



Further update of cancer incidence and cancer mortality in a cohort of semiconductor workers

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Further update of cancer incidence and cancer mortality in a cohort of semiconductor workers

Linda Nichols PhD

Tom Sorahan PhD,DSc,FFOM(Hon)

Institute of Occupational and Environmental

Medicine

University of Birmingham

Edgbaston

Birmingham, UK

B15 2TT

In this report, the mortality (1970-2002) and cancer morbidity (1971-2001) experienced by a cohort of 1,807 male and female employees from a semiconductor factory in the West Midlands (UK) have been investigated. The cohort comprised workers in employment on 1st January 1970, and workers commencing employment in the period 1970-1979. All workers had been employed for at least one month. Standardised mortality ratios (SMRs) and standardised registration ratios (SRRs) were used to assess mortality and morbidity respectively in the total cohort.

Expectations for both mortality and morbidity were based on sex-, age- and calendar year specific rates for the general population of England and Wales.

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Executive Summary

The mortality (1970-2002) and cancer morbidity (1971-2001) experienced by a cohort of 1,807 male and female employees from a semiconductor factory in the West Midlands (UK) have been investigated. The cohort comprised workers in employment on 1st January 1970, and workers commencing employment in the period 1970-1979. All workers had been employed for at least one month. Standardised mortality ratios (SMRs) and standardised registration ratios (SRRs) were used to assess mortality and morbidity respectively in the total cohort. Expectations for both mortality and morbidity were based on sex-, age- and calendar year-specific rates for the general population of England and Wales.

Overall mortality was close to expectation in males (Obs 86, Exp 87.08, SMR 99) and significantly below expectation in females (Obs 221, Exp 297.92, SMR 74). Cancer mortality (all sites) was slightly above expectation in males (Obs 29, Exp 25.93, SMR 112) and significantly below expectation in females (Obs 82, Exp 118.70, SMR 69). There were significant deficits for cancer of the oesophagus in males and females combined (Obs 0, Exp 4.03) and for cancer of the breast in females (Obs 13, Exp 27.38, SMR 47). Observed numbers for all other cancer sites were not significantly different from expectation.

Incidence of all sites of cancer was close to expectation in both sexes (males: Obs 46, Exp 35.44, SRR 130; females: Obs 193, Exp 204.51, SRR 94). Significantly elevated SRRs were found in males for cancer of the rectum (Obs 6, Exp 2.11, SRR 284), in females for cancer of the pancreas (Obs 10, Exp 4.43, SRR 226) and malignant melanoma (Obs 11, Exp 4.97, SRR 221) and in males and females combined for cancer of the rectum (Obs 19, Exp 9.57, SRR 199) and malignant melanoma (Obs 12, Exp 5.53, SRR 217).

Attempts to identify whether any of the excess risks might be occupationally related were limited to analyses of risks by year of hire, period from first employment and duration of employment. These limited analyses did not suggest that any of the three cancers in excess were occupationally related.

In conclusion, this study has found significantly elevated morbidity for cancer of the rectum and malignant melanoma in the total study cohort (males and females combined). In addition, there was significantly elevated morbidity for cancer of the pancreas, but in female employees only. There was no suggestion of excess risks in this cohort of semiconductor workers for stomach cancer, lung cancer, breast cancer and cancer of the brain. More specifically, there was a significant deficit of deaths for female breast cancer and the corresponding deficit for cancer incidence approached formal levels of statistical significance. Work history data were unavailable for analysis and elucidation of possible occupational cancer risks in the semiconductor manufacturing industry will require more detailed epidemiological analyses.

Introduction

An earlier investigation¹ studied mortality and cancer incidence in 1,807 workers employed at a factory manufacturing semiconductors in the West Midlands, UK. Mortality was investigated for the period 1970-82, and cancer incidence for the period 1971-81. The mortality findings were unexceptional, although an excess of borderline statistical significance was reported for the incidence of malignant melanoma (Obs 3, Exp 0.68, SRR 441, $p=0.06$). This excess was not associated with duration of employment, either in the plant as a whole or in the photomasking process, a procedure known to involve ultraviolet light exposure. A more recent update of this study, with a further seven years of follow-up, found no additional cases of malignant melanoma.²

In 2003, the Health and Safety Executive (HSE) reported cancer incidence and mortality in a cohort of 4,388 semiconductor manufacturing workers based at a factory in Scotland, following concern that there might be a cluster of cancers at the facility.³ Overall mortality and cancer incidence was below or close to expectation. Based on rates for the general population of Scotland, a statistically significant excess (incidence and mortality) of lung cancer was found in female workers, along with a significant excess of stomach cancer (based on three cases) and a non-significant excess of breast cancer (based on 20 cases). In male workers there was a non-significant excess of deaths from cancer of the brain, based on three deaths.

In the light of the findings of the HSE report, and editorials expressing concern about cancer risks in the semiconductor manufacturing industry,^{4,5} it was clear that further information was required on this topic. It was decided, therefore, to incorporate a further 13 years of mortality and cancer incidence data into the West Midlands study², with the aim of identifying causes of death or sites of cancer that merited further investigation.

Materials and Methods

Identification particulars were available for 1,807 (281 males and 1,526 females) workers employed at a semiconductor manufacturing facility. The cohort comprised a “census” cohort in employment on 1st January 1970 (758 employees) together with an “entry” cohort that commenced employment between 1st January 1970 and 31st December 1979 (1,049 employees). [A previous report noted 759 employees in the survivor population and 1,048 in the entry cohort.¹ These figures have been revised after checking the employment dates.] All workers had a minimum period of employment of one month. Some 88% of the cohort was employed for twelve months or more.

Semiconductor production started on the site in 1966. In the 1980s, departments included the plating shop, assembly, wafer plating, diffusion (incorporating photomasking), chemical processing and the test area. A wide variety of chemicals was in use at the plant including hydrochloric acid, sulphuric acid, nitric acid, phosphoric acid, boric acid, acetic acid, chloroauric acid, hydrofluoric acid, nickel sulphate, nickel chloride, sodium hydroxide, potassium hydroxide, gold potassium cyanide, copper cyanide, potassium cyanide, silver cyanide, tin sulphate, chromium trioxide, methylene chloride, trichloroethylene, trichloroethane, cyclohexane, methylated spirits, ethylmethylketone, acetone, ethoxyethanol, lead solder, and epoxy resin. Work history data currently available to the study team is limited to dates of hire and leaving employment; full work histories (dates of working in different departments) were not abstracted at the time of the study inception. In addition, duration of employment at the plant was based solely on periods of employment before 31st March 1983.

The National Health Service Central Register (NHSCR) of the Office for National Statistics (ONS) provided information on the vital status of each study subject on the closing date of the survey, 31st December 2002. Vital status information is summarised in Table 1. Mortality data were analysed for the period 1970-2002, with underlying cause of death coded by ONS (ICD-8 1970-2000, ICD-10 2001-2002). Cancer registration particulars were analysed for the period 1971-2001; national cancer registration data are not available before 1971. Site of cancer (ICD-8 1971-78, ICD-9 1979-94, ICD-10 1995-2001) was also supplied by ONS. At the time of the last update,² subjects who could not be traced by ONS were traced either by the Department of Social Security (DSS), by searching the electoral register or because they were still employed at the company. Further use has not been made of these latter tracing procedures.

The mortality experience of the cohort was compared with that which might have been expected to occur if mortality rates for the general population of England and Wales for the period 1966-2000 had been operating on the study cohort, having due regard to the composition of the study cohort by sex, age (five year age groups) and calendar period (five year calendar periods). Expectations based on person-years at risk (pyr) were calculated using the PersonYears computer program.⁶ Study subjects entered the pyr on completion of one month employment or 1st January 1970, whichever was later. Individuals ceased to contribute to the pyr on the date of death, date of embarkation, the date they were last confirmed to be alive or the closing date of the study, whichever was the earlier. Study subjects made no contribution to observed or expected numbers after their 85th birthday. There are three reasons for this censoring. Firstly, published mortality rates are only available for the “open ended” age group ≥ 85 years and the distribution of the cohort pyr by single years of age may be very different to that of the general population; secondly, the reliability of cause of death particulars is probably poorer at later ages; and thirdly, any study subjects incorrectly coded as traced alive at the end of the study would have a disproportionate effect on the expected numbers for the open ended age group.

In a similar manner, the cancer morbidity experience of the cohort was compared with expectations based on cancer incidence rates for England and Wales for the period 1971-2000. For these analyses subjects could not enter the pyr before 1st January 1971. Employees traced by sources other than the NHSCR are not included in analyses of cancer incidence.

Standardised mortality ratios (SMRs) and standardised registration ratios (SRRs) were calculated as the ratio of observed to expected numbers of deaths expressed as a percentage. In calculating p-values and 95% confidence intervals (95% CIs), deaths and cancer registrations were assumed to occur as a Poisson process. In addition, evidence was sought for any trend (linear component) in the pattern of SMRs or SRRs (e.g. any tendency for SMRs to increase or decrease with time since first employment).⁷ Tests of heterogeneity were also carried out (e.g. could the differences in SMRs by duration of employment represent no more than random variation in sub-groups).⁷ Both tests assume a similar null hypothesis; no trend and homogeneous SMRs or SRRs. Small P-values indicate statistical significance, either that the trend or the amount of heterogeneity is unlikely to have occurred by chance alone. All significance tests were two-tailed.

Results

Table 2 shows observed and expected numbers of deaths from main disease groupings for male and female employees. Compared with national rates, all causes mortality was close to expectation for males (Obs 86, Exp 87.08, SMR 99) and was significantly below expectation in females (Obs 221, Exp 297.92, SMR 74). Statistically significant deficits of deaths were found in females for all neoplasms (Obs 82, Exp 118.70, SMR 69), diseases of the circulatory system (Obs 83, Exp 105.11, SMR 79) and non-malignant diseases of the respiratory system (Obs 18, Exp 29.53, SMR 61).

Table 3 shows observed and expected numbers of deaths for individual sites of cancer for male and female employees. The only findings for which there were significant differences between observed and expected numbers were deficits for cancer of the breast in females (Obs 13, Exp 27.38, SMR 47) and cancer of the oesophagus in males and females combined (Obs 0, Exp 4.03).

Table 4 shows observed and expected numbers of cancer registrations for male and female employees. In males, there was a non-significant excess for all malignant neoplasms (Obs 46, Obs 35.44, SRR 130), although there was a significantly elevated SRR for cancer of the rectum (Obs 6, Exp 2.11, SRR 284). In females, cases of all malignant neoplasms were slightly below expectation (Obs 193, Exp 204.51, SRR 94) although there was a significantly elevated SRR for cancer of the pancreas (Obs 10, Exp 4.43, SRR 226) and malignant melanoma (Obs 11, Exp 4.97, SRR 221). In males and females combined, cases of all malignant neoplasms were close to expectation (Obs 239, Exp 239.95, SRR 100) although there was a significantly elevated SRR for cancer of the rectum (Obs 19, Exp 9.57, SRR 199) and malignant melanoma (Obs 12, Exp 5.53, SRR 217).

Sites of cancer that warranted further investigation were then selected. Cancers of the stomach, lung, brain and breast (female) were selected on the basis of findings from the HSE study of semiconductor workers.³ In addition, cancer of the rectum, cancer of the pancreas and malignant melanoma were selected because of the excess incidence of these cancers in the current study.

Observed and expected numbers of deaths by year of hire, time since first employment and duration of employment are shown for stomach cancer, rectal cancer, pancreatic cancer, lung cancer, malignant melanoma, breast cancer and cancer of the brain in Tables 5-11, respectively. Confidence intervals (95%) are only shown for those SMRs based on two or more observed deaths. In these analyses the numbers of deaths available were small and no significant trends or significant heterogeneity were found in any set of SMRs.

Table 12 shows observed and expected numbers of registrations for cancer of the stomach by year of hire, time since first employment and duration of employment. Numbers of cases were small and no significant trends or significant heterogeneity were found in any set of SRRs.

Table 13 shows observed and expected numbers of registrations for cancer of the rectum by year of hire, time since first employment and duration of employment. There was no significant trend or significant heterogeneity in any set of SRRs. There was a significantly elevated SRR for workers (males and females) first employed in the 1970s (Obs 11, Exp 4.45, SRR 247).

Table 14 shows observed and expected numbers of registrations for cancer of the pancreas by year of hire, time since first employment and duration of employment. There was no significant

trend or significant heterogeneity in any set of SRRs. All cases occurred in workers first employed in the period 1960-79.

Table 15 shows observed and expected numbers of registrations for cancer of the lung and bronchus by year of hire, time since first employment and duration of employment. There was no significant trend or significant heterogeneity in any set of SRRs, and all category-specific SRRs were unexceptional.

Table 16 shows observed and expected numbers of registrations for malignant melanoma by year of hire, time since first employment and duration of employment. There was no significant trend or significant heterogeneity in any set of SRRs. All cases occurred in workers first employed in the period 1960-79.

Table 17 shows observed and expected numbers of registrations for cancer of the breast by year of hire, time since first employment and duration of employment among female employees. SRRs by year of hire showed significant heterogeneity ($p=0.02$) and a significant negative trend with year of hire ($p=0.01$), i.e. there were lower SRRs with recent decades of hire. In addition, the positive trend with duration of employment approached statistical significance ($p=0.06$). This trend was based on unusually low incidence in the short duration of employment category ($<5y$) rather than unusually high incidence in the longest category of duration ($\geq 10y$).

Table 18 shows observed and expected numbers of registrations for cancer of the brain by year of hire, time since first employment and duration of employment. There were only two cases available for analysis.

Table 1 Study population of semiconductor workers at Mere Green site by vital status (as of 31st December, 2002) and sex

<i>Vital status</i>	<i>Males</i>	<i>Females</i>	<i>Total</i>	<i>(%)</i>
Flagged alive - NHSCR	185	1261	1446	(80.0)
Traced alive – DSS ^a	2	13	15	(0.8)
Traced alive – still employed ^b	0	4	4	(0.2)
Traced alive – electoral register ^c	0	1	1	(0.1)
Emigrated	4	18	22	(1.2)
No trace	0	0	0	(0.0)
Deceased	90	229	319	(17.7)
	281	1526	1807	(100.0)

a. to 01/03/1989

b. to 31/12/1982

c. to 31/12/1983

Table 2 Mortality from main disease groupings in semiconductor workers, Mere Green site, 1970-2002

Site of cancer	ICD-9	Males			Females			Total					
		Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)			
Infectious and parasitic diseases	1-139	0	0.49	0	-	0	0	0	0	0	-	-	-
All neoplasms	140-239	29	25.93	112	(75 to 161)	82	118.70	69(***)	(55 to 86)	111	144.63	77(**)	(63 to 92)
Endocrine nutritional and metabolic diseases	240-279	0	1.10	0	-	3	4.91	61	(13 to 179)	3	6.01	50	(10 to 146)
Diseases of blood	280-289	0	0.22	0	-	1	0.94	106	-	1	1.16	86	-
Mental disorders	290-319	0	0.62	0	-	2	2.41	83	(10 to 300)	2	3.03	66	(8 to 238)
Diseases of nervous system	320-389	1	1.32	76	-	4	5.95	67	(18 to 172)	5	7.27	69	(22 to 161)
Diseases of circulatory system	390-459	43	40.43	106	(77 to 143)	83	105.11	79(*)	(63 to 98)	126	145.54	87	(72 to 103)
Diseases of respiratory system	460-519	9	9.47	95	(43 to 180)	18	29.53	61(*)	(36 to 96)	27	39.00	69	(46 to 101)
Diseases of digestive system	520-579	4	2.62	152	(42 to 390)	12	11.54	104	(54 to 182)	16	14.16	113	(65 to 184)
Diseases of genitourinary system	580-629	0	0.80	0	-	2	3.07	65	(8 to 236)	2	3.87	52	(6 to 187)
Diseases of skin	680-709	0	0.05	0	-	1	0.38	260	-	1	0.44	228	-
Diseases of musculo skeletal system	710-739	0	0.25	0	-	2	2.38	84	(10 to 303)	2	2.64	76	(9 to 274)
Accidents	800-949	0	1.99	0	-	2	5.11	39	(5 to 141)	2	7.10	28	(3 to 102)
Suicide	950-959	0	1.03	0	-	1	2.76	36	-	1	3.79	26	-
All causes		86	87.08	99	(79 to 122)	221	297.92	74(***)	(65 to 85)	307	385.00	80(***)	(71 to 89)

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, () indicates deficit.

Table 3 Cancer mortality in semiconductor workers, Mere Green site, 1970-2002

Site of cancer	ICD-9	Males			Females			Total		
		Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)
Lip	140	0	0.01	0	0	0.01	0	0.01	0	-
Tongue	141	1	0.09	1107	0	0.23	0	1	0.33	307
Salivary gland	142	0	0.04	0	0	0.11	0	0	0.15	0
Mouth	143-145	0	0.09	0	0	0.23	0	0	0.32	0
Pharynx	146-149	1	0.19	540	0	0.50	0	1	0.69	145
Oesophagus	150	0	1.13	0	0	2.90	0	0	4.03	0(*)
Stomach	151	2	1.88	106 (13 to 384)	5	3.96	126	7	5.84	120 (48 to 247)
Small intestine	152	0	0.05	0	0	0.21	0	0	0.26	0
Large intestine	153	3	1.72	175 (36 to 511)	9	8.18	110	12	9.90	121 (63 to 212)
Rectum	154	2	1.08	185 (22 to 667)	2	3.36	60	4	4.44	90 (25 to 231)
Liver	155.0,155.1	0	0.26	0	0	0.88	0	0	1.14	0
Gallbladder	156	0	0.11	0	0	0.70	0	0	0.81	0
Pancreas	157	0	1.09	0	9	4.62	195	9	5.71	158 (72 to 299)
Peritoneum	158	0	0.04	0	0	0.19	0	0	0.23	0
Other digestive	159	0	0.17	0	1	0.76	131	1	0.93	108
Nose and sinuses	160	0	0.04	0	0	0.12	0	0	0.16	0
Larynx	161	0	0.24	0	0	0.33	0	0	0.58	0
Lung and bronchus	162	11	8.76	126 (63 to 225)	14	20.60	68	25	29.36	85 (55 to 126)
Pleura	163	0	0.15	0	0	0.16	0	0	0.31	0
Bone	170	0	0.05	0	0	0.15	0	0	0.20	0
Connective tissue	171	0	0.10	0	0	0.53	0	0	0.63	0
Melanoma	172	0	0.22	0	1	1.34	74	1	1.57	64
Skin, other	173	0	0.07	0	0	0.17	0	0	0.23	0
Breast	174,175	0	0.03	0	13	27.38	47(**)	13	27.41	47(**) (25 to 81)
Cervix	180	-	-	-	2	3.90	51	-	-	- (6 to 185)
Uterus	182	-	-	-	0	1.66	0	-	-	-
Ovary	183	-	-	-	5	9.37	53	-	-	- (17 to 125)
Prostate	185	3	1.98	152 (31 to 444)	-	-	-	-	-	-
Testis	186	0	0.06	0	-	-	-	-	-	-

Other genital	184,187	0	0.04	0	-	1	0.54	186	-	1	0.57	174	-
Bladder	188	0	0.96	0	-	2	1.73	115	(14 to 416)	2	2.70	74	(9 to 268)
Kidney	189,0	0	0.54	0	-	2	1.68	119	(14 to 429)	2	2.23	90	(11 to 324)
Other urinary	189.1-189.9	0	0.03	0	-	0	0.09	0	-	0	0.12	0	-
Eye	190	0	0.02	0	-	0	0.12	0	-	0	0.14	0	-
Brain	191-192	0	0.66	0	-	3	2.94	102	(21 to 298)	3	3.60	83	(17 to 243)
Thyroid	193	0	0.04	0	-	1	0.33	300	-	1	0.37	268	-
Other endocrine glands	194	0	0.02	0	-	0	0.12	0	-	0	0.14	0	-
Secondary and other cancers	195-199	3	1.87	160	(33 to 468)	6	8.78	68	(25 to 149)	9	10.65	84	(39 to 160)
Hodgkins disease	201	0	0.11	0	-	0	0.35	0	-	0	0.46	0	-
Lymphosarcoma	200,202	1	0.66	152	-	2	2.84	70	(9 to 254)	3	3.50	86	(18 to 250)
Multiple myeloma	203	1	0.36	280	-	0	1.60	0	-	1	1.95	51	-
Leukaemia	204-208	1	0.63	159	-	2	2.49	80	(10 to 291)	3	3.11	96	(20 to 282)
All neoplasms	140-239	29	25.93	112	(75 to 161)	82	118.70	69(***)	(55 to 86)	111	144.63	77(**)	(63 to 92)

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, () indicates deficit.

Table 4 Cancer incidence in semiconductor workers, Mere Green site 1971-2001

Site of cancer	ICD-9	Males			Females			Total			
		Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)	
Lip	140	0	0.08	0	0	0.10	0	0	0.18	0	-
Tongue	141	1	0.17	588	0	0.55	0	1	0.73	137	-
Salivary gland	142	0	0.08	0	0	0.39	0	0	0.46	0	-
Mouth	143-145	0	0.22	0	2	0.67	299	2	0.89	225	(27 to 812)
Pharynx	146-149	1	0.31	323	0	0.83	0	1	1.14	88	-
Oesophagus	150	0	1.07	0	1	3.06	33	1	4.13	24	-
Stomach	151	3	2.21	136	4	4.75	84	7	6.96	101	(40 to 207)
Small intestine	152	0	0.09	0	0	0.40	0	0	0.49	0	-
Large intestine	153	4	2.68	149	16	13.89	115	20	16.57	121	(74 to 186)
Rectum	154	6	2.11	284*	13	7.46	174	19	9.57	199**	(120 to 310)
Liver	155.0,155.1	0	0.31	0	0	0.95	0	0	1.26	0	-
Gallbladder	156	0	0.16	0	0	1.05	0	0	1.22	0	-
Pancreas	157	0	1.04	0	10	4.43	226*	10	5.47	183	(88 to 336)
Peritoneum	158	0	0.05	0	0	0.32	0	0	0.37	0	-
Other digestive	159	0	0.07	0	0	0.30	0	0	0.36	0	-
Nose and sinuses	160	0	0.08	0	1	0.29	345	1	0.37	270	-
Larynx	161	1	0.63	159	1	0.78	128	2	1.41	142	(17 to 512)
Lung and bronchus	162	10	8.93	112	15	21.84	69	25	30.77	81	(53 to 120)
Pleura	163	0	0.30	0	0	0.35	0	0	0.65	0	-
Bone	170	0	0.06	0	0	0.25	0	0	0.31	0	-
Connective tissue	171	1	0.18	556	0	0.89	0	1	1.07	93	-
Melanoma	172	1	0.56	179	11	4.97	221*	12	5.53	217*	(112 to 379)
Skin, other	173	5	6.08	82	31	26.60	117	36	32.68	110	(77 to 153)
Breast	174,175	0	0.08	0	54	68.93	78	54	69.01	78	(59 to 102)
Cervix	180	-	-	-	5	8.45	59	-	-	-	-
Uterus	182	-	-	-	8	9.79	82	-	-	-	-
Ovary	183	-	-	-	11	12.44	88	-	-	-	-
Prostate	185	5	4.32	116	-	-	-	-	-	-	-
Testis	186	1	0.36	278	-	-	-	-	-	-	-

Other genital	184,187	0	0.13	0	-	4	1.83	219	(60 to 560)	4	1.96	204	(56 to 523)
Bladder	188	2	2.60	77	(9 to 278)	6	4.67	128	(47 to 280)	8	7.27	110	(48 to 217)
Kidney and other urinary	189	0	0.95	0	-	4	3.05	131	(36 to 336)	4	4.01	100	(27 to 255)
Eye	190	0	0.07	0	-	0	0.39	0	-	0	0.47	0	-
Brain	191-192	0	0.73	0	-	2	3.27	61	(7 to 221)	2	4.00	50	(6 to 181)
Thyroid	193	0	0.09	0	-	1	1.22	82	-	1	1.31	76	-
Other endocrine glands	194	0	0.04	0	-	1	0.22	455	-	1	0.26	385	-
Secondary and other cancers	195-199	5	1.91	262	(85 to 611)	8	9.44	85	(37 to 167)	13	11.36	114	(61 to 196)
Hodgkins disease	201	1	0.24	417	-	1	0.77	130	-	2	1.01	198	(24 to 715)
Lymphosarcoma	200,202	1	1.12	89	-	8	5.35	150	(65 to 295)	9	6.47	139	(64 to 264)
Multiple myeloma	203	1	0.47	213	-	2	2.11	95	(11 to 342)	3	2.58	116	(24 to 340)
Leukaemia	204-208	2	0.86	233	(28 to 840)	3	3.28	91	(19 to 267)	5	4.13	121	(39 to 283)
All malignant neoplasms ^a	140-208	46	35.44	130	(95 to 173)	193	204.51	94	(82 to 109)	239	239.95	100	(87 to 113)

* $p < 0.05$, ** $p < 0.01$.

a. *excluding other skin.*

Table 5 Mortality from cancer of the stomach among semiconductor workers, Mere Green site, 1970-2002

	Males			Females			Total		
	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.17	0	0	0.00	0	0	0.17	0
1940-49	0	0.02	0	1	0.12	838	1	0.14	714
1950-59	0	0.29	0	0	0.23	0	0	0.52	0
1960-69	1	0.65	154	1	1.99	50	2	2.64	76 (9 to 274)
1970-79	1	0.76	132	3	1.62	185 (38 to 540)	4	2.38	168 (46 to 430)
<i>Period from first employment (years)</i>									
<10	1	0.27	370	0	0.46	0	1	0.73	137
10-19	1	0.56	178	2	1.02	196 (24 to 707)	3	1.58	189 (39 to 553)
20-29	0	0.60	0	2	1.62	124 (15 to 446)	2	2.21	90 (11 to 326)
>30	0	0.45	0	1	0.86	116	1	1.31	76
<i>Duration of employment (years)</i>									
<5	1	0.59	169	2	0.99	203 (25 to 372)	3	1.58	190 (39 to 555)
5-9	0	0.37	0	1	1.13	88	1	1.51	66
≥10	1	0.92	109	2	1.84	109 (13 to 392)	3	2.76	109 (22 to 318)
Total	2	1.88	106 (13 to 384)	5	3.96	126 (41 to 294)	7	5.84	120 (48 to 247)

Table 6 Mortality from cancer of the rectum among semiconductor workers, Mere Green site, 1970-2002

	Males			Females			Total		
	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.08	0	0	0.00	0	0	0.08	0
1940-49	0	0.01	0	0	0.09	0	0	0.10	0
1950-59	0	0.15	0	1	0.18	570	1	0.33	303
1960-69	0	0.36	0	0	1.63	0	0	1.99	0
1970-79	2	0.48	414 (50 to 1494)	1	1.46	69	3	1.94	155 (32 to 452)
<i>Period from first employment (years)</i>									
<10	1	0.13	762	0	0.35	0	1	0.48	207
10-19	0	0.31	0	0	0.88	0	0	1.19	0
20-29	1	0.38	265	1	1.42	71	2	1.79	112 (14 to 403)
>30	0	0.26	0	1	0.71	141	1	0.97	103
<i>Duration of employment (years)</i>									
<5	1	0.36	281	1	0.85	118	2	1.20	166 (20 to 601)
5-9	1	0.22	461	0	0.96	0	1	1.18	85
≥10	0	0.51	0	1	1.55	65	1	2.06	49
Total	2	1.08	185 (22 to 667)	2	3.36	60 (7 to 215)	4	4.44	90 (25 to 231)

Table 7 Mortality from cancer of the pancreas among semiconductor workers, Mere Green site, 1970-2002

	Males			Females			Total		
	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.08	0	0	0.00	0	0	0.08	0
1940-49	0	0.01	0	0	0.12	0	0	0.13	0
1950-59	0	0.15	0	0	0.24	0	0	0.39	0
1960-69	0	0.36	0	6	2.23	269 (99 to 586)	6	2.59	232 (85 to 504)
1970-79	0	0.50	0	3	2.03	148 (31 to 432)	3	2.53	119 (24 to 347)
<i>Period from first employment (years)</i>									
<10	0	0.13	0	1	0.32	310	1	0.46	219
10-19	0	0.31	0	1	1.06	95	1	1.37	73
20-29	0	0.38	0	6	2.13	282* (104 to 614)	6	2.51	239 (88 to 521)
>30	0	0.26	0	1	1.12	90	1	1.37	73
<i>Duration of employment (years)</i>									
<5	0	0.36	0	2	1.12	179 (22 to 646)	2	1.48	135 (16 to 488)
5-9	0	0.22	0	4	1.31	306 (84 to 785)	4	1.52	262 (72 to 672)
≥10	0	0.51	0	3	2.20	137 (28 to 399)	3	2.70	111 (23 to 325)
Total	0	1.09	0	9	4.62	195 (89 to 370)	9	5.71	158 (72 to 299)

* $p < 0.05$.

Table 8 Mortality from cancer of the lung and bronchus among semiconductor workers, Mere Green site, 1970-2002

	Males				Females				Total			
	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)
<i>Year of hire</i>												
Pre 1940	0	0.69	0	-	0	0.02	0	-	0	0.71	0	-
1940-49	0	0.06	0	-	1	0.51	196	-	1	0.57	175	-
1950-59	2	1.31	153	(18 to 551)	1	0.99	101	-	3	2.30	130	(27 to 381)
1960-69	3	2.98	101	(21 to 295)	7	9.85	71	(29 to 146)	10	12.83	78	(37 to 143)
1970-79	6	3.72	161	(59 to 351)	5	9.24	54	(18 to 126)	11	12.96	85	(42 to 152)
<i>Period from first employment (years)</i>												
<10	1	1.19	84	-	1	1.44	69	-	2	2.63	76	(9 to 275)
10-19	6	2.60	230	(85 to 501)	3	4.83	62	(13 to 181)	9	7.44	121	(55 to 230)
20-29	3	2.90	103	(21 to 302)	6	9.58	63	(23 to 136)	9	12.48	72	(33 to 137)
>30	1	2.06	48	(1 to 270)	4	4.75	84	(23 to 216)	5	6.81	73	(24 to 171)
<i>Duration of employment (years)</i>												
<5	6	2.81	214	(78 to 465)	5	4.96	101	(33 to 235)	11	7.77	142	(71 to 253)
5-9	2	1.74	115	(14 to 416)	0	5.75	0(*)	-	2	7.48	27(*)	(3 to 97)
≥10	3	4.21	71	(15 to 208)	9	9.90	91	(42 to 173)	12	14.11	85	(44 to 149)
Total	11	8.76	126	(63 to 225)	14	20.60	68	(37 to 114)	25	29.36	85	(55 to 126)

* $p < 0.05$, () indicates deficit.

Table 9 Mortality from melanoma among semiconductor workers, Mere Green site, 1970-2002

	Males			Females			Total		
	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.01	0	0	0.00	0	0	0.01	0
1940-49	0	0.00	0	0	0.02	0	0	0.02	0
1950-59	0	0.02	0	0	0.05	0	0	0.07	0
1960-69	0	0.07	0	1	0.58	171	1	0.65	154
1970-79	0	0.13	0	0	0.69	0	0	0.82	0
<i>Period from first employment (years)</i>									
<10	0	0.03	0	0	0.21	0	0	0.24	0
10-19	0	0.07	0	1	0.38	261	1	0.45	223
20-29	0	0.08	0	0	0.53	0	0	0.61	0
>30	0	0.04	0	0	0.23	0	0	0.27	0
<i>Duration of employment (years)</i>									
<5	0	0.09	0	0	0.42	0	0	0.51	0
5-9	0	0.05	0	0	0.40	0	0	0.45	0
≥10	0	0.08	0	1	0.52	191	1	0.61	164
Total	0	0.22	0	1	1.34	74	1	1.57	64

Table 10 Mortality from cancer of the breast among female semiconductor workers, Mere Green site, 1970-2002

	<i>Obs</i>	<i>Exp</i>	<i>SMR</i>	<i>(95% CI)</i>
<i>Year of hire</i>				
Pre 1940	0	0.02	-	-
1940-49	0	0.53	-	-
1950-59	0	1.13	-	-
1960-69	7	12.31	57	(23 to 117)
1970-79	6	13.39	45(*)	(16 to 98)
<i>Period from first employment (years)</i>				
<10	2	4.09	49	(6 to 177)
10-19	3	8.69	35	(7 to 101)
20-29	7	10.44	67	(27 to 138)
>30	1	4.16	24	(1 to 134)
<i>Duration of employment (years)</i>				
<5	2	8.03	25(*)	(3 to 90)
5-9	5	8.11	62	(20 to 144)
≥10	6	11.24	53	(20 to 116)
Total	13	27.38	47(**)	(25 to 81)

* $p < 0.05$, ** $p < 0.01$, () indicates deficit.

Table 11 Mortality from cancer of the brain among semiconductor workers, Mere Green site 1970-2002

	Males			Females			Total		
	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)	Obs	Exp	SMR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.02	0	0	0.00	0	0	0.02	0
1940-49	0	0.00	0	0	0.05	0	0	0.05	0
1950-59	0	0.06	0	1	0.11	888	1	0.17	588
1960-69	0	0.20	0	0	1.30	0	0	1.50	0
1970-79	0	0.37	0	2	1.48	135 (16 to 487)	2	1.85	108 (13 to 391)
<i>Period from first employment (years)</i>									
<10	0	0.12	0	0	0.44	0	0	0.56	0
10-19	0	0.21	0	1	0.88	114	1	1.09	92
20-29	0	0.22	0	2	1.17	171 (21 to 617)	2	1.39	144 (17 to 519)
≥30	0	0.11	0	0	0.46	0	0	0.56	0
<i>Duration of employment (years)</i>									
<5	0	0.26	0	0	0.89	0	0	1.15	0
5-9	0	0.15	0	1	0.86	116	1	1.01	99
≥10	0	0.25	0	2	1.20	167 (20 to 604)	2	1.44	139 (17 to 501)
Total	0	0.66	0	3	2.94	102 (21 to 298)	3	3.60	83 (17 to 243)

Table 12 Incidence of stomach cancer among semiconductor workers, Mere Green site, 1971-2001

	Males			Females			Total		
	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.15	0	0	0.01	0	0	0.16	0
1940-49	0	0.02	0	1	0.14	714	1	0.16	625
1950-59	0	0.33	0	0	0.26	0	0	0.59	0
1960-69	2	0.76	263 (32 to 951)	1	2.35	43	3	3.11	96 (20 to 282)
1970-79	1	0.96	104	2	1.99	101 (12 to 363)	3	2.95	102 (21 to 297)
<i>Period from first employment (years)</i>									
<10	1	0.30	333	0	0.50	0	1	0.80	125
10-19	2	0.69	290 (35 to 1047)	1	1.28	78	3	1.96	153 (32 to 447)
20-29	0	0.75	0	3	2.06	146 (30 to 426)	3	2.80	107 (22 to 313)
≥30	0	0.47	0	0	0.92	0	0	1.39	0
<i>Duration of employment (years)</i>									
<5	1	0.71	141	1	1.18	85	2	1.89	106 (13 to 382)
5-9	1	0.45	222	1	1.36	74	2	1.81	110 (13 to 399)
≥10	1	1.04	96	2	2.21	90 (11 to 327)	3	3.26	92 (19 to 269)
Total	3	2.21	136 (28 to 397)	4	4.75	84 (23 to 216)	7	6.96	101 (40 to 207)

Table 13 Incidence of cancer of the rectum among semiconductor workers, Mere Green site, 1971-2001

	Males			Females			Total		
	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)
<i>Year of hire</i>									
Pre 1940	1	0.11	909	0	0.01	0	1	0.12	833
1940-49	0	0.01	0	0	0.18	0	0	0.19	0
1950-59	1	0.27	370	1	0.35	286	2	0.62	323
1960-69	0	0.69	0	5	3.50	143	5	4.19	119
1970-79	4	1.03	388* (106 to 994)	7	3.42	205	11	4.45	247* (123 to 442)
<i>Period from first employment (years)</i>									
<10	1	0.23	435	0	0.65	0	1	0.88	114
10-19	3	0.61	492* (101 to 1437)	2	1.94	103	5	2.56	195
20-29	1	0.81	123	9	3.45	261* (119 to 495)	10	4.26	235* (113 to 432)
≥30	1	0.46	217	2	1.41	142	3	1.87	160
<i>Duration of employment (years)</i>									
<5	3	0.72	417	2	1.91	105	5	2.64	189
5-9	1	0.43	233	4	2.14	187	5	2.58	194
≥10	2	0.95	211	7	3.40	206	9	4.35	207
Total	6	2.11	284* (104 to 619)	13	7.46	174	19	9.57	199** (120 to 310)

* $p < 0.05$, ** $p < 0.01$.

Table 14 Incidence of cancer of the pancreas among semiconductor workers, Mere Green site, 1971-2001

	Males			Females			Total		
	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.06	0	0	0.00	0	0	0.06	0
1940-49	0	0.01	0	0	0.12	0	0	0.13	0
1950-59	0	0.14	0	0	0.23	0	0	0.37	0
1960-69	0	0.35	0	7	2.14	327* (132 to 674)	7	2.49	281* (113 to 579)
1970-79	0	0.48	0	3	1.94	155 (32 to 452)	3	2.42	124 (26 to 362)
<i>Period from first employment (years)</i>									
<10	0	0.13	0	1	0.31	323	1	0.44	227
10-19	0	0.31	0	1	1.07	93	1	1.39	72
20-29	0	0.37	0	6	2.12	283* (104 to 616)	6	2.49	241 (88 to 524)
≥30	0	0.22	0	2	0.93	215 (26 to 777)	2	1.15	174 (21 to 628)
<i>Duration of employment (years)</i>									
<5	0	0.35	0	2	1.07	187 (23 to 675)	2	1.42	141 (17 to 509)
5-9	0	0.21	0	4	1.26	317 (86 to 813)	4	1.47	272 (74 to 697)
≥10	0	0.48	0	4	2.11	190 (52 to 485)	4	2.58	155 (42 to 397)
Total	0	1.04	0	10	4.43	226* (108 to 415)	10	5.47	183 (88 to 336)

* $p < 0.05$.

Table 15 Incidence of cancer of the lung and bronchus among semiconductor workers, Mere Green site, 1971-2001

	Males			Females			Total		
	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.56	0	0	0.02	0	0	0.58	0
1940-49	0	0.06	0	1	0.53	189	1	0.59	169
1950-59	3	1.33	226 (47 to 659)	0	1.04	0	3	2.37	127 (26 to 370)
1960-69	3	3.05	98 (20 to 287)	8	10.40	77 (33 to 152)	11	13.45	82 (41 to 146)
1970-79	4	3.92	102 (28 to 261)	6	9.84	61 (22 to 133)	10	13.76	73 (35 to 134)
<i>Period from first employment (years)</i>									
<10	1	1.26	79	1	1.58	63	2	2.85	70 (8 to 253)
10-19	5	2.81	178 (58 to 415)	3	5.53	54 (11 to 159)	8	8.34	96 (41 to 189)
20-29	2	3.00	67 (8 to 241)	7	10.44	67 (27 to 138)	9	13.44	67 (31 to 127)
≥30	2	1.86	108 (13 to 388)	4	4.28	93 (25 to 239)	6	6.14	98 (36 to 213)
<i>Duration of employment (years)</i>									
<5	4	2.91	137 (37 to 352)	5	5.27	95 (31 to 221)	9	8.19	110 (50 to 209)
5-9	2	1.82	110 (13 to 397)	2	6.12	33 (4 to 118)	4	7.94	50 (14 to 129)
≥10	4	4.20	95 (26 to 244)	8	10.45	77 (33 to 151)	12	14.65	82 (42 to 143)
Total	10	8.93	112 (54 to 206)	15	21.84	69 (38 to 113)	25	30.77	81 (53 to 120)

Table 16 Incidence of melanoma among semiconductor workers, Mere Green site, 1971-2001

	Males			Females			Total		
	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.01	0	0	0.00	0	0	0.01	0
1940-49	0	0.00	0	0	0.07	0	0	0.07	0
1950-59	0	0.04	0	0	0.15	0	0	0.19	0
1960-69	0	0.16	0	5	2.01	249 (81 to 581)	5	2.17	230 (75 to 538)
1970-79	1	0.34	294	6	2.74	219 (80 to 477)	7	3.08	227 (91 to 468)
<i>Period from first employment (years)</i>									
<10	0	0.07	0	2	0.73	274 (33 to 990)	2	0.80	250 (30 to 903)
10-19	1	0.17	588	5	1.59	314* (102 to 734)	6	1.77	339* (124 to 738)
20-29	0	0.23	0	3	2.01	149 (31 to 436)	3	2.24	134 (28 to 391)
≥30	0	0.09	0	1	0.64	156	1	0.73	137
<i>Duration of employment</i>									
<5	1	0.23	435	4	1.68	238 (65 to 610)	5	1.91	262 (85 to 611)
5-9	0	0.13	0	3	1.49	201 (42 to 588)	3	1.62	185 (38 to 541)
≥10	0	0.20	0	4	1.80	222 (61 to 569)	4	2.00	200 (54 to 512)
Total	1	0.56	179	11	4.97	221* (110 to 396)	12	5.53	217* (112 to 379)

* $p < 0.05$.

Table 17 Incidence of breast cancer among female semiconductor workers, Mere Green site, 1971-2001

	<i>Obs</i>	<i>Exp</i>	<i>SRR</i>	<i>(95% CI)</i>
<i>Year of hire</i>				
Pre 1940	0	0.04	0	-
1940-49	3	1.05	286	(59 to 835)
1950-59	5	2.38	210	(68 to 490)
1960-69	22	28.95	76	(48 to 115)
1970-79	24	36.51	66(*)	(42 to 98)
<i>Period from first employment (years)</i>				
<10	6	9.73	62	(23 to 134)
10-19	16	21.60	74	(42 to 120)
20-29	22	28.77	76	(48 to 116)
≥30	10	8.83	113	(54 to 208)
<i>Duration of employment (years)</i>				
<5	12	21.84	55(*)	(28 to 96)
5-9	15	20.82	72	(40 to 119)
≥10	27	26.27	103	(68 to 150)
Total	54	68.93	78	(59 to 102)

* $p < 0.05$, () indicates deficit.

Table 18 Incidence of brain cancer among semiconductor workers, Mere Green site, 1971-2001

	Males			Females			Total		
	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)	Obs	Exp	SRR (95% CI)
<i>Year of hire</i>									
Pre 1940	0	0.02	0	0	0.00	0	0	0.02	0
1940-49	0	0.00	0	0	0.06	0	0	0.06	0
1950-59	0	0.07	0	1	0.12	833	1	0.19	526
1960-69	0	0.22	0	0	1.42	0	0	1.64	0
1970-79	0	0.43	0	1	1.67	60	1	2.10	48
<i>Period from first employment (years)</i>									
<10	0	0.14	0	0	0.50	0	0	0.64	0
10-19	0	0.24	0	1	1.01	99	1	1.26	79
20-29	0	0.25	0	1	1.31	76	1	1.56	64
≥30	0	0.11	0	0	0.44	0	0	0.55	0
<i>Duration of employment (years)</i>									
<5	0	0.30	0	0	1.00	0	0	1.30	0
5-9	0	0.17	0	1	0.96	104	1	1.12	89
≥10	0	0.27	0	1	1.31	76	1	1.57	64
Total	0	0.73	0	2	3.27	61 (7 to 221)	2	4.00	50 (6 to 181)

Discussion

This study has found significantly elevated morbidity for cancer of the rectum and malignant melanoma in the total study cohort (males and females combined). In addition, there was significantly elevated morbidity for cancer of the pancreas, but in female employees only. For cancer of the rectum and malignant melanoma the excess cancer morbidity risks were not mirrored in the corresponding mortality findings. Confident explanations for such disparities are not available. The overall excess of melanoma incidence incorporates the original reported excess¹, and this cohort study should be viewed as providing a single report of melanoma excess and not two such reports. There was no suggestion of excess risks in this cohort of semiconductor workers for stomach cancer, lung cancer, breast cancer or cancer of the brain. More specifically, there was a significant deficit of deaths for female breast cancer and the corresponding deficit for cancer incidence approached formal levels of statistical significance.

The most important limitation to be attached to this study is the absence of job history information and the consequent absence of exposure histories. [At the time of the original data abstraction in the 1980s, the intention was that work history data, if required, would be considered in nested case-control studies.] It was not possible therefore to make any comparisons between workers employed in different departments. Attempts to identify whether any of the excess risks might be occupationally related were limited to analyses of risks by year of hire, period from first employment and duration of employment. These analyses did not suggest that any of the three cancers in excess (cancer of the rectum, cancer of the pancreas, malignant melanoma) were occupationally related. The absence of work history data means, however, that these latter analyses are of limited value and, if work history records are still available, more informative analyses of occupational exposures need now to be carried out. A minor limitation of the study is that workers who ceased employment before 1970 could not be included in the cohort because factory records for these employees had been destroyed.

There is only one other cohort study (with published findings) of workers engaged in semiconductor manufacture.³ Excess risks reported by one study are not replicated in the other, and vice versa. This may indicate that occupational exposures in the two facilities are very different and that different sets of occupational cancer risks are present. Alternatively, it is possible that occupational factors are not involved in the cancer excesses at either facility. Various intermediate scenarios can also be envisaged. Elucidation of possible cancer risks in the semiconductor manufacturing industry will require more detailed epidemiological analyses and the initiation of further cohort studies. It will be important that such studies are carried out on complete cohorts of workers and not on volunteers.

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