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Mortality and cancer incidence among British agricultural pesticide users

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Background Although the acute effects of pesticides in humans are well known, uncertainty still exists about the health effects of chronic low-level exposure to pesticides.

Aims To compare mortality and cancer incidence experienced by a cohort of British pesticide users to that of the Great Britain (GB) population.

Methods The Pesticide Users Health Study (PUHS) comprises users of agricultural pesticides who have Certificates of Competence under the Control of Pesticides Regulations 1986. Participants were followed up between 1987 and 2004 (cancer incidence) or 2005 (mortality). Standardized mortality ratios (SMRs) and Standardized incidence ratios (SIRs) were estimated for outcomes of interest identified from the literature.

Results Altogether, 62 960 pesticide users were followed up for 829 709 person-years (to 31 December 2005). Most participants were male (94%) and based in England (86%). All-cause mortality was lower for both men [SMR 0.58, 95% confidence interval (CI) 0.55–0.60] and women (SMR 0.71, 95% CI 0.52–0.98) compared to the GB population. Mortality and incidence were below those expected for all cancers combined among men (SMR 0.71, 95% CI 0.66–0.77; SIR 0.85, 95% CI 0.81–0.90), particularly for cancers of the lip, oral cavity and pharynx, digestive organs and respiratory system. The incidence of testicular cancer, non-melanoma skin cancer and multiple myeloma were above expected. Mortality from injury by machinery was significantly above expected for men (SMR 4.21, 95% CI 2.11–8.42).

Conclusions This study suggests that pesticide users in the PUHS are generally healthier than the national population but may have excesses of non-melanoma skin cancer, testicular cancer and multiple myeloma.

Key words Cancer incidence; Great Britain; mortality; pesticide users.

Introduction

The acute effects of exposure to pesticides in humans are well documented and include headache, muscle twitching, runny nose, confusion, muscle weakness and fevers among others [1]. Current surveillance systems in Great Britain (GB) tend to focus on acute episodes of ill-health such as poisonings but there is concern over the potential effects of long-term low-level exposure to pesticides. Although chronic health effects such as cancer and adverse reproductive outcomes have been investigated extensively [2–7], any association with pesticide exposure remains uncertain, with methodological difficulties as a possible reason for observed inconsistencies [8, 9]. Currently in GB, there is no surveillance system to monitor the health of those exposed to low levels of pesticides on a longer term basis.

Since 1989, anyone applying agricultural pesticides on a commercial basis or agricultural pesticide users born after 31 December 1964 must first gain a Certificate of Competence in their safe use; this is a statutory requirement under the Control of Pesticides Regulations 1986 (COPR). City & Guilds Land Based Services (formerly City & Guilds NPTC, National Proficiency Tests Council) issues the Certificates of Competence and holds a database of all those who hold certificates in GB. The Health and Safety Executive (HSE) recognized the potential of this database to help monitor the use of pesticides and the health of pesticide users in GB. In 1996/1997, HSE conducted a feasibility study which concluded that pesticide users on the City & Guilds Land Based Services database would be a good group on which to base future research [10]. The Pesticide Users Health Study (PUHS) was therefore

established, comprising individuals on this database who had given permission for HSE to access their information.

The objective of the current analysis was to report on mortality and cancer incidence experienced by the pesticide users in the PUHS and to compare these to the national population of GB.

Methods

All individuals with Certificates of Competence issued by City & Guilds Land Based Services since 1987 are eligible for inclusion in the PUHS. At the time of application for certification, pesticide users are asked whether they give permission for HSE to access their details. Those who consent are included in the PUHS. The information held by City & Guilds Land Based Services is obtained from the application form for the module. It includes basic details on the individual (including name, address, sex and date of birth) and information on the module (such as type of module, date of test and test centre). The last update was received from City & Guilds Land Based Services in 2003 and the PUHS now comprises 65 910 pesticide users tested between 1987 and 2003.

Individuals on the PUHS are flagged for cancer and death registrations at the National Health Service Central Register (NHSCR) for England and Wales and the General Register Office for Scotland (GROS). Notifications are received quarterly from the National Health Service Information Centre. The HSE Research Ethics Committee approved the study.

The causes of death and cancers investigated were selected based on a review of the literature; diseases or conditions in previous studies of pesticide users or pesticide manufacturing workers were listed and used as the outcomes of interest. Primary cancers were included in the analysis of cancer incidence and underlying cause of death in the mortality analysis.

Standardized mortality ratios (SMRs) and Standardized incidence ratios (SIRs) were used to compare mortality and cancer incidence (respectively) among the pesticide users to that observed in the GB population. Only those with a valid date of first test, date of death (if dead), date of birth and region were included in the analysis; those not resident in GB were excluded.

There is a delay in obtaining cancer registrations compared to death notifications and so the end of the study period was 1 year earlier for the analysis of cancer incidence than the mortality analysis. For the mortality analysis, person-years were accumulated from the date of first test to the date of death, loss to follow-up or the end of the study period (31 December 2005), whichever occurred first. Similarly, for the analysis of cancer incidence, person-years were accumulated from the date of first test to the date of death, loss to follow-up or the end of the study period (31 December 2004) for those who did not have a cancer registration. Pesticide users with cancer were withdrawn from analyses of specific cancers on the date that specific cancer was diagnosed but remained at risk for other cancers. Therefore, total person-years at risk differed depending on the cancer type being analysed. In order to ensure that only incident, and not prevalent, cases were included, pesticide users with a cancer registration before their first test date did not contribute person-years to the analysis of that specific cancer.

Poisson regression was used to estimate SMRs/SIRs, with the number of observed deaths/cases as the dependent variable and the number of expected deaths/cases as the offset variable. The expected number of deaths/cases was estimated using age, sex, period and country (England and Wales or Scotland)-specific mortality/incidence rates. SMRs/SIRs with corresponding 95% confidence intervals (CIs) were calculated separately for males and females and a P-value of <0.05 was used to indicate statistical significance. All analyses were conducted in Stata/SE 11.1 for Windows [11].

Results

Altogether, there were 65,910 pesticide users in the PUHS. Around 96% (63,493) were successfully traced for follow-up with the NHSCR or GROS. Just 533 (0.8%) were excluded due to residence outside GB or because their first test date was missing. Therefore, 62,960 pesticide users were included in the analysis, followed-up for a total of 829,709 person-years (to 31 December 2005) with a mean of 13.2 years per participant.

Figure 1 shows the year of first test for pesticide users in the PUHS. Nearly 50% of all participants were first tested before 1991 as the implementation of the COPR resulted in those already using agricultural pesticides requiring certification.

Table 1 shows characteristics of the study participants. The majority of the pesticide users were male (94%) and based in England (86%). Around 10% of individuals had

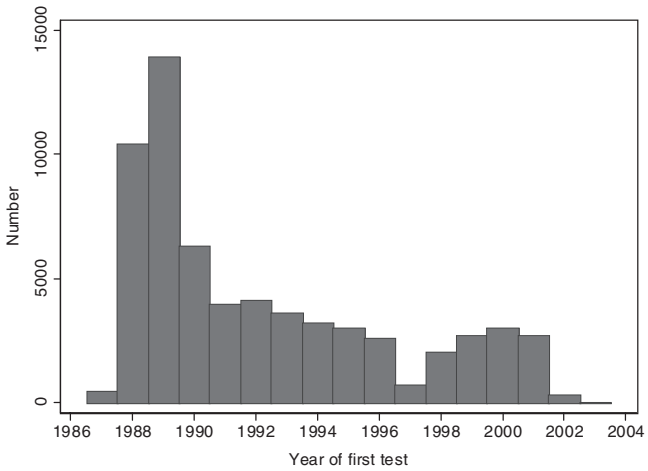

Figure 1. Number of pesticide users in the PUHS, by year of first test.

Table 1. Characteristics of pesticide users in the PUHS, 1987–2003

Characteristic	Men Number (%)	Women Number (%)	Total Number (%)
Total	59 085 (100)	3875 (100)	62 960 (100)
Region			
East	8343 (14)	600 (16)	8943 (14)
South East	11 872 (20)	1156 (30)	13 028 (21)
South West	7457 (13)	543 (14)	8000 (13)
Midlands	10 431 (18)	584 (15)	11 015 (18)
North	12 350 (21)	615 (16)	12 965 (21)
Scotland	6071 (10)	252 (7)	6323 (10)
Wales	2561 (4)	125 (3)	2686 (4)
Year of birth			
Before 1930	618 (1)	4 (0)	622 (1)
1930–39	3532 (6)	48 (1)	3580 (6)
1940–49	8344 (14)	290 (8)	8634 (14)
1950–59	13 264 (22)	598 (15)	13 862 (22)
1960–69	21 347 (36)	1698 (44)	23 045 (37)
1970–79	10 607 (18)	1157 (30)	11 764 (19)
1980 onwards	1373 (2)	80 (2)	1453 (2)
Age at first test			
<25	18 696 (32)	1689 (44)	20 385 (32)
25–29	10 428 (18)	876 (23)	11 304 (18)
30–34	8520 (14)	479 (12)	8999 (14)
35–39	6692 (11)	314 (8)	7006 (11)
40–44	5498 (9)	261 (7)	5759 (9)
45–49	3975 (7)	141 (4)	4116 (7)
50–	5276 (9)	115 (3)	5391 (9)
Modules taken			
Foundation (F)	6293 (11)	676 (18)	6969 (11)
F + ground crop sprayer	16 640 (28)	207 (5)	16 847 (27)
F + hand-held operator	28 693 (49)	2709 (70)	31 402 (50)
All three	2711 (5)	73 (2)	2784 (4)
All other combinations	4748 (8)	210 (5)	4958 (8)

Percentages may not sum to 100% due to rounding.

only completed the foundation module. This is not regarded as a Certificate of Competence under the COPR in its own right but needs to be accompanied by another module. Approximately 50% of pesticide users had completed hand-held operator modules (PA06 modules) and ~25% had completed the ground crop sprayer modules (PA02 modules). Most people (~50%) were <30 years of age at their first test, with a mean age at first test of 32.5 [standard deviation (SD) 11.0] years for males and 28.7 (SD 8.8) years for females.

Altogether, there were 1628 deaths among the cohort (1591 men, 37 women), including 602 (37%) from cancer and 270 (17%) from external causes. There were 1720 cancers registered during the study period (1645 among men, 75 among women). A single individual can be registered for multiple primary cancers and there were 1585 'first' registrations during follow-up (1514 among men, 71 among women). All-cause mortality was statistically significantly below that expected for both males [SMR 0.58, 95% CI 0.55–0.60] and females (SMR 0.71, 95% CI 0.52–0.98) (Table 2).

Tables 2 and 3 show SMRs and SIRs for cancer mortality and incidence, respectively. The trends of the SMRs and SIRs tended to be similar. For men, the SMRs/SIRs were statistically significantly <1 for all cancers combined (SMR 0.71, 95% CI 0.66–0.77; SIR 0.85, 95% CI 0.81–0.90). In particular, cancers of the lip, oral cavity and pharynx, digestive organs and respiratory system all showed statistically significant reductions compared to the general population (Tables 2 and 3). There were statistically significant excesses for incidence of non-melanoma skin cancer, cancer of the testis and multiple myeloma (Table 3). Corresponding SMRs were >1 but not statistically significantly so possibly due to the small number of deaths (particularly for non-melanoma skin cancer and cancer of the testis) resulting in wide CIs (Table 2).

There was no clear pattern in SMRs and SIRs among women due to the small numbers of deaths and cases and the resulting wide CIs (Tables 2 and 3). Incidence of non-melanoma skin cancer was statistically significantly above that expected (SIR 1.73, 95% CI 1.06–2.82) but there were no deaths from non-melanoma skin cancer to

Table 2. Mortality in the PUHS, 1987–2005

Cause of death	ICD-9	ICD-10	Men			Women		
			Obs	SMR	95% CI	Obs	SMR	95% CI
All causes	001–799, E800–E999	A00–R99, V01–Y98	1591	0.58	0.55–0.60***	37	0.71	0.52–0.98*
All malignant neoplasms	140–208	C00–C97	583	0.71	0.66–0.77***	19	0.85	0.54–1.34
All malignant neoplasms (excl. NMSC)	140–208 (excl. 173)	C00–C97 (excl. C44)	580	0.71	0.66–0.77***	19	0.85	0.54–1.34
Lip, oral cavity and pharynx	140–149	C00–C14	4	0.18	0.07–0.49**	0		
Digestive organs	150–159	C15–C26	192	0.78	0.68–0.90**	2	0.58	0.14–2.30
Oesophagus	150	C15	46	0.89	0.66–1.18	0		
Stomach	151	C16	30	0.88	0.61–1.26	1	2.33	0.33–16.5
Colon	153	C18	38	0.72	0.53–1.00*	0		
Rectum and anus	154	C19–C21	22	0.64	0.42–0.97*	0		
Liver	155–156	C22–C24	8	0.42	0.21–0.85*	0		
Pancreas	157	C25	38	1.02	0.74–1.40	1	1.55	0.22–11.0
Respiratory system	160–165	C30–C39	126	0.55	0.46–0.66***	1	0.34	0.05–2.42
Larynx	161	C32	3	0.34	0.11–1.05	0		
Trachea, bronchus and lung	162	C33–C34	118	0.55	0.46–0.66***	1	0.35	0.05–2.51
Skin	172–173	C43–C44	15	0.79	0.48–1.32	0		
Melanoma	172	C43	12	0.72	0.41–1.27	0		
NMSC	173	C44	3	1.34	0.43–4.15	0		
Soft tissue sarcoma	171	C49	3	0.93	0.30–2.87	1	8.77	1.24–62.3*
Breast	174–175	C50	1	1.24	0.17–8.82	6	0.94	0.42–2.08
Female genital system	179–184	C51–C58	NA			2	0.60	0.15–2.40
Ovarian and other uterine adnexa	183	C56–C57	NA			1	0.60	0.08–4.22
Male genital system	185–187	C60–C63	40	0.86	0.63–1.18	NA		
Prostate	185	C61	33	0.80	0.57–1.12	NA		
Testis	186	C62	7	1.95	0.93–4.09	NA		
Urinary system	188–189	C64–C68	34	0.72	0.51–1.00	0		
Kidney	189	C64	18	0.72	0.45–1.15	0		
Bladder	188	C67	14	0.66	0.39–1.11	0		
Eye, brain and central nervous system	190–192	C69–72	34	0.82	0.58–1.14	1	0.98	0.14–6.95
Eye	190	C69	0			0		
Brain	191	C71	20	0.78	0.51–1.22	0		
CNS and meninges	192	C70, C72	1	1.89	0.27–13.4	0		
Thyroid	193	C73	1	0.72	0.10–5.09	0		
Lymphatic and haematopoietic	200–208	C81–C96	73	0.94	0.75–1.18	6	3.48	1.56–7.74**
Hodgkin's disease	201	C81	4	0.82	0.31–2.20	0		
Non-Hodgkin's lymphoma	200, 202	C82–C85	26	0.77	0.53–1.14	2	3.03	0.76–12.1
Multiple myeloma	203	C90	15	1.28	0.77–2.12	2	10.8	2.70–43.2**
Leukaemia	204–208	C91–C95	26	0.96	0.66–1.42	2	2.83	0.71–11.3
Diseases of the:								
Nervous system and sense organs	320–389	G00–H95	28	0.40	0.28–0.59***	0		

Table 2. (*Continued*)

Cause of death	ICD-9	ICD-10	Men			Women		
			Obs	SMR	95% CI	Obs	SMR	95% CI
Parkinson's disease	3320	G20	0			0		
Motor neuron disease	3352	G122	9	0.81	0.42–1.56	0		
Alzheimer's disease	3310	G30	3	0.95	0.31–2.94	0		
Circulatory system	390–459	I00–I99	530	0.58	0.53–0.63***	4	0.43	0.16–1.14
Ischaemic heart disease	410–414	I20–I25	335	0.54	0.48–0.60***	1	0.27	0.04–1.90
Cerebrovascular disease	430–438	I60-I69	89	0.66	0.54–0.82***	2	0.71	0.18–2.85
Respiratory system	460–519	J00-J99	75	0.39	0.32–0.49***	1	0.32	0.04–2.26
COPD	490–492	J40-J44	15	0.30	0.18–0.49***	0		
Asthma	493	J45-J46	4	0.41	0.15–1.08	0		
Farmer's lung	4950	J670	0			0		
Digestive system	520–579	K00-K93	39	0.23	0.17–0.32***	2	0.56	0.14–2.25

ICD, International Classification of Diseases version 9 (ICD–9) and version 10 (ICD–10); NMSC, non–melanoma skin cancer; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; Obs, number of deaths observed; NA, not applicable.

*, Statistically significant at $P < 0.05$; **, statistically significant at $P < 0.01$; ***, statistically significant at $P < 0.001$.

enable estimation of an SMR. The SMRs for soft tissue sarcoma (SMR 8.77, 95% CI 1.24–62.3) and lymphatic and haematopoietic cancers (SMR 3.48, 95% CI 1.56–7.74) and both the SMR and SIR for multiple myeloma (SMR 10.8, 95% CI 2.70–43.2; SIR 10.9, 95% CI 4.10–29.1) were all statistically significantly >1, although the numbers of deaths/cases were small.

Among non-malignant diseases mortality was statistically significantly below that expected for diseases of the nervous system and sense organs (SMR 0.40, 95% CI 0.28–0.59) and circulatory (SMR 0.58, 95% CI 0.53–0.63), respiratory (SMR 0.39, 95% CI 0.32–0.49) and digestive (SMR 0.23, 95% CI 0.17–0.32) systems among men (Table 2).

The SMR for mortality from all external causes was statistically significantly lower than that expected compared with the GB population (SMR 0.69, 95% CI 0.62–0.78) (Table 4). Among male pesticide users, there was a statistically significant excess of deaths caused by 'injury by machinery' (SMR 4.21, 95% CI 2.11–8.42). There was also a statistically significant excess of deaths caused by slips, trips or stumbling among women (SMR 123, 95% CI 17.3–873) but this estimate was based on only one death.

Discussion

Men and women in the PUHS had reduced all-cause mortality compared to the GB population. Men in the PUHS had reduced cancer mortality and incidence. In particular, cancers of the lip, oral cavity and pharynx, cancers of the digestive organs and cancers of the respiratory system were significantly below that expected. Excesses were observed for cancer of the testis, non-melanoma skin cancer and multiple myeloma.

Members of the PUHS were recruited from all those who have passed Certificates of Competence in applying agricultural pesticides since 1987, so the cohort should be representative of those using agricultural pesticides in GB. However, the information held by the issuer's database is restricted to the information provided at the time of application for the certificate. The database lacks information on potential confounding factors, such as smoking history, physical activity and hours spent outdoors, which would need to be collected through additional research.

Around 10% of the PUHS cohort holds only the foundation module, which in isolation is not recognized as a Certificate of Competence under the COPR. However, individuals may use agricultural pesticides on a commercial basis without certification if supervised by someone who holds a valid Certificate of Competence. The cancer incidence analysis was repeated excluding those who had only completed the foundation module but the results were not substantially different to those presented, and so these individuals were retained in the analysis.

Other studies of farmers and pesticide applicators have also found reduced mortality and cancer incidence [2, 12, 13], which may in part reflect the 'healthy worker effect'. This may also be at least partially attributable to pesticide users having a healthier lifestyle than the general population in terms of, for example, greater physical activity levels and lower tobacco and alcohol consumption. The US Agricultural Health Study of 52,394 pesticide applicators

Table 3. Cancer incidence in the PUHS, 1987–2004

Cancer	ICD-9	ICD-10	Men			Women		
			Obs	SIR	95% CI	Obs	SIR	95% CI
All malignant neoplasms	140–208	C00–C97	1514	0.85	0.81–0.90***	71	0.94	0.74–1.18
All malignant neoplasms (excl. NMSC)	140–208 (excl. 173)	C00–C97 (excl. C44)	1187	0.80	0.75–0.85***	56	0.83	0.64–1.08
Lip, oral cavity and pharynx	140–149	C00–C14	21	0.36	0.23–0.55***	1	1.04	0.15–7.38
Digestive organs	150–159	C15–C26	282	0.76	0.68–0.86***	6	0.98	0.44–2.19
Oesophagus	150	C15	37	0.73	0.53–1.01	0		
Stomach	151	C16	44	0.77	0.57–1.03	1	1.55	0.22–11.0
Colon	153	C18	81	0.77	0.62–0.95*	3	1.31	0.42–4.06
Rectum and anus	154	C19–C21	67	0.76	0.59–0.96*	1	0.67	0.09–4.73
Liver and gall bladder	155–156	C22–C24	14	0.62	0.36–1.04	0		
Pancreas	157	C25	34	0.93	0.66–1.30	1	1.54	0.22–10.9
Respiratory system	160–165	C30–C39	139	0.52	0.44–0.61***	1	0.28	0.04–2.00
Larynx	161	C32	16	0.59	0.36–0.96*	0		
Trachea, bronchus and lung	162	C33–C34	118	0.51	0.43–0.61***	1	0.31	0.04–2.19
Skin	172–173	C43–C44	422	1.08	0.98–1.19	21	1.51	0.98–2.31
Melanoma	172	C43	62	0.94	0.73–1.21	5	1.06	0.44–2.56
NMSC	173	C44	363	1.11	1.00–1.23*	16	1.73	1.06–2.82*
Soft tissue sarcoma	171	C49	9	0.70	0.36–1.34	0		
Breast	174–175	C50	4	1.23	0.46–3.27	22	0.78	0.51–1.18
Female genital system	179–184	C51–C58	NA			10	0.81	0.43–1.50
Ovarian and other uterine adnexa	183	C56–C57	NA			3	0.75	0.24–2.32
Male genital system	185–187	C60–C63	310	1.11	0.99–1.24	NA		
Prostate	185	C61	205	1.07	0.93–1.22	NA		
Testis	186	C62	102	1.26	1.04–1.53*	NA		
Urinary system	188–189	C64–C68	100	0.78	0.64–0.94*	0		
Kidney	189	C64	41	0.84	0.62–1.14	0		
Bladder	188	C67	54	0.72	0.55–0.93*	0		
Eye, brain and CNS	190–192	C69–C72	44	0.79	0.59–1.07	0		
Eye	190	C69	5	1.10	0.46–2.63	0		
Brain	191	C71	38	0.78	0.57–1.07	0		
CNS and meninges	192	C70, C72	1	0.50	0.07–3.56	0		
Thyroid	193	C73	13	1.43	0.83–2.46	1	0.65	0.09–4.61
Lymphatic and haematopoietic	200–208	C81–C96	183	1.04	0.90–1.20	7	1.41	0.67–2.95
Hodgkin's disease	201	C81	24	0.92	0.62–1.37	0		
Non-Hodgkin's lymphoma	200, 202	C82–C85	74	0.92	0.73–1.15	1	0.47	0.07–3.35
Multiple myeloma	203	C90	31	1.49	1.05–2.13*	4	10.9	4.10–29.1***
Leukaemia	204–208	C91–C95	51	1.05	0.80–1.39	2	1.57	0.39–6.29

ICD, International Classification of Diseases version 9 (ICD–9) and version 10 (ICD–10); NMSC, non–melanoma skin cancer; CNS, central nervous system; Obs, number of cancers observed; NA, not applicable.

*, Statistically significant at $P < 0.05$; **, statistically significant at $P < 0.01$; ***, statistically significant at $P < 0.001$. Note: number of cases of NMSC plus all malignant neoplasms (excl. NMSC) do not sum to number of cases of all malignant neoplasms due to the method of calculating person–years.

Table 4. External causes of mortality in the PUHS, 1987–2005

Cause of death	ICD-9	ICD-10	Men			Women		
			Obs	SMR	95% CI	Obs	SMR	95% CI
All external causes	E800–E999	V01–Y98	264	0.69	0.62–0.78***	6	0.96	0.43–2.14
Transport accidents	E800–E848	V01–V99	67	0.74	0.58–0.94*	1	0.74	0.10–5.29
Accidental falls	E880–E888	W00–W19	17	0.74	0.46–1.20	1	3.14	0.44–22.3
Slips, trips or stumbling	E885	W01	1	1.66	0.23–11.8	1	123	17.3–873***
Injury by falling object	E916	W20	3	1.78	0.57–5.51	0		
Injury by machinery	E919	W30–W31	8	4.21	2.11–8.42***	0		
Injury by firearm	E922	W32–W33	1	5.03	0.71–35.8	0		
Accidents by submersion, suffocation and foreign bodies	E910–E915	W65–W84	6	0.45	0.20–1.00	0		
Injury by electric current	E925	W85–W87	2	1.33	0.33–5.31	0		
Accidental poisoning	E850–E863	X48–X49	6	0.34	0.15–0.75**	0		
Suicide & self–inflicted injury	E950–E959	X60–X84	101	0.80	0.66–0.97*	4	2.23	0.84–5.93
Injury, undetermined intent	E980–E989	Y10–Y34	25	0.43	0.29–0.64***	0		

ICD, International Classification of Diseases version 9 (ICD–9) and version 10 (ICD–10); Obs, number of deaths observed.

*, Statistically significant at $P < 0.05$; **, statistically significant at $P < 0.01$; ***, statistically significant at $P < 0.001$.

followed-up from 1993 to 2007 found an all cause SMR of 0.54 (95% CI 0.52–0.55) with an all cancer SMR of 0.61 (95% CI 0.58–0.64), which were similar to those found in the PUHS. They reported that just 17% of the pesticide applicators were current smokers [14] compared to 25% in the US population [15].

Agricultural workers tend to spend a greater number of hours outdoors than the general population, and so sun exposure cannot be ruled out as a possible explanation for the observed excess incidence of non-melanoma skin cancer. Few studies report on non-melanoma skin cancer, focussing mainly on malignant melanoma or skin cancer as a whole. One review of cancer risks among farmers did not find a significant association, obtaining a meta-relative risk of 1.04 (95% CI 0.93–1.15) for non-melanoma skin cancer (based on eight studies) [16]; the recent mortality analysis of the Agricultural Health Study cohort observed too few cases to estimate an SMR [14].

Men in the PUHS had significantly elevated incidence of testicular cancer with a non-significant excess in mortality. A recent article by Jones *et al.* [17] reviewed studies of workers in the crop protection product manufacturing industry, and the pooled SMR of 1.61 (95% CI 0.99–2.61) for testicular cancer (based on 20 cohorts) was of borderline statistical significance. There was no association observed in a meta-analysis of testicular cancer among farmers [18], and the Agricultural Health Study did not observe a significant excess of testicular cancer incidence [19].

Results in the PUHS for multiple myeloma were consistent across both the mortality and incidence analyses, with similar magnitudes observed for the SMRs and SIRs. Significant excesses were observed for incidence of multiple myeloma in both men and women and for mortality in women. There is substantial literature on the association between agricultural work or pesticide-related occupations and the risk of multiple myeloma, but it is not conclusive. The meta-analysis by Jones *et al.* [17] did not find a significant pooled SMR when considering 25 cohorts (SMR 1.26, 95% CI 0.89–1.77). Another review concentrated on case–control studies and investigated the occurrence of haematopoietic cancers in pesticide-related occupations [20]. Here, the meta-odds ratio was of borderline significance (meta-odds ratio 1.66, 95% CI 0.99–1.63; $P = 0.06$).

Significant excesses were observed for mortality from soft tissue sarcoma and lymphatic and haematopoietic cancer among women in the PUHS. However, due to the small numbers of deaths involved, these estimates are imprecise with large CIs and should be interpreted with care. They are also not consistent with those of male mortality from the two cancers or with the results of the incidence analysis. In addition to this, there have been multiple statistical tests performed during the analyses and some statistically significant results could be chance findings.

Considering the above strengths and limitations of the study and consistency of findings with other studies, the current study suggests that pesticide users in the PUHS are generally healthier than the national population but may have higher than expected numbers of non-melanoma skin cancer, cancer of the testis and multiple myeloma. However, this does not show a causal link between pesticide exposure and these cancers since there is no information available linking health outcomes with specific pesticides or working practices, and potential confounding from other factors cannot be ruled out. For excesses in mortality and cancer incidence that are not currently statistically significant or for those that have a small number of cases,

further follow-up may help to distinguish whether they are true associations or just chance findings.

The PUHS is the first national study of the long-term health of users of agricultural pesticides in GB. Future studies that more accurately measure personal exposure to pesticides and gauge the overall health of participants in terms of factors such as smoking, alcohol consumption and diet are needed to determine with greater certainty whether observed associations are in fact causal.

Key points

- This study suggests that pesticide users in the Great Britain Pesticide Users Health Study are generally healthier than the national population but may have higher than expected numbers of non-melanoma skin cancer, cancer of the testis and multiple myeloma.
- Further research is needed in order to gauge the overall health of participants in the Pesticide Users Health Study in terms of factors such as smoking, alcohol consumption and diet and also to collect more accurate information regarding personal exposures to pesticides.
- As the only national study of men and women in Great Britain who potentially experience long-term low-level pesticide exposure as part of their work, the Pesticide Users Health Study has the potential to make a substantial contribution to the scientific evidence base about the role of pesticides in human health and to help to inform future policy decisions.

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Conflicts of interest

None declared.

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