ORIGINAL ARTICLE

Cancer incidence among semiconductor and electronic storage device workers

T J Bender, C Beall, H Cheng, R F Herrick, A R Kahn, R Matthews, N Sathiakumar, M J Schymura, J H Stewart, E Delzell

Occup Environ Med 2007;**64**:30–36. doi: 10.1136/oem.2005.023366

Tables are available online at http://oem.bmjjournals.com/supplemental

See end of article for authors' affiliations

Correspondence to:
T J Bender, Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, 523 Ryals Building, 1665 University Blvd, Birmingham, AL 35294, USA; bender@uab.edu

Accepted 29 June 2006
Published Online First 17 July 2006

Aims: To evaluate cancer incidence among workers at two facilities in the USA that made semiconductors and electronic storage devices.

Methods: 89 054 men and women employed by International Business Machines (IBM) were included in the study. We compared employees' incidence rates with general population rates and examined incidence patterns by facility, duration of employment, time since first employment, manufacturing era, potential for exposure to workplace environments other than offices and work activity.

Results: For employees at the semiconductor manufacturing facility, the standardised incidence ratio (SIR) for all cancers combined was 81 (1541 observed cases, 95% confidence interval (CI) 77 to 85) and for those at the storage device manufacturing facility the SIR was 87 (1319 observed cases, 95% CI 82 to 92). The subgroups of employees with ⩾15 years since hiring and ⩾5 years worked had 6–16% fewer total incidents than expected. SIRs were increased for several cancers in certain employee subgroups, but analyses of incidence patterns by potential exposure and by years spent and time since starting in specific work activities did not clearly indicate that the excesses were due to occupational exposure.

Conclusions: This study did not provide strong or consistent evidence of causal associations with employment factors. Data on employees with long potential induction time and many years worked were limited. Further follow-up will allow a more informative analysis of cancer incidence that might be plausibly related to workplace exposures in the cohort.

Epidemiological research on cancer among workers in semiconductor manufacturing and related operations has been limited.[1–4] During the early years of manufacturing, use of chemicals was intense, and workers' handling of chemicals was frequent. Various known and suspected carcinogens, including ionising radiation, asbestos, arsenic and arsenical compounds, chromium compounds, sulphuric acid mist, ultraviolet light, trichloroethylene, carbon tetrachloride, nickel and antimony trioxide, have been used in these operations, but information on workers' exposure to such agents is not available.[4–6] 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.

We recently carried out a mortality study of 126 836 employees at three facilities owned by International Business Machines (IBM).[7] Two of the facilities, in East Fishkill, New York, USA, and in Burlington, Vermont, USA, made semiconductors, and the third, in San Jose, California, USA, made computer hard drives and other electronic storage devices.[5] Employees had fewer than expected deaths from all cancers combined and from most specific types of cancer. We found no firm evidence of a causal association between occupational factors and cancer, but several facility-specific and work activity-specific subgroups had more than expected deaths from central nervous system, prostate and several other cancers. To obtain a more thorough assessment of potential occupational associations of cancers with relatively long survival,[8 9] we carried out an additional investigation focused on cancer incidence rather than on mortality.

The present study evaluated incidence of cancer among employees at the East Fishkill and San Jose facilities in relation to duration of employment, time since first employment and type of work. Because it was not known whether semiconductor workers have been exposed to carcinogenic agents and because previous epidemiological studies have not provided evidence that exposures in the industry are associated with cancer, we did not evaluate hypotheses on specific agents and cancers as part of the present research. We did not include the Burlington facility because linkage with the Vermont cancer registry was not feasible.

PARTICIPANTS AND METHODS

To be eligible for the cancer incidence study, an IBM employee should have worked at either facility between 1965 and 1999, not been a foreign citizen on temporary assignment, and should have had records containing information on birth date, sex, race, social security number (SSN), IBM hire date and facility start date.[7] Follow-up ended in 1999 as this was the most recent year for which data were available from national and state sources when we conducted record linkages to determine vital status and to identify cancer cases. In addition, eligible employees at East Fishkill had to have lived in New York sometime between 1976 and 1999, and eligible employees at San Jose had to have lived in California sometime between 1988 and 1999. The additional eligibility requirements were necessary because of procedures used to identify cancer cases, described later.

Abbreviations: DMVs, departments of motor vehicles; IBM, International Business Machines; SES, socioeconomic status; SIR, standardised incidence ratio; SSN, social security number

We used IBM's electronic personnel files to identify employees and to develop a detailed work history file for each employee.[7] The data on each IBM position held by an employee, since 1 January 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.

We described in detail elsewhere[5 7] the historical operations at the study facilities and our development of facility-specific work groups based on division, department and job (DDJ) assignments; identification of three facility-specific manufacturing eras during which work environments were relatively stable (East Fishkill 1965–73, 1974–83, 1984–99; San Jose 1965–72, 1973–89, 1990–9); categorisation of work activities as ''potentially exposed'' (ie, entailing any type of work other than office work) or ''unexposed'' (ie, entailing office work only); and assignment of employees to one of three categories of socioeconomic status (SES), including group 1 (professional), group 2 (technical) and group 3 (production, clerical and other).

Assessment of eligibility required development of residential histories.[10] The work history file provided residential history for employees who were actively working for IBM or were retired, and provided residential history during active employment for employees who left the job without retiring. Postemployment residential histories of employees who left without retiring used information from departments of motor vehicles (DMVs) and voter registration records in New York and California, and from private vendors of residential data.

Information on vital status as of 31 December 1999 came from IBM records and from linkages with the Social Security Administration, the National Death Index, DMVs and voter registration records in New York and California, and several other sources.[7] Information related to cause of death came from the National Death Index[11] or from death certificates of employees if they died before 1979.

We identified cancer cases through record linkage with the New York State and California cancer registries. The registries described case reporting as being statewide and population-based beginning in 1976 for New York and in 1988 for California. We converted International Classification of Diseases for Oncology codes into 9th revision of International Classification of Diseases codes.[12] We counted as cases all invasive cancers plus in situ bladder cancers identified among employees during 1976–99 (East Fishkill) or during 1988–99 (San Jose) if the date of diagnosis was between their beginning and ending dates of follow-up for the incidence study and occured 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. Our study included employees who worked for short as well as for longer periods of time to enhance our ability to assess associations and trends with duration of employment. To minimise dilution of any true association between occupational factors and cancer resulting from the inclusion of short-term employees, we restricted some analyses to employee subgroups with long potential induction time (⩾15 years since first worked) and relatively long duration of employment (⩾5 years worked). Analyses of such subgroups accomplish the same objective as those using duration of employment restrictions to determine employees' eligibility.

External analyses compared employees' cancer incidence rates with the general population rates for the facility state (New York State minus New York City or California). 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 standardised incidence ratio (SIR) as the measure of association.[13] Person-year accumulation began on the latest of the cancer registry inception dates (New York, 1 January 1976; California, 1 January 1988), on the employee's first date of employment at the facility or on the date of entering a particular category of an employment factor, and ended on the earliest of the study closing dates, on the last date of residence in New York or California, on the date of loss to follow-up or on the death date. Between these beginning and ending dates, employees accrued only person-time while they were residing 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 with unexposed employees and to compute RRs for employees ever, compared with never, exposed in a particular work group at a facility. We also used Cox regression to evaluate the relationship between years 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, sex (except when analysing sex-specific cancers), race, SES and, for analyses of work groups, employment (ever *v* never or years) in other work groups.

To select results for detailed description from analyses of the overall group of employees and of subgroups specified according to years worked, years since hiring, manufacturing era and potential exposure, we used the criteria of at least five observed cases and an SIR of at least 120. We used more restrictive criteria in presenting results for work groups to reduce the role of random variability in producing positive results, focusing on associations having at least five observed cases, an SIR of ⩾150 and an RR of at least 1.5.[14]

The Institutional Review Boards of the University of Alabama at Birmingham and of Harvard University approved the research and monitored its conduct.

RESULTS

Of the 99 229 employees in the mortality study who worked at East Fishkill or at 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 sex: 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. Over 50% of employees at each facility started work in the two earliest manufacturing eras. The median values were 2.2 for years worked and 15.0 for years since first recorded work. At the end of follow-up, 92% of employees were alive, 4% were deceased, 4% were lost to follow-up, and employees' median age was 43 years. Person-years of follow-up were 499 445 at East Fishkill and 362 076 at San Jose.

Analyses of cancer incidence by facility indicated that for all cancers combined the SIR was 81 (1541 observed, 95% CI 77 to 85) at East Fishkill and 87 (1319 observed, 95% CI 82 to 92) at San Jose (table 2). In the total group of employees at each facility, all SIRs for specific forms of cancer were <120. Employee subgroups with ⩾15 years since hiring and ⩾5 years of employment had 6–16% fewer total incident cancers than expected; their SIRs were ⩾120 at East Fishkill only for ovarian cancer (9 observed, SIR 121, 95% CI 55 to 230) and at San Jose for soft tissue sarcoma (6 observed, SIR 144, 95% CI 53 to 314), prostate cancer (243 observed, SIR 120, 95% CI 106 to 136) and

Table 1 Number of subjects by selected characteristics for each facility and for all employees combined

	East Fishkill n (%)	San Jose n (%)
Total*	42 612 (100)	46 912 (100)
Sex/race or ethnicity		
Men, total	27 946 (100)	29 795 (100)
White	23 355 (84)	15 450 (52)
Hispanic	696 (2)	3519 (12)
Asian	1808 (6)	8683 (29)
African American	2016 (7)	2007 (7)
American Indian	35 (0)	108 (0)
Unknown	36 (0)	28 (0)
Women, total	14 666 (100)	17 117 (100)
White	11 047 (75)	7289 (43)
Hispanic	490 (3)	3371 (20)
Asian	651 (4)	4771 (28)
African American	2408 (16)	1585 (0.9)
American Indian	27 (0)	93 (1)
Unknown	43 (0)	8 (0)
Vital status		
Alive	38 927 (91)	43 541 (93)
Deceased	2359 (6)	1200 (3)
Unknown	1326 (3)	2171 (5)
Age at end of follow-up (years)		
<40	15 735 (25)	19 212 (41)
40–49	10 716 (25)	11 400 (24)
50–59	7940 (19)	9317 (20)
⩾60	8221 (19)	6983 (15)
Median	44	43
Sex and SES group		
Men		
Professionals	13 386 (48)	13 232 (44)
Technicians	4435 (16)	2559 (9)
Prod/cler/other	10 125 (36)	14 004 (47)
Women		
Professionals	2827 (19)	4012 (23)
Technicians	1119 (8)	450 (3)
Prod/cler/other	10 720 (73)	12 655 (74)
Manufacturing era†		
1	10 212 (24)	7490 (16)
2	11 775 (28)	19 103 (41)
3	20 625 (48)	20 319 (43)
Years worked at facility		
<1	13 834 (32)	18 756 (40)
1–4	11 276 (26)	13 869 (30)
⩾5	17 502 (41)	14 287 (30)
Median	3.1	1.6
Years since first record of employment at facility		
<15	18 347 (43)	26 605 (57)
⩾15	24 265 (57)	20 307 (43)
Median	15.9	11.4
IBM employment status		
Active	11 048 (26)	8378 (18)
Retired	9893 (23)	6989 (15)
Left without retiring	21 671 (51)	31 545 (67)
Exposure category		
Exposed, ever	31 686 (74)	31 133 (66)
Unexposed	10 391 (24)	15 221 (32)
Person-years	499 445	362 076

*The total is less than the sum of the number of employees at each facility because 470 employees worked at both facilities.
†East Fishkill era 1,1965–73; era 2, 1974–83; era 3, 1984–99; San Jose era 1, 1965–72; era 2, 1973–89; era 3, 1990–9.

Table 2 Observed number of cases of specific types of cancer, standardised incidence ratio* and 95% confidence interval among all employees and among those who had stayed for ≥15 years since first record of employment and worked for ≥5 years, by facility

	East Fishkill						San Jose					
	All employees			≥15 YSF, ≥5 YRS			All employees			≥15 YSF, ≥5 YRS		
Facility and type of cancer†	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI
All cancers	1541	81	77 to 85	822	84	79 to 90	1319	87	82 to 92	758	94	88 to 101
Oral cavity, pharynx	32	51	35 to 72	20	64	39 to 99	33	62	43 to 87	15	55	31 to 91
Oesophagus	7	27	11 to 56	5	34	11 to 78	9	56	26 to 107	6	61	23 to 133
Stomach	18	45	27 to 71	10	46	22 to 84	23	71	45 to 106	17	96	56 to 154
Colorectum	184	83	72 to 96	112	90	74 to 108	148	101	85 to 118	88	103	83 to 127
Liver	8	47	20 to 92	4	41	11 to 106	12	49	25 to 86	4	33	9 to 84
Pancreas	37	83	59 to 115	28	112	74 to 162	20	68	42 to 106	12	69	36 to 121
Larynx	14	40	22 to 67	11	58	29 to 103	12	64	33 to 112	7	62	25 to 127
Lung, men	159	60	51 to 70	90	57	46 to 70	97	57	46 to 69	83	75	60 to 93
Lung, women	40	73	52 to 100	17	74	43 to 119	26	68	44 to 99	11	69	34 to 123
Soft tissue	8	54	24 to 107	1	17	0 to 97	10	99	47 to 182	6	144	53 to 314
Melanoma of the skin	45	83	61 to 111	22	94	59 to 142	71	111	87 to 140	34	119	82 to 166
Breast	185	104	89 to 120	66	114	88 to 145	162	102	87 to 119	47	94	69 to 125
Cervix	20	95	58 to 147	2	[4.1]		12	59	31 to 104	5	118	38 to 275
Endometrium	29	90	61 to 130	10	88	42 to 161	17	73	43 to 117	7	84	34 to 174
Ovary	21	86	53 to 131	9	121	55 to 230	13	65	35 to 111	5	87	28 to 202
Prostate	277	101	89 to 113	202	107	93 to 123	334	115	103 to 128	243	120	106 to 136
Testis	17	69	40 to 111	1	[4.2]		13	106	56 to 181	3	[2.3]	
Bladder	99	93	75 to 113	61	97	74 to 125	55	85	64 to 111	37	87	61 to 120
Kidney	55	101	76 to 131	29	98	66 to 141	29	77	52 to 111	12	57	29 to 99
Central nervous system	34	94	65 to 132	14	94	52 to 158	21	91	56 to 139	13	126	67 to 215
Thyroid	19	71	43 to 111	4	53	14 to 135	25	105	68 to 155	7	106	43 to 219
NHL	74	94	74 to 118	36	98	69 to 136	60	91	69 to 117	34	110	76 to 154
Hodgkin's lymphoma	25	114	74 to 169	5	110	36 to 256	9	90	41 to 170	2	[2.7]	
Leukaemia	35	70	49 to 98	15	62	35 to 103	37	103	73 to 142	21	115	71 to 175
Multiple myeloma	21	103	64 to 157	13	114	61 to 196	13	79	42 to 135	9	96	44 to 183
Other cancer	78	69	54 to 86	35	64	45 to 90	58	53	40 to 68	30	60	40 to 85

Obs, observed; NHL, non-Hodgkin's lymphoma; SIR, standardised incidence ratio; YRS, years worked; YSF, years since first record of employment.
*The expected number is provided in square brackets, without the SIR and the 95% confidence interval, when the observed number and the expected number of cases were both <5.
†Endometrium includes the uterus, not otherwise specified.

central nervous system cancer (13 observed, SIR 126, 95% CI 67 to 215).

Analyses by manufacturing era indicated a deficit of total cancer incidence in each era at both facilities (data not displayed). The all-cancer SIR for the earliest manufacturing era was 82 (983 observed, 95% CI 77 to 88) at East Fishkill and 93 (745 observed, 95% CI 86 to 100) at San Jose. At East Fishkill, results by manufacturing era for specific forms of cancer were unremarkable. At San Jose, employees hired in the earliest manufacturing era had excesses of soft tissue sarcoma (7 observed, SIR 175, 95% CI 71 to 361), melanoma of the skin (45 observed, SIR 160, 95% CI 117 to 214) and prostate cancer (246 observed, SIR 120, 95% CI 105 to 136).

SIR analyses indicated that both unexposed employees and potentially exposed employees had cancer incidence rates that were less than or equal to the general population rates overall and for most cancers (table 3, panels 1 and 2). Among those potentially exposed at each facility, several SIRs for specific cancers were >120 and were based on at least five observed cases, but none of these results approached statistical significance, and none of the corresponding RRs indicated a moderate or strong association with potential exposure (all RRs were <2.5). At East Fishkill, analyses by manufacturing era of first potential exposure did not show any notable cancer excesses (data not displayed). San Jose employees potentially exposed in the earliest manufacturing era had an excess of melanoma of the skin (30 observed, SIR 198, 95% CI 134 to 283) that was concentrated in short-term workers (<5 years worked: 15 observed, SIR 353, 95% CI 198 to 582), and an excess of soft tissue sarcoma (6 observed, SIR 276, 95% CI 101 to 600) that was concentrated in the subgroup who had worked for ≥5 years (5 observed, SIR 317, 95% CI 103 to 739).

Table A1 provides the number of employees and person-years in each work group and table A2 the results of SIR and Cox regression analyses for specific cancers for employees ever, compared with those never, in each work group (see tables A1 and A2, online at http://oem.bmjjournals.com/supplemental). For work groups associated with specific cancers and having at least five observed cases, an SIR of ≥150 and an RR of at least 1.5, we examined incidence patterns by years worked, years since starting work and manufacturing era.

At East Fishkill, several results met the above criteria for detailed consideration, but further analysis found that the associations were limited mainly or entirely to short-term employees in the respective work groups and did not display a duration–response trend. Such associations 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's lymphoma, and process equipment maintenance and multiple myeloma. For these associations, results for employees with ≥15 years since starting and ≥5 years in the work group were based on 0, 1 or 2 observed cases, respectively, and expected numbers were <1.

Several other associations at East Fishkill met the criteria for further consideration, displayed a trend with years spent in the relevant work group, but were characterised by sparse data on employees with ≥15 years since starting and ≥5 years in the work group. These included other manufacturing and cervical cancer (overall: 6 observed, SIR 300, 95% CI 110 to 652;

Table 3 Observed number of cases of specific types of cancer, standardised incidence ratio* and 95% confidence interval (CI) among all employees who were unexposed, ever exposed, and exposed with ⩾15 years since first exposure and ⩾5 years of exposure, and rate ratio† and 95% CI for exposed compared with unexposed, by facility‡

	Unexposed			Exposed			Exposed, ⩾15 YSF, ⩾5 YRS			Ever exposed	Exposed, ⩾15 YSF, 5⩾ YRS
Facility and type of cancer§	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI	RR, 95% CI	RR, 95% CI
Panel 1 East Fishkill											
All cancers	311	77	69 to 86	1194	82	77 to 87	571	83	77 to 90	1.0, 0.9 to 1.2	1.0, 0.9 to 1.2
Oral cavity, pharynx	5	42	14 to 97	26	53	34 to 77	12	54	28 to 95	1.3, 0.5 to 3.1	1.2, 0.5 to 3.4
Oesophagus	1	[4.6]	—	6	29	11 to 63	4	37	10 to 95	—	—
Stomach	2	27	3 to 99	15	47	26 to 78	8	51	22 to 100	—	—
Colorectum	27	62	41 to 91	150	86	73 to 101	87	99	79 to 122	1.2, 0.8 to 1.8	1.4, 0.9 to 2.1
Liver	0	[3.1]	—	7	51	21 to 105	4	57	16 to 146	—	—
Pancreas	9	104	48 to 198	25	71	46 to 105	17	96	56 to 153	0.7, 0.3 to 1.3	0.8, 0.4 to 1.8
Larynx	1	16	0 to 86	12	43	22 to 76	9	67	30 to 126	—	—
Lung, men	31	69	47 to 97	123	57	47 to 68	53	47	35 to 61	0.7, 0.5 to 1.1	0.6, 0.4 to 0.9
Lung, women	9	52	24 to 100	31	85	58 to 120	11	77	39 to 138	1.8, 0.8 to 3.8	1.6, 0.6 to 4.0
Soft tissue	2	[3.2]	—	6	53	20 to 116	1	4	—	—	—
Melanoma of the skin	8	65	28 to 129	37	91	64 to 125	15	93	52 to 153	1.2, 0.6 to 2.7	1.0, 0.4 to 2.6
Breast	69	115	89 to 145	113	98	81 to 117	32	94	65 to 133	0.8, 0.6 to 1.1	0.8, 0.5 to 1.2
Cervix	3	42	9 to 124	17	125	73 to 199	2	[2.4]	—	—	—
Endometrium	7	65	26 to 134	22	106	66 to 160	7	103	41 to 212	1.8, 0.7 to 4.5	1.4, 0.4 to 4.1
Ovary	9	107	49 to 203	11	70	35 to 125	4	[4.3]	—	0.6, 0.2 to 1.4	—
Prostate	44	97	71 to 130	227	102	89 to 116	148	107	90 to 125	1.1, 0.8 to 1.6	1.2, 0.8 to 1.6
Testis	3	[4.5]	—	14	71	39 to 118	0	3	—	—	—
Bladder	17	86	50 to 137	79	93	74 to 116	45	101	73 to 135	1.0, 0.6 to 1.7	1.2, 0.7 to 2.0
Kidney	8	75	32 to 147	44	103	75 to 138	21	100	62 to 153	1.1, 0.6 to 2.3	1.1, 0.5 to 2.5
Central nervous system	6	77	28 to 168	28	101	67 to 147	12	116	60 to 203	1.2, 0.5 to 3.0	1.0, 0.3 to 2.8
Thyroid	6	80	30 to 175	12	63	33 to 111	2	40	5 to 144	0.6, 0.2 to 1.5	—
NHL	13	80	43 to 137	61	100	76 to 128	28	109	72 to 157	1.2, 0.6 to 2.2	1.2, 0.6 to 2.5
Hodgkin's lymphoma	4	76	21 to 196	21	129	80 to 197	1	[3.1]	—	—	—
Leukaemia	8	79	34 to 157	27	70	46 to 102	12	70	36 to 123	1.1, 0.5 to 2.4	1.1, 0.4 to 2.8
Multiple myeloma	4	[3.9]	—	17	105	61 to 168	11	136	68 to 243	—	—
Panel 2 San Jose											
All cancers	529	93	85 to 101	558	92	85 to 100	394	91	83 to 101	1, 0.9 to 1.1	1, 0.9 to 1.2
Oral cavity, pharynx	12	64	33 to 111	20	60	37 to 93	10	68	33 to 125	1, 0.5 to 2.1	1.2, 0.5 to 2.8
Oesophagus	5	88	29 to 206	3	30	6 to 88	1	19	1 to 104	—	—
Stomach	6	53	20 to 116	17	82	48 to 132	11	113	57 to 203	2.0, 0.7 to 5.1	2.4, 0.8 to 6.8
Colorectum	58	109	83 to 141	88	98	78 to 120	49	107	79 to 141	1, 0.7 to 1.4	1.1, 0.7 to 1.6
Liver	4	52	14 to 132	7	43	17 to 89	2	29	4 to 104	—	—
Pancreas	7	65	26 to 134	13	73	39 to 125	6	64	24 to 140	1.3, 0.5 to 3.3	1.4, 0.4 to 4.2
Larynx	5	74	24 to 173	7	61	25 to 126	4	65	18 to 166	0.8, 0.2 to 2.6	—
Lung, men	36	61	43 to 85	59	55	42 to 71	47	78	57 to 104	0.9, 0.6 to 1.4	1.3, 0.8 to 2.0
Lung, women	13	70	37 to 120	12	64	33 to 112	7	95	38 to 195	1.1, 0.5 to 2.4	1.3, 0.5 to 3.6
Soft tissue	2	[3.7]	—	8	128	55 to 251	5	223	73 to 521	—	—
Melanoma of the skin	27	110	72 to 160	42	111	80 to 150	16	105	60 to 171	1.1, 0.7 to 1.8	0.9, 0.5 to 1.8
Breast	80	109	87 to 136	80	97	77 to 121	19	80	48 to 125	1.2, 0.8 to 1.6	0.9, 0.5 to 1.6
Cervix	4	45	12 to 115	8	73	31 to 143	3	[2.1]	—	—	—
Endometrium	8	73	32 to 144	8	69	30 to 136	4	[3.9]	—	0.9, 0.3 to 2.6	—
Ovary	3	32	7 to 94	10	98	47 to 179	4	[2.7]	—	—	—
Prostate	123	123	102 to 147	201	109	95 to 125	117	106	87 to 127	0.9, 0.8 to 1.2	0.9, 0.7 to 1.1
Testis	3	[4.3]	—	10	127	61 to 233	3	[1.3]	—	—	—
Bladder	18	77	45 to 121	37	94	66 to 130	21	92	57 to 141	1.3, 0.7 to 2.2	1.2, 0.6 to 2.3
Kidney	16	115	66 to 187	13	57	30 to 98	7	62	25 to 127	0.6, 0.3 to 1.2	0.5, 0.2 to 1.4
Central nervous system	9	102	47 to 193	12	87	45 to 152	9	164	75 to 311	0.8, 0.3 to 1.9	1.6, 0.6 to 4.3
Thyroid	13	137	73 to 234	11	79	39 to 141	5	143	46 to 334	0.7, 0.3 to 1.6	1.5, 0.5 to 4.5
NHL	28	116	77 to 168	30	74	50 to 106	14	84	46 to 141	0.7, 0.4 to 1.1	0.7, 0.3 to 1.3
Hodgkin's lymphoma	5	134	44 to 313	4	65	18 to 166	2	[1.5]	—	—	—
Leukaemia	14	107	59 to 180	23	104	66 to 156	11	112	56 to 200	1.1, 0.5 to 2.2	1.1, 0.5 to 2.5
Multiple myeloma	5	85	28 to 199	7	69	28 to 141	6	118	43 to 257	0.7, 0.2 to 2.1	1.0, 0.3 to 3.3

Obs, observed; NHL, non-Hodgkin's lymphoma; SIR, standardised incidence ratio; YRS, years worked; YSF, years since first record of employment.
*The expected number is provided in square brackets, without the SIR and the 95% CI, when the observed number and the expected number of cases were both <5.
†RR, adjusted using Cox regression for year of birth, socioeconomic status, sex and race; computed when there were at least five cases, both among the unexposed and among the exposed.
‡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 division, department and job codes (DDJs) (535 at East Fishkill and 558 at San Jose).
§Endometrium includes the uterus, not otherwise specified.

subgroup with ⩾15 years since starting and ⩾5 years: 0 observed, 0.1 expected), other manufacturing and endometrial cancer (overall: 7 observed, SIR 195, 95% CI 78 to 401; subgroup with ⩾15 years since starting and ⩾5 years: 1 observed, 0.3 expected), and research and development and multiple myeloma (overall: 9 observed, SIR 251, 95% CI 115 to 477; subgroup with ⩾15 years since starting and ⩾5 years: 2 observed, 0.4 expected).

Work in process equipment maintainence was associated with central nervous system cancer at East Fishkill (8 observed, SIR 192, 95% CI 83 to 379; RR 1.5, 95% CI 0.6 to 3.5), as in the companion mortality study.[7] The excess was concentrated in employees with ⩾15 years since starting and ⩾5 years worked (4 observed, 0.8 expected), but there was no evidence of a positive trend (p = 0.80). The central nervous system cancer excess in this work group was largely limited to the first manufacturing era (5 observed, SIR 301, 95% CI 105 to 756).

Several results at San Jose also met the criteria for detailed examination. Some of these were limited mainly or entirely to employees with <5 years in the respective work groups and did not display a duration–response trend, including associations between 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 leukaemia. The excess of soft tissue sarcoma among potentially exposed employees at San Jose was concentrated in research and development (4 observed, 0.9 expected). We did not examine this association further due to the small number of observed cases.

At San Jose, several other associations displayed a positive trend with length of employment in a work group, but were characterised by sparse data on employees who had both many years since starting and relatively long duration. These included other manufacturing and melanoma (overall 18 observed, SIR 161, 95% CI 96 to 255; subgroup with ⩾15 years since starting and ⩾5 years: 4 observed, 2.5 expected), head fabrication and cervical cancer (overall: 6 observed, SIR 157, 95% CI 58 to 342; subgroup with ⩾15 years since starting and ⩾5 years: 2 observed, 0.3 expected), disk manufacturing and endometrial cancer (overall: 6 observed, SIR 361, 95% CI 132 to 785; subgroup with ⩾15 years since starting and ⩾5 years: 1 observed, 0.1 expected), and clean rooms (occasional) and testicular cancer (overall: 9 observed, SIR 195, 95% CI 89 to 370; subgroup with ⩾15 years since starting and ⩾5 years: 1 observed, 0.6 expected).

DISCUSSION

Our study included large numbers of employees, person-years and cases, and had several other strengths, including low potential for differential information bias, residential histories that allowed the inclusion of person-time after employees stopped working at the study facilities, and the ability to assess non-fatal and fatal cancers. Internal analyses allowed us to assess potential associations between employment variables and cancer incidence alongside reducing potential distortion due to confounding and detection bias stemming from the relatively high SES of employees compared with the general population.[15–21] For cancers associated with relatively long survival, the incidence study provided more precision than the companion mortality study.[7] For example, there were six times more cases of prostate cancer 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 employees' young age, possible selection bias due to temporal and geographical restrictions, lack of agent-specific exposure information and lack of data on non-occupational confounders. Selection bias was a concern because of temporal and geographic follow-up restrictions. Analyses presented in a companion paper indicated minimal evidence that these restrictions affected validity for the overall cohorts from the two facilities.[10] However, because the proportion of follow-up time lost due to the restrictions varied by work group, it is possible that selection bias influenced the results of work group analyses. As noted earlier, the semiconductor industry over time has used several established and suspected carcinogens.[4–6] We did not develop estimates of employees' exposure to such agents. External analyses of many types of cancer may have been positively or negatively confounded by correlates of SES, and internal analyses, although possibly reducing such a problem, could still have been compromised by residual confounding. Our analyses examined a multitude 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 the general population rates overall and those of 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, including cancers of the oral cavity and pharynx, oesophagus, liver, larynx, lung and bladder. When the latter forms of cancer were excluded, residual cancers were, collectively, associated with only a modest deficit (SIR 92) among all employees, and there was almost no deficit (SIR 98) among employees with ⩾15 years since first recorded work and ⩾5 years worked.

When compared with the general population, some employee subgroups had small increases in several cancers, including melanoma of the skin and cancers of the colon, breast, prostate and thyroid, results that are consistent with employees' relatively high SES. SES tends to be associated positively with these cancers because of positive correlations with non-occupational risk factors, better detection or both.[15–21]

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 insufficient data to determine whether a duration–response relationship or a consistent pattern with potential induction time was present. Although several work group associations displayed positive duration–response trends, the underlying data were limited to short-term employees 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 partly due to confounding by well-established non-occupational causes that may not have been completely controlled for in the internal analyses.

The incidence study and its companion mortality study had results that differed in many respects. 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 geographical 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.[10]

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.[7] The incidence study found a weak association between cancer of the central nervous system and process equipment maintenance at East Fishkill. The association was concentrated in employees who began in the earliest manufacturing era and who had many years since starting and long duration of employment, but Cox regression analyses did not find a duration–response trend. The mortality study found a 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[10] and 80% of the deaths due to central nervous system cancer. 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 or laboratories and prostate cancer at San Jose,[7] the incidence study did not. This difference might be partly due 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.[10]

Previous research on two groups of semiconductor industry workers in the UK 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] whereas McElvenney *et al*[4] reported a twofold increase in lung cancer incidence. The results of the present study are not consistent with those of the British investigations. Storage device manufacturing workers have not been studied previously.

CONCLUSIONS

This study found that IBM employees at East Fishkill and San Jose had fewer than expected cases of cancer compared with 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 non-occupational risk factors, imprecision and other limitations. There was no strong and consistent evidence suggesting that any type of cancer was associated causally with employment factors. Further follow-up will allow a more informative analysis of cancer incidence that might be plausibly related to workplace exposures in the cohort.

ACKNOWLEDGEMENTS

We thank Lawrence Kupper, Dimitrios Trichopoulos and Noel Weiss for their guidance throughout the conduct of the research and for their comments on this paper. We also thank all IBM employees who contributed to developing work history classifications and to other aspects of data development for the project.

....

Authors' affiliations

T J Bender, C Beall, H Cheng, R Matthews, N Sathiakumar, E Delzell, Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, Alabama, USA

R F Herrick, J H Stewart, Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA

A R Kahn, M J Schymura, New York State Cancer Registry, New York State Department of Health, Albany, New York, USA

Funding: This research was funded by the IBM Corporation. TJB also received support from the Medical Scientist Training Program at the University of Alabama at Birmingham.

Competing interests: None.

The collection of cancer incidence data used in this study was supported by the California Department of Health Services as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract N01-PC-35136 awarded to the Northern California Cancer Center, contract N01-PC-35139 awarded to the University of Southern California, and contract N02-PC-15105 awarded to the Public Health Institute; and the Centers for Disease Control and Prevention's National Program of Cancer Registries, under agreement #U55/CCR921930-02 awarded to the Public Health Institute. The ideas and opinions expressed herein are those of the authors, and endorsement by the State of California, Department of Health Services, the National Cancer Institute, and the Centers for Disease Control and Prevention or their contractors and subcontractors is not intended nor should be inferred.

REFERENCES

1 **Sorahan T**, Waterhouse JA, McKiernan MJ, *et al*. Cancer incidence and cancer mortality in a cohort of semiconductor workers. *Br J Ind Med* 1985;**42**:546–50.
2 **Sorahan T**, Pope DJ, McKiernan MJ. Cancer incidence and cancer mortality in a cohort of semiconductor workers: an update. *Br J Ind Med* 1992;**49**:215–16.
3 **Nichols L**, Sorahan T. *Further update of cancer incidence and cancer mortality in a cohort of semiconductor workers*, Research report RR265. Sudbury, Suffolk: HSE Books, 2004.
4 **McElvenny DM**, Darnton AJ, Hodgson JT, *et al*. Investigation of cancer incidence and mortality at a Scottish semiconductor manufacturing facility. *Occup Med (Lond)* 2003;**53**:419–30.
5 **Herrick RF**, Stewart JH, Beall C, *et al*. Exposure assessment for retrospective follow-up studies of semiconductor and storage device manufacturing workers. *J Occup Environ Med* 2005;**47**:983–95.
6 **Siemiatycki J**, Richardson L, Straif K, *et al*. Listing occupational carcinogens. *Environ Health Perspect* 2004;**112**:1447–59.
7 **Beall C**, Bender TJ, Cheng H, *et al*. Mortality among semiconductor and storage device manufacturing workers. *J Occup Environ Med* 2005;**47**:996–1014.
8 **Demers PA**, Vaughan TL, Checkoway H, *et al*. Cancer identification using a tumor registry versus death certificates in occupational cohort studies in the United States. *Am J Epidemiol* 1992;**136**:1232–40.
9 **Veys CA**. Towards causal inference in occupational cancer epidemiology—II. Getting the count right. *Ann Occup Hyg* 1993;**37**:181–9.
10 **Bender TJ**, Beall C, Cheng H, *et al*. Methodological issues in follow-up studies of cancer incidence among occupational groups in the United States. *Ann Epidemiol* 2006;**16**:170–9.
11 **Bilgrad R**. *National Death Index Plus: coded causes of death supplement to the National Death Index user's manual*. Hyattsville, MD: National Center for Health Statistics, Centers for Disease Control and Prevention, 1997.
12 **Ferlay J**. *IARCtools, Version 2.01*. Lyon, France: Unit of Descriptive Epidemiology, International Agency for Research on Cancer, World Health Organization, 2001.
13 **Marsh GM**, Youk AO, Stone RA, *et al*. OCMAP-PLUS: a program for the comprehensive analysis of occupational cohort data. *J Occup Environ Med* 1998;**40**:351–62.
14 **Greenland S**, Finkle WD. A retrospective cohort study of implanted medical devices and selected chronic diseases in Medicare claims data. *Ann Epidemiol* 2000;**10**:205–13.
15 **Faggiano F**, Partanen T, Kogevinas M, *et al*. Socioeconomic differences in cancer incidence and mortality. *IARC Sci Publ* 1997;**138**:65–176.
16 **Mackillop WJ**, Zhang-Salomons J, Boyd CJ, *et al*. Associations between community income and cancer incidence in Canada and the United States. *Cancer* 2000;**89**:901–12.
17 **Katz SJ**, Hofer TP. Socioeconomic disparities in preventive care persist despite universal coverage. Breast and cervical cancer screening in Ontario and the United States. *JAMA* 1994;**272**:530–4.
18 **Mandelblatt J**, Andrews H, Kao R, *et al*. The late-stage diagnosis of colorectal cancer: demographic and socioeconomic factors. *Am J Public Health* 1996;**86**:1794–7.
19 **Ionescu MV**, Carey F, Tait IS, *et al*. Socioeconomic status and stage at presentation of colorectal cancer. *Lancet* 1998;**352**:1439.
20 **Mandelblatt JS**, Yabroff KR, Kerner JF. Equitable access to cancer services: a review of barriers to quality care. *Cancer* 1999;**86**:2378–90.
21 **Hiatt RA**, Klabunde C, Breen N, *et al*. Cancer screening practices from national health interview surveys: past, present, and future. *J Natl Cancer Inst* 2002;**94**:1837–46.