2. Studies of Cancer in Humans

The available knowledge on the relationship between tobacco usage and a variety of human cancers is based primarily on epidemiological evidence. An immense amount of such evidence has been obtained, and, of necessity, only a small proportion can be referred to here. The cancers considered to be causally related to tobacco smoking in the previous *IARC Monograph* on tobacco smoking (IARC, 1986) included those of the lung, upper aerodigestive tract (oral cancer and cancer of the oropharynx, hypopharynx, larynx and oesophagus), urinary bladder and renal pelvis and pancreas. Since 1986, there have been numerous additional cohort and case–control studies on the relationship of cigarette smoking and other forms of tobacco use to these and other cancers in many different countries. The most comprehensive evidence, although often not the first or most detailed, has been obtained from several large cohort studies that are referred to repeatedly in this monograph with respect to different cancer sites and types of tobacco product. These cohort studies are described briefly below and in Table 2.1, listed by country. The case–control studies are described in the sections pertaining to particular cancer sites.

Description of cohort studies

(*a*) *Europe*

(i) *United Kingdom*

British Doctors' Study

In 1951, a questionnaire on smoking habits was sent to all British doctors included in the Medical Register; 34 440 men and 6194 women responded, representing 69% and 60%, respectively, of those doctors not known to have died at the time of the inquiry. [The exact number of men and women included in the study varies between publications as a number of women were misclassified as men in early reports.] Further questionnaires about changes in smoking habits were sent in 1957, 1966, 1972, 1978 and 1990 to men and in 1961 and 1973 to women; on each occasion, at least 94% of those alive responded. Reports were published on cause-specific deaths after 10, 20 and 40 years for men and after 10 and 22 years for women; more than 99% of the subjects had been traced. Information on causes of death was obtained principally from the Registrars General of the United Kingdom and, otherwise, from the records of the general Medical Council, the

Bristish Medical Association, relatives or friends. Because the subjects in the study were themselves physicians, they were a reasonably uniform socioeconomic group and the causes of death were certified more accurately than might have been the case among a sample of the general population. For the first 20 years of the study, confirmation of all deaths attributed to lung cancer was obtained from a chest physician who was unaware of the patient's smoking history (Doll & Hill, 1964a,b; Doll & Peto, 1976; Doll *et al*., 1980, 1994).

Whitehall Study

A total of 19 018 men aged 40–69 years from the British Civil Service were clinically examined between 1967 and 1969, and followed up for vital status until 1987 through the National Health Service Central Registry. Information on exposure was collected only at baseline. The study concentrated on residual risk after smoking cessation as well as comparing risk associated with different tobacco products (Ben-Shlomo *et al.*, 1994).

British United Provident Association (BUPA) Study

Wald and Watt (1997) studied a cohort of 21 520 professional and businessmen with a National Health Service identification number who attended a routine health examination between 1975 and 1982 at a British United Provident Association (BUPA) Medical Centre in London. At this examination, a detailed smoking history was obtained, including self-reported level of inhalation (rated as nil, slight, moderate or deep). In addition, a blood sample was collected and carboxyhaemoglobin saturation and cholesterol levels were measured. Causes of death of cohort members were obtained from records of the National Health Service and the Office of Population Censuses and Surveys records. The risks of mortality from three causes (i.e. ischaemic heart disease, lung cancer and chronic obstructive lung disease) were computed using Cox's proportional hazard analysis.

(ii) *Sweden*

Swedish Twin Registry Study

A cohort of 10 945 twin pairs of the same sex, identified using the Swedish Twin registry, was asked to complete a questionnaire in 1961. Zygosity was based on questions of childhood similarity. Mortality in twins was followed up by record linkage with the central registry of causes of death through 1997. The information from death certificates, hospital records and other data was collected for the period up until 1981 and was reviewed without prior knowledge of smoking status; the underlying cause of death was determined according to the ICD 8th revision. For the period after 1981, the underlying cause of death as stated in the death certificate was used (Floderus *et al.*, 1988; Steineck *et al.*, 1988; Grönberg *et al.*, 1996; Terry *et al.*, 1998, 1999, 2001).

Swedish Census Study

A sample of the Swedish population drawn from the 1960 census was stratified by sex, year of birth and residence (urban or rural). The objective was to determine the smoking

habits of the Swedish population by means of postal questionnaires, telephone interviews and home visits. A questionnaire was posted in 1963, and, of 55 074 eligible subjects, 89% responded. Information was collected by telephone or personal interview for another 5.3%. A sub-sample of 20% was sent a second questionnaire in 1969, with the aim of validating the accuracy of the replies and collecting information about changes in smoking patterns. Mortality in the cohort was ascertained through death certificates. In addition, cancer incidence was ascertained through the nationwide Swedish Cancer Registry, which recorded an estimated 95.5% of all cancers. The follow-up period extended from 1964 until 1989. Cancer outcomes were reported after 10 and 26 years for men and women combined (Cederlöf *et al.*, 1975; Nordlund *et al.*, 1999) and after 16 years for men only (Carstensen *et al.*, 1987) and after 26 years for women only (Nordlund *et al.*, 1997). Cox proportional hazards regression models were used to compute odds ratios stratified by age and place of residence.

Swedish Construction Workers' Study

A cohort of male Swedish construction workers was identified in 1971, when workers filled out a questionnaire, the answers to which included a detailed smoking history. The cohort included about 135 000 men recruited between 1971 and 1975 or 350 000 men recruited between 1971 and 1992. Each cohort member contributed person–years of observation from the date of first registration visit until the date of diagnosis, death, migration or end of follow-up (Adami *et al.*, 1996; Nyrén *et al.*, 1996; Adami *et al.*, 1998; Chow *et al.*, 2000). Data on cancer incidence were obtained through linkage with the population-based national cancer registry established in 1958. Each cohort member was identified by his national registration number, a unique personal identifier assigned to all residents in Sweden.

(iii) *Norway*

Norwegian Cohort Study

Heuch *et al.* (1983), Engeland *et al.* (1996a,b) and Kjaerheim *et al.* (1998) reported the cancer incidence of a cohort of 26 000 Norwegians who completed a self-administered questionnaire in 1964–1965. The target population was drawn from three sources: approximately 19 000 persons were randomly drawn from lists of residents of Norway from the 1960 population census, approximately 5200 were drawn from four selected counties, and approximately 13 000 were drawn from a cohort of Norwegians living in Norway who had siblings living in the USA. The final study population comprised 26 126 persons, contributing approximately 540 000 person–years for analysis (230 000 for men and 310 000 for women). At the initial assessment, 17% of the men reported never having been a smoker, whereas 68% of the women had never smoked. Information on cancer incidence was obtained through the population-based Norwegian Cancer Registry, which has been operational through the mandatory reporting of cancer cases by physicians since 1953. All cohort members were followed up from 1966 to the date of the first diagnosis of the cancer being considered, the date of emigration, the date of death, or until 31 December 1993. The

only exception was for cancers of the upper aerodigestive tract, where more than one diagnosis per person was allowed. Questionnaire data were not updated during the follow-up period. Analyses were performed using the Cox proportional hazards regression models.

Norwegian Screening Study

The Norwegian Screening study followed the cancer incidence in a random sample of adults from two cities and three counties in Norway who were screened for coronary heart disease between different time periods (see Table 2.1). Participants were followed until death or emigration up to 1988. The officially coded underlying cause of death was used as the end-point. Mortality rates were adjusted for age and area of residence and analysed with Cox proportional hazards models (Vatten & Kvinnsland, 1990; Tverdal *et al.*, 1993; Thune & Lund, 1994; Veierød *et al.*, 1997).

(iv) *Finland*

Finnish Men's Study

A cohort of 4604 Finnish–Norwegian men was interviewed in 1962 about their smoking habits and cardiorespiratory symptoms. The study subjects were selected from three urban areas in western and central Finland, and three rural areas in western and eastern Finland (Pedersen *et al.*, 1969). One hundred and thirty-two men who died or were diagnosed with lung cancer before 1964, and 20 who had not given details of their smoking habits at the interview, were excluded, leaving an effective cohort size of 4452 men. The follow-up period for analysis covered 1964–80. Lung cancer cases were identified through the population-based cancer registry in Finland, by use of the Finnish personal identification number. The effect of smoking and different respiratory symptoms on lung cancer incidence was assessed by a log-linear modelling technique (Tenkanen *et al.*, 1987; Hakulinen *et al.*, 1997).

Finnish Mobile Clinic Health Examination Study

Between 1966 and 1972, the Finnish Mobile Clinic Health Examination Survey performed multiphasic health examinations in rural, semiurban and industrial municipalities in different parts of Finland. A total of 62 440 white adults aged ≥ 15 years were invited to participate, and the participation rate was 83%. All participants completed a questionnaire that had been sent in advance and checked at baseline examination. Participants were followed up until 1991 (Knekt *et al.*, 1998; Heikkilä *et al.*, 1999).

(v) *Iceland*

Reykjavík Study

Tulinius *et al.* (1997) assembled a cohort of 22 946 adult Icelanders in five stages for a study on risk factors for cardiovascular disease. The first stage took place from 1967 to 1969, the second from 1970 to 1972, the third from 1974 to 1979, the fourth from 1979 to 1984 and the fifth from 1985 to 1991. The initial enrolment interview took place at a clinic visit at which the completion of a comprehensive questionnaire concerning various

risk factors was followed by a series of anthropometric and biochemical measurements. Although interviews were conducted at each stage, this study used only data from each subject's first interview. Overall, 73% of the initial target population was successfully recruited into the study. The cohort was linked with the Icelandic Cancer Registry, a population-based registry of the entire country that was begun in 1954. Linking to the registry was facilitated by the unique identification number assigned to all residents in Iceland. Cox's regression was used to analyse the predictive power of a number of variables on the incidence of first cancer after enrolment into the study.

(vi) *Netherlands*

Dutch Study

A cohort of 26 697 women from the city of Utrecht in the Netherlands answered a questionnaire and provided a 12-h urine sample at the beginning of the follow-up period. Follow-up continued from entry to the study for up to 15 years. The full cohort was drawn from two previously established screening programmes. The first was a population-based screening programme for the early detection of breast cancer in women aged 40–64 years, called the DOM project. This portion of the cohort had 14 697 women who were enrolled from early 1975 until mid-1977, 72% of whom participated. One year later, 81% of this group participated in a follow-up effort in which a second 12-h urine sample was collected. The second breast cancer screening programme (Lutine study) was undertaken in 1982–83 and included more than 12 000 women 40–49 years of age [exact number not stated by the author]. For this second screening programme, 12-h urine samples were taken on days 21–23 of three consecutive menstrual cycles. Participation in the second screening programme was only 44%, probably because of the demanding study protocol. An all-cause-of-death register was established for this study to which all medical practitioners in the city of Utrecht who saw cohort members in their practices reported. In 1987, a regional cancer register was established, making it possible to follow the entire study cohort for cancer incidence. There were three distinct follow-up periods (Ellard *et al.*, 1995; de Waard *et al.*, 1995; van Wayenburg *et al.*, 2000).

(vii) *Denmark*

Copenhagen City Heart Study

In 1976, a prospective epidemiological study was initiated in which participants were selected from 90 000 persons living in a defined area around the University Hospital of Copenhagen. An age-stratified sample of subjects aged 20 years or more was selected at random. Seventy-four per cent of those invited to participate (14 223 subjects) attended. The subjects were followed up until 1989. Notification of deaths and causes of death were obtained from the Central Death Registry of the National Board of Health (Lange *et al.*, 1992).

(*b*) *North America*

(i) *USA*

Framingham Heart Study

The Framingham Heart Study included 5209 subjects who were first examined between 1948 and 1952, and were aged 45–84 years at baseline examination. Participants were routinely examined every two years for 24 or 34 years. At these examinations, information on smoking status and other risk factors was updated. A tumour registry was set up for this cohort (Williams *et al.*, 1981; Freund *et al.*, 1993).

American Cancer Society (nine-state) Study

In 1952, more than 22 000 volunteers for the American Cancer Society each distributed a questionnaire to 10 white men aged 50–69 years whom the volunteer knew well. Smoking histories were collected from 204 547 men in nine states. After exclusion of unsuitable subjects, a cohort of 187 783 men was followed by the volunteers from 1952 through 1955 (average duration, 44 months). A total of 11 870 deaths (6.2%) and 1.1% losses to follow-up were recorded. Death certificates were obtained for all reported deaths and further information was sought from the physician, hospital or tumour registry whenever cancer was mentioned in the certificate (Hammond & Horn, 1958a,b). The distribution of smoking habits in the study population was in close agreement with that reported in a large survey on smoking habits in a sample of the US population (Haenszel *et al*., 1956).

US Veterans' Study

Beginning in January 1954, 293 958 holders of US government Life Insurance policies who had served in the armed forces at any time between 1917 and 1940 were sent a questionnaire on smoking habits; 198 834 (68%) responded and 49 361 additional replies were obtained by a subsequent mailing in 1957 (total response rate, 85%). Policy holders were almost exclusively white men of the middle and upper social classes. Subjects were followed up from 1954 until 1980 during which time there were 192 756 deaths. Whenever a claim was filed for payment of a policy, a copy of the death certificate was sent by the Veterans' Administration to the National Institutes of Health study office. 'Terminated' policies were also checked annually to ascertain if termination was due to death or to other reasons. Additional information on policy holders who had died was requested from a certifying physician or hospital. The 26-year follow-up was considered to be almost complete by Chow *et al.* (1995), with 95% of the death certificates of cohort members who had died having been obtained (Kahn, 1966; Rogot & Murray, 1980; Kinlen & Rogot, 1988; McLaughlin *et al.*, 1989; Hsing *et al*., 1990a; McLaughlin *et al.*, 1990a,b; Hsing *et al*., 1991; Heineman *et al.*, 1992; Zahm *et al.*, 1992; Chow *et al*., 1993; Heineman *et al.*, 1994; Chow *et al.*, 1995; McLaughlin *et al.*, 1995; Chow *et al.*, 1996).

Californian Study

Information on occupational exposures and smoking history was collected from self-administered questionnaires in 1954–57 from 68 153 male labour union members, aged 35–64 years, in California. Subjects were followed up for mortality up to December 1962 (average follow-up time, 7.1 years) through California death records. A total of 4706 deaths occurred in the cohort, 936 of which were from cancer (Weir & Dunn, 1970). [The Working Group noted that the data available on smoking habits were less extensive than those obtained in other studies.]

Cancer Prevention Study I (CPS-I)

Between October 1959 and February 1960, volunteers for the American Cancer Society in 25 states recruited more than one million subjects from among their friends, neighbours and acquaintances. Families were enrolled, with the condition that there be at least one person aged over 45 years in the family. All family members over 30 years of age were requested to fill out a detailed four-page questionnaire. Participants were predominantly white (97%), married (82%) and college-educated. For the 1 051 038 subjects enrolled, vital status was monitored by the volunteers, originally to September 1965 (Thun & Heath, 1997). Each subject was traced annually and every 2 years was requested to fill out a brief follow-up questionnaire. Of the subjects originally enrolled, 1% could not be traced in the follow-up, and 2% of the questionnaires were unusable. Death certificates were obtained from state or local authorities and, when cancer was mentioned, further information was sought from physicians. The underlying cause of death was coded according to the ICD 7th revision. During the first 6 years of follow-up, 76 888 subjects died and 14 029 (1.4%) were lost to follow-up; 483 519 white women and 358 422 white men alive at the end of 1966 were further followed up for mortality until 1972 with a success rate for follow-up of 99%. This is the largest of the early cohort studies on tobacco and mortality (Hammond & Garfinkel, 1961; Hammond, 1966; Garfinkel, 1980; Hammond & Seidman, 1980; Garfinkel, 1985; Stellman & Garfinkel, 1986, 1989a,b; Garfinkel & Boffetta, 1990; Thun *et al.*, 1995; Thun & Heath, 1997; Thun *et al.*, 1997a; Shanks & Burns, 1998).

Harvard Alumni Study

A cohort of undergraduates who had entered the University of Harvard between the years of 1916 and 1950 was identified when they responded to a health questionnaire sent out in 1962 or 1966. Updated information was obtained from 13 905 cohort members from periodic surveys that assessed lifestyle habits and medical history. The questions asked for information on daily amount of cigarette smoking, age at start and cessation of cigarette smoking, weight, height and physical activity. In surveys conducted in 1988 and 1993, participants were asked whether a cancer had been diagnosed by a physician. Deaths that occurred up to 1992 were traced using information from the alumni office to obtain death certificates. The authors claimed that mortality follow-up was virtually complete (Paffenbarger *et al.*, 1977, 1978).

Tecumseh Community Health Study

The Tecumseh Community Health Study involved subjects who participated in one or more rounds of physical examinations offered to 9794 persons from a semi-rural community in 1959–60, 1962–65 and 1967–69. Cigarette smoking history was taken at each examination cycle. A retrospective cohort was created from those participants aged 25 years and older and who were free of cancer (except for non-melanoma skin cancer) at baseline or within 1 year of entering the study. These criteria resulted in a fixed cohort of 3956 subjects, for whom complete follow-up data were available. In 1986–87, a comprehensive cancer incidence survey was conducted by means of a questionnaire sent to the participants or their next-of-kin. An estimated completeness of 95% was achieved. The reported cancer cases were verified, with the permission of the participant, by requesting abstracts of hospital records. A Cox proportional hazards model was used to examine lung cancer incidence in relation to smoking habits (Islam & Schottenfeld, 1994).

Kaiser Permanente Medical Care Program Study

The first cohort included approximately 175 000 subjects aged 15–94 years who underwent at least one multi-phasic health check-up between 1964 and 1973 within the Kaiser Permanente Medical Care Program. Cancer incidence was ascertained from the first health examination until 1988 through the San Francisco-Oakland Surveillance, Epidemiology and End Result (SEER) programme and the Northern California Kaiser Permanente Medical Care Program. Approximately 4.4% of the cohort were lost to the study (Hiatt & Bawol, 1984; Hiatt & Fireman, 1986; Friedman, 1993; Friedman & van den Eeden, 1993; Herrinton & Friedman, 1998; Iribarren *et al.*, 2001). Between 1978 and 1985, a similar cohort was established, which included a maximum of 120 000 subjects aged 30–89 years. In one study, the cohort was further followed up until 1987 (Sidney *et al.*, 1993). Cancer cases were ascertained as for the first cohort (Hiatt *et al.*, 1988; Klatsky *et al.*, 1988; Sidney *et al.*, 1993; Hiatt *et al.*, 1994; Herrinton & Friedman, 1998).

American Men of Japanese Ancestry Study

A cohort of 8006 American men of Japanese ancestry, born during the years 1900–19 and who resided on the Hawaiian island of Oahu, were interviewed and examined clinically from 1965 to 1968. Information obtained at the interview included age, smoking history, usual occupation, type of housing, education and religion. A 24-h dietary recall questionnaire was also administered. Newly diagnosed cases of cancer were identified through continuous surveillance of Oahu hospitals and linkage with the Hawaii Tumor Registry (Stemmermann *et al.*, 1988; Severson *et al.*, 1989; Nomura *et al.*, 1990a,b; Chyou *et al.*, 1992, 1993a,b, 1995; Nomura *et al.*, 1995; Chyou *et al.*, 1996).

Lutheran Brotherhood Insurance Study

A cohort of 17 633 white male life insurance policy holders of the Lutheran Brotherhood Insurance Society was identified in 1966. A response rate of 68.5% was achieved and little difference was observed between responders and non-responders to the ques-

tionnaire with regard to age, urban or rural residence, policy status and cancer mortality at 11.5 years of follow-up. The questionnaire included questions on tobacco use in the form of cigarettes, cigars, pipes and smokeless tobacco. Other questions asked for details of the longest held occupation, frequency of consumption of 35 food items and the consumption of coffee, beer and spirits. Death certificates were coded for underlying and contributory causes of death. Person–years were accumulated up to death, loss to follow-up or the end of the study in 1986. The age-adjusted relative risks for cancer mortality resulting from exposure to tobacco, occupation and dietary variables were computed using Poisson regression. Statistical interaction between smoking and other risk factors was also examined. About 23% of the cohort members were lost to follow-up (Hsing *et al.*, 1990b; Kneller *et al.*, 1991; Linet *et al.*, 1991; Chow *et al.*, 1992; Linet *et al.*, 1992; Zheng *et al.*, 1993; Hsing *et al.*, 1998).

MRFIT Study

The MRFIT study was conducted on a cohort of 361 662 men who were seen at an initial screening visit at 22 clinical centres throughout the USA and were thereby enrolled into the cohort in 1975. At the initial visit, 37% ($n = 133\ 117$) were current smokers, consuming an average of 26 cigarettes per day. A total of 12 866 participants were selected for an intervention trial based on a high risk score for coronary heart disease assigned at the baseline physical examination. High risk for coronary heart disease was determined by a combination of factors, using a logistic regression function derived from men in the same age group in the Framingham Heart Study, including cigarette smoking habits, diastolic blood pressure and serum cholesterol at the first screening visit (Kuller *et al.*, 1991).

Nurses' Health Study

In 1976, a cohort of 121 700 female registered nurses was assembled in the USA. At enrolment, the nurses completed a mailed questionnaire on risk factors for cancer and heart disease. Responses to food-frequency questionnaires were also collected in 1980, 1984, 1986 and 1990. The response rate to follow-up questionnaires was almost 96% through to 1990. Family members were the main source of vital status information for non-respondents but the National Death Index was also used. Multiple logistic regression models were used to compute odds ratios, after controlling for age, total energy intake and other potentially confounding variables (Willett *et al.*, 1987; Hunter *et al.*, 1990; Chute *et al.*, 1991; Giovannucci *et al.*, 1994a; Grodstein *et al.*, 1995; Kearney *et al.*, 1995; Fuchs *et al.*, 1996; Egan *et al.*, 2002).

Using the same cohort, Speizer *et al*. (1999) collected and updated information on smoking status and health status by means of a follow-up questionnaire distributed every 2 years from baseline until 1992.

Adventists' Health Study

A cohort of 34 198 non-Hispanic white Seventh-day Adventists in California (mean age, 55.4 years) was formed in 1976 when they completed a questionnaire concerning

lifestyle. During the period of follow-up from enrolment until December 1982, newly diagnosed cancers were ascertained by various means. First, a record linkage of the cohort members was made with two population-based cancer registries, the Cancer Surveillance Program in Los Angeles and the Resource for Cancer Epidemiology in San Francisco. Second, annual contact was maintained with every member of the cohort by means of a mailed questionnaire in which the study subject was asked to report whether he or she had been hospitalized in the previous 12 months. Study staff reviewed all medical records for evidence of cancer diagnoses. The authors stated that follow-up was 99% complete. Relative risks adjusted for permanent covariates were computed by use of the Cox proportional hazards model (Mills *et al.*, 1988, 1989a,b, 1990, 1991; Singh & Fraser, 1998).

Leisure World Study

A detailed health questionnaire was sent to all residents of a retirement community in California in 1981, and to new residents in 1982, 1983 and 1985. A response rate of 61% was achieved overall. Almost all of the residents were Caucasians of the upper-middle class; about two-thirds were women; and 80% were aged 65–86 years. Histological diagnosis of cancer was obtained from local hospitals. All participants were sent a follow-up questionnaire every 2 years (Wu *et al.*, 1987; Ross *et al.*, 1990; Shibata *et al.*, 1994).

Cancer Prevention Study II (CPS-II)

The Cancer Prevention Study II (CPS-II) is a nationwide prospective mortality cohort study of nearly 1.2 million adults enrolled by volunteers of the American Cancer Society in 1982. As in CPS-I, enrolment was based on families and excluded persons in institutions and military service and others who would be difficult to trace (Garfinkel, 1985). Each participant completed a confidential four-page postal questionnaire on tobacco and alcohol use, diet and other factors potentially related to cancer. Deaths were ascertained from month of enrolment until 31 December 1996 through personal enquiries made by the volunteers in 1984, 1986 and 1988 and later through linkage with the National Death Index. Most of the smoking-related analyses were based on follow-up through 1986, 1988 or 1989 to minimize misclassification of exposure of those smokers who quit during follow-up. By 1988, 1.8% of the cohort were lost to follow-up and 79 802 (6.7%) had died (Thun & Heath, 1997). The ninth revision (ICD-9) of the International Classification of Diseases was used to code the underlying cause of death. Participants in CPS-II were more likely to be white (93%), married (81%) and educated (high school graduates or above, 85.6%) than the general population of the USA. The analyses excluded former cigarette smokers and persons with incomplete or unclassifiable data on smoking status or on the frequency or duration of cigarette smoking; men who ever smoked a pipe or a cigar or for whom pipe or cigar smoking status was unclear, were also excluded (Garfinkel, 1985; Stellman & Garfinkel, 1986; Garfinkel & Stellman, 1988; Stellman & Garfinkel, 1989a; Garfinkel & Boffetta, 1990; Calle *et al.*, 1994; Thun *et al.*, 1995; Heath *et al.*, 1997; Thun & Heath, 1997; Thun *et al.*, 1997a,b; Kahn *et al.*, 1998; Chao *et al.*, 2000; Shapiro *et al.*, 2000; Chao *et al.*, 2002).

Iowa Women's Health Study

The Iowa Women's Health Study was conducted on a cohort of 41 837 women who completed a postal questionnaire (response rate, 42.7%) sent in 1986 to a random sample of women from the Iowa driver's licence list (Potter *et al*., 1992). The questionnaire covered information on age, smoking history, physical activity, level of education and alcohol consumption. Cigarette consumption was analysed as pack–years for both current and former smokers. Physical activity was ascertained by questionnaire and translated into a three-level physical activity score (low, medium and high). Incident cases of cancer were ascertained by the Health Registry of Iowa, which is a population-based cancer registry in the SEER Program of the National Cancer Institute (Bostick *et al.*, 1994; Harnack *et al.*, 1997; Parker *et al.*, 2000).

Health Professionals' Follow-up Study

In 1986, a cohort of 51 529 male dentists, optometrists, osteopaths, podiatrists, pharmacists and veterinarians in the USA were asked to respond to a postal questionnaire. The questionnaire included questions on age, current and past tobacco use, marital status, height and weight, ancestry, medications, disease history, physical activity and diet. Only men who completed the diet questionnaire adequately at baseline and who reported no cancer other than non-melanoma skin cancer were included in the analysis. After all baseline exclusions, 47 781 men comprised the analysis cohort. Follow-up questionnaires were sent in 1988, 1990, 1992 and 1994 to ascertain new cancer cases and to update smoking status. Family members and the National Death Index were the main source of information on vital status of non-respondents. After repeated mailings, the follow-up response rate was 94% up to 1994 and ascertainment of death was estimated to be 98%. Pooled logistic regression was used in analysis, which accounts for varying time to the outcome event and which is asymptotically equivalent to a Cox regression model with time-dependent covariate, given the short intervals and low probability of outcomes (Giovannuci *et al.*, 1994b; Kearney *et al.*, 1995; Fuchs *et al.*, 1996; van Dam *et al.*, 1999; Giovannuci *et al.*, 1999).

(ii) *Canada*

Canadian War Veterans' Study

After a pilot study to validate the questionnaire in 1955–56, 207 397 war veterans listed by the Canadian Pension Commission were sent a questionnaire on smoking habits, principal occupations and residence history. Approximately 118 000 forms (57%) were returned; after removal of duplicates and unusable forms some 92 000 (44%) (78 000 men and 14 000 women) remained. Follow-up was conducted from 1956 to 1962 through quarterly lists of deaths made available by the Department of Veterans Affairs. There were 9491 deaths among men and 1794 deaths among women; in most cases the cause of death was confirmed by autopsy (Best *et al*., 1961; Lossing *et al*., 1966).

National Breast Screening Study

The National Breast Screening Study is a multicentre, randomized controlled trial of mammography screening for breast cancer. Between 1980 and 1985, 89 835 women aged 40–59 years were recruited. In 1982, a second questionnaire was distributed to new attendees and previously enrolled women returning to the screening centres for further screening. A total of 56 837 women returned the questionnaires. Analyses are based mainly on respondents to the second questionnaire (Friedenreich *et al.*, 1993; Terry *et al.*, 2002).

(*c*) *Asia*

(i) *China*

Shanghai Factory Study

Chen *et al*. (1997) studied a cohort of 9351 adults from 11 factories in urban Shanghai. This cohort was identified in two stages: one during 1972–73 and the other during 1977–78, when members completed an interview based on a structured questionnaire. The questionnaire included questions on smoking, alcohol consumption, occupation, medical history and physical exercise. Vital status of the cohort members was monitored using factory records until 1 January 1993, with only 4% of subjects lost to follow-up. Cause of death was ascertained by examination of death certificates and the underlying cause of death was determined by two nosologists blinded to the smoking status of the individual. The Cox proportional hazards model was used for comparing a gradient of smoking categories with nonsmokers, while simultaneously adjusting for relevant covariates. At baseline, 61% of men and 7% of women smoked. Of the men, 46% consumed more than 20 cigarettes per day whereas only 11% of the female smokers consumed this number. Thirty-eight per cent of male smokers had started smoking prior to their twenty-fifth birthday, whereas among women, this figure was 25%.

Xi'an Factory Study

A cohort of 1696 persons was identified for a cross-sectional survey of coronary heart disease among employees of a machinery factory in Xi'an in May 1976. Employees were monitored for cause-specific mortality until 1996. Approximately 7% of the cohort members were subjected to occupationally hazardous exposures according to factory physicians. Vital status was ascertained from personnel and union records and confirmed through interviews of co-workers or relatives. The Cox regression model was used, adjusting for potential confounding factors including age, marital status, occupation, education, diastolic blood pressure and triglycerides and total cholesterol levels. During the 20 years of follow-up, 173 men and 45 women died (Lam *et al.*, 1997).

Shanghai Residential Study

A cohort of 213 800 residents from urban, suburban and surrounding rural areas of Shanghai were surveyed for smoking status. Subjects in urban areas were followed up annually for 12 years (January 1983 to December 1994) and subjects in suburban areas

and rural counties for 11 years (January 1984 to December 1994). The cause of deaths during the follow-up period was ascertained by medical professionals. Only data on subjects aged 40 years and over at enrolment were analysed. Because the prevalence of smoking among women aged 40 years and over in suburban and rural areas was very low (3.1% and 1.5%, respectively), data on women in these areas were excluded from the analysis. Person–years observed were calculated by sex, age, smoking status and area of residence. A Poisson regression model was used to estimate age-adjusted relative risks with 95% confidence limits for each cause of death (Gao *et al.*, 1999).

Linxian Intervention Trial Study

In the frame of an intervention trial for micronutrients, approximately 30 000 residents of the Linxian region were interviewed to obtain information on usual dietary intake, tobacco use, alcohol drinking, family history of cancer and other factors. The cohort was followed up from 1986 until 1991, with little loss to follow-up. Information on cause of death and incidence of cancer was collected from local hospitals or a study medical team. Relative risks were adjusted for potential confounders as well as the vitamin/mineral intervention group (Guo *et al.*, 1994).

Shanghai Men's Study

Ross *et al.* (1992) and Yuan *et al*. (1996) studied a cohort of 18 244 male residents of Shanghai, enrolled between 1986 and 1989 (80% of eligible subjects). A structured questionnaire was completed at a face-to-face interview. The information obtained included level of education, history of tobacco and alcohol use, current diet and medical history. At recruitment, 50% of study subjects were current smokers, half of whom smoked 20 or more cigarettes per day. Former smokers represented 7% of the cohort while 43% of cohort members had never smoked cigarettes regularly. Cancer incidence was ascertained through the population-based Shanghai Cancer Registry and vital status was ascertained by inspection of the Shanghai death certificate records. Only 50 subjects were lost to follow-up which continued until 1993.

Taiwanese Study

A cohort of 14 397 residents of metropolitan, urban and rural areas in Taiwan, China were recruited between 1982 and 1986. Information on sociodemographic characteristics, smoking status, alcohol drinking and food habits was collected at interview using a structured questionnaire. The cohort was followed up until 1994 by linkage with the death certification system in Taiwan. Causes of death were classified according to ICD-9. Cox proportional hazards regression models were used to derive relative risks for mortality and to examine dose–responses (Liaw & Chen, 1998).

(ii) *Japan*

Life Span Study

The Life Span Study cohort originally consisted of 100 000 survivors [sex distribution not reported] of the atomic bomb blasts in Hiroshima and Nagasaki. The cohort was expanded in 1968 and 1985 by adding approximately 10 000 survivors each time. The total cohort included approximately 120 000 individuals, of whom approximately 27 000 were non-exposed controls. Information on smoking was obtained from three interview surveys conducted on a subgroup of the entire cohort in 1963–64, 1964–68 and 1968–70, and four postal surveys conducted on various subgroups in 1965, 1969, 1979 and 1980. The cancer incidence in 61 505 survivors for whom smoking data were available was reported. For 42% of this group, information on smoking was available from at least two surveys. Information on cancer incidence and mortality was obtained from the Radiation Effects Research Foundation tumour registry and mortality database. Poisson regression models were used to fit log-linear relative risk and linear excess relative risk models (Akiba, 1994; Land *et al.*, 1994; Goodman *et al.*, 1995).

Japanese Physicians' Study

A survey of smoking and drinking habits among physicians in western Japan was carried out using self-administered questionnaires in 1965. From 6815 male respondents in nine prefectures (51% response rate), a cohort of 5477 male physicians was established. Vital status was followed until 1983 and confirmed by various medical associations. Copies of death certificates were obtained from the District Legal Affairs Bureau and the cause of death coded with the ICD-8. After exclusions, the analysis was done on 5130 men. Statistical analysis was performed using the Cox proportional hazards model (Kono *et al.*, 1987).

Six-prefecture Study

In 1965, 122 261 men and 142 857 women aged ≥ 40 years (95% of the census population) in 29 health centre districts from six prefectures in Japan were interviewed. The six prefectures were selected as being representative of the entire country. The questionnaire included questions on smoking, alcohol consumption and dietary habits, occupation, and marital status. A record linkage system was established for the annual follow-up. During the 16-year follow-up period, 8% of the cohort migrated from the original health districts. Deaths among cohort members were monitored by linkage to vital statistics kept at each public health centre. Cause of death was coded using the 7th revision of the International Classification of Diseases (Hirayama, 1967, 1975a,b, 1977a,b, 1978, 1981, 1982, 1985, 1989a,b,c; Mizuno *et al.*, 1989; Akiba & Hirayama, 1990; Hirayama, 1990; Kinjo *et al.*, 1998).

Regular male smokers who had started smoking between 18 and 22 years of age, and who were, at that time, between the ages of 40 and 79 years, were selected from the cohort for further analysis, resulting in a subcohort of 49 013 men (Mizuno *et al.*, 1989). [This

study was large and unique in that it involved a non-Caucasian population and was based on interviews rather than self-completed questionnaires.]

Chiba Center Association Study

The Chiba Center Association Study was a nested case–control study based on a cohort population of 17 200 male participants in a mass screening for gastric cancer by the Chiba Cancer Association in Japan in 1984. Cancer cases in cohort members were detected by record linkage to the Chiba Cancer Registry. The participants were followed from 1984 until 1993. For each cancer case, two controls were selected from the cohort population by matching on sex, birth year and area of residence (Murata *et al.*, 1996).

Fukuoka Study

A baseline survey was conducted from 1986 until 1989 among the general population of Fukuoka, the region with the highest liver cancer mortality in Japan. All inhabitants aged > 30 years were asked to answer a questionnaire, to which the response rate was 84.3%. A follow-up survey was conducted annually to verify the vital status of participants. For study subjects who had died, the cause of death was determined from the health certificate and classified according to ICD-9. The participants were followed up until 1996.

Women were excluded from this survey because of the small numbers of deaths and current smokers. After exclusions, 4050 men were included in the analysis. Cox proportional hazards regression analysis was employed to estimate relative risks and 95% confidence intervals (Mizoue *et al.*, 2000).

(*d*) *Others*

Seven-country Study

Jacobs *et al*. (1999) studied a cohort of 12 763 men in seven countries between 1957 and 1964, after administration of a standardized questionnaire. The questionnaire included questions about daily cigarette consumption at entry, years of smoking cessation for former smokers, age, weight and height. A physical examination at baseline included a comprehensive history of cardiovascular and cerebral vascular health. Information on vital status and cause of death was obtained during the 25 years of follow-up, by examining death certificates, collecting medical records from hospitals and from interviews with physicians and relatives. A Cox proportional hazards model was used to compute relative risk.

Israel Civil Service Centre Study

In 1963, Kark *et al*. (1995) studied a cohort of 9975 male civil servants between the ages of 40 and 69 years living in Haifa, Jerusalem and Tel Aviv, Israel. The initial examination included a physical examination, measurement of blood pressure, weight and height, electrocardiography and venipuncture. A questionnaire, which included questions on sociodemography, health behaviour, diet and psychosocial factors, was administered

by a trained interviewer. Further examinations were carried out in 1965 and 1968. The follow-up period ended on 31 December 1986 and included 198 298 person–years of cancer surveillance by linking the cohort list to both the National Cancer Registry and the National Death Registry. A total of 153 cases of lung cancer were identified. The Cox proportional hazards model was used to compute relative risk by including age as a continuous variable, and city of employment, cigarette smoking and body-mass index as dummy variables. The reference categories were never-smokers, resident in Haifa and Tel Aviv, and the upper fifth of the body-mass index frequency distribution.

Table 2.1. Cohort studies of cancer and cigarette smoking

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
United Kingdom								
British Doctors' Study	1951	Doll & Hill (1964a,b); Doll & Peto (1976); Doll *et al.* (1980, 1994)	1951–91	40 634 (34 440 men, 6194 women) British doctors [age not reported]	Postal questionnaire	Deaths	Lung, urinary bladder, kidney, upper aerodigestive tract (oesophagus, mixed), pancreas, stomach, colon, rectum, liver, leukaemia, ovary, non-Hodgkin lymphoma, multiple myelomas	Information on pipe and cigars
Whitehall Study	1967–69	Ben-Shlomo *et al.* (1994)	1967–87	19 018 men from the British Civil Service, clinically examined, aged 40–69 years	Interview	Deaths	Lung	Information on pipe and cigars
British United Provident Association (BUPA) Study	1975–82	Wald & Watt (1997)	1975–93	21 520 professional and businessmen, aged 35–64 years	Interview	Deaths	Lung	Information on pipe and cigars
Sweden								
Swedish Twin Registry Study	1961	Floderus *et al.* (1988); Steineck *et al.* (1988); Grönberg *et al.* (1996); Terry *et al.* (1998, 1999, 2001)	1961–97	10 942 same-sex twin pairs, born 1886–1925	Postal questionnaire	Deaths	Lung, urinary bladder, stomach, colon, rectum, endometrium, prostate	Information on pipe and cigars Floderus *et al.* mentioned 10 945 pairs.

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Swedish Census Study	1963	I: Cederlöf *et al.* (1975); Carstensen *et al.* (1987)	1963–72	Adults selected from the 1960 census population, aged 18–69 years I: 51 911 (25 444 men, 26 467 women)	Postal questionnaire (94%), telephone, interview	Deaths	Lung, urinary bladder, pancreas, colon, rectum, liver, endometrium, cervix	Information on pipe and cigars Stratified by urban-rural residence
		II: Nordlund *et al.* (1997, 1999)	1964–89	II: 41 710 (15 881 men, 25 829 women)	Postal questionnaire (87%), telephone, home visits	Cases	Lung, urinary bladder, kidney, upper aerodigestive tract (oral cavity, pharynx, oesophagus, mixed), pancreas, stomach, colon/ rectum, liver, breast, endometrium, cervix, leukaemia	Stratified by place of residence
Swedish Construction Workers' Study	1971–75 (I) 1971–91 (II) 1971–92 (III)	I: Adami *et al.* (1996); Nyrén *et al.* (1996) II: Adami *et al.* (1998) III: Chow *et al.* (2000)	1971–92	Male construction workers, aged ≥ 35 years I: 143 998 II: 334 957 III: 363 992	Self-administered questionnaire/ interview	Cases	Kidney, colon, rectum, prostate, leukaemia, non-Hodgkin lymphoma, Hodgkin lymphoma, multiple myelomas	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Norway								
Norwegian Cohort Study	1964–65	Heuch *et al.* (1983); Engeland *et al.* (1996a,b); Kjaerheim *et al.* (1998)	1966–93	26 132 subjects (11 863 men, 14 269 women) including a sample of the 1960 census population, a random sample from 4 selected counties and a sample of siblings living in Norway with a sibling living in the USA, aged 33–72 years	Postal questionnaire	Cases	Lung, urinary bladder, kidney, upper aerodigestive tract (mixed), pancreas, stomach, colon, rectum, breast, endometrium, cervix, prostate, leukaemia, ovary	
Norwegian Screening Study	1974–78 (I) 1972–78 (II) 1977–83 (III)	I: Vatten & Kvinnsland (1990) II: Tverdal *et al.* (1993); Thune & Lund (1994) III: Veierød *et al.* (1997)	1972–88	Participants in a health screening programme, aged 35–49 years I: 24 329 women II: 44 290 men, 24 535 women; 53 242 men III: 26 119 men	Interview	Deaths	Lung, pancreas, stomach, colon, rectum, breast, cervix, prostate	Information on pipe and cigars
Finland								
Finnish Men's Study	1962	Pedersen *et al.* (1969); Tenkanen *et al.* (1987); Hakulinen *et al.* (1997)	1964–80	4452 men from 3 urban and 3 rural areas, born 1898–1917	Interview	Cases	Lung, prostate	Hakulinen *et al.* (1997) also included subjects from another survey in 1972–77

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Finnish Mobile Clinic Health Examination Study	1966–72	Knekt *et al.* (1998); Heikkilä *et al.* (1999)	1966–91	56 973 subjects having received multiphasic health examination from the Mobile Clinic [sex distribution not reported]	Postal questionnaire, checked by interview	Cases	Colon, rectum, prostate	
Iceland								
Reykjavík Study	1967–91	Tulinius *et al.* (1997)	1968–95	22 946 (11 366 men, 11 580 women) residents of Reykjavík, born 1907–1954, aged 31–61 years	Self-administered questionnaire	Cases	Lung, urinary bladder, oesophagus, pancreas, stomach, colon, endometrium, cervix, prostate, leukaemia	
The Netherlands								
Dutch Study	1975–77, 1982–83	Ellard *et al.* (1995); de Waard *et al.* (1995); van Wayenburg *et al.* (2000)	1975–90	26 697 women from 2 breast cancer screening programmes (DOM project and Lutine Study) in Utrecht, aged 40–64 years	Self-administered questionnaire	Cases	Lung, colon/rectum	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Denmark								
Copenhagen City Heart Study	1976–78, 1981–83	Lange *et al.* (1992); Prescott *et al.* (1999)	1976–89	14 223 subjects (6511 men, 7703 women) randomly selected among 90 000 persons living in a defined area of Copenhagen, aged ≥ 20 years	Self-administered questionnaire	Deaths	Lung	The study by Prescott *et al.* (1999) was based on data from three cohorts, including the Copenhagen City Heart Study, the Centre of Preventive Medicine and the Copenhagen Male Study.
USA								
Framingham Heart Study	1948–52	Williams *et al.* (1981); Freund *et al.* (1993)	1948–82	5209 subjects receiving routine examinations at the Framingham Heart Study Clinic, MA	Interview	Cases	Lung, colon	
American Cancer Society (nine-state) Study	1952	Hammond & Horn (1958a,b)	1952–55	187 783 men from 9 states, aged 50–69 years	Self-administered questionnaire	Deaths	Lung, urinary bladder, upper aerodigestive tract (mixed), pancreas, colon, rectum	Information on pipe and cigars

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
US Veterans' Study	1954, 1957	Kahn (1966); Rogot & Murray (1980); Kinlen & Rogot (1988); McLaughlin *et al.* (1989); Hsing *et al.* (1990a); McLaughlin *et al.* (1990a,b); Hsing *et al.* (1991); Heineman *et al.* (1992); Zahm *et al.* (1992); Chow *et al.* (1993); Heineman *et al.* (1994); Chow *et al.* (1995); Heineman *et al.* (1995); McLaughlin *et al.* (1995); Chow *et al.* (1996)	1954–80	293 958 male holders of a US Government Life Insurance, aged 31–84 years	Postal questionnaire	Deaths	Lung, urinary bladder, kidney, upper aerodigestive tract (oral cavity, nasopharynx, larynx, pharynx, oesophagus), pancreas, stomach, colon, rectum, liver, leukaemia, soft-tissue sarcoma, brain, biliary ducts, adrenals, non-Hodgkin lymphoma, Hodgkin's lymphoma, multiple myelomas	Information on pipe and cigars
Californian Study	1954–57	Weir & Dunn (1970)	1954–62	68 153 male labour union members, aged 35–64 years	Postal questionnaire	Deaths	Lung, urinary bladder, upper aerodigestive tract (oral cavity, larynx, pharynx, oesophagus), pancreas	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Cancer Prevention Study I (CPS-I)	1959–60	Hammond & Garfinkel (1961); Hammond (1966); Garfinkel (1980); Hammond & Seidman (1980); Garfinkel (1985); Stellman & Garfinkel (1986, 1989a,b); Garfinkel & Boffetta (1990); Thun *et al.* (1995); Thun & Heath (1997); Thun *et al.* (1997a); Shanks & Burns (1998)	1959–72	1 051 038 adults from 25 states, aged > 30 years	Postal questionnaire	Deaths	Lung, urinary bladder, upper aerodigestive tract (oesophagus, mixed), pancreas, stomach, colon/rectum, liver, endometrium, cervix, leukaemia, biliary ducts	Information on pipe and cigars For women, all sites of the aerodigestive tract and all cancers of the haematopoietic system were grouped.
Harvard Alumni Study	1962, 1966	Paffenbarger *et al.* (1977, 1978)	1962–92	13 905 male Harvard alumni; mean age, 58.3 years	Postal questionnaire	Cases/ deaths	Leukaemia, Hodgkin lymphoma	
Tecumseh Community Health Study (I/II/III)	1962–69	Islam & Schottenfeld, 1994	1962–87	3956 residents (1857 men, 2099 women) of Tecumseh, MI, aged > 25 years	Interview	Cases	Lung	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Kaiser Permanente Medical Care Program Study	1964–73 (I) 1978–85 (II) 1964–91 (I+II)	I: Hiatt & Bawol (1984); Hiatt & Fireman (1986); Friedman (1993); Friedman & van den Eeden (1993); Iribarren *et al.* (1999, 2001) II: Hiatt *et al.* (1988); Klatsky *et al.* (1988); Sidney *et al.* (1993); Hiatt *et al.* (1994) I+II: Herrinton & Friedman (1998)	I: 1964–97 II: 1978–87 I + II: 1973–93	Members of the Kaiser Permanente Medical Care Program I: approx. 175 000 members aged 15–94 years II: approx. 80 000 members aged 30–89 years I+II: 252 836 members aged 16–84 years	Interview	Cases	Lung, pancreas, colon, rectum, breast, prostate, leukaemia, thyroid, non-Hodgkin lymphoma, multiple myelomas	Information on pipe and cigars Period of collection and age range of participants at baseline vary slightly between studies, leading to different cohort sizes
American Men of Japanese Ancestry Study	1965–68	Stemmermann *et al.* (1988); Severson *et al.* (1989); Nomura *et al.* (1990a,b); Chyou *et al.* (1992, 1993a,b, 1995); Nomura *et al.* (1995); Chyou *et al.* (1996)	1965–95	8 006 American men of Japanese ancestry residing in Hawaii, born 1900–19	Interview	Cases	Lung, urinary bladder, upper aerodigestive tract (mixed), stomach, colon, rectum, colorectal polyps, prostate	
Lutheran Brotherhood Insurance Study	1966	Hsing *et al.* (1990b); Kneller *et al.* (1991); Linet *et al.* (1991); Chow *et al.* (1992); Linet *et al.* (1992); Zheng *et al.* (1993); Hsing *et al.* (1998)	1966–86	17 633 male holders of a Lutheran Brotherhood Insurance policy, largely of Swedish, Norwegian or German descent, aged ≥ 35 years	Postal questionnaire	Deaths	Lung, pancreas, stomach, colon/rectum, leukaemia, non-Hodgkin lymphoma, multiple myelomas	Information on pipe and cigars
MRFIT Study	1975	Kuller *et al.* (1991)	1975–85	12 866 randomized participants initially selected for the MRFIT, aged 35–57 years	Interview	Deaths	Lung, urinary bladder, kidney, upper aerodigestive tract (oesophagus, mixed), pancreas	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Nurses' Health Study	1976	Willett *et al.* (1987); Hunter *et al.* (1990); Chute *et al.* (1991); Giovannucci *et al.* (1994a); Kearney *et al.* (1995); Grodstein *et al.* (1995); Fuchs *et al.* (1996); Speizer *et al.* (1999); Egan *et al.* (2002)	1976–92	121 700 female nurses from 11 states, aged 30–55 years	Postal questionnaire	Cases	Lung, colon, rectum, colorectal polyps, pancreas, breast, skin	
Adventists' Health Study	1976	Mills *et al.* (1988, 1989a,b, 1990, 1991); Singh & Fraser (1998)	1976–82	34 198 male and female Adventists, aged > 25 years	Postal questionnaire	Cases	Urinary bladder, breast, pancreas, colon, prostate, leukaemia, multiple myeloma	
Leisure World Study	1981–82 (I) 1981–85 (II)	I: Wu *et al*. (1987) II: Ross *et al.* (1990); Shibata *et al.* (1994)	1981–85	Retirees living in a retirement community I: 11888 II: 13 976 [sex distribution not reported]	Postal questionnaire	Cases	Pancreas, colon/rectum, prostate	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Cancer Prevention Study II (CPS-II)	1982	Garfinkel (1985); Stellman & Garfinkel (1986); Garfinkel & Stellman (1988); Stellman & Garfinkel (1989a); Garfinkel & Boffetta (1990); Calle *et al.* (1994); Thun *et al.* (1995); Heath *et al.* (1997); Thun & Heath (1997); Thun *et al.* (1997a,b); Kahn *et al.* (1998); Chao *et al.* (2000); Shapiro *et al.* (2000); Chao *et al.* (2002)	1982–96	1 185 106 adults from 25 states, aged > 30 years	Postal questionnaire	Deaths	Lung, kidney, stomach, colon/rectum, colorectal polyps, breast, leukaemia	Information on pipe and cigars
Iowa Women's Health Study	1986	Potter *et al.* (1992); Gapstur *et al.* (1992); Bostick *et al.* (1994); Harnack *et al.* (1997); Parker *et al.* (2000)	1986–98	41 837 women randomly selected from the Iowa driver's licence list, aged 55–69 years	Postal questionnaire	Cases	Lung, pancreas, colon, breast, non-Hodgkin lymphoma	
Health Professionals' Follow-up Study	1986	Giovannucci *et al.* (1994b); Kearney *et al.* (1995); Fuchs *et al.* (1996); van Dam *et al.* (1999); Giovannucci *et al.* (1999)	1986–94	47 781 male health professionals, aged 40–75 years	Postal questionnaire	Cases	Pancreas, colon/rectum, colorectal polyps, prostate, skin	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Canada								
Canadian War Veterans' Study	1956	Best *et al.* (1961); Lossing *et al.* (1966)	1956–62	92 000 war veterans (78 000 men, 14 000 women), aged 55–79 years	Postal questionnaire	Deaths	Lung, urinary bladder, pancreas	
National Breast Screening Study (NBSS)	1980–85	Friedenreich *et al.* (1993); Terry *et al.* (2002)	1980–93	Multicentre randomized controlled trial of mammography screening for breast cancer in almost 90 000 women, aged 40–59 years	Self-administered questionnaire	Cases	Breast, endometrium	Friedenreich *et al.* (1993) conducted a nested case–control study.
China								
Shanghai Factory Study	1972–73, 1977–78	Chen *et al.* (1997)	1972–93	9351 factory employees (6494 men, 2857 women) aged 35–64 years	Interview	Deaths	Lung, upper aerodigestive tract (oesophagus), stomach, colon/rectum, liver	Site-specific analyses conducted for men only
Xi'an Factory Study	1976	Lam *et al.* (1997	1976–96	1696 factory employees (1124 men, 572 women) aged ≥ 35 years	Interview	Deaths	Lung, upper aerodigestive tract (oesophagus), liver	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Shanghai Residential Study	1983–84	Gao *et al.* (1999)	1983–94	213 800 residents of urban, suburban and rural areas of Shanghai, aged > 20 years [sex distribution not reported]	Interview	Deaths	Lung, upper aerodigestive tract (oesophagus), stomach, liver	
Linxian Intervention Trial Study	1985	Guo *et al.* (1994)	1985–91	Approx. 30 000 residents of 4 communes in Linxian, aged 40–69 years [sex distribution not reported]	Interview	Cases	Upper aerodigestive tract (oesophagus), stomach	Nested case–control study
Shanghai Men's Study	1986–89	Ross *et al.* (1992); Yuan *et al.* (1996)	1986–93	18 244 male residents of 4 communities in Shanghai, aged 45–64 years	Interview	Cases	Lung, urinary bladder, upper aerodigestive tract (oesophagus, mixed), pancreas, stomach, colon, rectum, liver	Ross *et al.* (1992) conducted a nested case–control study on smoking and risk of colorectal adenomatous polyps.
China, Province of Taiwan								
Taiwanese Study	1982–86	Liaw & Chen (1998)	1982–94	14 397 residents (11 096 men, 3301 women) of Taiwan, aged > 41 years	Interview	Deaths	Lung, urinary bladder, upper aerodigestive tract (nasopharynx, oesophagus, mixed), stomach, colon/rectum, liver, pancreas, cervix	

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ deaths	Neoplasms analysed	Comments
Japan								
Life Span Study	1963, 1968, 1985	Akiba (1994); Land *et al.* (1994); Goodman *et al.* (1995)	1963–87	93 000 exposed survivors of the atomic blasts and 27 000 non-exposed controls [sex distribution not reported]	Postal questionnaire, interview	Cases	Lung, upper aerodigestive tract (nasal cavity and sinuses, larynx, oesophagus, mixed), colon, rectum, liver, breast	
Japanese Physicians' Study	1965	Kono *et al.* (1987	1965–83	5477 male physicians, aged 27–89 years	Self-administered questionnaire	Deaths	Lung, upper aerodigestive tract (oesophagus, mixed), stomach, colon/rectum, liver	
Six-prefecture Study	1965	Hirayama (1967, 1975a,b, 1977a,b, 1978, 1981, 1982, 1985, 1989a,b,c); Mizuno *et al.* (1989); Akiba & Hirayama (1990); Hirayama (1990); Kinjo *et al.* (1998)	1965–81	265 118 subjects (122 261 men, 142 857 women) covering > 90% of the census population from 29 districts, aged > 40 years	Interview	Deaths	Lung, urinary bladder, upper aerodigestive tract (larynx, oesophagus, mixed), pancreas, stomach, colon, rectum, liver, cervix	
Chiba Center Association Study	1984	Murata *et al.* (1996)	1984–93	17 200 male participants in a mass screening for gastric cancer	Self-administered questionnaire	Cases	Lung, urinary bladder, upper aerodigestive tract (mixed), pancreas, stomach, colon, rectum, liver	
Fukuoka Study	1986–89	Mizoue *et al.* (2000)	1986–96	13 270 residents of 4 towns in Fukuoka, aged ≥ 30 years [sex distribution not reported]	Self-administered questionnaire	Deaths	Stomach, liver	Results reported include only men because of the low prevalence of site-specific cancer deaths in women.

Table 2.1 (contd)

Country Name of study	Date of cohort sampling	References	Maximum years of follow-up	Cohort sample and age at beginning of follow-up	Collection of information	Cases/ Deaths	Neoplasms analysed	Comments
Others								
Seven-Country Study	1957–64	Jacobs *et al.* (1999)	25 years	12 763 men from 16 cohorts in Croatia, Finland, Greece, Italy, Japan, the Netherlands, Serbia and the USA, aged 40–59 years	Self-administered questionnaire	Deaths	Lung	
Israel Civil Service Centre Study	1963	Kark *et al.* (1995)	1963–86	9975 male civil servants in Israel, aged 40–69 years	Interview	Cases	Lung	

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