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Cancer incidence among semiconductor and storage device manufacturing workers.

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CANCER INCIDENCE AMONG SEMICONDUCTOR AND STORAGE DEVICE MANUFACTURING WORKERS

by

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A DISSERTATION

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ABSTRACT OF DISSERTATION
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This dissertation had two central goals. The first was to examine and clarify methodologic issues related to retrospective follow-up studies of cancer incidence among occupational groups in the United States. The second was to determine if employment factors were associated with the incidence of any type of cancer among 89,054 International Business Machines employees at a semiconductor facility and a storage device facility.

We used data from studies of microelectronics industry employees to assess methods for developing residential histories, which are required for a cancer incidence investigation, and to determine the relative informativeness of cancer incidence and mortality studies. Use of postemployment residential histories increased person-years by up to 62% and increased the observed number of cancers by up to 28%. The number of observed cancer cases in the incidence study was 60% higher than the number of observed cancer deaths in the mortality study.

We compared employees' incidence rates with general population rates and examined incidence patterns by facility, duration of employment, time since first employment, potential for exposure to workplace environments other than offices, and work activity. Employees had lower than expected incidence for all cancers combined (2,860 observed

cases, standardized incidence ratio = 84, 95% confidence interval = 81-87). Analysis of incidence patterns by potential exposure and by years spent and time since starting in specific work activities did not provide strong or consistent evidence of causal associations with employment factors.

Assumptions about residential history had little impact on validity in the incidence study. Despite geographic and temporal restrictions, incidence studies provide more data than mortality studies on cancers with good survival. Employees had fewer than expected cases of cancer compared to general populations. Incidence was increased for several cancers in some employee groups, but interpretation of these results was difficult because data on employees with long potential induction time and many years worked were sparse and because of potential confounding by nonoccupational risk factors, imprecision, and other limitations. There was no strong and consistent evidence that any form of cancer was associated causally with employment factors.

DEDICATION

This dissertation is dedicated to my parents, Richard and Sandra Bender.

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LIST OF ABBREVIATIONS

CA	California
CI	confidence interval
DMV	department of motor vehicles
IBM	International Business Machine Corporation
MRR	cancer mortality rate ratios
NHL	non-Hodgkin lymphoma
NY	New York
OR	odds ratio
RR	cancer incidence rate ratio
SES	socioeconomic status
SIR	standardized incidence ratio
SMR	standardized mortality ratio
UA	uncertainty analysis
US	United States
VR	voter registration

INTRODUCTION

This dissertation evaluates cancer incidence among employees at semiconductor and storage device manufacturing facilities. It also investigates methodologic issues related to retrospective follow-up studies of cancer incidence among occupational groups in the United States (US).

In the US the semiconductor and storage device manufacturing sectors of the microelectronics industry have undergone rapid and complex expansion since the 1950s and have had a major impact on the economy (1). The semiconductor industry employed 283,875 people in the US in 2000, and semiconductor sales by US companies totaled $102 billion in 2000 or 50% of total worldwide sales (2). The productivity growth in the US in the 1990s was attributable in large part to computer production and to advances in information technology that depended on the semiconductor industry (3, 4).

During the early years of semiconductor and storage device manufacturing, use of chemicals was intense, and workers' handling of chemicals was frequent (5, 6). High-use chemical categories included solvents, acids, alkalis, and metals. Although the potential for workers to be exposed to these agents has declined with the development of engineering controls and with increased use of automated, enclosed processes, concern remains about the possible health effects of past workplace exposures (1, 5-10).

Ten epidemiologic studies (11-24), conducted both in this country and abroad, have investigated the occurrence of spontaneous abortion, reduced fertility, and other adverse reproductive outcomes among semiconductor and other microelectronics industry

workers; however, information on mortality and cancer incidence is limited. Only two small studies have been conducted (25-28). Both were in the United Kingdom. The present study includes 89,054 subjects employed at semiconductor and storage device manufacturing facilities in the US between 1965 and 2000. It is the first major study of cancer incidence in this important industry.

Epidemiologists typically use retrospective follow-up studies of mortality to obtain information on a wide range of chronic diseases among occupational groups. However, incidence data may be of greater value in studies of certain types of cancer, particularly those types associated with relatively long survival (e.g., cancers of the colon, breast, prostate, and bladder and non-Hodgkin lymphoma). Because incidence data include both nonfatal and fatal cancers, incidence studies may provide a more comprehensive and informative assessment of cancer occurrence than mortality studies.

The existing epidemiologic literature does not completely address the methodologic challenges of retrospective cancer incidence studies. Ascertainment of nonfatal cancer cases is difficult in the US because a national cancer registry does not exist. Using a state or regional cancer registry for case ascertainment imposes temporal and geographic restrictions on the study base that are characteristic of the particular registry. Use of registries also requires the development of residential histories to determine the person-time that subjects contribute while living in the registry's catchment area. Case ascertainment through special surveys of individually traced subjects requires considerable time and other resources. Simply locating subjects who have separated from employment can be difficult, nonparticipation may affect validity and precision, and confirmation of self-reported cancers is problematic. Irrespective of the means of case ascertainment, per-

son-time specification for analyses of multiple types of cancer is an unresolved methodologic issue. This dissertation reviews current practices and proposes contemporary approaches for meeting these challenges based upon analyses of the data collected for the cancer incidence study of semiconductor and storage device manufacturing workers, described in the first paper of this dissertation, and its companion mortality study.

Background

Semiconductor and storage device manufacturing.[1] Semiconductor manufacturing involves the creation of electronic devices on the surface of a thin circular disc of silicon. Silicon's conductive properties allow for the creation of electronic on/off switches that indicate a value of one or zero in a computer's binary language. Hundreds of complex processing steps build the switches and connect them into circuits, millions of which can be placed on a single chip. The exact nature and number of steps needed to manufacture a semiconductor chip varies with its design and complexity, but the basic process remains the same.

Manufacturing processes involve many chemicals, physical agents, and tools, and there is potential for exposure associated with each process. In brief, ultrapure silicon is processed into cylinders that are sliced into thin, five- to eight-inch-diameter wafers on which hundreds of individual computer chips can be made. The wafers are cleaned, inspected, and placed in high temperature furnaces, where they are coated with nonconducting oxide film. A thin layer of light-sensitive plastic, called photoresist, is applied over the oxide. A glass "mask," containing the chip's circuit pattern, is placed over the

[1] The description of the manufacturing processes is based on direct observations of the workplace and unpublished documentation furnished by the International Business Machines Corporation (IBM).

wafer and precisely aligned. In a process called photolithography, ultraviolet light or an X-ray beam is projected through the mask to print each chip's circuit pattern on the wafer surface. Exposure of the photoresist causes polymerization (hardening) in some areas but not in others.

The photoresist that has not been hardened is washed away in solvent baths, exposing the oxide layer with the shape of the circuit pattern. Using either a wet or dry etch method, holes also are etched in the oxide layer. The wafer is then bombarded with ions (electrically charged particles) that penetrate the holes etched in the oxide surface. The depth and concentration of these materials ("dopants") determine the specific electrical characteristics of the chip. The processes of oxidation, photolithography, etching, and ion implanting are repeated to build transistors and other electronic circuitry that make up each chip.

Once the electronic components have been implanted in the silicon, interconnecting wiring is added to the chip by placing the wafer in a vacuum chamber and coating it with copper mixed with aluminum or other metals. The aluminum is etched away, leaving the desired wiring. A thin layer of material is added to protect the wafer. The wafer is then cut into individual chips by diamond-bladed saws and mounted in metal or plastic packages, called modules. These modules are tested, inserted into printed circuit boards, and eventually become part of a computer or computer system.

Storage device manufacturing mainly involves the development, production, and packaging of hard drives, network servers, magnetic tapes, and, more recently, microdrives. The production of hard drives entails head manufacturing, disk manufacturing, and head-disk-drive assembly. The manufacture of magnetic heads consists of the crea-

tion of integrated circuits on the surface of man-made garnet wafers by several processes, similar to those in semiconductor manufacturing. The wafers are then sliced, polished, and cut into individual heads. The heads are placed on a suspension mechanism and stacked together, enabling their assembly into a drive. Disks are manufactured from aluminum or glass substrates that can be magnetized to create peaks and valleys. The disks are tested by writing on them to ensure that all areas on the disk can be read. Next, the disks and the heads, along with a controller card and electrical connections, are assembled and encased in a plastic shell. With the exception of the head and the disk, all other components of hard drives usually are purchased from vendors.

The separation of components and the width of connections in many semiconductors and storage devices is microscopic, and so many of the semiconductor and storage device manufacturing steps described above must take place in the particle free environment of a "clean room." A clean room creates an environment wherein the humidity, temperature, and contamination are controlled precisely. Clean rooms are rated by the number of dust particles 0.5 μ or more in diameter contained in one cubic foot of air. Usual designations in increasing order of cleanliness are Class 10,000, Class 1,000, Class 100, Class 10, and Class 1. Temperature and humidity control also increases with class rating: a typical specification for a Class 1 space is 70°F ± 0.5°F and 50% relative humidity ± 5%.

The semiconductor and storage device manufacturing industries have undergone rapid technological advances, with concomitant changes in processes and in work environments. Concerns about occupational exposures center on the clean room environment and on the wide variety of agents that have been used in clean room processes. Clean

room and other semiconductor and storage device manufacturing employees have potential exposure to solvents, acids, metals, caustics, gases, dopants (e.g., arsenic, phosphorous, or boron), photoresists (e.g., polymethylmethacrylate and diazonapthoquinone-novolak), and physical agents including ionizing and nonionizing radiation. Some of these agents such as arsenic, chromium, dichlorobenzene, isopropyl alcohol, tetra and trichloroethylene, trichloroethane, ionizing radiation, and sulfuric acid are established or suspected carcinogens and may, under certain exposure conditions, produce acute or chronic respiratory, neurological, and other medical effects. However, it is not known whether actual exposures in the industry have been high enough to have any, or a detectable, impact on the occurrence of cancer or other chronic diseases among employees. Other agents, including glycol ethers and fluorides, are suspected causes of adverse reproductive outcomes, including spontaneous abortion, reduced fertility, and congenital malformations. A large amount of information is available on the occurrence of spontaneous abortion among semiconductor industry workers. In contrast, as noted earlier, relatively little is known about the occurrence of cancer and other chronic diseases.

Mortality and cancer incidence among semiconductor workers. The first study was reported in 1985 (26) and updated in 1992 (27) and again in 2004 (28). This study assessed mortality and cancer incidence among 1,807 semiconductor workers in the United Kingdom. The follow-up period of the most recent update was 1970 through 2002 for mortality and 2001 for cancer incidence. The original study was prompted by the occurrence of several skin cancers among employees, and it sought to determine if these cases might have been due to exposure to ultraviolet radiation in the photolithography

process. In the original report, workers had 52 observed compared to 73 expected deaths when compared to the general population of England and Wales (standardized mortality ratio (SMR) = 71, 95% confidence interval (CI) = 53-93) and had 25 observed/27 expected cancer deaths (SMR = 91, 95% CI = 59-135). In the first update, workers had 107/149 deaths (SMR = 72, 95% CI = 59-87) and had 46/58 cancer deaths (SMR = 79, 95% CI = 58-105). Cancer incidence data indicated 93/97 total cancer cases (standardized incidence ratio (SIR) = 96, 95% CI = 77-118) and 3/1.5 cases of melanoma. In the more recent update, workers had 307/385 deaths (SMR = 80, 95% CI = 71-89), 111/145 cancer deaths (SMR = 77, 95% CI = 63-92), and 239/240 cancer cases (SIR = 100, 95% CI = 87-113). The observed number of cases was higher than the expected number for cancer of the rectum (19/10) and melanoma of the skin (12/6) among all workers and cancer of the pancreas among women (10/4).

McElvenny et al. evaluated mortality during 1970-1999 and cancer incidence during 1970-1998 among 4,388 workers at another semiconductor facility in Scotland (25). Compared to the Scottish population, workers had a 34% deficit of deaths from all causes combined (71/108, SMR = 66, 95% CI = 51-84) and had 29 observed and 31 expected cancer deaths (SMR = 94, 95% CI = 63-134). There were 79 observed and 73 expected incident cancers (SIR = 108, 95% CI = 66-135). The observed number of cases was higher than the expected number for cancers of the lung (13/6.0), stomach (3/1.4), and female breast (20/16). There were 4 observed and 4.1 expected cases of melanoma of the skin. Men had more than expected cases of brain cancer (3/0.8); results for brain cancer were not reported for women.

Beall et al. conducted a case-control study of 149 decedents with a primary malignant intracranial neoplasm among US employees of International Business Machine Corporation (IBM) who died in 1975 through 1989 and who were active in 1968 or later (29). Of these 149 cases, 38 also were included in the present investigation. The odds ratio (OR) for all primary malignant intracranial neoplasms combined was slightly increased for subjects ever employed as engineers and technicians (OR = 1.2, 95% CI = 0.8-1.9), and the OR was 1.9 (95% CI = 1.0-3.6) for subjects employed for 10 years or more as engineers or technicians. This study did not include a separate evaluation of the risk of primary malignant intracranial neoplasms among workers at semiconductor manufacturing facilities.

Reproductive health among semiconductor workers. Ten studies evaluated the association between work in the microelectronics industry and spontaneous abortion or early fetal death, reduced fertility, and other adverse reproductive outcomes (11-24). Some of these studies reported that fabrication work (12, 13, 16-18, 21, 22), work in photolithography (12, 14, 17, 22), and potential exposure to ethylene glycol ethers (11, 12, 16, 17, 21-23) are weakly associated with spontaneous abortion and subfertility. However, not all studies found positive associations, and the interpretation of the positive results is uncertain because workers were potentially exposed to many agents, and, in one positive study, nonmanufacturing workers, with no chemical exposure, had an elevated risk of spontaneous abortion (16, 17, 21).

One of the studies that investigated spontaneous abortion in relation to work in the semiconductor industry also considered congenital malformations as an outcome of

interest (16), largely because toxicologic research has found that certain glycol ethers are teratogenic (30, 31). Although these investigations were informative with regard to common adverse reproductive outcomes such as spontaneous abortion, they were too small to provide useful information on congenital malformations. This is because the occurrence of spontaneous abortion in the general population is frequent (7-50% of all pregnancies end in spontaneous abortion), whereas the occurrence of congenital malformations is rare (2-5% of all live births have a congenital malformation) (32). Thus, current evidence is insufficient to determine whether occupational exposure to glycol ethers causes congenital malformations (33).

Other medical conditions among semiconductor workers. Pastides et al. examined general illness symptoms in a cross-sectional study of 744 semiconductor workers (14). The prevalence of self-reported symptoms was higher among women in photolithography than among women who were unexposed.

A cross-sectional study, sponsored by the Semiconductor Industry Association and conducted in the late 1980s, examined respiratory symptoms, dermatologic symptoms, headache, nausea, and musculoskeletal symptoms among 3,175 semiconductor fabrication workers (34, 35). Fabrication workers reported a variety of symptoms more frequently than nonfabrication workers. However, the symptoms were nonspecific, they did not cluster within any specific work group, and they did not seem to involve exposure to particular agents.

A cross-sectional study in Taiwan examined lung function among 246 semiconductor workers (36). Workers in photolithography and etching/diffusion experienced lower forced vital capacity when compared to nonfabrication workers.

A small cross-sectional study of 57 US microcircuit development workers assessed markers of neurologic function (37). Compared to nonexposed workers, workers exposed to solvents had neurobehavioral deficits as measured by tests of mood, reaction time, symbol substitution, vibration sensitivity, visual contrast, and grip strength.

Studies of other groups having exposures similar to those of semiconductor workers. Semiconductor fabrication workers are exposed potentially to a variety of solvents, metals, gases, and radiation. Some of these agents have been evaluated in other occupational groups. For example, the possible carcinogenic and neurological effects of solvents have been studied in aerospace workers, in dry cleaners, and in a variety of other manufacturing groups. The International Agency for Research on Cancer has classified trichloroethylene and tetrachloroethylene, both of which have been used historically in the fabrication of semiconductors, as possible human carcinogens (38). Arsenic is used in the doping of semiconductors and as a component of the substrate (i.e., gallium arsenide wafers). The International Agency for Research on Cancer has determined that inorganic arsenic compounds are skin and lung carcinogens (39). Recent studies of occupational and environmental arsenic exposure support this conclusion (40-50). Chromium is used in several stages of semiconductor manufacturing, from the making of masks to the terminal metals operations. The International Agency for Research on Cancer has determined that soluble hexavalent chromium is a definite human respiratory system carcino-

gen (51). Recent studies support this determination (40, 52-60), and one has suggested that insoluble trivalent chromium compounds also may be carcinogenic (55). The International Agency for Research on Cancer has classified ionizing radiation as a definite human carcinogen (61) and low-frequency magnetic fields as possible human carcinogens, based primarily on residential studies involving children (62). Low frequency electric fields have not been classified as human carcinogens (62). Most other forms of nonionizing radiation have not been evaluated for carcinogenic potential. It is not known if semiconductor industry workers have had exposures to any of the above-mentioned agents that were high enough to cause cancer or other chronic diseases.

The microelectronics industry employs many software engineers and computer programmers. In a recent hospital-based case-control study of occupation and glioma, De Roos et al. found that computer programmers and analysts had an elevated incidence of glioma (OR = 2.4, 95% CI = 1.0-3.8) (63). The association was restricted to men, and it was larger among men who had worked as programmers for 5 years or more (OR = 3.8, 95% CI = 1.2-12.3).

Retrospective follow-up studies of cancer incidence among occupational groups. Retrospective investigation of cancer in occupational groups is advantageous because of the long induction period characteristic of most types of cancer. Retrospective follow-up studies of cancer incidence may be of greater value than mortality studies for cancers associated with relatively long survival (e.g., cancers of the colon (63.0% 5-year survival, 1992-1999), breast (87.9%), prostate (98.4%), and bladder (82.6%) and non-Hodgkin lymphoma (57.2%)) (64). Research in this country and abroad consistently indicates that

cancer incidence studies are more informative than mortality studies for cancers associated with long survival because of the ability to identify both nonfatal and fatal cases (65-72). In studies with follow-up periods of similar length for mortality and cancer incidence, the number of cases of all types of cancer is about 1.5 to 2.0 times greater than the number of cancer deaths (65-67, 69, 70, 72). However, even in studies with cancer incidence follow-up periods that are as much as 20 years shorter than the mortality follow-up periods, cancer cases will often exceed the number of cancer deaths (68, 71). The advantages of incidence over mortality studies may be particularly strong for studying the relatively young workforce that characterizes the semiconductor manufacturing industry, which has been in existence only for the last several decades.

Despite the advantages of retrospective follow-up studies of cancer incidence, few such investigations have been done in the US (73-79) because of methodologic difficulties. Retrospective case ascertainment of nonfatal cancer cases is difficult in the US for several reasons. Workers often change their state of residence after they retire or separate from employment. The US does not have a centralized cancer registry that would facilitate the identification of cases among employees in multiple states, and there is not a uniform mechanism for conducting record linkage with all existing registries. The North American Association of Central Cancer Registries has member registries in all 50 states, the District of Columbia, and Puerto Rico. However, most of these registries are of recent origin, and many do not meet the 98% case ascertainment standard of the Surveillance, Epidemiology, and End Results program of the National Cancer Institute. Although the Surveillance, Epidemiology, and End Results program provides high quality data on incident cancer cases, only five state registries (Connecticut, Hawaii, Iowa, New Mexico, and

Utah) and two regional registries (Detroit and San Francisco-Oakland) have participated in the program since its inception in 1973. The Surveillance, Epidemiology, and End Results program has since added coverage for other selected state and regional registries including four counties in the San Jose-Monterey area south of San Francisco beginning in 1992 and Greater California in 2001. With its expansion in 2001, Surveillance, Epidemiology, and End Results program coverage increased from 14% to 26% of the US population (from about 39 million to nearly 74 million people).

Under circumstances where there is no state or regional cancer registry with a catchment area that includes a study facility, investigators may perform incidence surveys in which cancer information is obtained from interviews with employees or family members, with confirmation from medical records. Studies using special surveys for case ascertainment are seldom done because they require that investigators locate subjects, recruit them to participate in a questionnaire survey, and confirm self-reports of cancer diagnoses. These procedures require considerable time and other resources.

When case ascertainment relies on a cancer registry, it is necessary to develop residential histories and to estimate the person-time contribution of subjects while they are living in the area covered by the registry. If person-time enumeration is inaccurate, selection bias will occur. Other investigators who have used cancer registries to identify cases have described their efforts to develop residential histories (73-76, 79-84). However, only a few conducted analyses to assess the impact of inevitable uncertainties about residential history and person-time at risk (73, 79, 84).

The complexity of developing residential histories, especially for subjects who separated from employment without retiring, stems from the need to use records from

sources other than the employer to obtain residential information. Employer data constitute the main source of residential information on subjects while they are actively working and, if pension data are available, while they are retired. Employees who separate without retiring are the most difficult subjects for determining residential history because employers do not consistently have records of the postseparation residences of such subjects. Sources commonly used to determine postseparation residences include public records from departments of motor vehicles and voter registration rolls. Record linkage with these sources is difficult because it usually is not possible to use social security number to identify matches between subjects and people with records in the source database. Also, it is possible that reliance on such sources could lead to the selective inclusion in the study of cancer-free person-time. This is because diagnosis of cancer may be followed by death, and deceased subjects are less likely to have records from departments of motor vehicles and voter registration rolls than are living subjects. Data available from various private vendors of residential information, such as LexisNexis, have not been used widely in epidemiology other than for small studies (76, 77). Finally, death certificate information indicating the place of residence at the time of death has been used in some studies as a source of residential information, despite the possible selection bias inherent in such use. Some investigators have opted to avoid the complex task of developing residential histories by excluding the postseparation person-time of separated employees. The existing literature on cancer incidence studies does not thoroughly address the utility or pitfalls of the above information sources for determining residential history.

Irrespective of how cases are detected, proper analytic procedures for subjects who are cases, and especially for subjects with multiple primary cancers, are a matter of

debate. Options include counting a case's person-years of follow-up only until the first cancer diagnosis date in all analyses and excluding all second or subsequent primary cancers; counting a case's person-years until the diagnosis date in analyses of the particular type of cancer experienced by the case but leaving the case under follow-up in analyses of other types of cancer; or counting all of a case's person-years until death, loss to follow-up, or the closing date of the study. Other investigators truncated follow-up of cases on their diagnosis dates but did not report how their results would have differed had cases been allowed to remain under follow-up (76, 79, 80, 82, 85-87). Tsai et al. allowed cases to remain under follow-up after their diagnosis dates, and they also performed, but did not present findings for, an uncertainty analysis that truncated follow-up for cases on their diagnosis dates (84).

Overview of Dissertation Research

A central goal of this dissertation was to examine and clarify methodologic issues related to retrospective follow-up studies of cancer incidence among occupational groups in the US. Drawing on data from a study of cancer incidence, presented in the second part of the dissertation, and its companion mortality study that included the same workers (88), the objectives of this part of the dissertation were 1) to evaluate the completeness and accuracy of information sources used to develop residential histories, 2) to assess the impact on validity and precision of different procedures and assumptions used to develop residential histories, 3) to evaluate variation in the impact of follow-up restrictions among subcohorts specified on the basis of work activity, 4) to describe the relative informativeness of a recently completed cancer incidence study and a companion mortality study for

specific types of cancer, and 5) to evaluate different procedures that address person-time specification for subjects who experienced multiple primary diagnoses of one or more types of cancer.

Another goal was to evaluate cancer incidence among 89,054 employees at IBM's semiconductor manufacturing facility in East Fishkill, New York, and storage product device manufacturing facility in San Jose, California. The dissertation includes the first large investigation of cancer incidence in the semiconductor and storage device manufacturing sectors of the microelectronics industry. The purpose was to determine if patterns of cancer incidence were related to employment in the industry as a whole, in either of the two facilities, or in groups with particular work activities.

METHODOLOGIC ISSUES IN FOLLOW-UP STUDIES OF CANCER INCIDENCE AMONG OCCUPATIONAL GROUPS IN THE UNITED STATES

by

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Abstract

PURPOSE: Incidence studies of occupational factors and cancer in the United States are problematic because the use of population-based registries to identify cases requires development of historical data on subjects' residences and often severely restricts the time period of follow-up. This paper describes procedures for addressing these challenges.

METHODS: We used data from studies of cancer incidence and mortality among microelectronics industry employees to assess various methods for developing residential histories and the relative informativeness of the two studies.

RESULTS: We developed residential histories for 98% of 99,229 mortality study subjects. Analyses making alternative assumptions about residential histories yielded standardized incidence ratios varying by at most 6%. Use of postemployment residential histories increased person-years by up to 62% and increased the observed number of cancers by up to 28%. The proportion of mortality study person-years included in the cancer incidence study ranged from 40% to 77% among work activity subcohorts. The number of observed cancer cases in the incidence study was 60% higher than the number of observed cancer deaths in the mortality study.

CONCLUSIONS: Assumptions about residential history had little impact on validity. Use of information sources with national coverage to develop residential histories increased the incidence study's precision. Despite geographic and temporal restrictions, incidence studies provide more data than mortality studies on cancers with good survival. However, the potential for selection bias in incidence studies may vary considerably among subcohorts, indicating the need for cautious interpretation of such research.

Introduction

Follow-up studies of cancer incidence are potentially more comprehensive and informative than mortality studies but may pose several challenges (1, 2). Most incidence studies use record linkage with cancer registries to identify cases because obtaining incidence data directly from large numbers of subjects is problematic (3-5). Reliance on registries to identify cases requires development of historical data on subjects' residences to compute person-time at risk accurately because cancer registry coverage in the United States (US) is temporally and geographically limited (6, 7). This paper evaluates the completeness and accuracy of information sources used to develop residential histories, assesses the impact on validity and precision of procedures and assumptions used to develop residential histories, evaluates variation in the impact of follow-up restrictions among subcohorts specified on the basis of work activity, describes the informativeness of a recent cancer incidence study relative to its companion mortality study, and evaluates different procedures that address person-time specification for subjects who experienced multiple primary diagnoses of one or more types of cancer.

Methods

Data came from a mortality study of International Business Machines employees at three microelectronics facilities (8) and a cancer incidence study of employees at two of the three facilities (9). The latter two facilities were located in East Fishkill, New York (NY), and San Jose, California (CA). Electronic databases of personnel records were used to identify subjects and to develop work histories. We classified work histories according to manufacturing activity (15 "work groups" at East Fishkill and 19 at San Jose)

(8, 9). International Business Machines records and record linkage with several national and state databases provided information on vital status. Cause of death information came from death certificates and from the National Death Index. Subjects accumulated person-years of follow-up between the later of January 1, 1965, or the employee's facility hire date and the earliest of the date of loss to follow-up, death date, or December 31, 1999. Standardized mortality ratios compared the mortality rates of employees with the rates of the general population of the states where the facilities were located (10).

Subjects in the cancer incidence study were employees who were in the mortality study (8) and who 1) worked at East Fishkill between 1965 and 1999 and lived in NY at any time between 1976 and 1999 or 2) worked at San Jose between 1965 and 1999 and lived in CA at any time between 1988 and 1999 (9). These eligibility requirements were necessary because of procedures used to identify cancer cases, described later.

Employees' work histories included, for each job, a code indicating the state of employment, which we assumed was the state of residence. For retirees, work histories also contained records with address information for each year of retirement.

For employees who had separated without retiring, work histories provided residential history only during active employment. The postemployment residential histories of these employees came from state departments of motor vehicles (DMVs), voter registration records (VRs), and the EZFIND file from LexisNexis, a private vendor of residential information. Record linkage with DMVs and VRs used matching based on name and birth date. Linkage with LexisNexis records used Social Security number, name, and birth date. DMV and VR records provided one or more addresses and dates of activity (i.e., license issuance, registration). LexisNexis provided current and previous addresses

with associated dates. For decedents, LexisNexis often provided only information on the state of residence at death.

For each subject, we compiled data from all sources into a chronological series of addresses and estimated the dates of entry into and exit from NY or CA (the "facility state"). We assumed that separated employees for whom we had no postemployment residential history left the facility state after their last date of employment (11).

We identified cancer cases through record linkage with the NY State and CA cancer registries. We counted a case if the diagnosis date was between the beginning and ending dates of follow-up for the incidence study, was after starting work at the facility, and occurred when the residential history indicated the subject was living in the facility state (9).

Person-year accumulation began on the latest of the cancer registry inception date (NY, January 1, 1976; CA, January 1, 1988) or the subject's facility hire date and ended on the earliest of the study closing date, the last date of residence in NY or CA, the date of loss to follow-up, or the death date. Between these beginning and ending dates, subjects accrued person-time only while they lived in the facility state. We computed standardized incidence ratios (SIRs) to compare the cancer incidence rates of employees with rates of the facility state general population (10).

To assess the completeness of each external residential history source, we determined the proportion of subjects having a record and the median number of dated addresses in the record. To evaluate each source's accuracy, we compared states from work histories with those from external sources during periods of active employment or retirement. We evaluated the potential for each source to introduce selection bias by determin-

ing if the proportion of subjects having a record in the source differed by race, gender, vital status, age at the end of follow-up, socioeconomic status (SES), employment status, year of first work, year of separation, years worked, and years since first record of employment at the facility. We assigned each subject to one of three SES groups based on salary information for the job in which the subject worked longest (8).

Postemployment residential histories of separated employees had the greatest potential for inaccuracy and required the most effort to produce. We carried out five uncertainty analyses (UAs) to quantify the impact on validity and precision of different assumptions about these residential histories. The main analysis of the incidence study included the postemployment experience of separated workers; UA-A completely excluded this experience. The main analysis assumed that subjects lived continuously in or outside the facility state from one transition to the next; UA-B expanded postemployment follow-up of separated employees to include every person-year except those specific years in which an address *outside* NY or CA occurred, and UA-C restricted postemployment follow-up of separated employees to those specific years in which an address *in* NY or CA occurred. The main analysis allowed subjects to exit and reenter the facility state multiple times; UA-D restricted follow-up to experience before the first NY or CA exit date. The main analysis did not use death certificates to specify residential histories for decedents; UA-E expanded follow-up to include the entire postemployment experience of all employees who died in NY or CA.

To evaluate the impact on validity of the temporal and geographic restrictions imposed by using cancer registries to identify cases, we partitioned the total mortality study person-time into three categories: 1) included in the cancer incidence study; 2) lost from

the cancer incidence study (i.e., accrued before the registry period); and 3) lost (i.e., accrued during the registry period but while subjects were living outside NY or CA). We compared the distribution of mortality study person-time included in the cancer incidence study with the distribution of lost person-time according to selected demographic and employment characteristics. We used Poisson regression to compute cancer mortality rate ratios (MRRs) that compared rates for lost person-time with rates for included person-time. The MRRs provided an indirect assessment of potential bias, assuming that, if cancer mortality rates for lost person-time were similar to rates for included person-time, cancer incidence rates may also be similar for lost and included person-time. MRRs were adjusted for age, race, gender, SES, years worked, years since first record of employment, and, when possible, calendar time. We examined the variation in the proportion of mortality study person-time included in the cancer incidence study by work group.

To evaluate the impact of restrictions on precision, we compared expected number of cancer cases computed for the lost person-time with the expected number for included person-time. To determine expected numbers, we applied gender, race, age, calendar time, and state-specific cancer incidence rates to the corresponding distributions of person-time. To compute expected numbers for the time period before the state registries began, we used the earliest available rates (1976-1979 for NY and 1988-1989 for CA). Finally, to evaluate the informational gain from inclusion of nonfatal and fatal incident cases, we compared the observed number of cancer cases in the incidence study to the observed number of cancer deaths in the mortality study.

We evaluated alternative approaches for person-time specification for subjects who experienced multiple primary diagnoses from one or more types of cancer. This work is described in the Appendix.

Results

Assessment of information sources. Of the 99,229 employees in the mortality study, 96% had LexisNexis records (Table 1). LexisNexis records contained a median of six dated addresses for each subject. The proportion of subjects with DMV records was 47% overall, 60% for San Jose, and 32% for East Fishkill. DMV records contained a median of one dated address. Thirty-four percent of subjects had VR records, containing a median of one dated address. Only 388 subjects (<1% of all subjects) had DMV or VR records and lacked LexisNexis records. The average proportion of a subject's postemployment address records from each source was 77% LexisNexis, 10% DMV, and 13% VR.

Agreement with states listed in work histories during periods of active employment or retirement was 90% for LexisNexis states, 92% for DMV states, and 99% for VR states. Agreement was similar for East Fishkill and San Jose for LexisNexis and VR data but varied by facility for DMV data (83% for East Fishkill and 98% for San Jose subjects).

The proportion of subjects with LexisNexis records varied little by demographic and employment characteristics (Table 2). Having a LexisNexis record was more common among subjects who were alive (97%) at the end of follow-up for the mortality study than among subjects who were deceased (94%) or who had unknown vital status (80%).

The proportion of subjects with a DMV record and the proportion with a VR record also were higher for subjects who were alive than for subjects who had unknown vital status or were deceased. In addition, DMV records were more likely to be available for Hispanics and Asians, for subjects under age 60 years, for production workers, for subjects who separated in the 1990s, and for subjects with 5+ years of employment. VR records were most likely to be available for subjects ages 40-59 years, for professionals and technicians, for active employees, for subjects with 5+ years of employment, and for subjects with 15+ years since first record of employment.

Uncertainty analyses. The alternative assumptions used to specify residential histories for UAs resulted in modest to large changes in the numbers of person-years and cases as compared to the main analysis (Table 3). However, differences between the UAs and the main analysis with regard to SIRs for all types of cancer combined were small. The three analyses that restricted follow-up (Table 3: UA-A, C, and D) included fewer person-years and cases and produced slightly higher SIRs for most types of cancer. The postemployment person-time accrued by separated employees constituted 52% of the total follow-up at San Jose. In the UA that completely excluded this experience, the SIR in the uncertainty analysis for all cancers combined was 6% greater than the SIR in the main analysis (Table 3: A). At East Fishkill, where the postemployment person-time of separated employees constituted 28% of the total follow-up, the same UA produced an SIR for all cancers combined that was only 1% greater than the SIR in the main analysis. Of the analyses that expanded postemployment follow-up of separated employees, the analysis having the greatest impact on SIRs assumed that employees who died in the facility

state spent their entire postemployment residential history in that state (Table 3: E). In this analysis SIRs were higher than those in the main analysis for many types of cancer.

Relative informativeness of cancer incidence and mortality studies. Of the 99,229 mortality study subjects from the two facilities, 89,054 (90%) were eligible for the main analysis of the cancer incidence study. At East Fishkill, the cancer incidence study included 42,612 (94%) of the subjects and 61% of the person-time of the mortality study (Table 4). The person-time distributions of the mortality and cancer incidence studies were similar with regard to median values of calendar year, age, years worked, and years since first record of employment at the facility. Compared to the total mortality study, the cancer incidence study had a lower proportion of person-years among men and in the highest SES group. Most of the mortality study person-time lost from the cancer incidence study occurred during the operational period of the cancer registry but while subjects were living outside NY. If incident cancer cases had been detectable for all mortality study person-time, 3,005 cases would have been expected, which is 59% more than the expected number of cases (N = 1,892) in the cancer incidence study. Comparison of cancer mortality rates pertaining to person-time lost from the incidence study with rates for the included person-time yielded cancer MRRs at East Fishkill of 0.7 (0.5-1.0) for person-time that occurred before the registry period and 0.9 (0.8-1.1) for person-time that occurred during the registry period while subjects were living outside NY (Table 4).

At San Jose, the cancer incidence study included 46,912 (86%) of the subjects and 43% of the person-time of the mortality study (Table 4). The person-time distributions of the mortality and cancer incidence studies were similar with regard to years worked and

years since first record of employment but differed with regard to median values of calendar year (1988 vs. 1994) and age (39 vs. 42). Compared to the mortality study, the cancer incidence study had a higher median value of calendar year and of age and a lower proportion among Whites and men and in the highest SES group. Most of the lost person-time accrued before the registry period. If incident cancer cases had been detectable for all mortality study person-time, 2,925 cases would have been expected, which is 76% more than the expected number of cases (N = 1,496) computed for the cancer incidence study. With the included person-time as the referent, the MRR was 1.1 (0.9-1.3) for person-time that occurred before the registry period and 1.0 (0.9-1.2) for person-time that occurred during the registry period while subjects were living outside CA.

At East Fishkill, the proportion of mortality study person-years included in the cancer incidence study varied by work group from 65% to 77% (Table 5). At San Jose, the proportion of person-years included varied by work group from 40% to 66%.

Comparison of observed numbers of cases in the incidence study with deaths in the mortality study indicated that the number of cases was less than or equal to the number of decedents for types of cancer having poor survival, including cancers of the lung (322 cases vs. 463 decedents), ovary (34 vs. 35), and central nervous system (55 vs. 82) (Table 6). Incident cases outnumbered decedents for types of cancer having good survival, including cancers of the breast (338 vs. 112), prostate (611 vs. 101), bladder (154 vs. 29), and thyroid (44 vs. 9).

Discussion

Investigators in the United States have access to several information sources useful for developing residential histories. A source with national coverage, such as LexisNexis, should provide more complete residential history than state-specific DMVs or VRs, especially for people similar to our subjects who were relatively young, mobile, and of high SES. LexisNexis records contain more information than DMV and VR records, and the accuracy of that information is high and compares favorably with DMV and VR data. The accessibility, record linkage options, and record format also make LexisNexis more useful than DMV or VR data. The effort expended to obtain and process DMV and VR records was not justified in terms of the information yielded.

No residential history sources provided information for every postemployment year, and none provided much information that predated 1990. We are not aware of available data that would provide earlier residential history. Although 14% of subjects with VR records had addresses dated before 1990, VR records were available for a small proportion of our subjects. In any study that does not contact subjects directly, investigators must make assumptions about postemployment residential history that occurred between the last day worked and the earliest address from an external source.

Errors in the residential histories were unavoidable. Most dates of transition into and out of NY or CA were approximate. Inaccuracies in the external information could have occurred because of linkage errors or the external source's delay in recording when subjects moved. Other errors stemmed from assuming that subjects who lacked postemployment addresses did not live in NY or CA after their last date of active employment.

Although our residential histories had limitations, all UAs produced similar results. Alternative approaches that expand or restrict the inclusion of person-time and cases might have a greater impact in a future update or in another study with older subjects and more cancer cases. We would expect a larger difference between the main analysis and the UAs that completely excluded the postemployment experience of separated workers as the proportion of their contribution to total follow-up grows or that used death certificates as a source of residential history as the number of decedents grows.

Among the other investigations that used cancer registries to identify cases and described the development of residential histories (1, 12-20), only a few conducted UAs to evaluate assumptions about postemployment residential history (14, 17, 20). Those studies, like ours, found little impact on results.

Our comparison of cancer mortality rates for person-time included in the cancer incidence study with rates for lost person-time provided minimal evidence of an impact of temporal and geographic restrictions on validity for the overall cohorts from the two facilities. We expected this result at East Fishkill because the cancer incidence follow-up period included most of the mortality study follow-up period. At San Jose, where only 12 years were included in the cancer incidence follow-up, the included person-time and the total mortality study person-time differed with respect to several characteristics, suggesting an effect of the restricted observation period on validity of the incidence results. However, mortality rates for included and lost person-time were similar.

The proportion of mortality study person-years included in the cancer incidence study varied considerably by work group, particularly at San Jose, and the validity of the cancer incidence results also may vary considerably across these subcohorts. A compan-

ion paper describes in more detail the impact on the incidence study of selection bias due to follow-up restrictions (9). In the latter paper, when we found that the relation between a work group and a particular cancer differed in the mortality and cancer incidence studies, we examined the overlap of subjects counted as deaths vs. cases in the studies and determined that most of the differences in the results could be attributable to follow-up restrictions and consequent selection bias in the cancer incidence study (9). Thus, investigators should examine variation in the potential for selection bias due to restricted follow-up across cohort subgroups and should use this information in interpreting the results of cancer incidence studies that rely on cancer registries that do not cover the entire potential follow-up experience of the study group. At present, the only alternative to the reliance on such registries in retrospective studies of cancer incidence is to conduct a survey to identify cancer cases by directly contacting all cohort members. Although methodologically superior, an incidence survey is often not feasible because of difficulties locating cohort members or surrogates, recruiting their participation, and obtaining medical records for case confirmation. Thus, this approach has rarely been used (3-5).

Although cancer registration is being implemented in all states, most registries are of relatively recent origin. The methodologic issues discussed in this paper will persist as challenges for any study of cancer incidence with cohorts established before the inception date of one or more registries.

The number of cancer cases substantially exceeded the number of cancer deaths at both facilities. Although the follow-up period for the cancer incidence study at San Jose was quite limited compared to that for the mortality study, much of the person-time that was lost from the cancer incidence study was accrued before 1988 when most subjects

were young and when there were few cancer deaths or expected cases. The enhanced precision of the incidence study compared to the mortality study depended in part on developing postemployment residential histories, and the UA that eliminated the postemployment experience of separated employees discarded hundreds of cases and thousands of person-years.

Research in this country and abroad consistently indicates that, for cancers for which survival is relatively long, cancer incidence studies are more informative than mortality studies (21-30). In studies with follow-up periods of similar length for mortality and cancer incidence, the number of cases of all types of cancer is 50-100% greater than the number of cancer deaths (23-30). Even in studies with cancer incidence follow-up periods that are as much as 20 years shorter in duration than the mortality follow-up periods, cancer cases can exceed the number of cancer deaths (21, 22). Cancer incidence studies are also better in delineating occupational exposure with a certain subtype of cancer or specific histology (e.g. acute myeloid leukemia, B-cell lymphoma) as this information is often recorded by the registry but absent from death certificates (17).

Based on the data available for this study group, the small differences between SIRs for our main analysis and SIRs for UAs that alternatively removed all cases from follow-up on their first diagnosis date in all analyses or removed cases from follow-up on a cancer-specific basis do not justify the loss of precision and added analytical burden of these analyses (Appendix). Results could differ with a longer follow-up period for this study group or for a different study group.

Many of the challenges we described are specific to conducting cancer incidence studies in the United States. In Canada and several European countries, relying on record

linkage with cancer registries to identify cases does not require temporal restrictions on follow-up because registries have existed for many years (23-30). Furthermore, the national coverage of these foreign registries makes it unnecessary to develop detailed residential histories or to apply geographical restrictions.

In summary, development of optimal residential histories for cancer incidence studies in the United States should use information sources with national coverage. Conducting UAs to examine the limitations of the residential histories and the impact of various assumptions is prudent until there is an accepted standard for developing residential histories. The cancer incidence study had much more precision than our mortality results for evaluating cancers associated with relatively long survival. The temporal and geographic restrictions on our cancer incidence study did not appear to affect the validity of the results for the overall analysis, but the potential for selection bias varied considerably by work group subcohort. The proportion of mortality study follow-up included in a cancer incidence study and the overlap of individuals counted as cancer deaths vs. cases should be evaluated critically when interpreting the results for a cancer incidence study. The impact of cancer incidence follow-up restrictions may vary among studies, depending on the age distribution and mobility of the study groups and the relative survival of specific cancers of interest.

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TABLE 1. Number of subjects with records from LexisNexis, departments of motor vehicles (DMV), or voter registration (VR) records and time coverage provided by each source of residential history

	LexisNexis		DMV		VR	
	N	%	N	%	N	%
Any record	95,432	96	47,029	47	33,702	34
Yes	3,797	4	52,200	53	65,527	66
No	99,229	100	99,229	100	99,229	100
Total	95,432	96	47,029	47	33,702	34
Number of dates or dated addresses[a]						
0	2,873	3	103	0	0	0
1-4	30,447	32	45,615	97	25,319	75
5-9	54,956	58	1,276	3	6,764	20
10+	7,156	7	35	0	1,619	5
Total	95,432	100	47,029	100	33,702	100
Median (Range)	6 (0-16)		1 (0-15)		1 (1-25)	
Number of calendar years in which dates occur[b]						
1	5,927	6	35,219	75	20,708	61
2	11,635	13	8,624	18	1,842	5
3+	74,997	81	3,080	7	11,152	33
Total	92,559	100	46,926	100	33,702	100
Median (Range)	4 (1-10)		1 (1-9)		1 (1-15)	
Time span of dates (years)[b]						
<5	24,790	27	40,280	86	22,041	65
5-9	28,045	30	6,149	13	4,904	15
10-14	30,593	33	421	1	2,806	8
15+	9,131	10	76	0	3,951	12
Total	92,559	100	46,926	100	33,702	100
Median (Range)	8 (1-37)		1 (1-28)		1 (1-37)	
Median year of dates[b]						
<1990	3,016	3	743	2	4,552	14
1990-1994	21,518	23	9,444	20	4,001	12
1995-1999	49,674	54	23,726	51	17,996	53
2000+	18,351	20	13,013	28	7,153	21
Total	92,559	100	46,926	100	33,702	100
Median (Range)	1997 (1969-2001)		1998 (1973-2002)		1998 (1953-2003)	

[a]Among those with records.
[b]Among those with 1 or more dates.

TABLE 2. Number of subjects with records from LexisNexis, departments of motor vehicles (DMV), or voter registration (VR) by selected demographic and employment characteristics and percent of total subjects in each category

Demographic & employment characteristics	Total N	LexisNexis N	%	DMV N	%	VR N	%
Total	99,229	95,432	96	47,026	47	33,702	34
Gender/race or ethnicity							
Men, total	65,125	62,498	96	30,599	47	21,841	34
White	45,153	43,284	96	19,235	43	15,862	35
Hispanic	4,489	4,313	96	2,684	60	1,455	32
Asian	10,715	10,318	96	6,411	60	3,240	30
African American	4,512	4,343	96	2,156	48	1,217	27
American Indian	172	163	95	71	41	43	25
Unknown	84	77	92	42	50	24	29
Women, total	34,104	32,934	97	16,427	48	11,861	35
White	20,130	19,407	96	8,777	44	7,515	37
Hispanic	4,010	3,894	97	2,486	62	1,275	32
Asian	5,480	5,285	96	3,160	58	1,643	30
African American	4,293	4,161	97	1,917	45	1,369	32
American Indian	138	135	98	71	51	44	32
Unknown	53	52	98	16	30	15	28
Vital status[a]							
Alive	89,388	86,791	97	44,995	50	33,156	37
Deceased	5,379	5,074	94	707	13	33	1
Unknown	4,462	3,567	80	1,324	30	513	11
Age[a]							
<40	36,810	35,001	95	17,645	48	10,495	29
40-49	23,629	22,802	97	11,985	51	9,136	39
50-59	20,637	19,978	97	9,706	47	7,822	38
60+	18,153	17,651	97	7,690	42	6,249	34
Socioeconomic status group							
Professionals	38,045	36,456	96	17,257	45	13,800	36
Technicians	9,806	9,486	97	4,084	42	3,544	36
Production	51,378	49,490	96	25,685	50	16,358	32
Employment status[a]							
Active	20,367	19,505	96	9,621	47	8,991	44
Retired	19,305	18,919	98	8,412	44	7,045	36
Separated	59,557	57,008	96	28,993	49	17,666	30
Year first at facility							
<1965-1969	19,874	19,118	96	7,806	39	6,465	33
1970-1979	18,392	17,722	96	8,418	46	6,988	38
1980-1989	32,397	31,168	96	16,006	49	12,104	37
1990-1999	28,566	27,424	96	14,796	52	8,145	29
Median	1984	1984		1984		1982	
Separation date							
1965-1979	11,201	10,469	93	3,882	35	2,814	25
1980-1989	23,722	22,680	96	10,021	42	7,319	31
1990-1999	64,306	62,283	97	33,123	52	23,569	37
Median	1993	1993		1993		1993	

TABLE 2. (Continued)

Demographic & employment characteristics	Total N	LexisNexis N	%	DMV N	%	VR N	%
Years worked at facility[a]							
<1	35,730	33,910	95	16,282	46	10,033	28
1-<5	29,361	28,261	96	13,074	45	8,610	29
5+	34,138	33,261	97	17,670	52	15,059	44
Median	2	2		2		4	
Years since first record of employment at facility[a]							
<15	46,984	44,569	95	22,505	48	13,498	29
15+	52,245	50,863	97	24,521	47	20,204	39
Median	16	16		15		17	

[a]At the end of the mortality study.

TABLE 3. Number of person-years (PY) and cases included in each of several uncertainty analyses, the standardized incidence ratio (SIR) and 95% confidence interval (CI) for all forms of cancer combined, and a summary of the changes in the uncertainty analysis SIR (SIR_U) compared to the main analysis SIR (SIR_M) for 26 specific types of cancer, by facility

				All forms of cancer combined					Specific forms of cancer with $SIR_U > SIR_M$		Specific forms of cancer with $SIR_U \leq SIR_M$	
Facility, analysis[a]	PY	Change in PY	Change in PY (%)	Cases	Change in cases	Change in cases (%)	SIR, 95% CI	Change in SIR (%)	Number of forms	(+) Change in SIR (% range)	Number of forms	(–) Change in SIR (% range)
Panel 1. East Fishkill & San Jose												
Main	861,520			2,860			84, 81-87					
A.	531,903	– 329,618	– 38%	2,233	– 627	– 22%	86, 83-90	+ 3%	16	2- 21%	8	1- 13%
B.	940,092	+ 78,571	+ 9%	2,923	+ 63	+ 2%	82, 79-85	– 2%	6	1- 4%	18	1- 11%
C.	644,910	– 216,611	– 25%	2,443	– 417	– 15%	85, 81-88	+ 1%	16	1- 10%	8	0- 9%
D.	832,744	– 28,777	– 3%	2,759	– 101	– 4%	84, 81-87	+ 1%	14	0- 5%	10	0- 7%
E.	863,054	+ 1,533	+ <1%	2,927	+ 67	+ 2%	85, 82-89	+ 2%	15	1- 10%	9	<1%
Panel 2. East Fishkill												
Main	499,445			1,541			81, 77-85					
A.	359,560	– 139,885	– 28%	1,309	– 232	– 15%	82, 78-87	+ 1%	14	1- 20%	10	0- 22%
B.	566,377	+ 66,932	+ 13%	1,594	+ 53	+ 3%	79, 75-83	– 2%	6	1- 6%	18	1- 14%
C.	406,686	– 92,760	– 19%	1,393	– 148	– 10%	81, 77-86	+ 0%	11	1- 11%	13	0- 24%
D.	481,193	– 18,252	– 4%	1,490	– 51	– 3%	82, 78-86	+ 1%	16	0- 5%	8	0- 8%
E.	500,748	+ 1,303	+ <1%	1,593	+ 52	+ 3%	83, 79-88	+ 3%	14	0- 24%	10	0- 1%
Panel 3. San Jose												
Main	362,076			1,319			87, 82-92					
A.	172,344	– 189,732	– 52%	924	– 395	– 30%	92, 86-98	+ 6%	20	1- 36%	4	3- 15%
B.	373,714	+ 11,638	+ 3%	1,329	+ 10	+ 1%	86, 82-91	– 1%	7	0- 10%	17	1- 4%
C.	238,225	– 123,851	– 34%	1,050	– 269	– 20%	90, 84-95	+ 3%	16	1- 24%	8	0- 16%
D.	351,551	– 10,525	– 3%	1,269	– 50	– 4%	87, 82-92	+ 0%	13	0- 4%	11	0- 7%
E.	362,306	+ 230	+ <1%	1,334	+ 15	+ 1%	88, 83-93	+ 1%	8	1- 11%	16	<1%

[a]Procedure:

A: Completely excluded the postemployment experience of separated employees.

B: Expanded follow-up to include each year of postemployment experience for separated employees unless they were known to have been living outside the facility state during a specific year.

C: Restricted postemployment follow-up of separated employees to years when they were specifically known to have been living in the facility state.

D: Restricted follow-up to experience prior to employees' first facility state exit date.

E: Assumed that employees who died in the facility state spent their entire postemployment residential history living in the facility state.

TABLE 4. Mortality study person-years included in and lost from the cancer incidence study because of temporal and geographic restrictions imposed by using cancer registries to identify incident cases, by facility

Facility, demographic, & employment characteristics[a]	Included in Incidence	Lost			Total in Mortality
		During RP[b], outside state	Before RP[b]	Total	
Panel 1. East Fishkill					
Person-Years	496,049	212,794	105,118	317,911	813,961
Year	1989	1992	1971	1984	1988
Age	39	41	33	37	38
YRS	4	2	2	2	3
YSF	10	14	3	8	9
White	85%	82%	89%	85%	85%
Male	67%	74%	82%	76%	71%
SES 1	38%	47%	51%	48%	42%
Cancer cases:					
Observed	1,541				
Expected	1,892	964	149	1,113	3,005
SIR	81				
Cancer deaths:					
Observed	630	283	35	318	948
Expected	771	388	67	454	1,226
SMR (95% CI)	82 (75-88)	73 (65-82)	52 (37-73)	70 (63-78)	77 (73-82)
MRR (95% CI)	1.0 (referent)	0.9 (0.8-1.1)	0.7 (0.5-1.0)		
Panel 2. San Jose					
Person-Years	354,097	102,222	360,576	462,798	816,895
Year	1994	1994	1980	1982	1988
Age	42	46	36	38	39
YRS	2	2	2	2	2
YSF	11	16	5	7	9
White	56%	78%	79%	79%	69%
Male	64%	73%	74%	74%	70%
SES 1	39%	53%	50%	51%	46%
Cancer cases:					
Observed	1,319				
Expected	1,496	553	876	1,429	2,925
SIR	88				
Cancer deaths:					
Observed	414	167	249	416	830
Expected	539	205	327	531	1,070
SMR (95% CI)	77 (70-85)	82 (70-95)	76 (67-86)	78 (71-86)	78 (72-83)
MRR (95% CI)	1.0 (referent)	1.0 (0.9-1.2)	1.1 (0.9-1.3)		

[a]Number of person-years; median values and percentages for selected demographic and employment characteristics; observed and/or expected cancer cases, standardized incidence ratio (SIR); observed and expected cancer deaths, standardized mortality ratio (SMR); and cancer mortality rate ratio (MRR) comparing lost person-years to included person-years, adjusted for age, years worked (YRS), years since first record of employment (YSF), race, gender, socioeconomic status (SES), and, when possible, calendar year.
[b]Registry period.

TABLE 5. Number of person-years in the mortality and cancer incidence studies and the proportion of mortality study person-years included in the cancer incidence study, by facility and employment factor

Facility & work group[a]	Person-years A. Mortality Study	B. Cancer Incidence Study	% (B/A)[b]
Panel 1. East Fishkill			
Semiconductor fabrication	327,754	215,366	66
Masking	23,222	17,973	77
Packaging	173,830	125,387	72
Facilities/labs	87,613	57,724	66
Research & development	78,541	51,039	65
Process equipment maintenance	64,096	42,752	67
Test/probe/dicing/slicing/die removal/wire bonding	111,868	73,350	66
Other Manufacturing	65,453	47,340	72
Panel 2. San Jose			
Head fabrication	86,206	54,731	63
Disk manufacturing	70,870	40,869	58
Head wafer/tape head	52,505	34,692	66
Facilities/labs	61,013	26,972	44
Research & development	54,042	24,374	45
Test/slice/dice	75,783	36,027	48
Head suspension/head disk/ assembly/box	166,561	96,470	58
Other manufacturing	104,746	42,249	40
Assembly	134,152	63,432	47

[a]Work groups are not mutually exclusive.
[b]Proportion of mortality study person-years included in the cancer incidence study.

TABLE 6. Observed number of cases of or deaths from specific types of cancer by facility

Type of cancer	East Fishkill		San Jose		Total	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
All cancers	1,541	948	1,319	830	2,860	1,762
Oral cavity, pharynx	32	11	33	12	65	22
Esophagus	7	13	9	20	16	33
Stomach	18	26	23	28	41	54
Colorectum	184	102	148	96	332	196
Liver	8	21	12	18	20	39
Pancreas	37	65	20	42	57	107
Larynx	14	5	12	4	26	9
Lung	199	253	123	210	322	461
Melanoma of skin	45	32	71	14	116	45
Breast	185	56	162	56	347	111
Cervix	20	6	12	2	32	8
Endometrium[a]	29	5	17	1	46	3
Ovary	21	16	13	19	34	34
Prostate	277	48	334	53	611	100
Testis	17	3	13	3	30	6
Bladder	99	22	55	7	154	29
Kidney	55	28	29	19	84	45
Central nervous system	34	40	21	42	55	82
Thyroid	19	2	25	7	44	9
non-Hodgkin lymphoma	74	59	60	42	134	100
Hodgkin lymphoma	25	5	9	5	34	10
Leukemia	35	37	37	34	72	70
Multiple myeloma	21	21	13	17	34	38
Other cancer	86	72	68	79	154	151

[a]Endometrium includes uterus, not otherwise specified.
This table omits soft tissue sarcoma because the mortality study did not consider this form of cancer.

APPENDIX

Introduction

Person-time specification is not only complicated by subjects' residential histories but also by the possibility that subjects may have more than one cancer diagnosis. This Appendix evaluates different procedures that address person-time specification for subjects who experienced multiple primary diagnoses of one or more types of cancer.

Methods

We evaluated alternative approaches for person-time specification for subjects who experienced multiple primary diagnoses from one or more types of cancer. In the main analysis, we allowed cases to continue to accrue person-time after their diagnosis date in all analyses, regardless of the type of cancer. We compared the results from the main analysis to results obtained when we 1) removed all cases from follow-up on their first diagnosis date in all analyses, regardless of the type of cancer being analyzed or 2) removed cases with a particular type of cancer from follow-up for analyses of that type of cancer but allowed such cases to contribute person-years for analyses of other types of cancer.

Results

Removing all cases from follow-up on the first diagnosis date in all analyses had similar effects for East Fishkill and San Jose. The analysis included 1% fewer person-years and 6% fewer cases and yielded an uncertainty analysis standardized incidence ratio for all types of cancer that was 2% lower than the main analysis standardized inci-

dence ratio (Appendix Table 1). The number of specific types of cancer with an uncertainty analysis standardized incidence ratio less than the main analysis standardized incidence ratio was approximately equal to the number of types with an uncertainty analysis standardized incidence ratio greater than the main analysis standardized incidence ratio, and ranges of percent decreases and percent increases were comparable.

In analyses restricting postdiagnosis follow-up for cases in analyses of their particular type of cancer, East Fishkill and San Jose subjects accrued a median of 226 fewer person-years (range: 15-2,326; <1% decrease) than in the main analysis (Appendix Table 1). The analysis included between 3 and 9 fewer cases (1-5% decrease) of those cancers for which at least one subject experienced multiple primary diagnoses of the same type of cancer (oral, colorectal, lung, breast), but the observed number was unchanged for analyses of all other cancers. The uncertainty analysis SIR was equal to the main analysis SIR for most types of cancer.

Discussion

The small differences between standardized incidence ratios for our main analysis and standardized incidence ratios for uncertainty analyses that alternatively removed all cases from follow-up on their first diagnosis date or removed cases from follow-up on a cancer-specific basis do not justify the loss of precision and added analytical burden of these analyses. It is possible that the differences between these SIRs could increase slightly as the study group ages and a larger number of subjects develop multiple cancers. Subjects already diagnosed with cancer may be at higher risk of developing additional cancers than subjects never diagnosed, but attempting to adjust for this heterogeneity in

risk by partitioning first diagnoses from additional diagnoses and person-time at risk for first diagnoses from person-time at risk for additional diagnoses can be problematic. Doing so has the potential of introducing an information bias in external comparisons because registries do not make similar adjustments in computing rates for the general population. Furthermore, given the temporal and geographic restrictions of cancer registries, investigators cannot be certain that the first diagnosis recorded for a subject by the registry was not preceded by a diagnosis that occurred before the registry was operational or outside its catchment area. Other investigators truncated follow-up for cases on their diagnosis dates but did not report how their results would have differed had cases been allowed to remain under follow-up (1-7). Tsai et al. allowed cases to remain under follow-up after their diagnosis dates, and they also performed, but did not present findings for, an uncertainty analysis that truncated follow-up for cases on their diagnosis dates (8).

Conclusion

Truncating person-time for cases on their diagnosis dates serves no useful purpose.

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APPENDIX TABLE 1. Observed number of cases (Obs), standardized incidence ratio (SIR)[a] and 95% confidence interval (CI) for all subjects in the main analysis and in uncertainty analyses that 1) removed all cases from follow-up on their first diagnosis date in all analyses or 2) removed cases with a particular type of cancer from follow-up for analyses of that type of cancer but allowed such cases to contribute person-time for analyses of other types of cancer, by facility

Facility &	Main analysis			Uncertainty analysis #1			Uncertainty analysis #2			
type of cancer	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	Person-years
Panel 1. East Fishkill & San Jose										
Person-years:		861,521			851,141					
All cancers	2,860	84	81-87	2,688	82	79-85				
Oral cavity, pharynx	65	56	43-72	58	52	39-67	62	54	41-69	861,182
Esophagus	16	38	22-62	16	40	23-65	16	38	22-62	861,506
Stomach	41	57	41-77	38	55	39-75	41	57	41-77	861,455
Colorectum	332	90	81-100	303	86	77-97	327	89	80-100	860,247
Liver	19	50	30-78	19	52	31-81	19	50	30-78	861,494
Pancreas	57	77	59-100	54	77	58-100	57	77	59-100	861,473
Larynx	26	49	32-71	25	48	31-72	26	49	32-71	861,423
Lung	322	61	54-68	293	58	51-65	318	60	54-67	860,972
Soft tissue	18	73	43-115	18	74	44-118	18	73	43-115	861,443
Melanoma of skin	116	98	81-118	108	94	77-114	116	99	81-118	860,950
Breast	347	103	92-114	329	100	90-112	338	101	91-113	859,839
Cervix	32	78	53-110	32	79	54-111	32	78	53-110	861,326
Endometrium[b]	46	83	61-111	45	84	61-113	46	84	61-112	861,251
Ovary	34	76	53-107	33	76	52-107	34	76	53-107	861,393
Prostate	611	108	100-117	591	111	102-120	611	111	103-120	859,195
Testis	30	81	55-116	29	79	53-114	30	81	55-116	861,313
Bladder	154	90	76-105	136	84	70-99	154	90	77-106	860,681
Kidney	84	91	73-113	75	85	67-106	84	91	73-113	861,218
Central nervous system	55	93	70-121	55	96	72-124	55	93	70-121	861,415
Thyroid	44	87	63-117	42	84	61-114	44	87	63-117	861,293
non-Hodgkin lymphoma	134	93	78-110	131	94	78-111	134	93	78-110	861,056
Hodgkin lymphoma	34	107	74-149	34	108	75-151	34	107	74-149	861,252
Leukemia	72	84	66-106	66	80	62-102	72	84	66-106	861,295
Multiple myeloma	34	92	64-129	32	91	62-128	34	92	64-129	861,431

[a]The expected number is provided in brackets, without the SIR and the 95% confidence interval, when the observed number and the expected number of deaths were both <5.
[b]Endometrium includes uterus, not otherwise specified.

CANCER INCIDENCE AMONG SEMICONDUCTOR AND STORAGE DEVICE MANUFACTURING WORKERS

by

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Abstract

PURPOSE: Epidemiologic research on cancer among workers in semiconductor and related industries has been limited. We evaluated cancer incidence among 89,054 International Business Machines employees at a semiconductor facility and a storage device facility.

METHODS: We compared employees' incidence rates with general population rates and examined incidence patterns by facility, duration of employment, time since first employment, potential for exposure to workplace environments other than offices, and work activity.

RESULTS: Employees had lower than expected incidence for all cancers combined (2,860 observed cases, standardized incidence ratio = 84, 95% confidence interval = 81-87). Standardized incidence ratios were increased for a number of cancers in certain employee subgroups; however, analysis of incidence patterns by potential exposure and by years spent and time since starting in specific work activities did not provide strong or consistent evidence of causal associations with employment factors.

CONCLUSIONS: Interpretation of the results was difficult because data on employees with long potential induction time and many years worked were sparse and because of potential confounding by nonoccupational risk factors, imprecision, and other limitations. Further follow-up will permit a more informative analysis of cancer incidence in the cohort.

Introduction

Epidemiologic research on cancer among workers in semiconductor manufacturing has been limited (1-4). There have been no epidemiologic studies of storage device manufacturers. We recently carried out a mortality study of 126,836 employees at three facilities owned by International Business Machines (IBM) (5). Two of the facilities, in East Fishkill, New York (NY), and Burlington, Vermont, made semiconductors, and the third, in San Jose, California (CA), made computer hard drives and other electronic storage devices (6). Employees had fewer than expected deaths from all cancers combined and from most specific types of cancer. There was no firm evidence of a causal association between occupational factors and cancer, but several facility- and work activity-specific subgroups had more than expected deaths from central nervous system and prostate cancer and several other cancers.

The present study evaluated cancer incidence among employees at the East Fishkill and San Jose facilities. Investigation of cancer incidence in addition to mortality permitted a more thorough assessment of potential occupational associations for cancers with relatively long survival (7, 8). We did not include the Burlington facility because linkage with the Vermont cancer registry was not feasible.

Methods

To be eligible for the cancer incidence study, an IBM employee must have worked at either facility for at least one day between 1965 and 1999; not been a foreign citizen on temporary assignment; and had records containing information on birth date, gender, race, Social Security Number, IBM hire date, and facility start date (5). In addi-

tion, eligible subjects at East Fishkill had to have lived in NY sometime between 1976 and 1999, and eligible subjects at San Jose had to have lived in CA sometime between 1988 and 1999. The latter eligibility requirements were necessary because of procedures used to identify cancer cases, described later.

We used IBM's electronic personnel files to identify subjects and to develop a detailed work history file for each employee (5). The data on each IBM position held by an employee, since the later of January 1, 1965, or the IBM hire date, consisted of the start and end dates, location (facility) code, division code, division name, department code, department name, job code, and job title.

Assessment of eligibility required development of residential histories (9). The work history file provided residential history for employees who were actively working for IBM or retired and provided residential history during active employment for employees who separated without retiring. Postemployment residential histories of employees who separated without retiring used information from departments of motor vehicles and voter registration records in NY and CA and from private vendors of residential data.

We described in detail elsewhere (5, 6) the development of facility-specific work groups based on division, department, and job assignments; categorization of work activities as "potentially exposed" (i.e., entailing any type of work other than office work) or "unexposed" (i.e., entailing office work only); and assignment of subjects to one of three categories of socioeconomic status (SES).

Information on vital status as of December 31, 1999, came from IBM records and from linkages with the Social Security Administration, the National Death Index, departments of motor vehicles and voter registration records in NY and CA, and several

other sources (5). Cause of death information came from National Death Index (10) or from subjects' death certificates if they died before 1979.

We identified cancer cases through record linkage with the NY State and CA cancer registries. The registries described case reporting as being statewide and population-based beginning in 1976 for NY and in 1988 for CA. We converted International Classification of Diseases for Oncology codes into 9th revision International Classification of Disease codes (11). We counted as cases all invasive cancers plus in situ bladder cancers identified among subjects during 1976-1999 (East Fishkill) or 1988-1999 (San Jose) if the date of diagnosis was between their beginning and ending dates of follow-up for the incidence study and occurred when their residential histories indicated they were living in the facility state.

Cancer incidence analyses considered all subjects and subgroups specified by facility, years since first record of employment, years worked, potential exposure, and work group. External analyses compared employees' cancer incidence rates to the general population rates for the facility state (NY State minus NY City or CA). We also carried out analyses with the general populations of the counties surrounding each facility providing the referent rates. Results were similar to those of analyses using state population rates and are not presented.

External analyses used the standardized incidence ratio (SIR) as the measure of association (12). Person-year accumulation began on the latest of the cancer registry inception date (NY, January 1, 1976; CA, January 1, 1988), the subject's first date of employment at the facility, or the date of entering a particular category of an employment factor and ended on the earliest of the study closing date, the last date of residence in NY

or CA, the date of loss to follow-up, or the death date. Between these beginning and ending dates, subjects accrued person-time only while they lived in the facility state. When there were at least five observed or expected cancer cases, we computed SIRs and exact 95% confidence intervals (CIs) under the assumption that the observed number of cases followed a Poisson distribution.

Internal analyses used Cox regression to obtain maximum likelihood estimates of cancer rate ratios (RRs) for employees with potential exposure compared to unexposed employees and to compute RRs for employees ever, compared to never, exposed in a particular work group at a facility. We also used Cox regression to evaluate the relation between years of work in potentially exposed work groups and specific types of cancer. In all Cox regression analyses, age was the time variable; all exposure variables were time-dependent; and the models controlled for year of birth, gender (except when analyzing gender-specific cancers), race, SES, and, for analyses of work groups, employment (ever vs. never or years) in other work groups.

Results

Of the 99,229 employees in the mortality study who worked at East Fishkill or San Jose, 89,054 (90%) were eligible for the cancer incidence study (Table 1). Of those eligible, 64% were men, and 64% were White. Employees' distribution by SES differed by gender: 46% of men and 21% of women were in SES group 1, 12% of men and 5% of women were in SES group 2, and 42% of men and 74% of women were in SES group 3. Median values were 1984 for first recorded year of work at the facilities, 2.2 for years worked, and 15.0 for years since first recorded work. At the end of follow-up, 92% of

subjects were alive, 4% were deceased, 4% were lost to follow-up, and subjects' median age was 43 years. Person-years of follow-up were 861,521 in total, 499,445 at East Fishkill, and 362,076 at San Jose.

Overall, employees had 2,860 observed compared to 3,418 expected cancer cases (SIR = 84, CI = 81-87) (Table 2). SIRs at the two facilities combined were below 100 for 21 of 24 specific types of cancer; were substantially below 100 for cancers associated with smoking and alcohol except bladder cancer; and were marginally above 100 for breast cancer, prostate cancer, and Hodgkin lymphoma (Table 2, panel 1). Employee subgroups with 15+ years since first work and with 5+ years of employment or with 20+ years since first work and with 10+ years of employment had total cancer rates that were 9-11% lower than expected and did not have any large deficits or excesses of specific types of cancer. In these subgroups, SIRs ranged from 110 to 120 for cancers of the pancreas, breast, prostate, and central nervous system; for melanoma of the skin; and for multiple myeloma.

Analyses of specific cancers by facility indicated that for all cancers combined the SIR was 81 (1,541 observed, CI = 77-85) at East Fishkill and 87 (1,319 observed, CI = 82-92) at San Jose and that the subgroups with many years since hire and long duration of employment had cancer deficits of 3-16% (Table 2, panels 2 and 3). At each facility the subgroups with many years since hire and long duration of employment did not have any large excess or deficit of any type of cancer. In these subgroups, SIRs were slightly elevated and ranged from 110 to 143 for pancreas cancer, breast cancer, non-Hodgkin lymphoma, and multiple myeloma at East Fishkill and from 110 to 129 for melanoma of the skin, non-Hodgkin lymphoma, and cancers of the stomach, prostate, and central nervous

system at San Jose. The only increase that was based on substantial numbers was for prostate cancer at San Jose (all men: 334 observed, SIR = 115, CI = 103-128; men with 15+ years since starting and 5+ years of employment: 243 observed, SIR = 120, CI = 106-136).

SIR analyses indicated that both potentially exposed employees (70% of all subjects) and unexposed employees had cancer incidence rates that were less than or equal to the general population rates for most cancers (Table 3, panel 1). For specific cancers at each facility, no SIR was above 150 among the potentially exposed or approached statistical significance, and none of the corresponding RRs indicated a strong association with potential exposure (all RRs were <2.5).

Appendix B provides the number of subjects and person-years in each work group (Appendix Table 1) and results of SIR and Cox regression analyses for specific cancers for employees ever, compared to those never, in each work group (Appendix Table 2). Tables 4 and 5 present summary data for work groups associated with specific cancers and having at least five observed cases of the cancer of interest, an SIR of 150 or higher, and an RR of at least 1.5. For results meeting these criteria, we examined incidence patterns by years worked and years since starting in the work group.

At East Fishkill, some of the associations meeting the above criteria were limited mainly or entirely to short-term employees in the respective work groups and did not display a duration-response trend (Table 4). These results included masking and lung cancer among women, packaging and cervical cancer, research and development and central nervous system cancer, test/probe/dicing/slicing/die removal/wire bonding and Hodgkin lymphoma, and process equipment maintenance and multiple myeloma. For these three

work groups, results for employees with 15+ years since starting and 5+ years in the group were based on 0, 1, or 2 observed cases, respectively, and expected numbers were below 1.0.

Several other associations at East Fishkill displayed a trend with years spent in a work group (Table 4). These included other manufacturing and cervical cancer (6 observed, SIR = 300, CI = 110-652; RR = 4.7, CI = 1.7-12.7), other manufacturing and endometrial cancer (7 observed, SIR = 195, CI = 78-401; RR = 2.2, CI = 0.9-5.3), and research and development and multiple myeloma (9 observed, SIR = 251, CI = 115-477; RR = 4.1, CI = 1.5-11.1).

The process equipment maintenance work group was associated with central nervous system cancer at East Fishkill (8 observed, SIR = 192, CI = 83-379; RR = 1.5, CI = 0.6-3.5), as in the companion mortality study (5). The excess was concentrated in employees with 15+ years since starting and 5+ years worked (4.0 observed and 0.8 expected), but this duration-response relation was within the limits of chance ($\beta = 0.02$, se = 0.06, p = 0.80).

At San Jose, further examination of several associations indicated that they were limited mainly or entirely to employees with fewer than 5 years in the respective work groups and did not display a duration-response trend (Table 5). These associations included head wafer/tape head and melanoma, research and development and melanoma, head fabrication and ovarian cancer, assembly and bladder cancer, test/dice/slice and central nervous system cancer, and head fabrication and leukemia.

Other associations displayed a positive trend with length of employment in a work group at San Jose but were characterized by sparse data on employees who had both

many years since starting and relatively long duration (Table 5). These included other manufacturing and melanoma (18 observed, SIR = 161, CI = 96-255; RR = 1.7, CI = 0.9-3.1), head fabrication and cervical cancer (6 observed, SIR = 157, CI = 58-342; RR = 7.2, CI = 1.8-27.8), disk manufacturing and endometrial cancer (6 observed, SIR = 361, CI = 132-785; RR = 9.7, CI = 3.3-28.1), and cleanrooms-occasional and testicular cancer (9 observed, SIR = 195, CI = 89-370; RR = 4.5, CI = 1.4-14.8).

Discussion

Our study included large numbers of subjects, person-years, and cases and had several other strengths, including low potential for selection bias and differential information bias, residential histories that permitted the inclusion of person-time after employees stopped working at the study facilities, and the ability to assess nonfatal as well as fatal cancers. We conducted several uncertainty analyses to evaluate assumptions about postemployment residential history, and the consistency of these analyses indicated that our results were robust (9). Internal analyses allowed us to assess potential associations between employment variables and cancer incidence while reducing potential distortion due to confounding and detection bias stemming from the relatively high SES of subjects compared to the general population (13-19). For cancers associated with relatively long survival, the incidence study provided more precision than the companion mortality study (5). For example, there were six times more prostate cancer cases in the incidence study than deaths among East Fishkill and San Jose employees in the companion mortality study and five times more melanoma cases than deaths.

Limitations of the study were subjects' young age, lack of agent-specific exposure information, temporal and geographic restrictions due to the use of state-based cancer registries to identify cases, lack of adequate postemployment residential information predating 1990 (9), lack of information on specific agents in the workplace, and lack of data on nonoccupational confounders. External analyses of many types of cancer may have been positively or negatively confounded by correlates of SES, and internal analyses, while possibly reducing such a problem, could still have been compromised by residual confounding. Our analyses examined thousands of relationships, and some or all observed positive and inverse associations may have been due to chance.

Employees had total cancer incidence rates that were lower than general population rates overall and in subgroups with many years since starting and relatively long duration of employment. These deficits reflected employees' low incidence rates of most cancers related to smoking, alcohol, and nutritional deficits that are inversely correlated with SES.

When compared to the general population, some employee subgroups had small increases in several cancers, including melanoma and cancers of the colon, breast, prostate, and thyroid, which are results consistent with subjects' relatively high SES. SES tends to be associated positively with these cancers because of positive correlations with nonoccupational risk factors, better detection, or both (13-19).

The results of the study do not provide any strong evidence of a causal association between employment factors and cancer. Potential exposure to work environments other than offices was not consistently associated with any type of cancer in both SIR and RR analyses. Most associations with work group were based on small numbers, with insuffi-

cient data to determine if a duration-response relation or a consistent pattern with potential induction time were present. Several work group associations displayed positive duration-response, but the underlying data were limited to short-term employees and/or to employees with short potential induction time. Work group associations observed for lung cancer among women, melanoma, and cancers of the cervix and endometrium could have been due in part to confounding by well-established nonoccupational causes that may not have been completely controlled for in the internal analyses.

The incidence study and its companion mortality study characterized the same study group using similar analytical approaches, but the results differed in many respects. These inconsistencies should not be interpreted as undermining the credibility of either study. Divergent results could be attributed easily to differences in the observed numbers of cancers and person-years in the two studies. Differences appeared to stem mainly from temporal and geographic restrictions on follow-up for the incidence study that resulted in the loss of cases and person-years accrued outside the facility state or before the registry period and variation by work group of the proportion of lost mortality study follow-up (9).

Incidence results for central nervous system cancer at East Fishkill and for prostate cancer at San Jose warrant further consideration because of work group associations seen for these cancers in the companion mortality study (5). The incidence study found a weak association between central nervous system cancer and process equipment maintenance at East Fishkill, but chance could not be ruled out as an explanation for this association. The association was concentrated in the subgroup with many years since starting and long duration of employment, but Cox regression analyses did not find a duration-

response trend. The mortality study found similar, but stronger, association, with a positive duration-response trend. Because of geographic and temporal restrictions, the incidence study included only 67% of mortality study person-years in this work group (9) and 80% of the central nervous system cancer deaths. One of the decedents not included in the incidence study because he died out-of-state had worked about 22 years in process equipment maintenance, and the exclusion of this decedent from the incidence data had a large influence on the duration-response analysis. Although associations with central nervous system cancer might be more reliably assessed with results of the mortality rather than the incidence study, interpretation of both studies was hampered by small numbers.

Although the mortality study found an association between employment in facilities/laboratories and prostate cancer at San Jose (5), the incidence study did not. This difference may be due in part to the incidence study's inclusion in this work group of just 9 of 18 fatal prostate cancers and only 44% of the mortality study person-years (9).

Previous research on two groups of semiconductor industry workers in the United Kingdom have not consistently reported positive findings for any type of cancer (1-4). Nichols and Sorahan found a 50% excess of colorectal cancer cases and a twofold increase in the incidence of melanoma of the skin (3), and McElvenney et al. reported a twofold increase in lung cancer incidence (4). The results of the present study are not consistent with those of the British investigations. Storage device manufacturing workers have not been studied previously.

This study found that IBM employees at East Fishkill and San Jose had fewer than expected cases of cancer compared to general populations. Incidence was increased

for several cancers in some employee groups, but interpretation of these results was difficult because data on employees with long potential induction time and many years worked were sparse, particularly in specific work groups, and because of potential confounding by nonoccupational risk factors, imprecision, and other limitations. There was no strong and consistent evidence that any type of cancer was associated causally with employment factors. Further follow-up will permit a more informative analysis of cancer incidence in the cohort.

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TABLE 1. Number of subjects by selected characteristics for each facility and for all subjects combined

Demographic & employment characteristics	East Fishkill N	(%)	San Jose N	(%)	Total[a] N	(%)
Total	42,612	(100)	46,912	(100)	89,054	(100)
Gender/race or ethnicity						
Men, total	27,946	(100)	29,795	(100)	57,350	(100)
White	23,355	(84)	15,450	(52)	38,543	(67)
Hispanic	696	(2)	3,519	(12)	4,211	(7)
Asian	1,808	(6)	8,683	(29)	10,384	(18)
African American	2,016	(7)	2,007	(7)	4,005	(7)
American Indian	35	(0)	108	(0)	143	(0)
Unknown	36	(0)	28	(0)	64	(0)
Women, total	14,666	(100)	17,117	(100)	31,704	(100)
White	11,047	(75)	7,289	(43)	18,296	(58)
Hispanic	490	(3)	3,371	(20)	3,860	(12)
Asian	651	(4)	4,771	(28)	5,395	(17)
African American	2,408	(16)	1,585	(9)	3,982	(13)
American Indian	27	(0)	93	(1)	120	(0)
Unknown	43	(0)	8	(0)	51	(0)
Vital status						
Alive	38,927	(91)	43,541	(93)	82,019	(92)
Deceased	2,359	(6)	1,200	(3)	3,545	(4)
Unknown	1,326	(3)	2,171	(5)	3,490	(4)
Age at end of follow-up (years)						
<40	15,735	(37)	19,212	(41)	34,858	(39)
40-49	10,716	(25)	11,400	(24)	22,006	(25)
50-59	7,940	(19)	9,317	(20)	17,098	(19)
60+	8,221	(19)	6,983	(15)	15,092	(17)
Median	44		43		43	
Gender & socioeconomic status group						
Men						
Professionals	13,386	(48)	13,232	(44)	26,315	(46)
Technicians	4,435	(16)	2,559	(9)	6,929	(12)
Prod/cler/other	10,125	(36)	14,004	(47)	24,106	(42)
Women						
Professionals	2,827	(19)	4,012	(23)	6,792	(21)
Technicians	1,119	(8)	450	(3)	1,562	(5)
Prod/cler/other	10,720	(73)	12,655	(74)	23,350	(74)
Year first at facility						
<1965	0	(0)	0	(0)	0	(0)
1965-1969	7,840	(18)	6,591	(14)	14,520	(16)
1970-1979	8,315	(20)	7,408	(16)	15,528	(17)
1980-1989	18,002	(42)	12,594	(27)	30,440	(34)
1990-1999	8,455	(20)	20,319	(43)	28,566	(32)
Median	1983		1987		1984	
Years worked at facility						
<5	25,110	(59)	32,625	(70)	57,321	(64)
5+	17,502	(41)	14,287	(30)	31,733	(36)
Median	3.1		1.6		2.2	

TABLE 1. (Continued)

Demographic & employment characteristics	East Fishkill N	(%)	San Jose N	(%)	Total[a] N	(%)
Years since first record of employment at facility						
<15	18,347	(43)	26,605	(57)	44,649	(50)
15+	24,265	(57)	20,307	(43)	44,405	(50)
Median	15.9		11.4		15.0	
Employment status						
Active	11,048	(26)	8,378	(18)	19,243	(22)
Retired	9,893	(23)	6,989	(15)	16,731	(19)
Separated	21,671	(51)	31,545	(67)	53,080	(60)
Exposure category						
Exposed, ever	31,686	(74)	31,133	(66)	62,535	(70)
Unexposed	10,391	(24)	15,221	(32)	25,430	(29)
Person-years	499,445		362,076		861,521	

[a]Total is less than the sum of the number of employees at each facility because 470 subjects worked at both facilities.

TABLE 2. Observed number of cases (Obs) of specific types of cancer, standardized incidence ratio (SIR)[a] and 95% confidence interval (CI) among all subjects, those with 15+ years since first record of employment (YSF) and 5+ years worked (YRS), and those with 20+ YSF and 10+ YRS, by facility

Facility & type of cancer	All subjects			15+ YSF, 5+ YRS			20+ YSF, 10+ YRS		
	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI
Panel 1. East Fishkill & San Jose									
All cancers	2,860	84	81-87	1,580	89	84-93	1,086	91	86-96
Oral cavity, pharynx	65	56	43-72	35	60	42-83	18	47	28-75
Esophagus	16	38	22-62	11	45	22-80	9	53	24-101
Stomach	41	57	41-77	27	68	45-99	22	83	52-126
Colorectum	332	90	81-100	200	95	83-109	135	96	81-114
Liver	20	48	29-74	8	37	16-72	3	20	4-59
Pancreas	57	77	59-100	40	94	67-128	33	116	80-162
Larynx	26	49	32-71	18	59	35-93	11	55	27-98
Lung, Men	256	59	52-66	173	64	55-75	125	68	56-81
Lung, Women	66	71	55-90	28	72	48-104	18	77	46-122
Soft tissue	18	73	43-115	7	71	28-146	4	65	18-167
Melanoma of skin	116	98	81-118	56	107	81-140	40	120	85-163
Breast	347	103	92-114	113	105	86-126	63	110	85-141
Cervix	32	78	53-110	7	84	34-173	1	[3.7]	-
Endometrium[b]	46	83	61-111	17	86	50-138	11	101	50-180
Ovary	34	76	53-107	14	106	58-178	7	101	41-208
Prostate	611	108	100-117	445	114	103-125	331	113	101-126
Testis	30	81	55-116	4	61	17-156	2	[2.9]	-
Bladder	154	90	76-105	98	93	76-114	71	98	76-124
Kidney	84	91	73-113	41	81	58-110	28	82	55-119
Central nervous system	55	93	70-121	27	107	71-156	18	113	67-178
Thyroid	44	87	63-117	11	77	39-139	5	63	20-146
non-Hodgkin lymphoma	134	93	78-110	70	104	81-131	47	107	79-142
Hodgkin lymphoma	34	107	74-149	7	96	39-197	2	[4.0]	-
Leukemia	72	84	66-106	36	85	59-117	25	89	58-132
Multiple myeloma	34	92	64-129	22	106	67-161	16	115	66-187
Other cancer	136	61	51-72	65	62	48-79	41	60	43-82

TABLE 2. (Continued)

Facility & type of cancer	All subjects Obs	SIR	95% CI	15+ YSF, 5+ YRS Obs	SIR	95% CI	20+ YSF, 10+ YRS Obs	SIR	95% CI
Panel 2. East Fishkill									
All cancers	1,541	81	77-85	822	84	79-90	535	85	78-93
Oral cavity, pharynx	32	51	35-72	20	64	39-99	8	42	18-83
Esophagus	7	27	11-56	5	34	11-78	4	41	11-105
Stomach	18	45	27-71	10	46	22-84	7	50	20-104
Colorectum	184	83	72-96	112	90	74-108	73	92	72-116
Liver	8	47	20-92	4	41	11-106	2	31	4-111
Pancreas	37	83	59-115	28	112	74-162	23	143	91-214
Larynx	14	40	22-67	11	58	29-103	7	60	24-123
Lung, Men	159	60	51-70	90	57	46-70	60	59	45-76
Lung, Women	40	73	52-100	17	74	43-119	9	66	30-126
Soft tissue	8	54	24-107	1	17	0-97	1	[3.4]	-
Melanoma of skin	45	83	61-111	22	94	59-142	15	107	60-176
Breast	185	104	89-120	66	114	88-145	39	126	90-173
Cervix	20	95	58-147	2	[4.1]	-	0	[1.8]	-
Endometrium[b]	29	90	61-130	10	88	42-161	6	96	35-208
Ovary	21	86	53-131	9	121	55-230	3	[3.9]	-
Prostate	277	101	89-113	202	107	93-123	142	102	86-120
Testis	17	69	40-111	1	[4.2]	-	1	[1.7]	-
Bladder	99	93	75-113	61	97	74-125	42	102	74-138
Kidney	55	101	76-131	29	98	66-141	19	99	60-155
Central nervous system	34	94	65-132	14	94	52-158	9	102	46-193
Thyroid	19	71	43-111	4	53	14-135	1	[4.2]	-
non-Hodgkin lymphoma	74	94	74-118	36	98	69-136	25	110	71-162
Hodgkin lymphoma	25	114	74-169	5	110	36-256	0	[2.2]	-
Leukemia	35	70	49-98	15	62	35-103	11	73	36-131
Multiple myeloma	21	103	64-157	13	114	61-196	9	123	56-234
Other cancer	78	69	54-86	35	64	45-90	19	57	34-88

TABLE 2. (Continued)

Facility & type of cancer	All subjects Obs	SIR	95% CI	15+ YSF, 5+ YRS Obs	SIR	95% CI	20+ YSF, 10+ YRS Obs	SIR	95% CI
Panel 3. San Jose									
All cancers	1,319	87	82-92	758	94	88-101	551	97	89-105
Oral cavity, pharynx	33	62	43-87	15	55	31-91	10	53	25-97
Esophagus	9	56	26-107	6	61	23-133	5	70	23-162
Stomach	23	71	45-106	17	96	56-154	15	120	67-198
Colorectum	148	101	85-118	88	103	83-127	62	102	78-130
Liver	12	49	25-86	4	33	9-84	1	12	0-66
Pancreas	20	68	42-106	12	69	36-121	10	80	39-148
Larynx	12	64	33-112	7	62	25-127	4	48	13-122
Lung, Men	97	57	46-69	83	75	60-93	65	79	61-100
Lung, Women	26	68	44-99	11	69	34-123	9	93	42-176
Soft tissue	10	99	47-182	6	144	53-314	3	[2.8]	-
Melanoma of skin	71	111	87-140	34	119	82-166	25	129	84-190
Breast	162	102	87-119	47	94	69-125	24	92	59-136
Cervix	12	59	31-104	5	118	38-275	1	[1.9]	-
Endometrium[b]	17	73	43-117	7	84	34-174	5	108	35-252
Ovary	13	65	35-111	5	87	28-202	4	[3.0]	-
Prostate	334	115	103-128	243	120	106-136	189	123	106-141
Testis	13	106	56-181	3	[2.3]	-	1	[1.2]	-
Bladder	55	85	64-111	37	87	61-120	29	92	62-132
Kidney	29	77	52-111	12	57	29-99	9	60	27-114
Central nervous system	21	91	56-139	13	126	67-215	9	127	58-241
Thyroid	25	105	68-155	7	106	43-219	4	[3.8]	-
non-Hodgkin lymphoma	60	91	69-117	34	110	76-154	22	104	65-158
Hodgkin lymphoma	9	90	41-170	2	[2.7]	-	2	[1.7]	-
Leukemia	37	103	73-142	21	115	71-175	14	109	60-183
Multiple myeloma	13	79	42-135	9	96	44-183	7	105	42-217
Other cancer	58	53	40-68	30	60	40-85	22	64	40-97

[a]The expected number is provided in brackets, without the SIR and the 95% confidence interval, when the observed number and the expected number of cases were both <5.
[b]Endometrium includes uterus, not otherwise specified.

TABLE 3. Observed number of cases (Obs) of specific types of cancer, standardized incidence ratio (SIR)[a] and 95% confidence interval (CI) among all subjects who were unexposed, ever exposed, and exposed with 15+ years since first exposure (YSF) and 5+ years of exposure (YRS), and rate ratio (RR)[b] and 95% CI for exposed compared to unexposed, by facility[c]

Facility & type of cancer	Unexposed			Exposed			Exposed, 15+ YSF, 5+ YRS			Ever Exposed	Exposed, 15+ YSF, 5+ YRS
	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	RR, 95% CI	RR, 95% CI
Panel 1. East Fishkill & San Jose											
Oral cavity, pharynx	17	55	32-88	46	56	41-74	22	60	37-90	1.1, 0.6-1.9	0.8, 0.3-2.0
Esophagus	6	59	22-128	9	29	13-56	5	31	10-73	0.6, 0.2-1.6	0.8, 0.2-3.3
Stomach	8	43	19-85	32	61	42-86	19	75	45-116	1.6, 0.8-3.5	2.5, 1.0-6.4
Colorectum	85	88	70-109	238	90	79-102	136	101	85-120	1.1, 0.8-1.4	1.3, 0.9-1.8
Liver	4	37	10-94	14	47	26-78	6	43	16-94	-	-
Pancreas	16	83	47-134	38	72	51-99	23	85	54-127	0.8, 0.5-1.5	1.2, 0.6-2.6
Larynx	6	45	17-99	19	49	29-76	13	66	35-113	1.0, 0.4-2.5	1.0, 0.3-3.4
Lung, Men	67	64	50-82	182	56	48-65	100	57	47-70	0.8, 0.6-1.1	0.9, 0.6-1.3
Lung, Women	22	62	39-93	43	78	56-105	18	83	49-132	1.4, 0.8-2.4	0.8, 0.3-2.4
Soft tissue	4	59	16-150	14	80	44-134	6	96	35-210	-	-
Melanoma of skin	35	95	66-132	79	100	79-125	31	99	67-140	1.1, 0.8-1.7	1.1, 0.6-2.1
Breast	149	112	94-131	193	97	84-112	51	89	66-116	1.0, 0.8-1.2	0.8, 0.5-1.3
Cervix	7	44	18-90	25	101	66-150	5	112	36-261	2.4, 1.0-5.8	3.2, 0.6-16.5
Endometrium[d]	15	69	39-114	30	92	62-132	11	103	52-185	1.4, 0.7-2.7	2.0, 0.7-5.4
Ovary	12	68	35-118	21	81	50-123	8	114	49-225	1.1, 0.5-2.3	1.5, 0.4-5.6
Prostate	167	115	98-134	428	105	95-115	265	106	94-120	1.0, 0.8-1.2	1.1, 0.9-1.4
Testis	6	69	25-150	24	87	55-129	3	[4.3]	-	1.3, 0.5-3.3	-
Bladder	35	81	56-112	116	94	77-112	66	98	76-125	1.1, 0.8-1.7	1.5, 0.9-2.4
Kidney	24	97	62-145	57	87	66-113	28	87	58-125	0.8, 0.5-1.4	0.9, 0.5-1.8
Central nervous system	15	90	51-149	40	97	69-132	21	133	82-203	1.0, 0.5-1.8	1.3, 0.6-3.0
Thyroid	19	112	67-175	23	70	44-105	7	82	33-170	0.6, 0.3-1.2	-
non-Hodgkin lymphoma	41	102	73-138	91	90	72-110	42	99	72-134	0.9, 0.6-1.3	0.8, 0.4-1.4
Hodgkin lymphoma	9	100	46-191	25	111	72-164	3	[4.6]	-	1.3, 0.6-3.0	-
Leukemia	22	95	60-144	50	82	61-109	23	86	54-128	1.1, 0.6-1.9	0.5, 0.2-1.3
Multiple myeloma	9	92	42-175	24	91	58-135	17	129	75-206	0.9, 0.4-2.0	1.2, 0.5-3.3

TABLE 3. (Continued)

Facility & type of cancer	Unexposed			Exposed			Exposed, 15+ YSF, 5+ YRS			Ever Exposed	Exposed, 15+ YSF, 5+ YRS
	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	RR, 95% CI	RR, 95% CI
Panel 2. East Fishkill											
Oral cavity, pharynx	5	42	14-97	26	53	34-77	12	54	28-95	1.3, 0.5-3.1	1.2, 0.5-3.4
Esophagus	1	[4.6]	-	6	29	11-63	4	37	10-95	-	-
Stomach	2	27	3-99	15	47	26-78	8	51	22-100	-	-
Colorectum	27	62	41-91	150	86	73-101	87	99	79-122	1.2, 0.8-1.8	1.4, 0.9-2.1
Liver	0	[3.1]	-	7	51	21-105	4	57	16-146	-	-
Pancreas	9	104	48-198	25	71	46-105	17	96	56-153	0.7, 0.3-1.3	0.8, 0.4-1.8
Larynx	1	16	0-86	12	43	22-76	9	67	30-126	-	-
Lung, Men	31	69	47-97	123	57	47-68	53	47	35-61	0.7, 0.5-1.1	0.6, 0.4-0.9
Lung, Women	9	52	24-100	31	85	58-120	11	77	39-138	1.8, 0.8-3.8	1.6, 0.6-4.0
Soft tissue	2	[3.2]	-	6	53	20-116	1	[4.0]	-	-	-
Melanoma of skin	8	65	28-129	37	91	64-125	15	93	52-153	1.2, 0.6-2.7	1.0, 0.4-2.6
Breast	69	115	89-145	113	98	81-117	32	94	65-133	0.8, 0.6-1.1	0.8, 0.5-1.2
Cervix	3	42	9-124	17	125	73-199	2	[2.4]	-	-	-
Endometrium[d]	7	65	26-134	22	106	66-160	7	103	41-212	1.8, 0.7-4.5	1.4, 0.4-4.1
Ovary	9	107	49-203	11	70	35-125	4	[4.3]	-	0.6, 0.2-1.4	-
Prostate	44	97	71-130	227	102	89-116	148	107	90-125	1.1, 0.8-1.6	1.2, 0.8-1.6
Testis	3	[4.5]	-	14	71	39-118	0	[3.0]	-	-	-
Bladder	17	86	50-137	79	93	74-116	45	101	73-135	1.0, 0.6-1.7	1.2, 0.7-2.0
Kidney	8	75	32-147	44	103	75-138	21	100	62-153	1.1, 0.6-2.3	1.1, 0.5-2.5
Central nervous system	6	77	28-168	28	101	67-147	12	116	60-203	1.2, 0.5-3.0	1.0, 0.3-2.8
Thyroid	6	80	30-175	12	63	33-111	2	40	5-144	0.6, 0.2-1.5	-
non-Hodgkin lymphoma	13	80	43-137	61	100	76-128	28	109	72-157	1.2, 0.6-2.2	1.2, 0.6-2.5
Hodgkin lymphoma	4	76	21-196	21	129	80-197	1	[3.1]	-	-	-
Leukemia	8	79	34-157	27	70	46-102	12	70	36-123	1.1, 0.5-2.4	1.1, 0.4-2.8
Multiple myeloma	4	[3.9]	-	17	105	61-168	11	136	68-243	-	-

TABLE 3. (Continued)

Facility & type of cancer	Unexposed			Exposed			Exposed, 15+ YSF, 5+ YRS			Ever Exposed	Exposed, 15+ YSF, 5+ YRS
	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	RR, 95% CI	RR, 95% CI
Panel 3. San Jose											
Oral cavity, pharynx	12	64	33-111	20	60	37-93	10	68	33-125	1.0, 0.5-2.1	1.2, 0.5-2.8
Esophagus	5	88	29-206	3	30	6-88	1	19	1-104	-	-
Stomach	6	53	20-116	17	82	48-132	11	113	57-203	2.0, 0.7-5.1	2.4, 0.8-6.8
Colorectum	58	109	83-141	88	98	78-120	49	107	79-141	1.0, 0.7-1.4	1.1, 0.7-1.6
Liver	4	52	14-132	7	43	17-89	2	29	4-104	-	-
Pancreas	7	65	26-134	13	73	39-125	6	64	24-140	1.3, 0.5-3.3	1.4, 0.4-4.2
Larynx	5	74	24-173	7	61	25-126	4	65	18-166	0.8, 0.2-2.6	-
Lung, Men	36	61	43-85	59	55	42-71	47	78	57-104	0.9, 0.6-1.4	1.3, 0.8-2.0
Lung, Women	13	70	37-120	12	64	33-112	7	95	38-195	1.1, 0.5-2.4	1.3, 0.5-3.6
Soft tissue	2	[3.7]	-	8	128	55-251	5	223	73-521	-	-
Melanoma of skin	27	110	72-160	42	111	80-150	16	105	60-171	1.1, 0.7-1.8	0.9, 0.5-1.8
Breast	80	109	87-136	80	97	77-121	19	80	48-125	1.2, 0.8-1.6	0.9, 0.5-1.6
Cervix	4	45	12-115	8	73	31-143	3	[2.1]	-	-	-
Endometrium[d]	8	73	32-144	8	69	30-136	4	[3.9]	-	0.9, 0.3-2.6	-
Ovary	3	32	7-94	10	98	47-179	4	[2.7]	-	-	-
Prostate	123	123	102-147	201	109	95-125	117	106	87-127	0.9, 0.8-1.2	0.9, 0.7-1.1
Testis	3	[4.3]	-	10	127	61-233	3	[1.3]	-	-	-
Bladder	18	77	45-121	37	94	66-130	21	92	57-141	1.3, 0.7-2.2	1.2, 0.6-2.3
Kidney	16	115	66-187	13	57	30-98	7	62	25-127	0.6, 0.3-1.2	0.5, 0.2-1.4
Central nervous system	9	102	47-193	12	87	45-152	9	164	75-311	0.8, 0.3-1.9	1.6, 0.6-4.3
Thyroid	13	137	73-234	11	79	39-141	5	143	46-334	0.7, 0.3-1.6	1.5, 0.5-4.5
non-Hodgkin lymphoma	28	116	77-168	30	74	50-106	14	84	46-141	0.7, 0.4-1.1	0.7, 0.3-1.3
Hodgkin lymphoma	5	134	44-313	4	65	18-166	2	[1.5]	-	-	-
Leukemia	14	107	59-180	23	104	66-156	11	112	56-200	1.1, 0.5-2.2	1.1, 0.5-2.5
Multiple myeloma	5	85	28-199	7	69	28-141	6	118	43-257	0.7, 0.2-2.1	1.0, 0.3-3.3

[a]The expected number is provided in brackets, without the SIR and the 95% confidence interval, when the observed number and the expected number of cases were both <5.
[b]RR, adjusted using Cox regression for year of birth, socioeconomic status, gender, and race; computed when there were at least five cases, both among the unexposed and among the exposed.
[c]Totals of exposed and unexposed exclude employees who worked only in jobs that could not be classified according to exposure because of missing or uninterpretable DDJs (535 at East Fishkill, 558 at San Jose, and 1,089 at both facilities combined).
[d]Endometrium includes uterus, not otherwise specified.

TABLE 4. Summary of results of analyses for specific types of cancer by work group, including observed number of cases (Obs), standardized incidence ratio (SIR)[a] and 95% confidence interval (CI), rate ratio (RR)[b] and 95% CI, and Cox regression results[c], East Fishkill

Type of cancer, work group, & subgroup[d]	Obs	SIR, 95% CI	RR, 95% CI	ß, se (p-value)
Lung cancer among women in masking				
Ever in work group	6	203, 75-442	3.2, 1.3-7.7	0.03, 0.13 (0.81)
15+ YSF, 5+ YRS	1	[0.5]		
Cervical cancer in packaging				
Ever in work group	10	191, 92-351	3.1, 1.3-7.5	0.07, 0.10 (0.49)
15+ YSF, 5+ YRS	0	[0.4]		
Cervical cancer in other manufacturing				
Ever in work group	6	300, 110-652	4.7, 1.7-12.7	0.40, 0.14 (0.01)
15+ YSF, 5+ YRS	0	[0.1]		
Endometrial cancer in other manufacturing				
Ever in work group	7	195, 78-401	2.2, 0.9-5.3	0.23, 0.10 (0.02)
15+ YSF, 5+ YRS	1	[0.3]		
Central nervous system cancer in research and development				
Ever in work group	10	188, 90-346	1.6, 0.7-3.5	<0.01, 0.10 (0.97)
15+ YSF, 5+ YRS	0	[0.5]		
Central nervous system cancer in process equipment maintenance				
Ever in work group	8	192, 83-379	1.5, 0.6-3.5	0.02, 0.06 (0.80)
15+ YSF, 5+ YRS	4	[0.8]		
Hodgkin lymphoma in test/probe/dicing/slicing/die removal/wire bonding				
Ever in work group	6	194, 71-423	2.1, 0.8-5.4	-0.04, 0.15 (0.81)
15+ YSF, 5+ YRS	0	[0.3]		
Multiple myeloma in research and development				
Ever in work group	9	251, 115-477	4.1, 1.5-11.1	0.18, 0.07 (0.01)
15+ YSF, 5+ YRS	2	[0.4]		
Multiple myeloma in process equipment maintenance				
Ever in work group	5	192, 62-448	2.1, 0.7-6.3	0.07, 0.08 (0.37)
15+ YSF, 5+ YRS	1	[0.6]		

[a]The expected number is provided in brackets, without the SIR and the 95% confidence interval, when the observed number and the expected number of cases were both <5.

[b]Rate ratio, ever-employed compared to never-employed in the work group; Cox regression used to adjust for year of birth, gender (except for gender-specific analyses), race, socioeconomic status, and ever-'exposed' in other work groups.

[c]ß, Cox regression coefficient for years spent in the work group (continuous variable), adjusted for year of birth, gender (except for gender-specific analyses), race, socioeconomic status, and years spent in other work groups entailing potential exposure; se, standard error of the regression coefficient; p-value of regression coefficient, equivalent to p-value for linear trend.

[d]YSF, years since first record of employment in the work group; YRS, years spent in the work group. Criteria for inclusion of results for a work group in this table: for subjects ever in the work group, observed number of cases = 5, SIR = 150, and RR = 1.5.

TABLE 5. Summary of results of analyses for specific types of cancer by work group, including observed number of cases (Obs), standardized incidence ratio (SIR)[a] and 95% confidence interval (CI), rate ratio (RR)[b] and 95% CI, and Cox regression results[c], San Jose

Type of cancer, work group, & subgroup[d]	Obs	SIR, 95% CI	RR, 95% CI	ß, se (p-value)
Melanoma of the skin in head wafer/tape head				
Ever in work group	9	160, 73-303	1.8, 0.9-3.6	0.12, 0.07 (0.12)
15+ YSF, 5+ YRS	0	[0.4]		
Melanoma of the skin in research and development				
Ever in work group	10	160, 77-295	1.6, 0.8-3.1	0.02, 0.06 (0.78)
15+ YSF, 5+ YRS	2	[1.2]		
Melanoma of the skin in other manufacturing				
Ever in work group	18	161, 96-255	1.7, 0.9-3.1	0.11, 0.04 (0.01)
15+ YSF, 5+ YRS	4	[2.5]		
Cervical cancer in head fabrication				
Ever in work group	6	157, 58-342	7.2, 1.8-27.8	0.23, 0.06 (<0.01)
15+ YSF, 5+ YRS	2	[0.3]		
Endometrial cancer in disk manufacturing				
Ever in work group	6	361, 132-785	9.7, 3.3-28.1	0.20, 0.08 (0.01)
15+ YSF, 5+ YRS	1	[0.1]		
Ovarian cancer in head fabrication				
Ever in work group	7	193, 77-397	5.9, 1.7-20.0	0.13, 0.08 (0.09)
15+ YSF, 5+ YRS	2	[0.4]		
Testicular cancer in cleanrooms occasional				
Ever in work group	9	195, 89-370	4.5, 1.4-14.8	0.17, 0.06 (<0.01)
15+ YSF, 5+ YRS	1	[0.6]		
Bladder cancer in assembly				
Ever in work group	19	152, 91-237	2.2, 1.2-4.0	0.04, 0.05 (0.48)
15+ YSF, 5+ YRS	4	[2.5]		
Central nervous system cancer in test/dice/slice				
Ever in work group	5	175, 57-408	2.2, 0.8-6.5	-0.03, 0.16 (0.84)
15+ YSF, 5+ YRS	0	[0.4]		
Leukemia in head fabrication				
Ever in work group	7	150, 60-310	1.7, 0.7-4.1	0.02, 0.11 (0.87)
15+ YSF, 5+ YRS	1	[0.5]		

[a]The expected number is provided in brackets, without the SIR and the 95% confidence interval, when the observed number and the expected number of cases were both <5.

[b]Rate ratio, ever-employed compared to never-employed in the work group; Cox regression used to adjust for year of birth, gender (except for gender-specific analyses), race, socioeconomic status, and ever-'exposed' in other work groups.

[c]ß, Cox regression coefficient for years spent in the work group (continuous variable), adjusted for year of birth, gender (except for gender-specific analyses), race, socioeconomic status, and years spent in other work groups entailing potential exposure; se, standard error of the regression coefficient; p-value of regression coefficient, equivalent to p-value for linear trend.

[d]YSF, years since first record of employment in the work group; YRS, years spent in the work group. Criteria for inclusion of results for a work group in this table: for subjects ever in the work group, observed number of cases = 5, SIR = 150, and RR = 1.5.

APPENDIX TABLE 1. Number of subjects and of person-years by facility and exposed work group

Facility and work group[a]	Subjects	Person-years
Panel 1. East Fishkill		
Cleanrooms, always/frequently	18,516	223,594
Semiconductor fabrication	18,022	215,366
Masking	1,185	17,973
Cleanrooms, occasional[b]	22,568	262,781
Packaging	11,590	125,387
Facilities/laboratories/environmental health & safety	4,476	57,724
Research & development	3,771	51,039
Process equipment maintenance	3,443	42,752
Test/probe/dicing/slicing/die removal/wire bonding	5,856	73,350
Other manufacturing	3,455	47,340
Panel 2. San Jose		
Cleanrooms, always/frequently[c]	9,360	60,917
Head fabrication	8,718	54,731
Cleanrooms, occasional†	17,062	127,349
Disk manufacturing	6,271	40,869
Head wafer/tape head	5,491	34,692
Facilities/laboratories/environmental health & safety	2,706	26,972
Research & development	2,586	24,374
Test/probe/dicing/slicing	4,594	36,027
Head suspension/head disk assembly/box	12,564	96,470
Other manufacturing	4,845	42,249
Assembly	7,173	63,432

[a]Work groups are not mutually exclusive.
[b]This category included some work groups that were not analyzed due to small numbers. At East Fishkill, the work groups were chem mix, field service and chemical mechanical planarization/backlap; at San Jose the groups were chem mix, process equipment maintenance and quality control/quality assurance.
[c]At San Jose this category included two work groups, VLSI/semiconductor and masking, that were not analyzed due to small numbers.

APPENDIX TABLE 2. Observed number of cases (Obs) of specific types of cancer, standardized incidence ratio (SIR)[a] and 95% confidence interval (CI), and rate ratio (RR)[b] and 95% CI, by facility and exposed work group

	Oral cavity & pharyngeal			Esophageal			Stomach		
Facility and work group	Obs	SIR, 95% CI	RR, 95% CI	Obs	SIR, 95% CI	RR, 95% CI	Obs	SIR, 95% CI	RR, 95% CI
Panel 1. East Fishkill									
Work group, exposed									
Cleanrooms, regular	19	59, 36-92	1.5, 0.7-3.1	5	37, 12-85	2.6, 0.5-13.4	10	49, 23-89	1.1, 0.4-2.8
Semiconductor fabrication	19	61, 37-95	1.6, 0.8-3.4	5	38, 12-88	2.8, 0.5-14.8	10	50, 24-92	1.2, 0.4-3.1
Masking	0	[3.0]	-	0	[1.3]	-	0	[2.0]	-
Cleanrooms, occasional	18	46, 27-73	0.7, 0.3-1.5	5	30, 10-70	1.4, 0.3-7.2	13	51, 27-88	1.4, 0.5-4.2
Packaging	8	47, 20-92	1.0, 0.4-2.2	2	27, 3-99	-	3	27, 6-80	-
Facilities/labs	4	36, 10-93	-	2	[4.9]	-	1	13, 0-75	-
Resesearch & development	8	69, 30-136	1.2, 0.5-2.9	2	38, 5-138	-	6	80, 29-173	2.3, 0.8-6.7
Process equipment maintenance	1	12, 0-67	-	2	[3.7]	-	4	73, 20-186	-
Test/dice/probe[c]	7	58, 23-120	1.2, 0.5-2.7	2	38, 5-138	-	4	51, 14-131	-
Other Manufacturing	7	87, 35-179	1.8, 0.8-4.2	3	[3.6]	-	1	19, 1-103	-
Panel 2. San Jose									
Work group, exposed									
Cleanrooms, regular	7	84, 34-173	1.4, 0.6-3.4	0	[2.4]	-	4	75, 20-192	-
Head fabrication	7	99, 40-205	1.7, 0.7-4.1	0	[2.0]	-	2	[4.5]	-
Cleanrooms, occasional	14	62, 34-105	1.0, 0.5-2.2	2	28, 3-102	-	14	100, 55-167	1.8, 0.7-4.7
Disk manufacturing	3	45, 9-132	-	1	[2.0]	-	6	147, 54-320	2.5, 0.9-6.5
Head wafer/tape head	7	142, 57-292	2.8, 1.2-6.6	0	[1.5]	-	3	[3.2]	-
Facilities/labs	4	64, 18-165	-	2	[2.2]	-	5	124, 40-289	1.7, 0.6-4.7
Resesearch & development	4	67, 18-172	-	0	[2.0]	-	5	135, 44-315	1.8, 0.6-5.1
Test/dice/slice	5	68, 22-158	1.2, 0.5-3.4	1	[2.4]	-	4	[4.5]	-
Head suspension/head disk/assembly/box	9	68, 31-128	1.0, 0.4-2.3	1	[3.9]	-	8	96, 41-188	1.4, 0.6-3.6
Other manufacturing	7	66, 27-136	1.2, 0.5-3.0	0	[3.7]	-	7	105, 42-216	1.4, 0.5-3.7
Assembly	5	46, 15-107	0.7, 0.3-2.0	1	[3.3]	-	5	74, 24-173	1.0, 0.3-2.7

APPENDIX TABLE 2. (Continued)

Facility and work group	Colorectal Obs	Colorectal SIR, 95% CI	Colorectal RR, 95% CI	Liver Obs	Liver SIR, 95% CI	Liver RR, 95% CI	Pancreatic Obs	Pancreatic SIR, 95% CI	Pancreatic RR, 95% CI
Panel 1. East Fishkill									
Work group, exposed									
Cleanrooms, regular	88	78, 63-97	0.8, 0.6-1.1	4	45, 12-114	-	19	83, 50-130	1.0, 0.5-1.9
Semiconductor fabrication	84	77, 62-96	0.8, 0.6-1.1	4	46, 13-118	-	19	86, 52-134	1.1, 0.5-2.1
Masking	11	98, 49-175	1.2, 0.6-2.1	0	[0.8]	-	2	[2.3]	-
Cleanrooms, occasional	120	88, 73-106	1.2, 0.9-1.6	5	46, 15-107	0.9, 0.2-3.8	23	84, 53-126	1.2, 0.6-2.4
Packaging	58	97, 74-126	1.2, 0.9-1.6	1	[4.9]	-	7	57, 23-118	0.7, 0.3-1.6
Facilities/labs	37	93, 65-128	1.2, 0.8-1.7	2	[3.1]	-	8	101, 44-199	1.3, 0.6-2.9
Resesearch & development	33	84, 58-118	1.0, 0.7-1.5	2	[3.2]	-	7	88, 35-181	1.0, 0.4-2.3
Process equipment maintenance	22	76, 48-115	0.8, 0.5-1.3	0	[2.3]	-	3	52, 11-151	-
Test/dice/probe[c]	44	104, 75-139	1.3, 0.9-1.8	2	[3.4]	-	8	93, 40-183	1.3, 0.6-2.9
Other Manufacturing	35	117, 82-163	1.5, 1.0-2.1	1	[2.3]	-	5	82, 27-192	1.1, 0.4-2.9
Panel 2. San Jose									
Work group, exposed									
Cleanrooms, regular	21	91, 56-139	0.9, 0.6-1.5	1	[4.3]	-	5	110, 36-256	1.8, 0.6-5.3
Head fabrication	21	108, 67-165	1.2, 0.7-1.9	1	[3.7]	-	5	131, 43-306	2.2, 0.7-6.2
Cleanrooms, occasional	59	95, 73-123	0.9, 0.6-1.3	5	46, 15-108	0.9, 0.3-3.1	9	73, 34-139	1.3, 0.5-3.4
Disk manufacturing	15	87, 49-144	0.9, 0.5-1.5	0	[3.4]	-	1	[3.4]	-
Head wafer/tape head	14	103, 56-173	1.1, 0.6-1.9	1	[2.6]	-	2	[2.7]	-
Facilities/labs	25	134, 87-198	1.5, 1.0-2.4	3	[2.8]	-	3	[3.7]	-
Resesearch & development	17	103, 60-164	1.0, 0.6-1.7	2	[2.7]	-	1	[3.4]	-
Test/dice/slice	18	90, 54-143	0.8, 0.5-1.4	2	[3.5]	-	5	124, 40-290	2.6, 0.9-7.7
Head suspension/head disk/assembly/box	33	91, 63-128	0.9, 0.6-1.3	2	30, 4-108	-	2	28, 3-101	-
Other manufacturing	27	88, 58-128	0.8, 0.5-1.3	2	[4.8]	-	3	48, 10-141	-
Assembly	25	84, 55-124	0.8, 0.5-1.2	2	37, 5-135	-	6	101, 37-219	1.4, 0.5-3.9

APPENDIX TABLE 2. (Continued)

Facility and work group	Laryngeal Obs	Laryngeal SIR, 95% CI	Laryngeal RR, 95% CI	Lung, Men Obs	Lung, Men SIR, 95% CI	Lung, Men RR, 95% CI	Lung, Women Obs	Lung, Women SIR, 95% CI	Lung, Women RR, 95% CI
Panel 1. East Fishkill									
Work group, exposed									
Cleanrooms, regular	8	44, 19-87	1.1, 0.4-3.2	69	50, 39-63	0.7, 0.5-1.0	23	93, 59-139	1.8, 0.9-3.4
Semiconductor fabrication	7	40, 16-82	0.8, 0.3-2.4	67	50, 38-63	0.8, 0.5-1.0	19	80, 48-126	1.2, 0.6-2.3
Masking	2	[1.7]	-	11	83, 42-149	1.4, 0.7-2.5	6	203, 75-442	3.2, 1.3-7.7
Cleanrooms, occasional	11	49, 25-88	2.1, 0.5-8.0	103	58, 47-70	1.0, 0.7-1.3	17	77, 45-124	1.1, 0.6-2.0
Packaging	7	74, 30-152	2.4, 0.8-7.0	44	60, 44-81	1.1, 0.8-1.5	8	57, 25-112	0.7, 0.3-1.4
Facilities/labs	1	15, 0-82	-	35	61, 43-85	1.0, 0.7-1.4	2	[2.1]	-
Resesearch & development	5	70, 23-164	2.3, 0.7-7.6	32	55, 37-77	1.1, 0.7-1.6	3	[1.7]	-
Process equipment maintenance	3	59, 12-171	-	25	58, 37-85	1.0, 0.7-1.6	0	[0.5]	-
Test/dice/probe[c]	3	44, 9-128	-	27	51, 33-74	0.9, 0.6-1.3	10	120, 58-221	1.8, 0.9-3.8
Other Manufacturing	1	[4.7]	-	20	55, 34-85	0.9, 0.6-1.5	4	59, 16-150	-
Panel 2. San Jose									
Work group, exposed									
Cleanrooms, regular	1	[2.7]	-	15	62, 35-103	1.2, 0.7-2.1	7	93, 37-191	1.7, 0.6-4.7
Head fabrication	0	[2.2]	-	11	58, 29-104	1.1, 0.6-2.0	7	96, 39-198	1.8, 0.7-5.0
Cleanrooms, occasional	6	73, 27-158	1.1, 0.3-4.0	47	59, 44-79	1.1, 0.7-1.7	8	87, 37-171	1.4, 0.5-3.7
Disk manufacturing	1	[2.3]	-	15	68, 38-113	1.4, 0.8-2.5	1	[2.6]	-
Head wafer/tape head	1	[1.7]	-	11	73, 36-131	1.5, 0.8-2.9	4	[3.7]	-
Facilities/labs	3	[2.5]	-	19	74, 45-116	1.3, 0.8-2.2	2	[1.6]	-
Resesearch & development	0	[2.4]	-	10	42, 20-76	0.8, 0.4-1.5	0	[0.8]	-
Test/dice/slice	3	[2.8]	-	17	65, 38-104	1.3, 0.7-2.2	2	[3.0]	-
Head suspension/head disk/assembly/box	2	[4.4]	-	27	69, 45-100	1.4, 0.8-2.2	10	91, 44-168	2.0, 0.7-5.2
Other manufacturing	2	[4.3]	-	26	62, 40-91	1.3, 0.8-2.1	4	[3.7]	-
Assembly	2	[3.8]	-	26	76, 49-111	1.4, 0.9-2.3	4	52, 14-133	-

APPENDIX TABLE 2. (Continued)

Facility and work group	Soft tissue sarcoma Obs	SIR, 95% CI	RR, 95% CI	Melanoma Obs	SIR, 95% CI	RR, 95% CI	Breast, Women Obs	SIR, 95% CI	RR, 95% CI
Panel 1. East Fishkill									
Work group, exposed									
Cleanrooms, regular	4	57, 15-145	-	17	66, 38-105	0.5, 0.3-1.0	74	99, 78-124	0.9, 0.7-1.2
Semiconductor fabrication	4	59, 16-150	-	17	68, 39-108	0.6, 0.3-1.1	69	97, 75-123	0.9, 0.6-1.2
Masking	0	[0.6]	-	3	[2.3]	-	7	88, 35-181	0.8, 0.4-1.8
Cleanrooms, occasional	4	47, 13-121	-	34	110, 76-153	2.1, 1.0-4.4	61	92, 70-118	0.8, 0.6-1.1
Packaging	2	[3.9]	-	15	108, 60-178	1.4, 0.7-2.6	37	85, 60-118	0.8, 0.5-1.1
Facilities/labs	1	[2.2]	-	11	130, 65-232	1.4, 0.7-2.9	6	87, 32-188	0.9, 0.4-2.0
Resesearch & development	1	[2.1]	-	7	84, 34-174	0.8, 0.3-1.8	6	134, 49-293	1.4, 0.6-3.3
Process equipment maintenance	0	[1.6]	-	4	62, 17-159	-	0	[1.7]	-
Test/dice/probe[c]	0	[2.5]	-	13	141, 75-241	1.7, 0.9-3.4	22	96, 60-146	0.9, 0.6-1.4
Other Manufacturing	0	[1.7]	-	2	33, 4-118	-	12	66, 34-114	0.6, 0.3-1.1
Panel 2. San Jose									
Work group, exposed									
Cleanrooms, regular	2	[1.6]	-	7	73, 29-150	0.7, 0.3-1.5	26	85, 55-124	1.0, 0.6-1.5
Head fabrication	2	[1.4]	-	2	24, 3-87	-	25	85, 55-126	1.0, 0.6-1.5
Cleanrooms, occasional	7	178, 71-366	2.7, 0.6-11.6	28	113, 75-163	1.0, 0.6-1.7	36	90, 63-125	0.9, 0.6-1.3
Disk manufacturing	2	[1.2]	-	9	123, 56-234	1.2, 0.6-2.4	6	51, 19-110	0.5, 0.2-1.1
Head wafer/tape head	1	[0.9]	-	9	160, 73-303	1.8, 0.9-3.6	12	74, 38-129	0.8, 0.4-1.4
Facilities/labs	1	[1.0]	-	7	103, 41-212	0.8, 0.4-1.8	7	106, 43-218	0.9, 0.4-2.0
Resesearch & development	4	[0.9]	-	10	160, 77-295	1.6, 0.8-3.1	5	131, 42-305	1.1, 0.4-2.6
Test/dice/slice	3	[1.2]	-	9	114, 52-217	1.0, 0.5-2.0	12	108, 56-189	1.1, 0.6-2.0
Head suspension/head disk/assembly/box	1	[2.6]	-	14	91, 50-153	0.8, 0.4-1.5	29	65, 44-94	0.6, 0.4-0.9
Other manufacturing	4	[1.7]	-	18	161, 96-255	1.7, 0.9-3.1	10	78, 38-144	0.7, 0.4-1.4
Assembly	2	[1.9]	-	13	108, 57-184	1.0, 0.5-1.8	28	99, 66-144	1.1, 0.7-1.8

APPENDIX TABLE 2. (Continued)

Facility and work group	Cervical Obs	Cervical SIR, 95% CI	Cervical RR, 95% CI	Endometrial Obs	Endometrial SIR, 95% CI	Endometrial RR, 95% CI	Ovarian Obs	Ovarian SIR, 95% CI	Ovarian RR, 95% CI
Panel 1. East Fishkill									
Work group, exposed									
Cleanrooms, regular	12	135, 70-236	2.1, 0.9-5.3	16	115, 66-187	1.4, 0.7-3.1	10	96, 46-177	1.3, 0.5-3.1
Semiconductor fabrication	11	130, 65-233	1.9, 0.8-4.7	15	113, 63-187	1.4, 0.6-2.9	9	91, 42-173	1.2, 0.5-2.9
Masking	2	[0.9]	-	2	[1.6]	-	1	[1.1]	-
Cleanrooms, occasional	12	149, 77-261	2.4, 1.0-6.0	15	122, 68-201	1.6, 0.7-3.4	6	65, 24-141	0.7, 0.2-1.7
Packaging	10	191, 92-351	3.1, 1.3-7.5	5	63, 21-148	0.6, 0.2-1.7	4	67, 18-173	-
Facilities/labs	0	[0.9]	-	1	[1.3]	-	0	[1.0]	-
Resesearch & development	3	[0.5]	-	3	[0.9]	-	2	[0.6]	-
Process equipment maintenance	0	[0.2]	-	2	[0.3]	-	0	[0.2]	-
Test/dice/probe[c]	4	[2.6]	-	6	135, 50-295	1.4, 0.6-3.6	1	[3.2]	-
Other Manufacturing	6	300, 110-652	4.7, 1.7-12.7	7	195, 78-401	2.2, 0.9-5.3	4	[2.5]	-
Panel 2. San Jose									
Work group, exposed									
Cleanrooms, regular	6	149, 55-325	6.5, 1.7-25.2	1	[4.5]	-	7	184, 74-379	5.6, 1.6-19.4
Head fabrication	6	157, 58-342	7.2, 1.8-27.8	1	[4.3]	-	7	193, 77-397	5.9, 1.7-20.0
Cleanrooms, occasional	3	56, 12-163	-	7	122, 49-252	3.7, 1.2-10.9	4	80, 22-205	-
Disk manufacturing	1	[1.6]	-	6	361, 132-785	9.7, 3.3-28.1	0	[1.5]	-
Head wafer/tape head	2	[2.2]	-	2	[2.3]	-	1	[2.0]	-
Facilities/labs	1	[0.9]	-	0	[1.0]	-	2	[0.9]	-
Resesearch & development	0	[0.5]	-	1	[0.5]	-	0	[0.5]	-
Test/dice/slice	0	[1.3]	-	3	[1.7]	-	1	[1.4]	-
Head suspension/head disk/assembly/box	5	87, 28-204	2.0, 0.5-7.3	2	31, 4-111	-	5	91, 29-212	0.9, 0.3-2.9
Other manufacturing	3	[1.4]	-	3	[2.0]	-	3	[1.6]	-
Assembly	3	[3.3]	-	3	[4.4]	-	3	[3.4]	-

APPENDIX TABLE 2. (Continued)

Facility and work group	Prostate Obs	Prostate SIR, 95% CI	Prostate RR, 95% CI	Testicular Obs	Testicular SIR, 95% CI	Testicular RR, 95% CI	Bladder Obs	Bladder SIR, 95% CI	Bladder RR, 95% CI
Panel 1. East Fishkill									
Work group, exposed									
Cleanrooms, regular	166	114, 97-133	1.3, 1.0-1.7	8	72, 31-143	1.0, 0.4-2.8	57	105, 79-136	1.3, 0.9-2.0
Semiconductor fabrication	163	115, 98-134	1.3, 1.0-1.7	7	65, 26-135	0.9, 0.3-2.5	56	106, 80-138	1.4, 0.9-2.1
Masking	12	86, 44-150	0.8, 0.5-1.5	1	[0.7]	-	8	149, 65-294	1.7, 0.8-3.5
Cleanrooms, occasional	186	100, 86-115	0.9, 0.7-1.2	8	55, 24-109	0.6, 0.2-1.7	65	95, 74-122	1.1, 0.7-1.7
Packaging	83	105, 84-130	1.0, 0.8-1.3	3	47, 10-137	-	31	108, 73-153	1.3, 0.8-1.9
Facilities/labs	60	99, 75-127	1.0, 0.8-1.4	2	[3.3]	-	18	84, 50-133	0.9, 0.6-1.6
Resesearch & development	76	123, 97-154	1.2, 0.9-1.5	1	[2.5]	-	15	71, 40-117	0.7, 0.4-1.2
Process equipment maintenance	50	108, 80-142	1.0, 0.7-1.4	2	[2.8]	-	22	137, 86-208	1.7, 1.0-2.9
Test/dice/probe[c]	61	108, 82-138	1.0, 0.8-1.4	1	[3.8]	-	13	63, 34-108	0.6, 0.3-1.1
Other Manufacturing	41	106, 76-144	1.1, 0.8-1.5	1	[2.2]	-	14	98, 54-165	1.1, 0.6-1.9
Panel 2. San Jose									
Work group, exposed									
Cleanrooms, regular	46	112, 82-150	1.0, 0.8-1.4	2	[1.7]	-	8	90, 39-178	1.0, 0.5-2.2
Head fabrication	40	126, 90-172	1.2, 0.9-1.7	2	[1.5]	-	8	114, 49-225	1.3, 0.6-2.8
Cleanrooms, occasional	140	101, 85-120	0.8, 0.6-1.0	9	195, 89-370	4.5, 1.4-14.8	24	83, 53-124	0.8, 0.4-1.4
Disk manufacturing	43	115, 83-155	1.1, 0.8-1.5	3	[1.6]	-	8	106, 46-209	1.2, 0.6-2.6
Head wafer/tape head	27	104, 68-151	0.9, 0.6-1.4	4	[1.0]	-	5	92, 30-215	1.1, 0.4-2.7
Facilities/labs	44	96, 69-128	0.8, 0.6-1.2	2	[1.0]	-	9	92, 42-175	1.0, 0.5-2.0
Resesearch & development	47	110, 81-147	1.0, 0.7-1.3	1	[1.0]	-	4	46, 13-118	-
Test/dice/slice	43	96, 69-129	0.8, 0.6-1.2	1	[1.3]	-	12	129, 66-225	1.5, 0.8-3.0
Head suspension/head disk/assembly/box	69	104, 81-131	0.9, 0.7-1.2	3	[3.1]	-	15	104, 58-172	1.2, 0.7-2.4
Other manufacturing	86	115, 92-142	1.0, 0.8-1.3	1	[1.5]	-	9	59, 27-112	0.6, 0.3-1.3
Assembly	55	95, 71-123	0.8, 0.6-1.1	1	[2.2]	-	19	152, 91-237	2.2, 1.2-4.0

APPENDIX TABLE 2. (Continued)

Facility and work group	Kidney			Central nervous system			Thyroid		
	Obs	SIR, 95% CI	RR, 95% CI	Obs	SIR, 95% CI	RR, 95% CI	Obs	SIR, 95% CI	RR, 95% CI
Panel 1. East Fishkill									
Work group, exposed									
Cleanrooms, regular	32	115, 79-162	1.4, 0.8-2.3	16	92, 53-150	0.8, 0.4-1.6	6	51, 19-110	0.5, 0.2-1.4
Semiconductor fabrication	31	115, 78-163	1.3, 0.8-2.3	15	89, 50-147	0.8, 0.4-1.5	5	44, 14-102	0.4, 0.2-1.3
Masking	3	[2.6]	-	2	[1.5]	-	1	[1.0]	-
Cleanrooms, occasional	33	98, 67-137	0.9, 0.5-1.5	25	120, 78-177	1.6, 0.7-3.7	7	54, 22-111	0.5, 0.2-1.4
Packaging	15	100, 56-165	1.0, 0.5-1.8	9	95, 44-181	1.0, 0.4-2.1	3	44, 9-129	-
Facilities/labs	7	72, 29-148	0.7, 0.3-1.5	8	145, 63-286	1.3, 0.6-2.9	1	[2.7]	-
Resesearch & development	10	100, 48-184	0.9, 0.4-1.9	10	188, 90-346	1.6, 0.7-3.5	2	[2.4]	-
Process equipment maintenance	9	122, 56-232	1.1, 0.5-2.4	8	192, 83-379	1.5, 0.6-3.5	0	[1.8]	-
Test/dice/probe[c]	10	96, 46-177	0.9, 0.5-1.8	9	145, 67-276	1.4, 0.6-3.0	1	[3.8]	-
Other Manufacturing	6	85, 31-185	0.8, 0.4-2.0	4	[4.1]	-	3	[2.6]	-
Panel 2. San Jose									
Work group, exposed									
Cleanrooms, regular	3	53, 11-154	-	2	[3.5]	-	3	[4.2]	-
Head fabrication	3	[4.7]	-	2	[3.0]	-	2	[3.9]	-
Cleanrooms, occasional	12	76, 39-133	1.2, 0.5-2.7	11	123, 61-220	1.6, 0.7-4.0	6	77, 28-167	0.7, 0.3-1.9
Disk manufacturing	3	[4.5]	-	4	[2.6]	-	2	[2.4]	-
Head wafer/tape head	2	[3.4]	-	2	[2.0]	-	2	[2.4]	-
Facilities/labs	4	[4.7]	-	3	[2.4]	-	2	[1.7]	-
Resesearch & development	5	115, 37-268	1.6, 0.6-4.5	3	[2.3]	-	2	[1.4]	-
Test/dice/slice	4	76, 21-195	-	5	175, 57-408	2.2, 0.8-6.5	2	[2.2]	-
Head suspension/head disk/assembly/box	4	44, 12-113	-	5	90, 29-209	1.1, 0.4-3.3	4	63, 17-161	-
Other manufacturing	5	63, 21-148	0.8, 0.3-2.3	6	148, 54-321	2.1, 0.7-6.0	4	[2.7]	-
Assembly	6	79, 29-172	1.5, 0.6-4.1	3	[4.4]	-	1	[4.1]	-

APPENDIX TABLE 2. (Continued)

Facility and work group	Non-Hodgkin lymphoma Obs	SIR, 95% CI	RR, 95% CI	Hodgkin lymphoma Obs	SIR, 95% CI	RR, 95% CI	Leukemia Obs	SIR, 95% CI	RR, 95% CI
Panel 1. East Fishkill									
Work group, exposed									
Cleanrooms, regular	45	116, 84-155	1.5, 1.0-2.5	9	95, 43-180	0.7, 0.3-1.7	19	77, 47-121	1.3, 0.6-2.5
Semiconductor fabrication	42	112, 81-151	1.4, 0.9-2.2	9	98, 45-187	0.8, 0.4-1.8	18	76, 45-120	1.2, 0.6-2.3
Masking	4	[3.5]	-	1	[0.7]	-	2	[2.3]	-
Cleanrooms, occasional	47	101, 74-134	1.1, 0.6-1.7	12	105, 54-183	1.0, 0.4-2.3	20	67, 41-103	0.9, 0.5-1.9
Packaging	25	118, 76-173	1.3, 0.8-2.1	6	113, 41-245	1.0, 0.4-2.4	9	68, 31-130	0.9, 0.4-2.0
Facilities/labs	10	80, 38-147	0.8, 0.4-1.6	2	[2.6]	-	8	95, 41-187	1.7, 0.7-3.8
Resesearch & development	13	107, 57-182	1.2, 0.6-2.3	2	[2.2]	-	7	85, 34-176	1.4, 0.6-3.5
Process equipment maintenance	7	75, 30-154	0.7, 0.3-1.6	2	[1.9]	-	2	32, 4-116	-
Test/dice/probe[c]	18	128, 76-202	1.4, 0.8-2.3	6	194, 71-423	2.1, 0.8-5.4	5	55, 18-129	0.8, 0.3-2.0
Other Manufacturing	11	117, 58-208	1.2, 0.6-2.2	3	[2.0]	-	7	114, 46-234	1.8, 0.8-4.2
Panel 2. San Jose									
Work group, exposed									
Cleanrooms, regular	5	49, 16-114	0.5, 0.2-1.4	1	[1.6]	-	8	145, 63-286	1.7, 0.7-3.8
Head fabrication	3	34, 7-100	-	1	[1.4]	-	7	150, 60-310	1.7, 0.7-4.1
Cleanrooms, occasional	22	83, 52-125	1.0, 0.5-1.7	3	[3.6]	-	13	88, 47-151	0.6, 0.3-1.3
Disk manufacturing	3	38, 8-111	-	1	[1.1]	-	2	[4.2]	-
Head wafer/tape head	4	67, 18-173	-	0	[0.9]	-	3	[3.2]	-
Facilities/labs	3	41, 9-120	-	1	[0.8]	-	3	[4.3]	-
Resesearch & development	10	149, 71-274	2.0, 1.0-4.2	0	[0.8]	-	4	[3.8]	-
Test/dice/slice	8	94, 41-185	1.2, 0.6-2.6	1	[1.0]	-	5	108, 35-251	0.9, 0.4-2.5
Head suspension/head disk/assembly/box	11	67, 34-120	0.8, 0.4-1.6	2	[2.5]	-	11	125, 63-224	1.4, 0.7-3.0
Other manufacturing	10	83, 40-153	0.9, 0.4-1.9	1	[1.3]	-	7	102, 41-210	0.9, 0.4-2.1
Assembly	12	92, 48-161	1.2, 0.6-2.3	1	[1.8]	-	5	72, 23-167	0.6, 0.2-1.6

APPENDIX TABLE 2. (Continued)

Facility and work group	Obs	Multiple myeloma SIR, 95% CI	RR, 95% CI
Panel 1. East Fishkill			
Work group, exposed			
Cleanrooms, regular	11	104, 52-186	0.9, 0.4-2.3
Semiconductor fabrication	11	108, 54-192	1.0, 0.4-2.5
Masking	0	[1.0]	-
Cleanrooms, occasional	15	119, 66-195	1.7, 0.6-4.8
Packaging	5	87, 28-204	0.8, 0.3-2.1
Facilities/labs	3	[3.5]	-
Resesearch & development	9	251, 115-477	4.1, 1.5-11.1
Process equipment maintenance	5	192, 62-448	2.1, 0.7-6.3
Test/dice/probe[c]	4	[4.0]	-
Other Manufacturing	1	[2.8]	-
Panel 2. San Jose			
Work group, exposed			
Cleanrooms, regular	1	[2.7]	-
Head fabrication	1	[2.3]	-
Cleanrooms, occasional	6	86, 32-187	1.5, 0.5-5.0
Disk manufacturing	2	[2.0]	-
Head wafer/tape head	0	[1.6]	-
Facilities/labs	2	[2.0]	-
Resesearch & development	3	[1.8]	-
Test/dice/slice	2	[2.3]	-
Head suspension/head disk/assembly/box	2	[4.2]	-
Other manufacturing	2	[3.4]	-
Assembly	2	[3.4]	-

[a]The expected number is provided in brackets, without the SIR and the 95% confidence interval, when the observed number and the expected number of cases were both <5.
[b]RR, rate ratio; in work group analyses, adjusted for year of birth, gender, race, socioeconomic status and employment in other exposed work groups; RR not computed when the observed number was <5.
[c]Test/probe/dicing/slicing/die removal/wire bonding.

CONCLUSIONS

Concerns about the possible health effects of past exposures in semiconductor and storage device manufacturing have arisen because of intensive use of chemicals and other agents during the early years of operation (1, 5-10). Information on employees' disease patterns is limited (26-28, 89). To address this deficiency, we carried out a mortality study at three facilities, and we evaluated cancer incidence at two of the three facilities.

We investigated cancer incidence in addition to mortality because incidence studies may yield more information on cancers with relatively long survival. Also, incidence studies may detect an occupational association earlier than mortality studies or provide more definitive reassurances that such an association does not exist, especially when the employment group is relatively young (81, 90). Incidence data therefore may offer enhanced precision and an earlier opportunity to detect and to minimize the impact of health hazards. However, investigators in the US must confront several methodologic challenges when conducting a study of cancer incidence.

A central goal of this dissertation was to examine and clarify methodologic issues related to retrospective follow-up studies of cancer incidence among occupational groups in the US. Another goal was to evaluate cancer incidence among employees at two microelectronics facilities owned by IBM in order to determine if employment factors are associated with the occurrence of any type of cancer.

This dissertation addressed five main objectives relating to the conduct of cancer incidence studies in occupational groups in the US. The first was to evaluate the

completeness and accuracy of information sources used to develop residential histories. We found that investigators in the US have access to several information sources useful for developing residential histories. A source with national coverage, such as LexisNexis, should provide more complete residential history than state-specific departments of motor vehicles and voter registration records, especially for people similar to our subjects who were relatively young, mobile, and of high socioeconomic status. The accuracy of LexisNexis data was high and compared favorably with departments of motor vehicles and voter registration data. None of our external residential history sources provided information for every postemployment year, and none provided much information that predated 1990.

The second objective was to assess the impact on validity and precision of different procedures and assumptions used to develop residential histories. In any study that does not contact subjects directly, investigators must make assumptions about postemployment residential history that occurred between the last day worked and the earliest address from an external source. Although our residential histories had limitations, all the uncertainty analyses we performed to consider alternate assumptions produced similar results. The assumptions we adopted for the main analysis therefore seemed reasonable, and our results were robust.

The third objective was to evaluate variation in the impact of follow-up restrictions among subcohorts specified on the basis of work activity. The proportion of mortality study person-years included in the cancer incidence study varied considerably by work group, particularly at San Jose, and the validity of the cancer incidence results also may vary considerably across these subcohorts. In the second paper, when we found that

the relation between a work group and a particular cancer differed in the mortality and cancer incidence studies, we examined the overlap of subjects counted as deaths vs. cases in the studies and determined that most of the differences in the results could be attributable to follow-up restrictions and consequent selection bias in the cancer incidence study. Thus, investigators should examine variation in the potential for selection bias due to restricted follow-up across cohort subgroups and should use this information in interpreting the results of cancer incidence studies that rely on cancer registries that do not cover the entire potential follow-up experience of the study group.

The fourth objective was to determine the relative informativeness of the cancer incidence study of IBM employees and the companion mortality study for specific types of cancer. Our comparison of cancer mortality rates for person-time included in the cancer incidence study with rates for lost person-time provided minimal evidence of an impact of temporal and geographic restrictions on validity: mortality rates for included and lost person-time were similar. The number of cancer cases substantially exceeded the number of cancer deaths at both facilities. The enhanced precision of the incidence study compared to the mortality study depended in part on developing postemployment residential histories, and the uncertainty analysis that eliminated the postemployment experience of separated employees discarded hundreds of cases and thousands of person-years. The results illustrated that, as others have consistently found, cancer incidence studies are more informative than mortality studies for cancers with relatively long survival (65-72).

The fifth objective was to evaluate different procedures that address person-time specification for subjects who experienced multiple primary diagnoses of one or more types of cancer. The small differences between SIRs for our main analysis and SIRs for

uncertainty analyses that alternatively removed all cases from follow-up on their first diagnosis date in all analyses or removed cases from follow-up on a cancer-specific basis do not justify the loss of precision and added analytical burden of these analyses. Results are presented in Appendix A.

The next part of the dissertation sought to determine if the incidence of cancer might be related to employment at the study facilities. This was accomplished by comparing employees' cancer incidence rates to the general population rates for the facility state (New York State minus New York City or California) or by comparing the cancer incidence rates of potentially exposed employees (any non-office work) with the rates of unexposed employees (office work only).

Employees had total cancer incidence rates that were lower than general population rates overall and in subgroups with many years since starting and relatively long duration of employment. These deficits reflected employees' low incidence rates of most cancers related to smoking, alcohol, and nutritional deficits that are inversely correlated with socioeconomic status.

When compared to the general population, some employee subgroups had small increases in several cancers, including melanoma and cancers of the colon, breast, prostate, and thyroid, results which are consistent with subjects' relatively high socioeconomic status. Socioeconomic status tends to be associated positively with these cancers because of positive correlations with nonoccupational risk factors, better detection, or both (91-97).

The results of the study provide, at most, limited evidence of a causal association between employment factors and cancer. Potential exposure to work environments other

than offices was not consistently associated with any type of cancer in both SIR and rate ratio analyses. Most associations with work group were based on small numbers, with insufficient data to determine if a duration-response relation or a consistent pattern with potential induction time were present. Several work group associations displayed positive duration-response, but the underlying data were limited to short-term employees and/or to employees with short potential induction time. Work group associations observed for lung cancer among women, melanoma, and cancers of the cervix and endometrium could have been due in part to confounding by well-established nonoccupational causes that may not have been completely controlled for in the internal analyses.

The incidence study and its companion mortality study characterized the same study group using similar analytical approaches, but the results differed in many respects. These inconsistencies should not be interpreted as undermining the credibility of either study. Divergent results could be attributed easily to differences in the observed numbers of cancers and person-years in the two studies. Differences appeared to stem mainly from temporal and geographic restrictions on follow-up for the incidence study that resulted in the loss of cases and person-years accrued outside the facility state or before the registry period and variation by work group of the proportion of lost mortality study follow-up (98).

Incidence results for central nervous system cancer at East Fishkill and for prostate cancer at San Jose warrant further consideration because of work group associations seen for these cancers in the companion mortality study (5). The incidence study found a weak association between central nervous system cancer and process equipment maintenance at East Fishkill. The association was concentrated in the subgroup with many years

since starting and long duration of employment, but Cox regression analyses did not find a duration-response trend. The mortality study found similar, but stronger, association, with a positive duration-response trend. Because of geographic and temporal restrictions, the incidence study included only 67% of mortality study person-years in this work group (98) and 80% of the central nervous system cancer deaths. One of the decedents not included in the incidence study had worked about 22 years in process equipment maintenance, and the exclusion of this decedent from the incidence data had a large influence on the duration-response analysis. Although associations with central nervous system cancer might be more reliably assessed with results of the mortality rather than the incidence study, interpretation of both studies was hampered by small numbers.

Although the mortality study found an association between employment in facilities/laboratories and prostate cancer at San Jose (88), the incidence study did not. This difference may be due in part to the incidence study's inclusion in this work group of just 9 of 18 fatal prostate cancers and only 44% of the mortality study person-years (98).

Previous research on two groups of semiconductor industry workers in the United Kingdom has not consistently reported positive findings for any type of cancer (26-28, 89). Nichols and Sorahan found a 50% excess of colorectal cancer cases and a twofold increase in the incidence of melanoma of the skin (28), whereas McElvenney et al. reported a twofold increase in lung cancer incidence (89). The results of the present study are not consistent with those of the British investigations. Storage device manufacturing workers have not been studied previously.

In summary, assumptions about residential history had little impact on validity in the incidence study. Use of information sources with national coverage to develop resi-

dential histories increased the incidence study's precision. The temporal and geographic restrictions on our cancer incidence study did not appear to affect the validity of the results for the overall analysis, but the potential for selection bias varied considerably by work group subcohort. This study found that IBM employees at East Fishkill and San Jose had fewer than expected cases of cancer compared to general populations. Incidence was increased for several cancers in some employee groups, but interpretation of these results was difficult because data on employees with long potential induction time and many years worked were sparse, particularly in specific work groups, and because of potential confounding by nonoccupational risk factors, imprecision, and other limitations. There was no strong and consistent evidence that any type of cancer was associated causally with employment factors. Further follow-up will permit a more informative analysis of cancer incidence in the cohort.

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APPENDIX

UNIVERSITY OF ALABAMA AT BIRMINGHAM INSTITUTIONAL REVIEW BOARD APPROVAL LETTER

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office of Human Research Protections (OHRP). The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56 and ICH GCP Guidelines. The Assurance became effective on November 24, 2003 and the approval period is for three years. The Assurance number is FWA00005960.

Principal Investigator:	DELZELL, ELIZABETH
Co-Investigator(s):	
Protocol Number:	**X991109001**
Protocol Title:	*An Epidemiologic Investigation at Three Semiconductor or Storage Device Manufacturing Facilities*

The IRB reviewed and approved the above named project on 3-15-05. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

project received EXPEDITED review.

IRB Approval Date: 3-15-05

Date IRB Approval Issued: 3-15-05

HIPAA Waiver Approved?: No

Marilyn Doss

Marilyn Doss, M.A.
Vice Chair of the Institutional Review
Board for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

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GRADUATE SCHOOL
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DISSERTATION APPROVAL FORM
DOCTOR OF PHILOSOPHY

Name of Candidate Thomas John Bender

Graduate Program Epidemiology

Title of Dissertation Cancer Incidence Among Semiconductor and Storage Device Manufacturing Workers

I certify that I have read this document and examined the student regarding its content. In my opinion, this dissertation conforms to acceptable standards of scholarly presentation and is adequate in scope and quality, and the attainments of this student are such that he may be recommended for the degree of Doctor of Philosophy.

Dissertation Committee:

Name		Signature
Elizabeth S. Delzell	**, Chair**	
Christopher Coffey		
Ellen M. Funkhouser		
Nalini Sathiakumar		
Shan Tsai		

Director of Graduate Program

Dean, UAB Graduate School

Date