarized. Where possible, an estimate is made of the percentage of current U.S. cancer mortality that might have been caused or avoided by that category of factors. These estimates are based chiefly on evidence from epidemiology, as the available evidence from animal and other laboratory studies cannot provide reliable human risk assessments. By far the largest reliably known percentage is the 30% of current U.S. cancer deaths that are due to tobacco, although it is possible that some nutritional factor(s) may eventually be found to be of comparable importance. The percentage of U.S. cancer deaths that are due to tobacco is still increasing, and must be expected to continue to increase for some years yet due to the delayed effects of the adoption of cigarettes in earlier decades. Trends in mortality and in onset rates for many separate types of cancer are studied in detail in appendixes to this paper. Biases in the available data on registration of new cases produce apparent trends in cancer incidence which are spurious. Biases also produce spurious trends in cancer death certification rates, especially among old people. In (and before) middle age, where the biases are smaller, there appear to be a few real increases and a few real decreases in mortality from some particular types of cancer, but there is no evidence of any generalized increase other than that due to tobacco. Moderate increases or decreases due to some new agent or habit(s) might of course be overlooked in such large-scale analyses. But such analyses do suggest that, apart from cancer of the respiratory tract the types of cancer that are currently common are not diseases and are likely to depend chiefly on some long-established factors. (A prospective study utilizing both questionnaires and stored blood and other biological materials might help elucidate these factors.) The proportion of current U.S. cancer deaths attributed to occupational factors is provisionally estimated as 4.9% (lung cancer the major contributor to this). This is far smaller than has recently been suggested by various U.S. Government agencies. The matter could be resolved directly by a "case-control" study of lung cancer two or three times larger than the recently completed U.S. National Bladder Cancer Study but similar to it in methodology and unit costs; there are also other reasons for such a study. A fuller summary of conclusions and recommendations comprises the final section of this report. -JNCI 1981; 66:1191-1308. J1c:1, tY)l.. tdi. Ntl. 1,, J1:1t.. 19M1

ABSTRACT—Evidence that the various common types of cancer are largely avoidable diseases is reviewed. Life-style and other environmental factors are divided into a dozen categories, and for each category the evidence relating those particular factors to cancer onset rates is summarized. Where possible, an estimate is made of the percentage of current U.S. cancer mortality that might have been caused or avoided by that category of factors. These estimates are based chiefly on evidence from epidemiology, as the available evidence from animal and other laboratory studies cannot provide reliable human risk assessments. By far the largest reliably known percentage is the 30% of current U.S. cancer deaths that are due to tobacco, although it is possible that some nutritional factor(s) may eventually be found to be of comparable importance. The percentage of U.S. cancer deaths that are due to tobacco is still increasing, and must be expected to continue to increase for some years yet due to the delayed effects of the adoption of cigarettes in earlier decades.

Trends in mortality and in onset rates for many separate types of cancer are studied in detail in appendixes to this paper. Biases in the available data on registration of new cases produce apparent trends in cancer incidence which are spurious. Biases also produce spurious trends in cancer death certification rates, especially among old people. In (and before) middle age, where the biases are smaller, there appear to be a few real increases and a few real decreases in mortality from some particular types of cancer, but there is no evidence of any generalized increase other than that due to tobacco. Moderate increases or decreases due to some new agent(s) or habit(s) might of course be overlooked in such large-scale analyses. But, such analyses do suggest that, apart from cancer of the respiratory tract, the types of cancer that are currently common are not peculiarly modern diseases and are likely to depend chiefly on some long-established factor(s). (A prospective study utilizing both questionnaires and stored blood and other biological materials might help elucidate these factors.)

The proportion of current U.S. cancer deaths attributed to occupational factors is provisionally estimated as 4% (lung cancer being the major contributor to this). This is far smaller than has recently been suggested by various U.S. Government agencies. The matter could be resolved directly by a "case-control" study of lung cancer two or three times larger than the recently completed U.S. National Bladder Cancer Study but similar to it in methodology and unit costs; there are also other reasons for such a study.

A fuller summary of conclusions and recommendations comprises the final section of this report.—JNCI 1981; 66:1191-1308.

Avoidable Risks of Cancer in the U.S. 1195 TABLE OF CONTENTS

PREFACE 1196
 1. DEFINITION OF AVOIDABILITY OF CANCER 1197
 2. EVIDENCE FOR THE AVOIDABILITY OF CANCER 1198
 2.1 Differences in Incidence Between Communities 1198
 2.2 Changes in Incidence on Migration 1200
 2.3 Changes in Incidence Over Time 1201
 2.4 Identification of Causes 1202
 2.5 Role of Genetic Factors, Luck, and Age 1202
 3. PROPORTION OF U.S. CANCERS THAT ARE KNOWN TO BE AVOIDABLE 1205
 4. ATTRIBUTION OF RISK 1207
 4.1 Increases and Decreases in U.S. Cancer Rates 1207
 4.2 Prediction From Laboratory Experiments 1212
 4.3 Use of Epidemiological Observations 1217
 4.4 Shared Responsibility: Two Avoidable Causes of One Case of Cancer 1219
 5. AVOIDABLE CAUSES 1220
 5.1 Tobacco 1220
 5.2 Alcohol 1224
 5.3 Diet 1226
 5.4 Food Additives 1235
 5.5 Reproductive and Sexual Behavior 1237
 5.6 Occupation 1238
 5.7 Industrial Products 1245
 5.8 Medicines and Medical Procedures 1251
 5.9 Geophysical Factors 1252
 5.10 Infection 1253
 5.11 Unknown Causes 1254
 6. SUMMARY AND CONCLUSIONS 1255
 REFERENCES 1260
 APPENDIX A: Age-Standardization Procedures 1266
 APPENDIX B: Population Estimation for Calculation of Age-Specific Rates 1268
 APPENDIX C: Sources of Bias in Estimating Trends in Cancer Mortality, Incidence, and Curability 1270
 APPENDIX D: U.S. Age-Standardized Cancer Death Rates During the Past Few Decades 1128
 APPENDIX E: Trends in Lung Cancer Death Rates in Relation to Cigarette Usage and Tar Yields 1-292
 APPENDIX F: Examination of the Arguments and Conclusions in "Estimates of the Fraction of Cancer in the United States Related to Occupational Factors" (OSHA, Sept. 15, 1978) 1305
 JN(1:101; tipi, \U, ti, JV1F., 1981

Avoidable Risks of Cancer in the U.S. 1195

TABLE OF CONTENTS

PREFACE 1196
 1. DEFINITION OF AVOIDABILITY OF CANCER 1197
 2. EVIDENCE FOR THE AVOIDABILITY OF CANCER 1198
 2.1 Differences in Incidence Between Communities 1198
 2.2 Changes in Incidence on Migration 1200
 2.3 Changes in Incidence Over Time 1201
 2.4 Identification of Causes 1202
 2.5 Role of Genetic Factors, Luck, and Age 1202
 3. PROPORTION OF U.S. CANCERS THAT ARE KNOWN TO BE AVOIDABLE 1205
 4. ATTRIBUTION OF RISK 1207
 4.1 Increases and Decreases in U.S. Cancer Rates 1207
 4.2 Prediction From Laboratory Experiments 1212
 4.3 Use of Epidemiological Observations 1217
 4.4 Shared Responsibility: Two Avoidable Causes of One Case of Cancer 1219
 5. AVOIDABLE CAUSES 1220
 5.1 Tobacco 1220
 5.2 Alcohol 1224
 5.3 Diet 1226
 5.4 Food Additives 1235
 5.5 Reproductive and Sexual Behavior 1237
 5.6 Occupation 1238

5.5 Reproductive and Sexual Behavior	1237
5.6 Occupation	1238
5.7 Pollution	1245
5.8 Industrial Products	1251
5.9 Medicines and Medical Procedures	1252
5.10 Geophysical Factors	1253
5.11 Infection	1254
5.12 Unknown Causes	1255
6. SUMMARY AND CONCLUSIONS	1256
REFERENCES	1260
APPENDIX A: Age-Standardization Procedures	1266
APPENDIX B: Population Estimation for Calculation of Age-Specific Rates	1268
APPENDIX C: Sources of Bias in Estimating Trends in Cancer Mortality, Incidence, and Curability	1270
APPENDIX D: U.S. Age-Standardized Cancer Death Rates During the Past Few Decades	1281
APPENDIX E: Trends in Lung Cancer Death Rates in Relation to Cigarette Usage and Tar Yields	1292
APPENDIX F: Examination of the Arguments and Conclusions in "Estimates of the Fraction of Cancer in the United States Related to Occupational Factors" (OSHA, Sept. 15, 1978)	1305

2025030547

JNCL VOL. 66, NO. 6, JUNE 1981

Page 5: [dbe35e00](#) [Log in](#) for more options!

1196 Doll and Peto PREFACE The percentage of today's fatal cancers that might, by suitable preventive measures, have been avoided is subject to some dispute. Indeed, the percentage avoidable by certain particular categories of preventive measure is subject to such vigorous dispute that the non-specialist (to whom the present review is addressed) may wonder whether research has yet discovered any solid facts at all about the avoidance of human cancer. The truth seems to be that there is quite good evidence that cancer is largely an avoidable (although not necessarily a modern) disease; but, with some important exceptions, frustratingly poor evidence as to exactly what are the really important ways of avoiding a reasonable percentage of today's cancers. Perhaps because of this uncertainty, the number of different areas of current research into hypothetical ways of avoiding cancer is enormous. As a convenient framework in which to seek an overview of them all, we have divided the various hypothetical ways of increasing or decreasing cancer onset rates into a dozen groups, and for each such group we have attempted to review what is known about the percentage of current U.S. cancer deaths that might thereby be avoidable. In some groups (e.g., smoking habits) the quantitative knowledge already available is quite reliable, whereas in others (e.g., dietary habits) it is not, and we have had to fall back on reviewing various current lines of research whose eventual outcome is still unknown. The "percentages" (of current cancer mortality thus avoidable) that we eventually cite for the separate groups are therefore not really comparable with each other. Some are fairly precisely known, whereas others are much less so. More importantly, some relate to quite specific preventive measures on which action would, at least in principle, be possible on present knowledge alone, whereas others relate to preventive measures (e.g., modification of dietary factors) where the changes that would be beneficial have not yet been reliably characterized. Moreover, even if two particular agents (e.g., asbestos and sunlight) happen to account for a similar percentage of all cancer deaths, that which is the more easily controlled is obviously of greater public health significance. Despite all these drawbacks, the "percentages" that we have attributed to each way or group of ways of avoiding cancer remain for us a useful summary of certain facts, and the estimation of those "percentages" remains a convenient way of structuring our review of the quantitative information that is already available or is emerging about the determinants of human cancer. Our report consists of a review of the evidence that cancer is largely an avoidable disease, a review of recent upward or downward trends in the onset rates of various types of cancer, a review of our reasons for preferring an epidemiological rather than a laboratory-based approach to the quantitative attribution of human risk, and then a dozen separate sections, one on each: of the possible ways or groups of ways of avoiding cancer. The final section then summarizes and brings together our principal conclusions. We have relegated most of our detailed discussions of trends and certain other matters to appendixes, for although these details might be of interest to the specialist our principal aim has been to explain matters to interested non-specialists. Of course some isolated pockets of detail remain in the text, but we have used paragraph subheadings fairly liberally throughout in the hope that wherever any reader feels the amount of detail excessive a few pages can be skipped without losing the general sense of our argument. Finally, following Russell (1946), a few words of apology and explanation are called for, chiefly addressed to the specialists on the various subjects we touch on. Most of these subjects, with the possible exception of tobacco, are better known to some others than to us. If reports covering a wide field are to be written at all, it is inevitable, since we are not immortal, that those who write them should spend less time on any one part than can be spent by someone who concentrates on a single subject. Some, whose scholarly austerity is unbending,

will conclude that reports covering a wide field should not be written at all, or, if written, should consist of chapters by a multitude of authors. There is, however, something lost when many authors cooperate. If any balance is to be achieved between the findings in laboratory experiments and the distribution of disease that actually occurs in the population as a whole, and if the major and minor causes of death are to be seen in proper perspective, then the various aspects should be synthesized in a consistent way, which would have increased in difficulty exponentially with the number of authors. $N \sim N \sim C \sim O \sim \dots \sim pc.t.$
 Vc,t.,A. :vu i., 1Vvt V#Ht

1196 Doll and Peto

PREFACE

The percentage of today's fatal cancers that might, by suitable preventive measures, have been avoided is subject to some dispute. Indeed, the percentage avoidable by certain particular categories of preventive measure is subject to such vigorous dispute that the non-specialist (to whom the present review is addressed) may wonder whether research has yet discovered any solid facts at all about the avoidance of human cancer.

The truth seems to be that there is quite good evidence that cancer is largely an avoidable (although not necessarily a modern) disease; but, with some important exceptions, frustratingly poor evidence as to exactly what are the really important ways of avoiding a reasonable percentage of today's cancers. Perhaps because of this uncertainty, the number of different areas of current research into hypothetical ways of avoiding cancer is enormous. As a convenient framework in which to seek an overview of them all, we have divided the various hypothetical ways of increasing or decreasing cancer onset rates into a dozen groups, and for each such group we have attempted to review what is known about the percentage of current U.S. cancer deaths that might thereby be avoidable.

In some groups (e.g., smoking habits) the quantitative knowledge already available is quite reliable, whereas in others (e.g., dietary habits) it is not, and we have had to fall back on reviewing various current lines of research whose eventual outcome is still unknown. The "percentages" (of current cancer mortality thus avoidable) that we eventually cite for the separate groups are therefore not really comparable with each other. Some are fairly precisely known, whereas others are much less so. More importantly, some relate to quite specific preventive measures on which action would, at least in principle, be possible on present knowledge alone, whereas others relate to preventive measures (e.g., modification of dietary factors) where the changes that would be beneficial have not yet been reliably characterized. Moreover, even if two particular agents (e.g., asbestos and sunlight) happen to account for a similar percentage of all cancer deaths, that which is the more easily controlled is obviously of greater public health significance. Despite all these drawbacks, the "percentages" that we have attributed to each way or group of ways of

avoiding cancer remain for us a useful summary of certain facts, and the estimation of those "percentages" remains a convenient way of structuring our review of the quantitative information that is already available or is emerging about the determinants of human cancer.

Our report consists of a review of the evidence that cancer is largely an avoidable disease, a review of recent upward or downward trends in the onset rates of various types of cancer, a review of our reasons for preferring an epidemiological rather than a laboratory-based approach to the quantitative attribution of human risk, and then a dozen separate sections, one on each of the possible ways or groups of ways of avoiding cancer. The final section then summarizes and brings together our principal conclusions. We have relegated most of our detailed discussions of trends and certain other matters to appendixes, for although these details might be of interest to the specialist our principal aim has been to explain matters to interested non-specialists. Of course some isolated pockets of detail remain in the text, but we have used paragraph subheadings fairly liberally throughout in the hope that wherever any reader feels the amount of detail excessive a few pages can be skipped without losing the general sense of our argument.

Finally, following Russell (1946), a few words of apology and explanation are called for, chiefly addressed to the specialists on the various subjects we touch on. Most of these subjects, with the possible exception of tobacco, are better known to some others than to us. If reports covering a wide field are to be written at all it is inevitable, since we are not immortal, that those who write them should spend less time on any one part than can be spent by someone who concentrates on a single subject. Some, whose scholarly austerity is unbending, will conclude that reports covering a wide field should not be written at all, or, if written, should consist of chapters by a multitude of authors. There is, however, something lost when many authors cooperate. If any balance is to be achieved between the findings in laboratory experiments and the distribution of disease that actually occurs in the population as a whole, and if the major and minor causes of death are to be seen in proper perspective, then the various aspects should be synthesized in a consistent way, which would have increased in difficulty exponentially with the number of authors.

2025030548

Page 6: [dbe35e00](#) [Log in](#) for more options!

Avoidable Risks of Cancer In the U.S. 1197 1. DEFINITION OF AVOIDABILITY OF CANCER The various human cancers are diseases in which one of the many cells of which the human body is composed is altered in such a way that it, inappropriately replicates itself again and again, producing millions of similarly affected self-replicating descendant cells, some of which may spread to other parts of the body and eventually overwhelm it. Some cancers are easily curable, whereas others are almost always completely incurable by the time they are diagnosed, depending largely on the organ of the body (lung, larynx, large intestine, etc.) in which the first altered cell originated. The symptoms produced and the approach to treatment also vary with the site of origin, so that it has been customary for doctors to regard tumors originating from different organs as different diseases. Gradually, it has come to be realized that agents or habits which greatly increase or decrease the likelihood of one particular type of cancer arising (in humans or experimental animals) may have little effect on most other types of cancer, so that the prevention of each type also must be considered separately. This realization reinforces the need to consider cancers of different organs, as largely independent diseases, just as we have to consider separately different infectious diseases such as syphilis, smallpox, and tuberculosis. When we consider them separately, we see at once that although there are several dozen different organs from which tumors may arise, cancers of three organs (lung, breast, and large intestine) are at present of outstanding importance as they currently account for half the U.S. cancer deaths (table 1). A substantial reduction in any of these three cancers, particularly lung cancer, would materially reduce total U.S. cancer death rates, whereas such reductions in any other type of cancer would have relatively little effect. That the common fatal cancers occur in large part as a result of life-style and other environmental factors and are in principle preventable was recognized by an expert committee of the WHO in 1964. The committee, which had been appointed to consider how existing knowledge could be applied to prevent cancer, began its report (Wolman, 1964) by stating that: "The potential scope of cancer prevention is limited by the proliferation of human cancers in which extrinsic factors are responsible. These factors include all environmental causes (whether identified or not) as well as 'intrinsic factors' such as our 'inherited' or 'intrinsic' origin (e.g., hormonal imbalance; dietary deficiencies and nutritional defects): The rate of cancer that are thus influenced, directly or indirectly, by extrinsic factors include, tumors of the skin and mouth, respiratory, tumor and "healing" have similar meanings, but strictly the word "cancer" refers only to the solid tumors of certain tissues. However, most lung tumors, are "tumors" that we shall sometimes use this term to include all lung cancers of death. TABLE 1.-Numbers of deaths certified as being due to various types of tumor: United States, 1978

Type of tumor	No. of deaths	Percent of all deaths from tumors
Cancer of the Lung	95,086	24
Large bowel (colon and rectum)	53,269	13.46
Breast	34,609	9
Prostate	21,674	5
Pancreas	20,777	5
Stomach	14,452	4
29 other types or categories	128,705	32
Each contributing less than 3% of deaths		
Other or unspecified tumors	33,383	8
Total, all tumors	401,955	100

The annual number of lung cancer deaths is changing rapidly and will probably be 105,000 by 1981. If it is, cancers of the lung, breast, and large intestine will account for just over half of all deaths from tumors where the site of origin of the tumor was specified on the death certificate (see footnote c). Including all leukemias as one category. (A detailed breakdown by sex and site is available in tables 17-19, pp. 1243-1244.) Comprising 4,963 deaths, attributed to tumors of benign or unspecified histology, and 28,420 deaths attributed to cancer for which the site of origin was not specified; at least half of the latter probably originated from the six commonest sites: gastrointestinal and urinary tracts, hormone dependent organs, (such as the breast, thyroid and uterus), hematopoietic and lymphopoietic systems, which, collectively, account for more than three-quarters of human cancers. It could be seen, therefore, that the majority of human cancer is potentially preventable. Many individuals had already expressed this belief previously, and the committee's report merely served to indicate that a consensus among most cancer research workers had been achieved. In the years since that report was published, advances in knowledge have consolidated these opinions and few if any competent research workers now question its main conclusion. Individuals, indeed, have gone further and have substituted figures of 80 or even 90% as the proportion of potentially preventable cancers in place of the 1964 committee's cautious estimate of "the majority." Unfortunately, the phrase "extrinsic factors" (or the phrase "environmental factors," which is often substituted for it), has been misinterpreted by many people to mean only "man-made chemicals," which was certainly not the intent of the WHO committee. The committee included, in addition to man-made or natural carcinogens, viral infections, nutritional deficiencies or excesses, reproductive activities, and a variety of other factors determined wholly or partly by personal behavior. To avoid similar misunderstandings, we shall refer throughout this report to the percentages of cancers that "might be avoidable" in various ways, rather than to the percentages that are due to various "extrinsic" or "environmental" factors, and have used the term "avoidable" in our title. We have had in mind throughout the avoidance of cancer, by INCI. 1<ri.. twi! NU: 6, Jt\); 1981

1. DEFINITION OF AVOIDABILITY OF CANCER

The various human cancers are diseases in which one of the many cells of which the human body is composed is altered in such a way that it inappropriately replicates itself again and again, producing millions of similarly affected self-replicating descendant cells, some of which may spread to other parts of the body and eventually overwhelm it.¹ Some cancers are easily curable, whereas others are almost always completely incurable by the time they are diagnosed, depending largely on the organ of the body (lung, larynx, large intestine, etc.) in which the first altered cell originated. The symptoms produced and the approach to treatment also vary with the site of origin, so that it has been customary for doctors to regard tumors originating from different organs as different diseases. Gradually, it has come to be realized that agents or habits which greatly increase or decrease the likelihood of one particular type of cancer arising (in humans or experimental animals) may have little effect on most other types of cancer, so that the prevention of each type also must be considered separately. This realization reinforces the need to consider cancers of different organs as largely independent diseases, just as we have to consider separately different infectious diseases such as syphilis, smallpox, and tuberculosis. When we consider them separately, we see at once that although there are several dozen different organs from which tumors may arise, cancers of three organs (lung, breast, and large intestine) are at present of outstanding importance as they currently account for half the U.S. cancer deaths (table 1). A substantial reduction in any of these three cancers, particularly lung cancer, would materially reduce total U.S. cancer death rates, whereas such reductions in any other type of cancer would have relatively little effect.

That the common fatal cancers occur in large part as a result of life-style and other environmental factors and are in principle preventable was recognized by an expert committee of the WHO in 1964. The committee, which had been appointed to consider how existing knowledge could be applied to prevent cancer, began its report (WHO, 1964) by stating that:

The potential scope of cancer prevention is limited by the proportion of human cancers in which extrinsic factors are responsible. These [factors] include all environmental carcinogens (whether identified or not) as well as 'modifying factors' that favour neoplasia of apparently intrinsic origin (e.g., hormonal imbalances, dietary deficiencies and metabolic defects). The categories of cancer that are thus influenced, directly or indirectly, by extrinsic factors include many tumours of the skin and mouth, the respiratory,

¹ "Tumor" and "neoplasm" have similar meanings, but strictly the word "cancer" relates only to invasive solid tumors of certain tissues. However, most fatal tumors are "cancers" and we shall sometimes use this familiar term loosely to include both solid and diffuse malignant neoplasms plus sometimes even the fatal benign tumors, as well.

TABLE 1.—Numbers of deaths certified as being due to various types of tumor: United States, 1978

Type of tumor	No. of deaths	Percent of all deaths from tumors
Cancer of the Lung ^a	95,086	24
Large bowel (colon and rectum)	53,269	13
Breast	34,609	9
Prostate	21,674	5
Pancreas	20,777	5
Stomach	14,452	4
29 other types or categories, ^b each contributing less than 3% of deaths	128,705	32
Other or unspecified tumors ^c	33,383	8
Total, all tumors	401,955	100

^a The annual number of lung cancer deaths is changing rapidly and will probably be ≈105,000 by 1981. If it is, cancers of the lung, breast, and large intestine will account for just over half of all deaths from tumors where the site of origin of the tumor was specified on the death certificate (see footnote c).

^b Including all leukemias as one category. (A detailed breakdown by sex and site is available in tables 17-19, pp. 1243-1244.)

^c Comprising 4,963 deaths attributed to tumors of benign or unspecified histology, and 28,420 deaths attributed to cancer for which the site of origin was not specified; at least half of the latter probably originated from the six commonest sites.

gastrointestinal and urinary tracts, hormone dependent organs (such as the breast, thyroid and uterus), haematopoietic and lymphopoietic systems, which, collectively, account for more than three-quarters of human cancers. It would seem, therefore, that the majority of human cancer is potentially preventable.

Many individuals had already expressed this belief previously, and the committee's report merely served to indicate that a consensus among most cancer research workers had been achieved. In the years since that report was published, advances in knowledge have consolidated these opinions and few if any competent research workers now question its main conclusion. Individuals, indeed, have gone further and have substituted figures of 80 or even 90% as the proportion of potentially preventable cancers in place of the 1964 committee's cautious estimate of "the majority."

Unfortunately, the phrase "extrinsic factors" (or the phrase "environmental factors," which is often substituted for it) has been misinterpreted by many people to mean only "man-made chemicals," which was certainly not the intent of the WHO committee. The committee included, in addition to man-made or natural carcinogens, viral infections, nutritional deficiencies or excesses, reproductive activities, and a variety of other factors determined wholly or partly by personal behavior. To avoid similar misunderstandings, we shall refer throughout this report to the percentages of cancers that "might be avoidable" in various ways, rather than to the percentages that are due to various "extrinsic" or "environmental" factors, and have used the term "avoidable" in our title. We have had in mind throughout our report the avoidance of cancer only by

means that might conceivably be socially acceptable, either now or in some plausible social atmosphere in the reasonably near future. (Potentially acceptable measures might, for example, include a continuation of the current decrease in cigarette smoking or tar yields, which would reduce the risk of lung cancer, but would not include a first pregnancy for most females by 15 years of age, though this would reduce the risk of breast cancer.) Even with this restriction, however, two ambiguities remain in what is meant by the "avoidability" of cancer.

First, by the year 2100 advances in basic research in biology may permit prevention of cancer by means now utterly unforeseen. No useful estimate of the likelihood of such progress can be made, and we have therefore tried to restrict our attention chiefly to the avoidability of cancer by means whose effects on cancer risks are already reasonably certain or by means that might well be devised over the next decade or two rather than in the indefinite future. For this we have not assumed that the mechanisms underlying such means are known or will be known in the near future, but chiefly that it should be possible to identify those things which different groups of people already do, or have done to them, that account for the marked differences in cancer risk between or within communities and that this identification will in many instances lead to preventive strategies which are based either directly or indirectly on the ways in which some people already live and are therefore reasonably practical.

A second, more trivial, ambiguity in what we mean by the "avoidability" of cancer arises simply because everybody is bound to die sooner or later. (If there are about two million births per year in the United States, there are in the long run also bound to be about two million deaths per year.) If exactly half the cancer deaths that now occur were somehow magically prevented and nothing else changed, those people who would have died of cancer might live on for a further 5, 10, 20, or 30 more years (the average being 10 or 15 extra years), but they must eventually die of something and that something would for some of them be a second cancer. Even so, we would still describe such a change as a *halving* of the cancer rate. To take an opposite example, if every cause of death other than cancer were suddenly abolished then of course everyone would eventually die of cancer, although it might be misleading to describe such a change in terms of an increase in either the risk of cancer or the average age at death from cancer, especially if one were interested in the causes of cancer. The usual means of avoiding such absurdities is to avoid basing inferences on the percentage of people who "will eventually" die of cancer, on "crude" cancer rates, or on "the mean age at death from cancer." Instead, it is usual to restrict attention to "age-specific" or "age-standardized" cancer rates (see appendixes A and B). When we speak of the avoidance of a certain percentage of cancer, we therefore have in mind a reduction by that percentage in the age-standardized rates. (This may sound complicated,

but it is merely the arithmetic equivalent of not advising people that the most reliable way of avoiding cancer is to commit suicide.)

In summary, the aim of our report is to review the established evidence and current research relating to each of several different possible ways or groups of ways of avoiding cancer and to estimate the percentage reduction in today's age-standardized U.S. cancer death rates that they might confer, now or in the medium-term future.

2. EVIDENCE FOR THE AVOIDABILITY OF CANCER

The evidence that much human cancer is avoidable can be summarized under four heads: differences in the incidence of cancer among different settled communities, differences between migrants from a community and those who remain behind, variations with time in the incidence of cancer within particular communities, and the actual identification of many specific causes or preventive factors. Genetic factors and age also affect cancer onset rates, of course, but this does not affect the conclusion that much human cancer is avoidable.

2.1 Differences in Incidence Between Communities

Evidence of differences in the incidence² of particular types of cancer between different parts of the world has accumulated slowly over the past 50 years. At first the only quantitative data available referred to mortality² rates in particular areas or, even more crudely, to the proportion of patients admitted to hospital suffering from different diseases. Such data were grossly affected by the age distribution of the population, the efficacy of treatment, and the frequency of other diseases. But even then data were sufficient to show that the incidence of some cancers among people of a given age in different parts of the world must vary by at least ten and possibly by a hundredfold. More recently, this evidence has been reinforced by the results of special surveys or by the establishment of registries in which records are consistently sought of all cases of cancer diagnosed in a defined population over a long period. Registry data also need care in interpretation owing to trends with time, or differences between different parts of the world, in the provision of medical services and in the extent to which they are used (especially by old people, among whom a large proportion of fatal cancers may never be diagnosed at all). Reasonably reliable comparisons between different areas are obtained only if comparisons are limited to men and women in middle life (or earlier, for some specific types of cancer), when a sufficient number of cases can be anticipated for onset rates to be reliably estimated and yet efforts at diagnosis are still likely to be

² Definition: The *incidence* (rate) depends on the total number of new cases of cancer (per year), while the *mortality* (rate), also called the death rate, ignores non-fatal cases.

Avoidable Risks of Cancer In the U.S. 1199 thorough. The International Union Against Cancer (1970) and IARC (1976) have recommended that, for the cancers of adult life, attention be chiefly directed to the risks in the truncated age range of 35-64 years (and many artifacts of interpretation of trends in U.S. cancer data might be avoided if this simple precaution were generally adopted). Table 2 shows for 119 common types of cancer their range of variation, among those cancer registries that have produced data sufficiently reliable to be published for the purposes of: international comparison by the IARC (1976) and the International Union Against Cancer (1966 and 1970). Types of cancer have been included if they are common enough somewhere to affect more than 1% of men (or women) by 75 years of age in the absence of other causes of death, and ranges of variation are shown for standardized incidence rates between 35 and 64 years of age. The range of variation (table 2) is never less than sixfold and is commonly much more. Some of this variation may be artifactual, due to different standards of medical service, case registration, and population enumeration, despite the care taken to exclude unreliable data; but in many cases the true ranges will be 'The incidence of: most types of cancer increases with age so rapidly that it may be misleading to compare disease onset rates among people in one part of the world with those of people elsewhere if the proportions of people of different ages in the populations being compared are not the same; this particular difficulty may be circumvented by the use of age-standardized incidence rates (see Table 2) and the rates in Table 2 are standardized as recommended by the IARC (1976). First, large gaps remain in the cancer map of the world, and some extreme figures may have been overlooked because no accurate surveys have been practicable in the least developed areas, these being just the areas that are likely to provide the biggest contrasts (both high and low) with Western society. Second, the rates cited in table 2 refer to cancers of whole organs, and in one particular organ such as the stomach, liver, or skin there may be many different types of cells that are affected differently by different carcinogens or protective factors; for example, in the skin the few cancers arising from the cells that are responsible for the manufacture of the dark pigment melanin in blacks or in suntanned whites are called "melanomas," and differ greatly in etiology and prognosis from the many "non-melanoma skin cancers." Third, various anatomic parts of one single organ such as the colon or skin may be affected differently by different factors; for example, cancers of the skin have different principal causes in the populations where they are common depending on whether they chiefly appear on the face, abdomen, forearm, or legs. Finally, although cancers of the skin are so common in certain parts of the world that they outnumber all other cancers, most are so easily cured that they engender little medical interest and are commonly not reported to; or in some cases sought by, even some of the best cancer registries. For these reasons and because the extremes of variation in skin cancer incidence between different communities are affected by skin color as well as by the means of avoidance which chiefly interest us, skin cancers (other than melanomas) are perhaps of less interest than any other type of cancer in table 2. TABLE 2: -Range, of incidence rates for common cancers among males (and for certain cancers among females) Site of origin of cancer High incidence area ex Cumulative incidence, % in high incidence area Ratio of highest rate to lowest rate Low incidence area Skin (chiefly non-melanoma) Australia, Queensland a >20 >200 India, Bombay Esophagus Indian, northeast section a 20 300 Nigeria Lung and bronchus England a, 11 35 Nigeria Stomach Japan a 11 25 Uganda Cervix uteri Colombia 4' 100 15 Israel: Jewish Prostate United States: blacks a 9 40 Japan Liver Mozambique 8 100- En land ver Breast Canada, British Columbia 4' 7 7 g Israel: non-Jewish N Colon United States, Connecticut: & 3 10- Nigeria Corpus uteri United States, California 9 3 30 Japan Buccal cavity Bombay India a 2 25 Denmark - Rectum, Denmark & 2 20: Nigeria Bladder United States, Connecticut & 2 6 Japan Ovary Denmark Y 2 6 Japan - Nasopharynx Singapore: Chinese a 2 40 England Pancreas New Zealand: Maori a 2 8' Bombay India Liver Brazil São Paulo a 2 10 . Japan Liver Pharynx, Bombay India a 2 20 p Denmark Cervix uteri, Parls of Uganda ; a, 1 300 Israel: Jewish w ' By age 75 yr, in the absence of other causes of death, -" At ages :55-64 yr, standardized for age as in IARC (1976); At these ages, even the data from cancer registries, in -poor countries are likely to be reasonably reliable (although at older ages serious underreporting may affect the data). JN(a. Vol. . t,t; . - r,iU.E t9rst

thorough. The International Union Against Cancer (1970) and IARC (1976) have recommended that, for the cancers of adult life, attention be chiefly directed to the risks in the truncated age range of 35-64 years (and many artifacts of interpretation of trends in U.S. cancer data might be avoided if this simple precaution were generally adopted).

Table 2 shows for 19 common types of cancer their range of variation among those cancer registries that have produced data sufficiently reliable to be published for the purposes of international comparison by the IARC (1976) and the International Union Against Cancer (1966 and 1970). Types of cancer have been included if they are common enough somewhere to affect more than 1% of men (or women) by 75 years of age in the absence of other causes of death, and ranges of variation are shown for standardized incidence rates between 35 and 64 years of age.³

The range of variation (table 2) is never less than sixfold and is commonly much more. Some of this variation may be artifactual, due to different standards of medical service, case registration, and population enumeration, despite the care taken to exclude unreliable data; but in many cases the true ranges will be

greater. First, large gaps remain in the cancer map of the world, and some extreme figures may have been overlooked because no accurate surveys have been practicable in the least developed areas, these being just the areas that are likely to provide the biggest contrasts (both high and low) with Western society. Second, the rates cited in table 2 refer to cancers of whole organs, and in one particular organ such as the stomach, liver, or skin there may be many different types of cells that are affected differently by different carcinogens or protective factors; for example, in the skin the few cancers arising from the cells that are responsible for the manufacture of the dark pigment melanin in blacks or in suntanned whites are called "melanomas," and differ greatly in etiology and prognosis from the many "non-melanoma skin cancers." Third, various anatomic parts of one single organ such as the colon or skin may be affected differently by different factors; for example, cancers of the skin have different principal causes in the populations where they are common depending on whether they chiefly appear on the face, abdomen, forearm, or legs. Finally, although cancers of the skin are so common in certain parts of the world that they outnumber all other cancers, most are so easily cured that they engender little medical interest and are commonly not reported to, or in some cases sought by, even some of the best cancer registries. For these reasons and because the extremes of variation in skin cancer incidence between different communities are affected by skin color as well as by the means of avoidance which chiefly interest us, skin cancers (other than melanomas) are perhaps of less interest than any other type of cancer in table 2.

³ The incidence of most types of cancer increases with age so rapidly that it may be misleading to compare disease onset rates among people in one part of the world with those of people elsewhere if the proportions of people of different ages in the populations being compared are not the same. This particular difficulty may be circumvented by the use of age-standardized incidence rates (see appendix A), and the rates in table 2 are standardized as recommended by the IARC (1976).

TABLE 2.—Range of incidence rates for common cancers among males (and for certain cancers among females)

Site of origin of cancer	High incidence area	Sex	Cumulative incidence, ^a % in high incidence area	Ratio of highest rate to lowest rate ^b	Low incidence area
Skin (chiefly non-melanoma)	Australia, Queensland	♂	>20	>200	India, Bombay
Esophagus	Iran, northeast section	♂	20	300	Nigeria
Lung and bronchus	England	♂	11	35	Nigeria
Stomach	Japan	♂	11	25	Uganda
Cervix uteri	Colombia	♀	10	15	Israel: Jewish
Prostate	United States: blacks	♂	9	40	Japan
Liver	Mozambique	♂	8	100	England
Breast	Canada, British Columbia	♀	7	7	Israel: non-Jewish
Colon	United States, Connecticut	♂	3	10	Nigeria
Corpus uteri	United States, California	♀	3	30	Japan
Buccal cavity	India, Bombay	♂	2	25	Denmark
Rectum	Denmark	♂	2	20	Nigeria
Bladder	United States, Connecticut	♂	2	6	Japan
Ovary	Denmark	♀	2	6	Japan
Nasopharynx	Singapore: Chinese	♂	2	40	England
Pancreas	New Zealand: Maori	♂	2	8	India, Bombay
Larynx	Brazil, São Paulo	♂	2	10	Japan
Pharynx	India, Bombay	♂	2	20	Denmark
Penis	Parts of Uganda	♂	1	300	Israel: Jewish

^a By age 75 yr, in the absence of other causes of death.

^b At ages 35-64 yr, standardized for age as in IARC (1976). At these ages, even the data from cancer registries in poor countries are likely to be reasonably reliable (although at older ages serious underreporting may affect the data).

2025030551

1200 Doll and Peto Variation in incidence is not, of course, limited to the types of cancer that are common enough some- where in the world! to have been included in table 2. For example, Burkitt's lymphoma: has nowhere been found in over 0.1% of the population, but even so is 100 times less common in North America than in the West Nile district of Uganda. Also; Kaposi's sarcoma, which is extremely rare in most of the world, is so common in parts of Central Africa that it accounted for more than 10% of all tumors seen in the (mostly young): males in one hospital (Cook and Burkitt, 1971). Some few rather rare types of cancer, such as the nephroblastoma of childhood, may perhaps eventually be shown to occur with approximately the same frequency in all communities; but no common types of cancer will be found to do so. In the absence of other causes of death, cancer of: the breast would affect about 60 of U.S. women before the age of 75 years as against only 1% of non-Jewish Israeli women, and it is possible that an even lower percentage would be affected in certain other populations where reliable cancer regis- tries do not yet exist. With breast cancer as the only possible exception, for each type of cancer a popula- tion exists where the cumulative incidence by the age of 75 years is .well under P%a: In other words, every type of cancer that is common in one district is rare somewhere else. Most of the figures in table 2 refer to the incidence of cancer in different communities defined by the area in which they live. Communities can, however, be defined in other ways and no matter how they are defined (whether by ethnic origin, religion, or economic status) similar or sometimes even greater differences will be found. Of particular interest are some of the differences that have been observed in the United States between members of different religious groups. For example, in comparison with members of other religious groups living in: the same States, the Mormons of Utah and the Seventh-day Adventists and Mormons of California experience low incidence rates for cancers of the respiratory, gastrointestinal, and genital systems. Of course, it is unlikely that any one single com- munity will by chance have the highest rates in the world for every single type of cancer, just as it is unlikely that any one single community will by chance have the lowest rates in the world for every single type of cancer. Consequently, when we consider total cancer rates, which are obtained by adding the rates for each separate type of cancer, in various communities we find less extreme variation (only threefold) between communities arotnu the world than was found for many separate single types of cancer. I-loweever, there is if, anything still more variation in these total cancer incidence rates than would have been expected if for ' G)r eA•x: tmplc; thc p:rtxA•rs from the recnt workshop on (:nrnrr and DInt-tality in Relil;irrus Gruups"i Lyon eti crl.. 19HQa; I.yun ct :rllA, l'.lttOh; ; f:n.uirnt, l!)NO; West et al., 1980; hhillips,ct al., IS/Hft; Martin ca ;rl., 1980; 6King , :md lsw'kr, lF1KU:r. each community the rates for the separate single types of cancer had been picked at random from the corre- sponding rates around the world for single types of cancer (Peto J: Unpublished calculations based on IARC, 1976). Consequently; the relative constancy of total cancer incidence rates around the world does not suggest that if one cancer is prevented another will tend to replace it;s it merely shows that if many things are added up, irregularities will tend to be averaged out. Apart from cancer of the skin, the risk of which is much greater for whites than for blacks (an& possibly also apart from the consistent lack among people of Chinese or Japanese descent of certain lymphoprolifer- ative conditions) it does not seem likely that most of the large differences in cancer onset rates between communities could be chiefly due to genetic factors (see section 2.5), and such factors certainly cannot explain the differences observed'n on migration or with the passage oE time that are described in the following sections.

2.2 Changes in Incidence on Migration Evidence of a change in the incidence of cancer in a migrant group (from that in the homeland they have left toward that of their new country of residence) provides good evidence of the importance of life-style or other environmental factors in the production of the disease. That such changes have occurred and are occurring is beyond reasonable doubt, but strictly controlled quantitative evidence cornparing incidence rates in the three populations (original! country, mi- grant group, and new country) is hard to come by. Black Americans, for example, experience cancer inci- dence rates that are generally much more like those of white Americans than like those of the black popula- tion in West Africa from which they were originally drawn, as is indicated for selected sites6 in table 3. From the strict scientific point of view, this compari- son is unsatisfactory because the ancestors of black Americans would have come from many different parts of (chiefly West) Africa, some of which are likely to have cancer rates somewhat different from those ob- served in Nigeria. Nevertheless, the contrast is so great that there can be little doubt that new factors were ' The suggestion that environmental and life-style factors do not usuA•ally have much effect on whether or when an individual gets cancer, but merely affect the site at which a(hypotheticaly)' predestined cancer will appear, has recurred fronr titne to time for half a century ever since Cramer (1931) overlooketil the fact that the coefficient of variation of total cancer rates must of necessity be less than that of individual cancer rates. It is easily, disproved by noting that people exposed to hazards (cg., carcinogens in industry or cigarette smoke: lkrIt, 1978) which affect sfxA•cific tyfxA•s of cancer do not have reduced risks of cancer of any other tyllle. The cune is, of coursa, true arnaml; exfxfrirental anim: tIs. ' We ornittcd data for (:utcer si(cs for whIch the lbadan rates nA•wmbble the U_S. while rates (e.g., ese)(phagus and sturnach)- JN(a. 1't)t.. 1.6, 1;t, o. (t-t.F 1981

Variation in incidence is not, of course, limited to the types of cancer that are common enough somewhere in the world to have been included in table 2. For example, Burkitt's lymphoma has nowhere been found in over 0.1% of the population, but even so is 100 times less common in North America than in the West Nile district of Uganda. Also, Kaposi's sarcoma, which is extremely rare in most of the world, is so common in parts of Central Africa that it accounted for more than 10% of all tumors seen in the (mostly young) males in one hospital (Cook and Burkitt, 1971). Some few rather rare types of cancer, such as the nephroblastoma of childhood, may perhaps eventually be shown to occur with approximately the same frequency in all communities; but no common types of cancer will be found to do so. In the absence of other causes of death, cancer of the breast would affect about 6% of U.S. women before the age of 75 years as against only 1% of non-Jewish Israeli women, and it is possible that an even lower percentage would be affected in certain other populations where reliable cancer registries do not yet exist. With breast cancer as the only possible exception, for each type of cancer a population exists where the cumulative incidence by the age of 75 years is well under 1%. In other words, every type of cancer that is common in one district is rare somewhere else.

Most of the figures in table 2 refer to the incidence of cancer in different communities defined by the area in which they live. Communities can, however, be defined in other ways and no matter how they are defined (whether by ethnic origin, religion, or economic status) similar or sometimes even greater differences will be found. Of particular interest are some of the differences that have been observed in the United States between members of different religious groups.⁴ For example, in comparison with members of other religious groups living in the same States, the Mormons of Utah and the Seventh-day Adventists and Mormons of California experience low incidence rates for cancers of the respiratory, gastrointestinal, and genital systems.

Of course, it is unlikely that any one single community will by chance have the highest rates in the world for every single type of cancer, just as it is unlikely that any one single community will by chance have the lowest rates in the world for every single type of cancer. Consequently, when we consider total cancer rates, which are obtained by adding the rates for each separate type of cancer, in various communities we find less extreme variation (only threefold) between communities around the world than was found for many separate single types of cancer. However, there is if anything still *more* variation in these total cancer incidence rates than would have been expected if for

⁴ See, for example, the papers from the recent workshop on "Cancer and Mortality in Religious Groups": Lyon et al., 1980a; Lyon et al., 1980b; Enstrom, 1980; West et al., 1980; Phillips et al., 1980; Martin et al., 1980; King and Locke, 1980a.

each community the rates for the separate single types of cancer had been picked at random from the corresponding rates around the world for single types of cancer (Peto J: Unpublished calculations based on IARC, 1976). Consequently, the relative constancy of total cancer incidence rates around the world does not suggest that if one cancer is prevented another will tend to replace it;⁵ it merely shows that if many things are added up, irregularities will tend to be averaged out.

Apart from cancer of the skin, the risk of which is much greater for whites than for blacks (and possibly also apart from the consistent lack among people of Chinese or Japanese descent of certain lymphoproliferative conditions) it does not seem likely that most of the large differences in cancer onset rates between communities could be chiefly due to genetic factors (see section 2.5), and such factors certainly cannot explain the differences observed on migration or with the passage of time that are described in the following sections.

2.2 Changes in Incidence on Migration

Evidence of a change in the incidence of cancer in a migrant group (from that in the homeland they have left toward that of their new country of residence) provides good evidence of the importance of life-style or other environmental factors in the production of the disease. That such changes have occurred and are occurring is beyond reasonable doubt, but strictly controlled quantitative evidence comparing incidence rates in the three populations (original country, migrant group, and new country) is hard to come by. Black Americans, for example, experience cancer incidence rates that are generally much more like those of white Americans than like those of the black population in West Africa from which they were originally drawn, as is indicated for selected sites⁶ in table 3. From the strict scientific point of view, this comparison is unsatisfactory because the ancestors of black Americans would have come from many different parts of (chiefly West) Africa, some of which are likely to have cancer rates somewhat different from those observed in Nigeria. Nevertheless, the contrast is so great that there can be little doubt that new factors were

⁵ The suggestion that environmental and life-style factors do not usually have much effect on whether or when an individual gets cancer, but merely affect the site at which a (hypothetically) predestined cancer will appear, has recurred from time to time for half a century ever since Cramer (1934) overlooked the fact that the coefficient of variation of total cancer rates must of necessity be less than that of individual cancer rates. It is easily disproved by noting that people exposed to hazards (e.g., carcinogens in industry or cigarette smoke: Doll, 1978) which affect specific types of cancer do not have reduced risks of cancer of any other type. The same is, of course, true among experimental animals.

⁶ We omitted data for cancer sites for which the Ibadan rates resemble the U.S. white rates (e.g., esophagus and stomach).

Avoidable Risks of Cancer In the U.S. 1201 TABLE 3, Comparison of cancer incidence rates^a for Ibadan, Nigeria, and for two populations of blacks and whites in the United States Primary site of cancer Patients' sex Annual incidence/million people^a

Ibadan, United States' Nigeria, 1960-69 Blacks Whites Colon a 34 349 294 353 335 Rectum a 34 159 217 248 232 Liver 6 272 . 67 39 86 32 Pancreas a 55 200 126 250 122 Larynx a 37 236 141 149 141 Lung \$ 27 1,546 983 1,517 979 Prostate a 134 724 318 577 232 Breast Q 337 1,268 1,828 1,105 1,472 Cervix uteri Q 559 507 249 631 302 Corpus uteri Q 42 235 695 208! 441 Lymphosarcoma^a a 133 10! 4 at ages <15 yr 5 3 ^a From IARC (1976): 6 Ages 35-64 yr, standardized for age as in IARC (1976) j For brevity, wherever possible only the male rates have been presented, and sites for which the rates among U.S. whites resemble those in the country of origin of the non-^awhite migrants have been omitted. ^a For each type of cancer, upper entry shows incidence in San Francisco Bay area, 1969-73; lower entry shows incidence in Detroit, 1969-71. ^b Including Burkitt's lymphoma. The cited rates are the average of the age-specific rates at ages 0-4, 5-9 and 10-14 yr: introduced with migration. These, it would appear, are not chiefly the result of genetic dilution by inter- breeding, for at most major sites the differences between black and white Americans in defined areas seem largely independent of the degree of admixture of white-derived genes among the blacks in those areas (Petraakis, 1971). A similar comparison can be made between the Japanese and Caucasian residents in Hawaii and the Japanese in two particular prefectures of Japan (table 4): The close approximation of the rates in the two prefectures gives some justification for believing that they may be typical of the areas from which the Japanese migrants to Hawaii (or their ancestors); origi- nated, although the mii;rants will have come from other parts of Japan as wc^a•III For every type of cancer except cancer of the lung, the rates for the migrants are more like those for the (:aucasian resider.ts than for those in Japan. Other groups for which data :uc available include Indians who went tr, :ulti' Sccluth Africa (and Irlst their high risk ol devrli/l>ing oral c: In(terr), liritolls .who went to Fiji' (and acquired a high risk of' skin cancer),, and Central Europeans who went to North America and Australia. Data for some of these groups were reviewed in 1969, under the auspices of the Interna- tional Agency for Research on Cancer (Haenszel, 1970; Kmet, 1970), and recent data on cancer patterns in different ethnic groups within the United States were reviewed in 1980 under the auspices of the National Cancer Institute (Kolonel, 1980; King and Locke, 1!980b; Locke and King, 1980; Lanier et al., '1980).

2.3 Changes In Incidence Over Time Changes in the incidence of! particular types of cancer with the passage of time provide conclusive evidence that extrinsic factors affect those types of cancer. Such changes are, however, notoriously diffi- cult to estimate reliabliy^a, chiefly because it is difficult to compare the efficiency of case finding at different periods and partly because few incidence data have been collected for a sufficiently long time, so that we have to compare mortality rates, which record only fatal cases and thus may be influenced by changes in treatment. There are no uniform rules for deciding which of the many apparent changes in cancer inci- dence are real. Each set of incidence data and each~ type of cancer must be assessed', individually. It is relatively easy to be sure about changes in the incidence of cancer of the esophagus, because the disease can be diagnosed without complex investigations and its oc- TABLE 4. Comparison of cancer incidence rates^a in Japan and for Japanese and Caucasians in Hawaii Primar Annual incidence/million people^b y site of Patients' sex j Hawaii, 1968-72 cancer Japan Japanese Caucasians Esophagus 3' 150 46 75 112 Stomach a 1,331 397 217 1,291 Colon a 78 371 368 87 Rectum \$ 95 297 204 90 Lung a 237 379 962 299 Prostate a 14 154 343 13 B reast 9 335 1,221 1,869 N ' 295 0 Cervix uteri Q 329 398 149 . 243 N Corpus uteri 9 32 407 714 ~ 20 ~ Ovary 9 51, 160 274 ~ 55 a From IARC (1976). w1 ^a Ages 35-64 yr. standardized for age as in IARC (1976).CA ^b Male only, wherever possible; sites selected as in, table 3'~ ^a For each typt of, cancer, upper entry shows incidence in Miyagi prefecture, 1968-71: lower entry shost s incidence in Osaka prefocture; 1970-71. J1(:1, \A•Ul.. ta,, '.. ~, J1'tiE19M1

Avoidable Risks of Cancer In the U.S. 1201

TABLE 3.—Comparison of cancer incidence rates^a for Ibadan, Nigeria, and for two populations of blacks and whites in the United States

Primary site of cancer	Patients' sex ^c	Annual incidence/million people ^b		
		Ibadan, Nigeria, 1960-69	United States ^d	
			Blacks	Whites
Colon	♂	34	349	294
			353	335
Rectum	♂	34	159	217
			248	232
Liver	♂	272	67	39
			86	32
Pancreas	♂	55	200	126
			250	122
Larynx	♂	37	236	141
			149	141
Lung	♂	27	1,546	983
			1,517	979
Prostate	♂	134	724	318
			577	232
Breast	♀	337	1,268	1,828
			1,105	1,472
Cervix uteri	♀	559	507	249
			631	302
Corpus uteri	♀	42	235	695
			208	441
Lymphosarcoma ^a at ages <15 yr	♂	133	10	4
			5	3

^a From IARC (1976).

went to Fiji (and acquired a high risk of skin cancer), and Central Europeans who went to North America and Australia. Data for some of these groups were reviewed in 1969, under the auspices of the International Agency for Research on Cancer (Haenszel, 1970; Kmet, 1970), and recent data on cancer patterns in different ethnic groups within the United States were reviewed in 1980 under the auspices of the National Cancer Institute (Kolonel, 1980; King and Locke, 1980b; Locke and King, 1980; Lanier et al., 1980).

2.3 Changes In Incidence Over Time

Changes in the incidence of particular types of cancer with the passage of time provide conclusive evidence that extrinsic factors affect those types of cancer. Such changes are, however, notoriously difficult to estimate reliably, chiefly because it is difficult to compare the efficiency of case finding at different periods and partly because few incidence data have been collected for a sufficiently long time, so that we have to compare mortality rates, which record only fatal cases and thus may be influenced by changes in treatment. There are no uniform rules for deciding which of the many apparent changes in cancer incidence are real. Each set of incidence data and each type of cancer must be assessed individually. It is relatively easy to be sure about changes in the incidence of cancer of the esophagus, because the disease can be

at ages 0-14 yr.

^a From IARC (1976).

^b Ages 35-64 yr, standardized for age as in IARC (1976).

^c For brevity, wherever possible only the male rates have been presented, and sites for which the rates among U.S. whites resemble those in the country of origin of the non-white migrants have been omitted.

^d For each type of cancer, upper entry shows incidence in San Francisco Bay area, 1969-73; lower entry shows incidence in Detroit, 1969-71.

^e Including Burkitt's lymphoma. The cited rates are the average of the age-specific rates at ages 0-4, 5-9 and 10-14 yr.

introduced with migration. These, it would appear, are not chiefly the result of genetic dilution by interbreeding, for at most major sites the differences between black and white Americans in defined areas seem largely independent of the degree of admixture of white-derived genes among the blacks in those areas (Petrakis, 1971).

A similar comparison can be made between the Japanese and Caucasian residents in Hawaii and the Japanese in two particular prefectures of Japan (table 4). The close approximation of the rates in the two prefectures gives some justification for believing that they may be typical of the areas from which the Japanese migrants to Hawaii (or their ancestors) originated, although the migrants will have come from other parts of Japan as well. For every type of cancer except cancer of the lung, the rates for the migrants are more like those for the Caucasian residents than for those in Japan.

Other groups for which data are available include Indians who went to Fiji and South Africa (and lost their high risk of developing oral cancer), Britons who

easy to be sure about changes in the incidence of cancer of the esophagus, because the disease can be diagnosed without complex investigations and its oc-

TABLE 4.—Comparison of cancer incidence rates^a in Japan and for Japanese and Caucasians in Hawaii

Primary site of cancer	Patients' sex ^c	Annual incidence/million people ^b		
		Japan ^d	Hawaii, 1968-72	
			Japanese	Caucasians
Esophagus	♂	150	46	75
		112		
Stomach	♂	1,331	397	217
		1,291		
Colon	♂	78	371	368
		87		
Rectum	♂	95	297	204
		90		
Lung	♂	237	379	962
		299		
Prostate	♂	14	154	343
		13		
Breast	♀	335	1,221	1,869
		295		
Cervix uteri	♀	329	149	243
		398		
Corpus uteri	♀	32	407	714
		20		
Ovary	♀	51	160	274
		55		

^a From IARC (1976).

^b Ages 35-64 yr, standardized for age as in IARC (1976).

^c Male only, wherever possible; sites selected as in table 3.

^d For each type of cancer, upper entry shows incidence in Miyagi prefecture, 1968-71; lower entry shows incidence in Osaka prefecture, 1970-71.

2025030553

JNCL, VOL. 66, NO. 6, JUNE 1981

Text Control

Hide Citation

(above)

Highlight Text:

OCR Text Alignment:

Image Control

Image Rotation:

Image Size:

Document Navigation

View - of 117
Range:

[NEXT >](#)

[Home](#) | [Collections](#) | [Profiles](#) | [Other Resources](#)

© 1999-2010 Tobacco Documents Online