Mortality and cancer incidence of aircraft maintenance workers exposed to trichloroethylene and other organic solvents and chemicals: extended follow up

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Abstract

***Objectives*—To extend the follow up of a cohort of 14 457 aircraft maintenance workers to the end of 1990 to evaluate cancer risks from potential exposure to trichloroethylene and other chemicals.**

***Methods*—The cohort comprised civilians employed for at least one year between 1952 and 1956, of whom 5727 had died by 31 December 1990. Analyses compared the mortality of the cohort with the general population of Utah and the mortality and cancer incidence of exposed workers with those unexposed to chemicals, while adjusting for age, sex, and calendar time.**

***Results*—In the combined follow up period (1952–90), mortality from all causes and all cancer was close to expected (standardised mortality ratios (SMRs) 97 and 96, respectively). Significant excesses occurred for ischaemic heart disease (SMR 108), asthma (SMR 160), and cancer of the bone (SMR 227), whereas significant deficits occurred for cerebrovascular disease (SMR 88), accidents (SMR 70), and cancer of the central nervous system (SMR 64). Workers exposed to trichloroethylene showed non-significant excesses for non-Hodgkin's lymphoma (relative risk (RR) 2.0), and cancers of the oesophagus (RR 5.6), colon (RR 1.4), primary liver (RR 1.7), breast (RR 1.8), cervix (RR 1.8), kidney (RR 1.6), and bone (RR 2.1). None of these cancers showed an exposure-response gradient and RRs among workers exposed to other chemicals but not trichlorethylene often had RRs as large as workers exposed to trichloroethylene. Workers exposed to solvents other than trichloroethylene had slightly increased mortality from asthma, non-Hodgkin's lymphoma, multiple myeloma, and breast cancer.**

***Conclusion*—These findings do not strongly support a causal link with trichloroethylene because the associations were not significant, not clearly dose-related, and inconsistent between men and women. Because findings from experimental investigations and other epidemiological studies on solvents other than trichloroethylene provide some biological plausibility, the suggested links between these chemicals and non-Hodgkin's lymphoma, multiple myeloma, and breast cancer found here deserve further attention. Although this extended follow up cannot rule out a connection between exposures to solvents and some diseases, it seems clear that these workers have not experienced a major increase in cancer mortality or cancer incidence.**

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In the early 1980s the National Cancer Institute (NCI) assembled a cohort of workers employed at Hill Air Force Base in Utah to evaluate potential disease risks associated with exposure to organic solvents, including trichloroethylene, and other chemicals. Organic solvents are of interest because of their widespread use at the base and because experimental[1] and epidemiological studies[2–4] have raised concern that these chemicals may present a cancer hazard to humans. However, except for benzene no organic solvent is classified as a human carcinogen.[1] Several solvents (tetrachloroethylene, methylene chloride, chloroform, and carbon tetrachloride) are classified in the possible or probable category.[1] This study provided the opportunity to evaluate possible associations between exposure to various solvents and the risk of cancer.

In the earlier follow up, the cohort experienced slight but significant deficits from all causes of death, all malignant neoplasms, ischaemic heart disease, non-malignant respiratory disease, and accidents, compared with mortalities for the general population of Utah.[5] Non-significant excesses were found for a few causes of death including multiple myeloma, non-Hodgkin's lymphoma, cancer of the biliary passages and liver, and asthma. Because the numbers of deaths from these cancers were small, mortality follow up of the cohort was extended from 1982 to the end of 1990 to more clearly evaluate the potential for disease risks from solvent and other workplace exposures.

Methods

Details on assembly of the cohort and assessment of exposures have been previously published.[5 6] Briefly, all civilians employed at Hill Air Force Base for at least one year between 1 January 1952 and 31 December 1956 were enrolled in the cohort. A cohort of 14 457 workers who met these criteria was

Table 1 Cause specific SMRs and 95% confidence intervals adjusted for age, sex, and calendar year (using Utah population rates as the referent)

Cause of death (ICDA-8)	Combined early and recent follow up		
	SMR	Observed/expected	95% CI
All causes (000–999)	97	5727/5932.0	94 to 99
All cancer (140–209)	96	1048/1096.2	90 to 102
Buccal cavity/pharynx (140–149)	98	19/19.4	62 to 153
Digestive organs (150-159)	94	275/293.9	83 to 105
Oesophagus (150)	84	15/17.9	51 to 139
Stomach (151)	99	53/53.6	76 to 129
Colon (153)	97	99/101.9	80 to 118
Rectum (154)	78	17/21.8	49 to 126
Biliary passages and liver (155,156)	110	27/24.5	76 to 161
Primary liver (155)	115	7/6.1	55 to 242
Pancreas (157)	94	59/62.9	73 to 121
Larynx (161)	69	6/8.6	31 to 155
Lung (162)	98	213/216.7	86 to 112
Breast (174)	82	49/59.7	62 to 109
Cervix (180)	147	11/7.5	81 to 265
Prostate (185)	95	107/112.3	79 to 115
Kidney (189)	122	30/24.7	85 to 174
Bladder (188)	103	28/27.2	71 to 149
Melanoma of skin (172.0–172.4, 172.6–172.9)	111	20/18.0	72 to 172
Central nervous system (191,192)	64	21/33.0	41 to 98
Endocrine (193,194)	74	4/5.4	28 to 197
Bone (170)	227	7/3.1	108 to 476
Lymphatic or haematopoietic (200–209)	105	134/128.1	88 to 124
Non-Hodgkin's lymphoma (200,202)	114	49/42.9	86 to 151
Leukaemia (204–207)	82	41/50.0	60 to 111
Hodgkin's disease (201)	68	7/10.2	33 to 144
Multiple myeloma (203)	140	32/22.8	99 to 198
Diabetes mellitus (250)	102	124/121.6	86 to 122
Cerebrovascular disease (430–438)	88	385/439.2	79 to 97
Ischaemic heart disease (410–414)	108	1868/1729.4	103 to 113
Non-malignant respiratory disease (460–519)	95	454/478.3	87 to 104
Bronchitis (490,491)	89	19/21.3	57 to 140
Emphysema (492)	99	91/91.5	81 to 122
Asthma (493)	160	19/11.9	102 to 251
Cirrhosis of liver (571)	101	94/93.4	82 to 123
Accidents (800–949)	70	244/349.6	62 to 79
Motor vehicle accidents (800–823)	66	92/149.5	54 to 80
Suicides (950–959)	83	90/111.4	67 to 101

identified from individual earnings records stored at the National Personnel Records Center in St Louis, Missouri. From the personnel records we obtained each worker's name, date of birth, race, sex, and a complete history of employment at the base. The work histories included job titles, department codes, and dates the jobs were held.

Vital status for the original follow up was determined with information obtained from the United States Office of Personnel Management, records from the Department of Veteran's Affairs, motor vehicle records, and the national death index. Ninety seven per cent of the cohort was successfully traced to 31 December 1982. Vital status from the current follow up (to December 1990) was determined solely through linkage of the cohort with the national death index, which has been available since 1979. The underlying and contributing causes of death were determined by an experienced nosologist according to the rules of the international classification of diseases (ICDA) in effect at the time of death and were assigned numerical codes according to the eighth revision of the ICDA (ICDA-8). The cohort was also linked with the Utah tumour registry to obtain information on cancer incidence. The registry was established in 1973 and is part of the NCI surveillance, epidemiology, and end results programme of tumour registries (SEER).

A comprehensive exposure assessment effort was undertaken in the initial study to characterise various exposures likely to be associated with various jobs held and to provide semi-quantitative estimates of exposure to trichloroethylene, the main solvent used at the base.[6] The evaluations of exposure covered the time from the first job to the end of 1982. Job titles from personnel records were collapsed into 43 000 job-department code combinations. A further reduction was not possible because of the difficulty in identifying the department of assignment from the personnel records. To characterise the work environment, industrial hygienists conducted walk through surveys and interviews with management and labour and reviewed historical records, monitoring data, chemical inventories, organisation charts, technical orders, and job descriptions. Because a main focus of the study was exposure to trichloroethylene, particular attention was paid to areas where this solvent was used. There were two main uses for trichloroethylene: dipping of large parts in vapour degreasers to remove oils or other contaminants and cleaning small electrical parts with squeeze bottles or other small containers at work benches. Exposure to chemicals other than trichloroethylene was assessed on a qualitative (ever or never exposed) basis. The exposure estimates developed for the earlier follow up were used in the analysis of the extended mortality follow up without additional assessment of exposures for jobs held in the years since 1982.

An exposure score for trichloroethylene was assigned to each job based on possible exposure intensity, frequency, and duration of peak exposures from vapour degreasing and of low level exposures at the work bench.[6] Information from two surveys of vapour degreaser in the 1960s and 1970s on work practices at the degreasers and other potential exposures[7 8] was used to create an intensity index of exposure to trichloroethylene for various periods (600 for the years 1939–54, 400 for 1955–67, and 200 for 1968–78). These scores provide an indication of the relative exposures over time, but they should not be viewed as ppm. After 1978, trichloroethylene in the degreasers was replaced by 1,1,1,-trichloroethane. Frequency of use of the vapour degreasers and the time spent at the degreaser for each episode were evaluated for each job. People who used the vapour degreasers tended to work, regardless of the work areas to which they were assigned, at degreasers either about twice a day or less often, twice a week. The time spent at the degreasers was about the same for all jobs, 15 minutes. Trichloroethylene was also used in bench top work until 1968. Measurement data on solvents other than trichloroethylene used in bench work indicated exposures were at relatively low levels, <15 ppm. No measurements were available for trichloroethylene. An intensity score of 15 for trichloroethylene from work bench use was assigned based on measurements of solvents other than trichloroethylene. The frequency of solvent use at the work bench varied by job title. Workers in some jobs went to the degreaser to clean parts about 15 times a day, whereas others cleaned parts less often (four times a day). Peak scores,

representing estimates of typical high levels of exposure from vapour degreasers, were derived by multiplying the exposure intensity appropriate for the year of exposure, by the frequency of use, and by the duration of use per day for each job held. The exposure score of low level exposure was derived similarly. A subject's cumulative exposure score (defined as unit-years) was the sum of multiplication products for each job—that is, duration multiplied by the exposure score for peaks plus duration multiplied by the score for low level exposure.

Relative risks were estimated with standardised mortality ratios (SMRs) based on the mortality experience of the Utah population and the rate ratios (RRs) for mortality and cancer incidence from comparison of exposed and unexposed cohort members by Poisson regression, adjusting for date of birth, calendar year of death, and sex where appropriate.[9] The starting date of person-year accumulation for the mortality analyses for the overall cohort was 1 January 1953 or one year after first employment, whichever was later. The starting date for person-year accumulation for the incidence analyses was 1 January 1973, the start of the Utah tumour registry. The end of person-year accumulation for mortality and incidence analyses was 31 December 1990 or date of death or diagnosis(for cancer incidence). All 95% confidence intervals (95% CIs) were calculated assuming Wald type confidence bounds.[9] Internal comparisons were made to reduce biases that may arise with use of the general population as referents.[10]

Results

The 14 457 workers consisted of 9400 white men, 3138 white women, 269 non-white men, 122 non-white women, and 1061 men and 467 women of unknown race. In the analyses, workers of unknown race were classified as white because those of known race were overwhelmingly white (97%). Only forty seven deaths occurred among non-white people and 30 had cancer as the underlying cause. The detailed analyses presented here include white people only. A search of the national death index identified 1866 former Hill workers (white only) who died between 1983 and the end of 1990. We also found 29 previously undiscovered deaths that occurred before

Table 2 Rate ratios (95% CI and number of events) for selected causes of deaths among workers with exposure to trichloroethylene by follow up period (cohort members with no chemical exposures as referents)

	Combined early and recent follow up			*Follow up to the end of 1982**			*Follow up 1983–90*		
Cause of death (ICDA-8)	*Rate ratio**	*Exposed/unexposed deaths*	*95% CI*	*Rate ratio*	*Exposed/unexposed deaths*	*95% CI*	*Rate ratio*	*Exposed/unexposed deaths*	*95% CI*
All causes (000–999)	1.0	2813/1382	1.0 to 1.1	1.0	1804/930	0.9 to 1.1	1.1	1009/452	1.0 to 1.2
All cancer (140–209)	1.1	528/253	1.0 to 1.3	1.1	309/163	0.9 to 1.3	1.1	219/90	0.9 to 1.5
Buccal cavity/pharynx (140–149)	1.4	9/3	0.4 to 5.2	1.0	6/3	0.2 to 4.3	—	3/0	—
Digestive organs (150–159)	1.2	142/58	0.9 to 1.7	1.2	87/38	0.8 to 1.8	1.2	55/20	0.7 to 2.1
Oesophagus (150)	5.6	10/1	0.7 to 44.5	3.4	6/1	0.4 to 28	—	4/0	—
Stomach (151)	0.9	23/13	0.4 to 1.9	0.9	15/14	0.4 to 2.0	1.0	8/3	0.2 to 4.1
Colon (153)	1.4	54/19	0.8 to 2.4	1.2	30/11	0.6 to 2.6	1.6	24/8	0.7 to 3.8
Rectum (154)	0.4	5/5	0.1 to 1.5	0.8	5/3	0.2 to 3.5	0.0	0/2	—
Biliary passages and liver (155,156)	1.3	15/6	0.5 to 3.4	1.1	10/5	0.4 to 3.3	2.3	5/1	0.2 to 20
Primary liver (155)	1.7	4/1	0.2 to 16.2	0.8	2/1	0.1 to 8.8	—	2/0	—
Pancreas (157)	1.2	33/13	0.6 to 2.3	1.6	19/7	0.6 to 3.8	0.8	14/6	0.3 to 2.0
Lung (162)	0.9	109/51	0.6 to 1.3	0.9	68/31	0.6 to 1.4	0.9	41/20	0.5 to 1.6
Breast (174)	1.8	20/20	0.9 to 3.3	1.8	14/13	0.8 to 3.9	1.6	6/7	0.5 to 5.0
Cervix (180)	1.8	5/5	0.5 to 6.5	1.8	4/4	0.4 to 7.6	1.7	1/1	0.1 to 31
Prostate (185)	1.1	54/20	0.6 to 1.8	1.0	21/10	0.5 to 2.2	1.1	33/10	0.5 to 2.3
Kidney (189)	1.6	15/4	0.5 to 5.1	1.2	9/3	0.3 to 4.7	2.8	6/1	0.3 to 24
Bladder (188)	1.2	17/7	0.5 to 2.9	1.2	11/5	0.4 to 3.4	1.3	6/2	0.3 to 6.7
Melanoma of skin (172.0–172.4, 172.6–172.9)	1.0	9/5	0.3 to 3.1	1.2	6/3	0.3 to 5.2	0.6	3/2	0.1 to 4.2
Central nervous system (191,192)	0.8	11/5	0.2 to 2.2	0.8	9/4	0.2 to 2.9	0.5	2/1	0.1 to 5.2
Endocrine (193,194)	0.7	2/2	0.1 to 5.4	—	1/0	—	0.4	1/2	0.1 to 4.4
Bone (170)	2.1	5/1	0.2 to 18.8	1.5	3/1	0.2 to 15	—	2/0	—
Lymphatic or haematopoietic (200–209)	1.1	66/33	0.7 to 1.8	1.3	42/21	0.7 to 2.2	0.9	24/12	0.4 to 1.9
Non-Hodgkin's lymphoma (200,202)	2.0	28/8	0.9 to 4.6	1.9	17/6	0.7 to 5.0	2.2	11/2	0.4 to 10
Leukaemia (204–207)	0.6	16/16	0.3 to 1.2	0.7	11/9	0.3 to 1.9	0.3	5/7	0.1 to 1.2
Hodgkin's disease (201)	1.4	5/1	0.2 to 12.0	1.1	4/1	0.1 to 66	—	1/0	—
Multiple myeloma (203)	1.3	14/7	0.5 to 3.4	1.2	8/5	0.4 to 3.9	1.5	6/2	0.3 to 8.7
Diabetes mellitus (250)	1.3	61/29	0.8 to 2.2	1.4	38/15	0.8 to 2.6	1.2	23/14	0.6 to 2.5
Cerebrovascular disease (430–438)	1.0	161/100	0.8 to 1.3	1.0	111/66	0.7 to 1.4	0.9	50/34	0.6 to 1.4
Ischaemic heart disease (410–414)	1.1	948/409	1.0 to 1.3	1.1	641/286	1.0 to 1.3	1.1	307/123	0.9 to 1.4
Non-malignant respiratory disease (460–519)	1.2	234/98	0.9 to 1.5	0.9	117/62	0.7 to 1.3	1.6	117/36	1.1 to 2.4
Bronchitis (490,491)	2.4	10/2	0.5 to 11.3	3.8	7/1	0.5 to 31	1.1	3/1	0.1 to 10
Emphysema (492)	0.9	44/21	0.5 to 1.6	0.7	32/20	0.4 to 1.2	7.2	12/1	0.9 to 60
Asthma (493)	1.7	11/4	0.5 to 5.5	1.2	6/3	0.3 to 5.0	3.2	5/1	0.3 to 28
Cirrhosis of liver (571)	1.1	44/19	0.6 to 1.9	1.0	32/15	0.5 to 1.9	1.4	12/4	0.4 to 4.5
Accidents (800–949)	1.1	128/51	0.8 to 1.6	1.0	95/43	0.7 to 1.5	1.8	33/8	0.8 to 4.1
Motor vehicle accidents (800–823)	1.1	52/22	0.6 to 1.8	1.1	43/19	0.6 to 2.0	1.1	9/3	0.3 to 4.0
Suicides (950–959)	0.8	53/25	0.5 to 1.3	1.0	45/18	0.5 to 1.7	0.4	8/7	0.1 to 1.2

*Workers not exposed to any chemicals serve as referents. Rate ratios adjusted for age, calendar time, and sex.

Table 3 Rate ratios (95% CI) and number of events for selected causes of deaths among workers with no exposure to trichloroethylene and by cumulative exposure to trichloroethylene in unit-years (cohort members with no chemical exposures as referents)

	Men				*Women*
Cause of death	*No exposure*	*<5 unit-y*	*5–25 unit-y*	*>25 unit-y*	*No exposure*
All causes	1.1 (1.0 to 1.2) 1320	1.0 (0.9 to 1.1) 927	1.0 (0.9 to 1.1) 573	1.1 (1.0 to 1.2) 889	1.2 (1.0 to 1.4) 212
All cancer	1.1 (0.9 to 1.4) 141	1.1 (0.9 to 1.4) 230	1.1 (0.9 to 1.4) 109	1.2 (0.9 to 1.5) 155	1.0 (0.7 to 1.4) 372
Buccal cavity and pharynx	1.4 (0.3 to 5.5) 6	1.2 (0.3 to 5.7) 4	0.5 (0.1 to 5.3) 1	1.1 (0.2 to 5.4) 3	0 deaths
Oesophagus	3 deaths*	3 deaths	2 deaths	4 deaths	2.2 (0.2 to 42) 1
Stomach	1.1 (0.5 to 2.5) 17	0.8 (0.3 to 2.1) 7	1.2 (0.4 to 3.3) 6	1.1 (0.4 to 2.7) 9	0 deaths
Colon	1.5 (0.7 to 3.3) 21	1.5 (0.7 to 3.3) 19	1.5 (0.7 to 3.6) 12	1.5 (0.7 to 3.3) 15	1.6 (0.5 to 4.8) 5
Biliary passages and liver	0.5 (0.1 to 2.4) 3	1.1 (0.3 to 4.1) 6	0.9 (0.2 to 4.3) 3	0.7 (0.2 to 3.2) 3	4.2 (0.7 to 25.0) 3
Pancreas	0.7 (0.3 to 1.7) 10	0.8 (0.3 to 1.9) 10	0.8 (0.3 to 2.2) 6	1.1 (0.5 to 2.6) 11	2.7 (0.4 to 19.1) 3
Lung	1.0 (0.7 to 1.6) 51	1.0 (0.6 to 1.6) 43	0.9 (0.5 to 1.6) 23	1.1 (0.7 to 1.8) 38	0.4 (0.1 to 1.6) 2
Prostate	1.2 (0.7 to 2.1) 33	0.9 (0.5 to 1.8) 19	1.0 (0.5 to 2.1) 13	1.3 (0.7 to 2.4) 22	
Breast					1.4 (0.6 to 3.1) 9
Cervix					0.6 (0.1 to 5.4) 1
Kidney	2.5 (0.7 to 8.9) 10	2.0 (0.5 to 7.6) 8	0.4 (0.1 to 4.0) 1	1.2 (0.3 to 4.8) 4	3.2 (0.2 to 51.2) 1
Bladder	0.7 (0.2 to 2.8) 4	1.8 (0.5 to 6.2) 7	2.1 (0.6 to 8.0) 5	1.0 (0.2 to 5.1) 3	0 deaths
Central nervous system	1.2 (0.3 to 4.9) 5	0.7 (0.1 to 3.3) 3	2.0 (0.5 to 8.4) 5	0.9 (0.2 to 4.4) 32	0 deaths
All lymphatic and haematopoietic	1.3 (0.7 to 2.3) 32	1.1 (0.6 to 2.1) 21	1.0 (0.4 to 2.1) 11	1.3 (0.7 to 2.5) 21	0.6 (0.2 to 2.0) 3
Leukaemia	1.0 (0.4 to 2.9) 9	1.0 (0.3 to 3.2) 7	0 deaths	1.2 (0.4 to 3.6) 7	0 deaths
Multiple myeloma	1.7 (0.5 to 5.5) 10	1.0 (0.2 to 4.2) 4	0.8 (0.1 to 4.4) 2	1.2 (0.3 to 4.7) 4	1.0 (0.1 to 9.9) 11
Non-Hodgkin's lymphoma	1.6 (0.5 to 4.5) 11	1.8 (0.6 to 5.4) 10	1.9 (0.6 to 6.3) 6	1.1 (0.3 to 3.8) 5	2.0 (0.3 to 12.2) 2
Diabetes mellitus	1.1 (0.6 to 2.1) 27	1.0 (0.5 to 2.0) 18	1.2 (0.6 to 2.5) 12	0.7 (0.3 to 1.6) 11	1.6 (0.6 to 4.1) 7
Cerebrovascular disease	1.2 (0.9 to 1.6) 105	0.7 (0.5 to 1.1) 43	0.6 (0.4 to 1.0) 21	1.2 (0.8 to 1.7) 62	1.5 (0.9 to 2.7) 19
Ischaemic heart disease	1.1 (1.0 to 1.3) 448	1.0 (0.9 to 1.2) 317	1.1 (1.0 to 1.4) 207	1.2 (1.0 to 1.4) 311	1.3 (1.0 to 1.8) 63
Non-malignant respiratory disease	1.2 (0.9 to 1.7) 111	1.0 (0.7 to 1.5) 70	1.1 (0.8 to 1.6) 45	1.7 (1.2 to 2.4) 96	1.0 (0.5 to 2.0) 11
Bronchitis	5.0 (0.6 to 40.4) 7	5.8 (0.7 to 49.9) 5	0 deaths	6.4 (0.8 to 55.2) 5	0 deaths
Emphysema	0.9 (0.5 to 1.6) 24	0.5 (0.2 to 1.0) 10	0.9 (0.4 to 1.8) 11	1.1 (0.6 to 2.0) 20	6.7 (0.6 to 74.0) 2
Cirrhosis of the liver	1.5 (0.8 to 2.8) 26	0.6 (0.2 to 1.3) 10	0.8 (0.3 to 1.9) 9	1.2 (0.6 to 2.4) 17	2.5 (0.8 to 8.1) 5
Accidents	1.2 (0.8 to 1.8) 57	0.9 (0.6 to 1.4) 37	1.4 (0.8 to 2.3) 33	1.2 (0.8 to 2.0) 41	1.2 (0.5 to 2.7) 8
Motor vehicle accidents	0.9 (0.41 to 7) 21	0.6 (0.3 to 1.3) 11	1.3 (0.6 to 2.8) 15	1.2 (0.6 to 2.3) 18	1.2 (0.3 to 4.5) 3
Suicide	0.5 (0.2 to 1.1) 13	0.8 (0.4 to 1.5) 23	0.7 (0.4 to 1.5) 121	0.6 (0.3 to 1.3) 14	0.5 (0.1 to 3.8) 1

*No deaths occurred among non-exposed male workers so rate ratios could not be calculated.

1983. With 3832 deaths already identified before 1983,[5] there was a total of 5727 events.

Table 1 presents SMRs for white workers (n=14 066) for the combined follow up (1952–90) with Utah mortality rates as the referent, adjusted for age, sex, and calendar time. Small, but significant, deficits occurred for total mortality (SMR 97) and total cancer mortality (SMR 96). This average level of mortality overall was composed of some causes in excess and some in deficit. Significant deficits also occurred for cancer of the central nervous system (SMR 64), cerebrovascular disease (SMR 88), accidents (SMR 70), and motor vehicle accidents (SMR 66). Significant excesses occurred for mortality from cancer of the bone (SMR 227), ischaemic heart disease (SMR 108), and asthma (SMR 160). The SMR for bone cancer was increased in both follow up periods—that is, early SMR 191 (five observed) and recent SMR 427 (two observed).

In the earlier follow up, two causes of death had significant excesses (multiple myeloma (SMR 156, 21 observed) and asthma (SMR 185, 13 observed)) and two had significant deficits (cerebrovascular disease (SMR 88, 272 observed) and accidents (SMR 64, 187 observed)). In the more recent follow up both multiple myeloma and asthma excesses were smaller (SMR 117, 11 observed and SMR 124, six observed, respectively).

We also calculated SMRs with rates from the United States population as referents. The SMRs were similar to those based on Utah rates, although generally smaller (data not shown). For example the SMRs were 84 for all causes, 69 for all cancer, 48 for colon cancer, 48 for lung cancer, 69 for breast cancer, and 96 for cancer of the lymphatic and haematopoietic system.

About half of the workers at Hill Air Force Base (6153 white men and 1051 white women) were exposed to trichloroethylene with 2389 deaths among men and 424 deaths among women. Table 2 shows risks for selected causes of death for workers ever holding jobs in which exposure to trichloroethylene may have occurred. Rates among exposed workers were compared with those with no chemical exposures adjusting for age, calendar time, and sex. Mortality from all causes and all cancer was about as expected. No significant deficits occurred. Significant excesses occurred for ischaemic heart disease in the early and combined follow up periods and for non-malignant respiratory disease in the recent follow up period. Non-significant excesses occurred for cancers of the oesophagus (in the combined, early, and recent follow up periods), colon (combined, early, and recent period), primary liver (recent period), breast (combined, early, and recent periods), cervix (combined, early, and recent periods), kidney (combined and recent periods), bone (combined, early, and recent periods), non-Hodgkin's lymphoma (combined, early, and recent periods), and multiple myeloma (recent period). Excesses occurred from mortality due to bronchitis in the early follow up period and emphysema and asthma in the recent follow up period.

Table 3 shows the RRs for four categories of workers, those with exposure to chemicals but not trichloroethylene and those in three levels of cumulative exposure (the sum of low level and peak exposures) to trichloroethylene. Mortalities in each category were compared with workers with no exposure to chemicals.

Table 3 continued

<5 unit-y	*5-25 unit-y*	*>25 unit-y*
1.1 (0.9 to 1.3) 151	0.8 (0.6 to 1.1) 47	1.1 (1.0 to 1.3) 226
1.3 (0.9 to 1.9) 36	0.6 (0.3 to 1.4) 7	1.1 (0.8 to 1.6) 42
1 exposed, 0 unexposed	1 exposed, 0 unexposed	0 deaths
3.6 (0.2 to 58) 1	0 deaths	0 deaths
0 deaths	0 deaths	1.2 (0.1 to 12.3) 1
1.2 (0.3 to 4.6) 3	0 deaths	1.5 (0.5 to 4.4) 5
1.6 (0.2 to 18.2) 1	0 deaths	2.3 (0.3 to 16.7) 2
2.4 (0.4 to 14.3) 3	0 deaths	3.3 (0.7 to 15.0) 4
0.6 (0.1 to 2.4) 2	0.6 (0.1 to 4.7) 11	0.4 (0.1 to 1.8) 2
2.4 (1.1 to 5.2) 10	1.2 (0.3 to 5.4) 21	1.4 (0.6 to 3.2) 8
0.9 (0.1 to 8.3) 1	0 deaths	3.0 (0.8 to 11.7) 4
0 deaths	9.8 (0.6 to 157) 1	3.5 (0.2 to 56.4) 1
0 deaths	0 deaths	0.8 (0.1 to 7.5) 1
0 deaths	0 deaths	0 deaths
1.5 (0.6 to 4.0) 6	0.7 (0.1 to 4.9) 1	1.1 (0.4 to 3.0) 6
0.4 (0.1 to 3.2) 1	0 deaths	0.3 (0.1 to 2.4) 1
3.2 (0.5 to 19.8) 2	4.3 (0.4 to 43.4) 1	1.3 (0.1 to 13.2) 1
3.8 (0.8 to 18.9) 3	0 deaths	3.6 (0.8 to 16.2) 4
2.7 (1.1 to 6.4) 9	2.2 (0.6 to 7.8) 31	1.7 (0.7 to 4.2) 5
0.5 (0.2 to 1.3) 5	1.0 (0.4 to 2.8) 4	1.8 (1.1 to 2.9) 26
1.1 (0.7 to 1.5) 39	0.6 (0.3 to 1.1) 8	1.2 (0.9 to 1.6) 66
0.6 (0.3 to 1.5) 6	1.0 (0.3 to 2.7) 4	1.0 (0.5 to 1.9) 13
0 deaths	0 deaths	0 deaths
0 deaths	0 deaths	11.5 (1.1 to 118) 3
2.4 (1.4 to 13.7) 6	1.8 (0.2 to 15.0) 1	0.6 (0.1 to 4.8) 1
1.5 (0.7 to 3.5) 8	1.5 (0.4 to 5.0) 3	0.8 (0.3 to 2.1) 6
2.1 (0.6 to 7.2) 4	1.4 (0.2 to 11.0) 1	1.2 (0.3 to 4.6) 3
0 deaths	2.3 (0.3 to 19.4) 1	2.1 (0.5 to 8.7) 33

The workers who had been exposed to trichloroethylene experienced about the same rate of total mortality as workers unexposed to any chemicals and those exposed to chemicals other than trichloroethylene (RRs across the cumulative exposure categories for trichloroethylene ranged from 0.8 to 1.2). The RR for total mortality was significant among men and women with no exposure to trichloroethylene and with cumulative exposures of ⩾25 unit-years. Significant excesses also occurred in the highest cumulative exposure category for cerebrovascular disease among women (RR 1.8), ischaemic heart disease among men (RR 1.1), non-malignant respiratory disease among men (RR 1.7), and emphysema among women (RR 11.5). We found no significant deficits. Non-significant excesses associated with exposure to trichloroethylene occurred for cancers of the colon among men and women (RRs 1.2–1.6), biliary passages and liver among women (RRs 1.6–2.3), pancreas among women (RRs 2.4–3.3), breast among women (RRs 1.2–2.4), uterine (RRs 1.3–1.4), kidney among women (RRs 3.5–9.8), bladder among men (RRs 1.0–2.1), multiple myeloma among women (RRs 1.3–4.3), and non-Hodgkin's lymphoma among men and women (RRs 1.1–3.8). Also, men had RRs for non-malignant respiratory disease of 1.0–1.7 and for bronchitis from no deaths to an RR of 6.4. Women had RRs for diabetes of 1.7–2.7, cirrhosis of the liver of 0.6–2.4, and motor vehicle accidents of 1.2–2.1. None of these diseases showed a positive exposure-response gradient and risks in workers exposed to chemicals other than trichloroethylene were similar to those among workers exposed to trichloroethylene.

No deaths from asthma occurred among men in the cohort who were unexposed to chemicals so it was not possible to use internal comparisons for analysis of this cause of death. We were able, however, to calculate SMRs. Compared with men in the general Utah population, men exposed to trichloroethylene more often died from asthma (SMR 222; 95% CI 115 to 423; nine deaths). The SMRs by cumulative level of exposure to trichloroethylene were 181 (three observed; 95% CI 58 to 561) for <5 unit-years, 397 (four observed; 95% CI 149 to 1058) for the 5–25 unit-years, and 141 (two observed; 95% CI 35 to 563) for the >25 unit-years. Only two of the women exposed to trichloroethylene died from asthma (SMR 136; 95% CI 34 to 542), both fell in the lowest cumulative exposure category.

We also examined the risks among workers exposed to trichloroethylene who had exposure to no other chlorinated solvents (n=3363). These risk patterns (data not shown) were very similar to those in table 3.

Table 4 shows the RRs for selected causes of death by type of exposure to trichloroethylene, intermittent low level, continuous low level, or frequent peaks. Results from infrequent low level showed no unusual patterns and are not presented. As workers could hold multiple jobs

Table 4 Rate ratios (95% CI) and observed numbers for selected causes of death by type of trichloroethylene exposure (workers not exposed to any chemical as referents)

	Men			*Women*		
Cause of death	*Low level intermittent exposure*	*Low level continuous exposure*	*Frequent peaks*	*Low level intermittent exposure*	*Low level continuous exposure*	*Frequent peaks*
All causes	1.0 (0.9 to 1.1) 1564	1.0 (0.9 to1.1) 1146	1.1 (1.0 to 1.2) 1120	1.1 (1.0 to 1.3) 203	1.0 (0.8 to 1.2) 107	1.1 (0.9 to 1.3) 267
All cancers	1.1 (0.9 to 1.3) 309	1.2 (1.0 to 1.5) 225	1.1 (0.9 to 1.4) 194	1.4 (1.0 to 1.9) 48	1.0 (0.6 to 1.7) 19	1.1 (0.8 to 1.5) 49
Stomach	1.2 (0.5 to 2.8) 16	1.5 (0.6 to 3.6) 14	0.9 (0.4 to 2.2) 9	0 deaths	0 deaths	1.0 (0.1 to 10.4) 1
Colon	1.7 (0.8 to 3.5) 36	1.8 (0.8 to 3.7) 25	1.6 (0.7 to 3.4) 20	1.6 (0.5 to 4.8) 5	0.5 (0.1 to 4.1) 1	1.2 (0.4 to 3.5) 5
Biliary passages and liver	1.3 (0.4 to 4.1) 12	0.6 (0.2 to 2.6) 4	0.7 (0.2 to 3.0) 4	2.8 (0.4 to 20.3) 2	0 deaths	1.8 (0.2 to 13.0) 2
Liver	1.6 (0.2 to 14.5) 4	0 deaths	0.7 (0.1 to 11.0) 1	0 deaths	0 deaths	0 deaths
Pancreas	0.8 (0.4 to 1.8) 19	1.0 (0.4 to 2.2) 14	1.0 (0.4 to 1.2) 12	1.7 (0.3 to 10.5) 2	0 deaths	2.8 (0.6 to 12.4) 4
Breast	0 deaths	0 deaths	0 deaths	3.1 (1.5 to 6.2) 15	3.4 (1.4 to 8.0) 8	1.4 (0.7 to 3.2) 10
Kidney	2.1 (0.6 to 7.5) 12	2.2 (0.6 to 8.1) 9	1.4 (0.3 to 5.7) 5	0 deaths	0 deaths	5.7 (0.5 to 63.3) 2
Bladder	1.5 (0.4 to 4.8) 10	2.0 (0.6 to 6.4) 9	1.2 (0.3 to 4.4) 5	0 deaths	0 deaths	0.6 (0.1 to 6.3) 1
Multiple myeloma	0.5 (0.1 to 1.9) 4	0.8 (0.2 to 3.2) 4	0.8 (0.2 to 3.3) 4	4.4 (1.0 to 20.4) 4	2.4 (0.2 to 24.3) 1	0.9 (0.1 to 8.9) 1
Non-Hodgkin's lymphoma	1.5 (0.5 to 4.3) 15	1.8 (0.6 to 5.2) 12	1.5 (0.5 to 4.4) 9	3.9 (0.8 to 17.7) 4	3.4 (0.5 to 21.7) 2	3.8 (0.9 to 16.2) 5
Non-malignant respiratory disease	1.0 (0.7 to 1.4) 119	1.6 (1.1 to 2.1) 121	1.6 (1.1 to 2.1) 113	1.0 (0.5 to 1.9) 5	0.8 (0.3 to 1.8) 6	0.9 (0.5 to 1.7) 15
Bronchitis	4.2 (0.5 to 36.9) 5	8.6 (1.0 to 73.6) 7	7.1 (0.8 to 59.7) 6	0 deaths	0 deaths	0 deaths
Diabetes	1.0 (0.5 to 1.8) 28	0.8 (0.4 to 1.6) 15	1.0 (0.5 to 2.0) 19	2.7 (1.2 to 6.2) 11	0.8 (0.2 to 3.4) 2	1.8 (0.8 to 4.1) 10
Motor vehicle accidents	0.6 (0.3 to 1.2) 22	1.0 (0.5 to 2.0) 23	1.2 (0.6 to 2.3) 26	2.2 (0.7 to 6.9) 5	0 deaths	1.4 (0.4 to 4.7) 4

Table 5 Rate ratios (95% CI) number of events for incident cancers by cumulative exposure to trichloroethylene and sex (cohort members with no chemical exposures as the controls)

	Men				*Women*
Cause of death	*No exposure*	*< 5 units-y*	*5-25 unit-y*	*> 25 unit-y*	*No exposure*
All cancer	1.1 (0.9 to 1.4) 191	1.2 (1.0 to 1.5) 213	1.1 (0.9 to 1.4) 125	1.2 (1.0 to 1.6) 171	0.7 (0.4 to 1.1) 182
Buccal cavity and pharynx	1.0 (0.4 to 2.4) 10	1.2 (0.5 to 3.0) 13	0.7 (0.2 to 2.2) 5	0.8 (0.3 to 2..2) 7	1.8 (0.2 to 19.6) 1
Stomach	1.5 (0.4 to 6.0) 6	0.3 (0.1 to 2.6) 1	3.1 (0.8 to 12.1) 7	2.0 (0.5 to 8.1) 6	0 cases
Colon	4.1 (1.4 to 11.8) 22	2.9 (1.0 to 8.9) 15	4.3 (1.4 to 13.0) 14	5.7 (2.0 to 16.7) 23	0.3 (0.1 to 2.6) 1
Biliary passages and liver	0.2 (0.1 to 2.4) 1	0.6 (0.1 to 3.1) 3	0.6 (0.1 to 3.8) 2	1.1 (0.2 to 4.8) 4	6.5 (0.6 to 71.4) 2
Liver	0.8 (0.1 to 12.0) 1	1.2 (0.1 to 13.8) 2	1.0 (0.1 to 16.0) 1	2.6 (0.3 to 25.0) 3	0 cases
Pancreas	0.7 (0.2 to 2.3) 6	0.7 (0.2 to 2.1) 6	0.4 (0.1 to 1.8) 2	0.7 (0.2 to 2.4) 51	1 observed/0 unexposed
Lung	1.0 (0.5 to 1.9) 22	1.0 (0.6 to 2.0) 24	0.8 (0.4 to 1.6)11	0.8 (0.4 to 1.7) 15	0 cases
Prostate	1.0 (0.7 to 1.4) 61	1.1 (0.7 to 1.6) 64	1.0 (0.6 to 1.6) 38	1.2 (0.8 to 1.8) 56	
Breast					0.4 (0.2 to 1.3) 4
All uterine cancers					1.3 (0.04 to 4.1) 4
Kidney	1.6 (0.5 to 5.4) 9	1.4 (0.4 to 4.7) 9	1.3 (0.3 to 4.7) 5	0.4 (0.1 to 2.3) 2	0 cases
Bladder	1.3 (0.5 to 3.5) 10	1.7 (0.6 to 4.4) 13	1.7 (0.6 to 4.9) 9	1.4 (0.5 to 4.1) 9	0 cases
Central nervous system	2.2 (0.2 to 21.2) 3	2.0 (0.2 to 19.7) 3	3.9 (0.4 to 34.9) 4	0.8 (0.1 to 13.2) 1	0 cases
All lymphatic and haematopoietic	1.0 (0.5 to 2.1) 16	0.8 (0.4 to 1.7) 12	0.7 (0.3 to 1.8) 7	1.4 (0.6 to 2.9) 17	0.3 (0.1 to 2.4) 1
Leukaemia	1.0 (0.3 to 3.7) 6	0.4 (0.1 to 2.0) 2	0 cases	0.9 (0.2 to 3.7) 4	0 cases
Multiple myeloma	3.7 (0.4 to 31.7) 5	0.8 (0.1 to 12.7) 1	3.8 (0.4 to 37.4) 3	5.1 (0.6 to 43.7) 5	1 observed/0 expected
Non-Hodgkin's lymphoma	0.5 (0.2 to 1.7) 5	0.9 (0.3 to 2.6) 8	0.7 (0.2 to 2.6) 4	1.0 (0.4 to 2.9) 7	0 cases

these are not mutually exclusive categories. Small excesses of colon cancer occurred in each exposure category among men. Among women excesses occurred only among those in the intermittent, low level exposure category. Risk of breast cancer was significantly associated with intermittent (RR 3.1) and continuous low level (RR 3.4), but not with peak (RR 1.4) exposures. Kidney cancer was doubled among men with intermittent and continuous low levels of exposure. Women with frequent peaks experienced an RR for kidney cancer of 5.7 (based on only two exposed deaths). Four of the five women with multiple myelomas had held jobs with intermittent low level exposure, yielding a significantly increased RR of 4.4 for this category. The RR for non-Hodgkin's lymphoma did not vary much by category among men or women. Mortality from non-malignant respiratory disease was significantly increased from continuous low level (RR 1.6) and frequent peak (RR 1.6) exposures among men, but not among women. Women who had experienced intermittent low level exposures to trichloroethylene had an increased risk of diabetes (RR 2.7) and men with low level continuous exposure had a significant excess mortality from bronchitis (RR 1.6).

Table 5 shows the RRs for incident cancers that occurred since 1973, comparing workers exposed to trichloroethylene with those not exposed to any chemicals. Colon cancer among men was significantly increased with RRs of 2.9, 4.3, and 5.7 from the lowest to the highest exposure categories for trichloroethylene; however, an RR of 4.1 for colon cancer was also found among those exposed to other chemicals but not to trichloroethylene. Among men, an RR of 2.6 was found for liver cancer in the highest exposure category (based on three incident cases). Multiple myeloma among men showed some evidence of an exposure-response gradient with trichloroethylene (the RR rose from 0.8 in the lowest exposure category to 5.1 in the highest, based on nine cases), but an RR of 3.7 was also found among workers exposed to chemicals, but not trichloroethylene. Among men there were two bone cancers (one in the lowest exposure category and one in the middle category). No bone cancers occurred among women or unexposed men. Women exposed to trichloroethylene showed no excess cancer incidence, although for many diseases there were no or very few cases.

Workers at Hill Air Force Base had the potential for exposure to many chemicals other than trichloroethylene. We assessed the possible associations between selected causes of death and exposure to 25 chemicals. The number of person-years of follow up among workers potentially exposed to specific chemicals varied from 2200 to 110 000 among men and 100 to 65 000 among women. These exposure categories are not mutually exclusive. For some chemicals the number of workers exposed was too small for meaningful analysis and they are not presented here. Some men (n=1801, 16% of the cohort) and many women (n=1938, 62% of the cohort) held no jobs in which they were likely to have been exposed to any chemicals.

Tables 6–8 show RRs for selected causes of death for the combined follow up period by selected other exposures. For many combinations of exposure and disease, the number of deaths was very small. Also, the overlap of exposures further limits our ability to evaluate disease risks from exposure to individual chemicals. For example, there were 11 men who died from non-Hodgkin's lymphoma with exposure to freon, solder flux, isopropyl alcohol, trichloroethane, or methylene chloride. Four of these were exposed to all five chemicals and four more were exposed to four of the five chemicals. Four of the five women who died from non-Hodgkin's lymphoma who had exposure to freon, solder flux, isopropyl alcohol, or acetone had likely contact with four of the five chemicals. Similar exposure overlaps occurred for multiple myeloma, breast cancer, and asthma. We also considered broad categories of exposure including mixed solvents, or any solvent.

Workers with potential exposure to any solvent or mixed solvents experienced non-significant excesses of non-Hodgkin's lymphoma (table 6). The RRs among women

Table 5 continued

< 5 units-y	5-25 unit-y	> 25 unit-y
0.7 (0.4 to 1.2) 13	0.6 (0.2 to 1.5) 5	0.8 (0.5 to 1.4) 22
0 cases	0 cases	0 cases
0 cases	0 cases	1.0 (0.1 to 10.9) 1
0.8 (0.2 to 3.8) 2	0 cases	0.9 (0.2 to 3.2) 3
0 cases	8.3 (0.5 to 135) 1	0 cases
0 cases	0 cases	0 deaths
1 observed/0 unexposed	1 observed/0 unexposed	1 observed/0 unexposed
0.6 (0.1 to 5.3) 1	0 cases	0 cases
0.3 (0.1 to 1.4) 20	0.4 (0.1 to 2.9) 11	0.4 (0.1 to 1.2) 3
0.8 (0.2 to 3.9) 2	1.0 (0.1 to 7.8) 1	0 cases
0 cases	0 cases	3.6 (0.5 to 25.6) 2
1.1 (0.1 to 10.8) 1	0 cases	1.0 (0.1 to 9.1) 1
0 cases	0 cases	0 cases
1.2 (0.3 to 4.4) 3	1.9 (0.4 to 8.8) 2	0.9 (0.2 to 3.3) 3
0 cases	2.4 (0.3 to 21.8) 1	0 cases
2 observed/0 expected	1 observed/0 expected	1 observed/0 expected
0.6 (0.1 to 5.0) 1	0 cases	0.9 (0.2 to 4.5) 2

were usually larger than those among men and based on fewer deaths. Several significant excesses were associated with several chemicals among women, whereas no significant excesses from any chemical occurred among men. Women with potential exposure to any solvent, mixed solvents, and some specific solvents experienced excesses for multiple myeloma (table 7). Few, however, were significant. Smaller excesses were found in men (RR 1.3). Deaths from breast cancer were in excess among women exposed to any solvent, mixed solvents, and several other solvents (table 8).

Because mortality from ischaemic heart disease and asthma was increased in the total cohort we also assessed their risks by specific exposures. Analyses of heart disease by individual chemicals generally showed RRs of about 1.1, similar to the RRs for the entire overall cohort (not shown). The only significant excess occurred among men exposed to toluene (RR 1.2, 207 observed). Men exposed to other chemicals but not toluene had an RR of 1.1. Only six women died from asthma. Four of these had no exposure to any chemical. Thirteen men died from asthma, all of them exposed to at least one chemical. Compared with Utah mortalities, SMRs were significant for exposure to any solvents (SMR 1.8), mixed solvents (SMR 1.8), methylene chloride (SMR 2.3), and Stoddard solvent (SMR 2.4).

In the earlier report on this cohort,[5] we noted that three women who died from multiple myeloma had worked in fabric handling operations. No additional deaths from multiple myeloma occurred during the extended follow up among any of the women ever employed in these operations (RR 8.9, 95% CI 1.6 to 48.1, three deaths). Other causes of death for this group showed non-significant excesses, including cancers of the liver and biliary passages (RR 4.2, 95% CI 0.6 to 30.4, two deaths) and breast (RR 2.3, 95% CI 0.9 to 5.8, six deaths). Men once employed in fabric handling had no significant excesses for a cause of death, but several non-significant increases were found including non-Hodgkin's lymphoma (RR 4.0, 95% CI 0.8 to 20.7, two deaths), cancer of the colon (RR 3.3, 95% CI 0.9 to 12.2, three deaths), and ischaemic heart disease (RR 1.4, 95% CI 1.0 to 1.9, 40 deaths).

Discussion

We conducted this study of the mortality and cancer incidence of civilian workers at Hill Air Force Base because of concern about possible ill health effects from exposure to organic solvents and other chemicals used in the repair and maintenance of aircraft. Several of the chemicals currently or previously used at the base cause cancer in animals, including chloroform, methylene chloride, isopropyl alcohol, silica, perchloroethylene, and trichloroethylene, and some have been linked with human cancer in epidemiological investigations.[1–4] An earlier follow up of the cohort to the end of 1982 found mortality excesses from asthma, multiple myeloma, non-Hodgkin's lymphoma, and cancers of the liver, bone, and breast.[5] Too few deaths occurred in each of these combinations of exposure and cause of death to draw firm conclusions, so we continued to follow up the cohort from 1982 to 1990 to obtain additional information. This new follow up identified 1895 additional deaths, including 408 cancer deaths. During the second follow up, the cohort was also linked to the Utah cancer registry to provide information on cancer incidence. Incidence data are especially valuable for cancers of the liver, bone, and endocrine glands because these cancers are especially susceptible to diagnostic misclassifi-

Table 6 Rate ratios for mortality from non-Hodgkin's lymphoma among workers with exposure to selected chemicals (compared with those with no such exposure)

	Men			Women		
Chemical	RR	Cases (n)	95% CI	RR	Cases (n)	95% CI
Any solvent	1.6	31	0.6 to 4.1	2.8	9	0.8 to 4.5
Solvents, unspecified	1.6	31	0.6 to 4.1	2.9	9	0.8 to 10.6
Stoddard solvent	1.3	16	0.5 to 3.5	2.4	5	0.6 to 9.9
Carbon tetrachloride	1.2	14	0.4 to 3.3	3.3	8	0.9 to 12.7
Jet fuel (JP4)	1.7	10	0.6 to 5.1	2.7	2	0.4 to 16.1
Freon	1.9	8	0.6 to 5.8	5.6	2	0.9 to 33.7
Solder flux	1.8	7	0.5 to 5.7	6.5	2	1.1 to 39.1
Isopropyl alcohol	1.8	7	0.6 to 5.8	5.8	2	1.0 to 34.6
Other alcohols	2.1	3	0.5 to 9.0	—	0	
Zinc chromate	1.6	6	0.5 to 5.2	3.7	3	0.7 to 18.5
Trichloroethane	2.3	8	0.7 to 7.5	—	0	
Acetone	1.7	6	0.5 to 5.5	1.3	1	0.1 to 12.8
Toluene	1.0	3	0.2 to 4.2	2.2	2	0.4 to 13.1
Methyl ethyl ketone	1.4	4	0.4 to 5.1	1.6	1	0.2 to 15.7
Methylene chloride	3.0	6	0.9 to 10.0	—	0	

Table 7 Rate ratios for mortality from multiple myeloma among workers with exposure to selected chemicals (compared with those with no such exposure)

	Men			Women		
Chemical	*RR*	*Cases (n)*	*95% CI*	*RR*	*Cases (n)*	*95% CI*
Any solvent	1.3	19	0.4 to 3.8	1.9	5	0.4 to 8.2
Solvents, unspecified	1.3	19	0.4 to 3.8	2.0	5	0.4 to 8.5
Stoddard solvent	1.0	96	0.3 to 3.2	1.6	3	0.3 to 8.2
Carbon tetrachloride	1.2	14	0.4 to 3.3	3.3	8	0.9 to 12.7
Jet fuel (JP4)	1.4	60	0.4 to 5.2	—	0	
Freon	1.8	5	0.4 to 6.8	—	0	
Solder flux	1.5	4	0.4 to 6.2	—	0	
Isopropyl alcohol	1.5	4	0.4 to 6.4	—	0	
Other alcohols	1.7	2	0.3 to 9.6	—	0	
Zinc chromate	—	0		3.6	3	0.7 to 18.1
Trichloroethane	—	0		13.2	2	2.2 to 80.4
Acetone	1.6	4	0.4 to 6.7	3.8	2	0.6 to 23.8
Toluene	0.9	2	0.2 to 4.8	5.0	4	1.1 to 23.1
Methyl ethyl ketone	0.4	1	0.1 to 4.0	4.6	3	0.9 to 23.2
Methylene chloride	3.4	5	0.9 to 13.2	—	0	

cation on death certificates,[11] and for cancers with good survival such as breast, prostate, and bladder.

Mortality after 1982 tended to follow the same patterns found in the original report.[5] Mortality from all causes and all cancer during the extended period were about the same as in the Utah population. The SMRs were slightly larger during the recent follow up period than in the period before 1982 where small but significant deficits occurred for all causes combined and all cancers combined. The increase in SMRs for all causes and all cancer with additional follow up may reflect a diminution of the healthy worker effect, which is often attenuated as a working cohort ages.[10 12]

Trichloroethylene was the main solvent used historically at the base and consequently it was an important focus of this study. Experimental investigations have reported excesses of hepatocellular carcinomas, lung cancer, and lymphomas in mice, and possibly renal cancer in rats exposed to trichloroethylene.[13] We found no significant excess of any cancer among workers exposed to trichloroethylene, although non-significant excesses occurred in both follow up periods for cancers of the oesophagus, colon, breast, cervix, kidney, bone, and non-Hodgkin's lymphoma. These associations do not seem to be specific to trichloroethylene because workers who were exposed to other chemicals, but not trichloroethylene, also experienced increased risks for these cancers; patterns differed between men and women; and no clear exposure-response gradient was evident. An exception was colon cancer, in which the RR for incident cancer rose with cumulative exposure among men, but no such pattern occurred among women. The non-significant excess of mortality from liver and biliary cancer among women and incidence among men is interesting because this is one of the tumours found in bioassays of trichloroethylene and other solvents[13] and because it is a cancer often misclassified on death certificates.[11]

Table 8 Rate ratios for mortality from breast cancer among women with exposure to selected chemicals (compared with those with no such exposure)

Chemical	*RR*	*Cases (n)*	*95% CI*
Any solvent	1.6	28	0.9 to 2.8
Solvents, unspecified	1.6	27	0.9 to 2.8
Stoddard solvent	1.2	15	0.6 to 2.4
Carbon tetrachloride	1.3	18	0.7 to 2.5
Jet fuel (JP4)	1.0	50	0.4 to 2.7
Freon	3.8	8	1.7 to 8.8
Solder flux	3.7	7	1.6 to 8.9
Isopropyl alcohol	3.7	8	1.6 to 8.4
Other alcohols	2.8	2	0.7 to 12.2
Zinc chromate	1.6	8	0.7 to 3.8
Trichloroethane	3.3	3	1.0 to 11.2
Acetone	1.9	7	0.8 to 4.6
Toluene	2.0	10	0.9 to 4.2
Methyl ethyl ketone	2.1	8	0.9 to 4.7
Methylene chloride	3.0	4	1.0 to 8.8

The larger excess for mortality from kidney cancer in the recent follow up (RR 2.8) than in the earlier follow up (RR 1.2) is based on only one death and may simply be a chance finding. Although numbers are small, RRs by level and type of exposure do not implicate trichloroethylene in the aetiology of kidney cancer in this study.

Excess mortality from breast cancer occurred among the women exposed to trichloroethylene in both follow up periods, but the highest RR was in the category exposed to trichloroethylene at the lowest level (RR 2.4). Mortality by type of exposure, intermittent low level, continuous low level, or frequent peaks, and data on cancer incidence also showed some associations, but these were not consistent.

Non-significant associations occurred between multiple myeloma and non-Hodgkin's lymphoma and trichloroethylene. The RR for incident multiple myeloma rose with cumulative exposure to trichloroethylene among men, but mortality was not increased. Men exposed to other chemicals, but not trichloroethylene, also had an excess of multiple myeloma. Mortality and incident excesses of multiple myeloma occurred among women, but no exposure-response gradients were found. Mortality from non-Hodgkin's lymphoma was slightly increased among men and women, but its incidence was not. Inconsistencies by sex and exposure level do not make a strong case for an association between these two cancers and exposure to trichloroethylene.

Our findings can be compared with previous investigations of workers exposed to trichloroethylene.[14–16] Colon cancer has not been linked with trichloroethylene in other epidemiological investigations. This and the lack

of consistent results among men and women and by incidence and mortality in our study do not make a strong case for a link between exposure to trichloroethylene and colon cancer. Small excesses of liver cancer were found among men, but not women, in studies in Finland[15] and Sweden,[14] but no excess occurred in a mortality study in the United States.[16] We cannot compare our slight excess for breast cancer with earlier reports because the other studies did not present data on breast cancer. An excess of kidney cancer was recently reported among German workers exposed to trichloroethylene,[17] but no excess was found in other investigations.[14–16] The excess found here was limited mainly to the recent follow up and showed no clear pattern with cumulative exposure and it was as large among workers exposed to other chemicals as among those exposed to trichloroethylene. Non-significant excesses were reported for multiple myeloma in the Finnish study[15] and for non-Hodgkin's lymphoma in the Finnish[15] and Swedish[14] studies. Excesses from reported exposure to solvents in general were found in case-control studies from Sweden for lymphoma[18] and for colon cancer.[19] Siemiatycki[20] found no associations between non-Hodgkin's lymphoma and cancers of colon, pancreas, and kidney and occupational exposure to trichloroethylene. Thus, data from this study and others in the scientific literature, although somewhat limited, do not strongly support a link between any specific cancer and exposure to trichlorethylene.

If the apparent lack of any strong carcinogenic effects specifically from exposure trichloroethylene is somewhat reassuring, the long term health effects from solvents as a class of exposures may be less so. Excesses of non-Hodgkin's lymphoma and multiple myeloma were typically found among workers potentially exposed to any solvents, mixed solvents, and several individual solvents. The RRs were larger among women than men and the excesses were smaller during the recent period. Unfortunately, because of small numbers and overlapping exposures it was not possible to clearly evaluate risks from individual chemicals. The inconsistency in level of risk between men and women and the general diminution in risk in the recent follow up period do not present compelling evidence for a causal link with occupational exposures. It is not easy, however, to simply dismiss as spurious the associations between non-Hodgkin's lymphoma and multiple myeloma to clusters of solvents because various lymphatic and haematopoietic cancers have been linked with several organic solvents (benzene, methylene chloride, trichloroethylene, and tetrachloroethylene) in experimental studies[13] and in some epidemiological studies.[18 21–30]

Although breast cancer was not excessive in the total cohort, non-significant excesses occurred among women exposed to any solvent and mixed solvents, whereas significant excesses occurred among those exposed to freon, solder flux, trichloroethane, methylene chloride, metal fumes and dusts, isopropyl alcohol, and other alcohols. Numbers of deaths from breast cancer associated with any one chemical were small, there was a considerable overlap of exposures, and the associations could be due to chance or confounding. Confounding would not seem to be simply from some social factor linked to working at the base because there was a deficit of breast cancer in the entire cohort for both the earlier and recent follow up. Any bias or confounding would have to be chemical specific and thus is less plausible. Few environmental causes of breast cancer are known, but several chemicals cause mammary cancer in rodents including the solvents benzene, butadiene, methylene chloride, and trichloropropane.[31] Cantor *et al*[32] with a job exposure matrix for a death certificate case-control study found suggestive associations between breast cancer and occupational exposure to organic solvents, carbon tetrachloride, methylene chloride, styrene, paints, metals, and solder. The significant association we found with occupational exposure to isopropyl alcohol and non-significant association with other alcohols is interesting in the light of the suspected link with consumption of alcohol.[33] Goldberg and Labreche,[34] in a recent review of breast cancer and occupation exposures, noted the lack of high quality investigations in this area. The findings from this cohort study underscore the need for future evaluation of breast cancer risks associated with occupational exposures.

It was not possible to control for reproductive factors that are major risk factors for breast cancer.[35] For example, these women could have delayed their first pregnancy because they were employed. Any confounding would have to be exposure specific as the cohort as a whole shows no excess of breast cancer mortality. Habel *et al*[36] in a recent publication showed that RRs for breast cancer by occupation were barely changed by adjustment for established risk factors.

Mortality from ischaemic heart disease was significantly increased in the recent follow up, but not during the earlier period. Small but significant excesses occurred among men exposed to trichloroethylene and a non-significant excess occurred among women. No striking association was found between ischaemic heart diseases and any other specific chemical exposures. Although the epidemiological literature is sparse, exposure to organic solvents (with the exception of carbon disulphide) has generally not been associated with an increased risk of heart disease.[37] Carbon disulphide affects mortality from heart disease,[38 39] but this chemical was not known to be used at Hill Air Force Base. Methylene chloride is metabolised to carbon monoxide, which could pose a risk,[37] but neither men nor women potentially exposed to methylene chloride in this cohort experienced an excess. In other studies, heart disease was not increased among workers exposed to various solvents including perchloroethylene,[25 40] styrene,[41 42] methylene chloride,[43] isopropanol,[44] benzene,[28] tetrachloroethane,[45] and trichloroethylene.[46]

Mortality from asthma was increased during both follow up periods, although it was smaller and not significant during the recent follow up,

it was significantly increased among men exposed to any solvents and mixed solvents. Although asthma is a disease not well investigated by mortality, it has been reported among workers exposed to paint,[47] isocyanates,[48] dust and fumes,[49] and organic solvents,[50] and solvents have been found to cause a decline in lung function among people with bronchial hyperactivity and asthma.[51] There were no identifiable patterns of exposures when the jobs of the cases were examined. Hagmar *et al*[52] found no excess of asthma among chemical workers in Sweden exposed to urethane, ethylene oxide, formaldehyde, and organic solvents.

This study has several strengths. It follows a large cohort of workers (n=14 457), many of them women (n=3138), who were exposed to several different chemicals, particularly various organic solvents. The potential exposures were carefully evaluated by industrial hygienists. The extended follow up provided 1866 additional deaths for analysis. About 40 years have elapsed since these workers were first exposed (generally in the 1950s), so effects with long latent periods could be detected. In fact, the generally lower RR for several cancers in the period after 1982 could indicate that the cohort is past the period of peak risk. Use of internal comparisons minimise the potential for selection and socioeconomic problems associated with use of the general population for comparison.[10 12] Finally, availability of data on cancer incidence is helpful for some cancers, the liver in particular.

Certain limitations need to be considered when evaluating study results. In the complex work environment at the base, exposures were not mutually exclusive and it is not possible to evaluate risks from exposure to individual chemicals while controlling for other exposures, particularly for rarer causes of death. Multiple comparisons were made and some significant excesses and deficits would be expected due to chance alone. Information on lifestyle and other non-occupational risk factors for various diseases—for example, tobacco and alcohol use and diet—were not available. Confounding by tobacco probably poses no major problem as smoking is not strongly associated with cancers that were increased in this cohort, non-Hodgkin's lymphoma, multiple myeloma, or cancers of the liver or breast.[53] Also, the lack of an excess for cancers related to tobacco (lung, oesophagus, and bladder) suggests that the smoking habits of exposed workers in this cohort were not significantly different from those of the general population of Utah. Others have found that tobacco seldom confounds risk estimates in occupational studies.[53–56] Finally, most analyses used an internal control which compared exposed people in the cohort with unexposed cohort members. Use of an internal working population for comparison should minimise differences in tobacco use and other potential confounders between the exposed and comparison population and diminish the chances of confounding from various lifestyle factors.

The extended follow up of this large cohort of workers provided the opportunity to evaluate risks of cancer and other diseases from potential exposure to various chemicals including trichloroethylene. We did not find any large relative risks with clear exposure-response gradients for any particular combination of exposure and disease. Although it is not possible to state with certainty whether some exposures may have caused a small excess for a particular disease, it is reasonably clear that the cohort has not experienced any major mortality or cancer excess. We continue, however, to find non-significant excesses of non-Hodgkin's lymphoma, multiple myeloma, and breast cancer among workers with exposures to various solvents. Little is known about occupational causes of breast cancer, but lymphatic and haematopoietic cancers have been associated with solvent exposure in both animal and human studies.

The conclusions in this paper are those of the authors and do not necessarily reflect the views of the United States Air Force, Department of Defense, or the American Federation of Government Employees. Financial support for the study was provided to the National Cancer Institute by the United States Air Force. We are grateful for the technical advice provided by the Air Force and the American Federation of Government Employees in conducting this investigation.

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Medical editors' trial amnesty

As described in an editorial in the *British Medical Journal*,[1] medical editors of nearly 100 international medical journals are taking action to try to ensure that the results of unpublished randomised controlled trials become available to be included in systematic reviews. This could have important benefits for patient care.

Any reader who would like to take up this opportunity to register the results of a trial that did not get published can do so on a special *unreported trial registration form*. Copies are available from the *Occupational and Environmental Medicine* editorial office.

I do not expect that many *Occupational and Environmental Medicine* readers will need to take up this offer, given the nature of our field, but perhaps I will be proved wrong.

ANNE COCKCROFT
Editor

1 R Smith, I Roberts. An amnesty for unpublished trials. *BMJ* 1997;**315**:622.