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ScienceDirect
Environmental Research 104 (2007) 282–289
Environmental Research
www.elsevier.com/locate/envres

Agricultural exposures and gastric cancer risk in Hispanic farm workers in California

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Received 16 June 2006; received in revised form 8 November 2006; accepted 14 November 2006
Available online 29 December 2006

Abstract

Previous studies have indicated that farm workers may be at increased risk of gastric cancer. Meta-analyses, ecological, case-control, and cohort studies suggest that some aspects of the agricultural environment may be implicated in the elevated risk. Hispanic farm workers in California are exposed to a multitude of potentially toxic substances in the work site, including excessive sunlight, fertilizers, diesel fumes, and pesticides. A previous analysis of a cohort of California farm workers who had been members of a farm labor union, the United Farm Workers of America (UFW) found a proportionate cancer incidence ratio for stomach cancer of 1.69 when using the California Hispanic population as the standard. The aim of the current study was to further evaluate associations between gastric cancer and the types of crops and commodities UFW members cultivate and the associated pesticide use as recorded by the California Department of Pesticide Regulation (DPR).

We conducted a nested case-control study of gastric cancer embedded in the UFW cohort and identified 100 cases of newly diagnosed gastric cancer between 1988 and 2003. We identified 210 control participants matched on age, gender, ethnicity, and who were known to be alive and resident in California up to the date of the cases' diagnosis. Both stratified analyses and unconditional logistic regression were used to calculate adjusted odds ratios (OR) and 95% confidence intervals (95% CI).

Work in the citrus industry was associated with increased gastric cancer (OR = 2.88; 95% CI = 1.02–8.12) although no other specific crops or commodities were associated with this disease. Working in areas with high use of the phenoxyacetic acid herbicide 2,4-D was associated with gastric cancer (OR = 1.85; 95% CI = 1.05–3.25); use of the organochlorine insecticide chlordane was also associated with the disease (OR = 2.96; 95% CI = 1.48–5.94). Gastric cancer was associated with use of the acaricide propargite and the herbicide triflurin (OR = 2.86; 95% CI = 1.56–5.23 and 1.69, 95% CI = 0.99–2.89, respectively).

Gastric cancer in California Hispanic farm workers is associated with work in the citrus fruit industry and among those who work in fields treated with 2,4-D, chlordane, propargite, and trifluin. These findings may have larger public health implications especially in those areas of the country where these pesticides are heavily used and where they may be found in the ambient atmosphere.

Keywords: Gastric cancer; Farm workers; Pesticides; Cancer registries

1. Introduction

The overall age-adjusted incidence rate of gastric cancer has been declining in the U.S. for several decades. Hispanics experience higher rates than non-Hispanic whites and survival continues to be rather poor (24% at five years) (Ries et al., 2006). Moreover there are diverging trends in the incidence between the two major types of stomach cancer, diffuse, and intestinal, with declines in the intestinal types (which comprise three quarters of all gastric cancers) but increases in the diffuse type (Henson et al., 2004). Environmental factors appear to play a more important role in the occurrence of intestinal gastric cancer (Lauren and Nevalainen, 1993).

Farmers experience elevated stomach cancer risk in comparison to the general population in most studies. Meta-analyses of agricultural populations show elevation in risk among farmers with relative risks ranging from 1.05 to 1.12 in magnitude (Acquavella et al., 1998; Blair et al.,

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doi:10.1016/j.envres.2006.11.008

1992). More recent studies of gastric cancer from Italy indicate elevated mortality in male farm workers (standardized mortality ratio = 1.25; 95% CI = 1.13–1.39) (Bucchi et al., 2004) and an ecological study revealed mortality odds ratios (OR) in agricultural workers for stomach cancer ranging from 1.22 to 1.81 (Meyer et al., 2003).

An earlier analysis of proportionate cancer incidence in California Hispanic farm workers who had been members of a farm labor union, the United Farm Workers of America (UFW) reported an age- and sex-adjusted proportionate cancer incidence ratio (PCIR) for stomach cancer of 1.69 (95% CI = 1.24–2.27) (Mills and Kwong, 2001). This PCIR was based on 50 cases observed from 1987–1997 and used the California Hispanic population as the standard. The PCIR was higher in males (PCIR = 1.87, 95% CI = 1.32–2.54) than in females (PCIR = 0.98, 95% CI = 0.49–2.52). Survival with gastric cancer is poor and mortality patterns in the UFW cohort were also evaluated for the years 1973–2000 and proportionate mortality ratios (PMR) were calculated for several types of cancer. Compared to U.S. whites, the PMR for stomach cancer in the UFW members was 2.67 (95% CI = 2.09–3.37) based on 72 deaths. However, when Hispanic deaths in California were used as the standard the PMR was 1.38 (0.98–1.88) suggesting that Hispanic ethnicity may explain, in part, the elevated ratio when using total U.S. white population as the standard (Mills et al., 2006).

California is a leading agricultural state and accounted for 22% of all agricultural pesticide use in the U.S. in 1992 (Aspelin, 1994) and there are more than 850 pesticide active ingredients applied to the fields each year throughout the state. The crops and commodities cultivated throughout California are largely labor intensive and require extensive human contact for cultivation and harvest. Since the 1950s, the agricultural industry in California has evolved from a largely family run farming operation where farm owners and their family members accounted for 40% of the agricultural labor force to a business with an 85% hired workforce (Villarejo et al., 2000). California's hired farm workers are predominantly foreign born (92%) and Hispanic (96%). A majority receives less than seven years of formal education and are often unable to speak English, impoverished and undocumented (Villarejo et al., 2000; Carroll et al., 2005). Furthermore, 70% of the workforce lacks health insurance. As members of the agricultural industry, hired farm workers are exposed to physically demanding working conditions and a multitude of potentially toxic compounds including fumes, diesel exhaust, chemical fertilizers, pesticides and dust all of which may adversely affect health (Blair and Zahm, 1995).

Based on these observations we evaluated the role of exposure to specific crops and commodities and exposure to commonly used pesticides in stomach cancer risk in California Hispanic farm workers.

2. Materials and methods

We conducted a nested case-control study embedded in a cohort of known farm workers in California utilizing several resources including the California Cancer Registry (CCR), the population-based cancer registry of the state of California, as well as the membership listing of the UFW labor union and the California Department of Pesticide Regulation (DPR).

The state of California has maintained a population-based cancer registry since 1988 and reporting is currently greater than 95% complete through 2003. The CCR consists of 10 regional registries reporting to a central registry in Sacramento, California. The regional registries are all current members of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program with the San Francisco—Oakland region first joining in 1973 followed by Los Angeles County and the San Jose—Monterey region in 1992 and the remaining counties (Greater California) in 2001 (National Cancer Institute, 2005). CCR's regional registries also attained North American Association of Central Cancer Registries (NAACCR) certification at the gold (for the majority of regions) or silver level since NAACCR began certification in 1995 (North American Association of Central Cancer Registries, 2006).

CCR collects data on all malignant cancer diagnoses (excluding basal and squamous cell skin cancers and in situ cancer of the uterine cervix) among California's 33.8 million residents (State of California, Department of Finance, 2005). Standardized data collection and quality control procedures were mandated with the creation of the registry (Cancer Reporting in California, vol. II, 1997; Cancer Reporting in California, vol. III, 1997; Cancer Reporting in California, vol. IV, 1998; Cancer Reporting in California, vol. I, 1997) and involve both active (contact with hospitals and physician's offices) and passive (linkage with databases including state mortality records and Department of Motor Vehicles registration files) methods for case ascertainment and follow-up. A majority of cancer cases are actively identified from California hospitals with cancer programs approved by the American College of Surgeons. CCR case reporting is 95% complete within 18 months of the close of each calendar year and follow-up is 95% complete as demonstrated by Laurent et al. (2005). The specific CCR methods are reported elsewhere (California Cancer Registry Data Standards and Quality Control Unit, 2003).

Farm workers were identified from a roster of individuals who were ever a member of the UFW between 1973 and 1996. The roster was generated by combining records of individuals enrolled in two benefits programs offered to all union members—the Robert F. Kennedy Medical Plan and the Juan de la Cruz Pension Program. Several validation checks were used to verify the records within the roster including SSNChecker (identifies invalid and out of range social security numbers) and cross-linking with Medi-Cal (California's health insurance program for low income individuals) and California Department of Motor Vehicles databases. When any part of the identification record was determined invalid, the entire entry was removed from the roster.

Except for linkages with the CCR database to detect newly diagnosed cancers and linkages with the Death Certificate Master Files to identify and remove deaths, there was no active follow-up of this cohort. We identified farm workers who were members of the UFW at some point in time between 1973 and 1996, and have used data on when they joined and for how long they were dues-paying members. In this study, we did not censor study members and did not calculate person-years at risk for the entire group of 139,000. It may be more accurate to refer to a "roster of workers" of the UFW in this study rather than a true cohort.

2.1. Cases

Stomach cancer cases (C = 16.0–16.9) were identified by electronically linking the edited roster of UFW members to the CCR database to identify UFW members diagnosed in California between 1988 and 2003. AUTOMATCH calculated probability scores based on the degree of similarity in linkage variables (social security number, first and last name, date of birth, gender and city of residence) between the UFW and CCR databases. User-defined cut points distinguished matches from nonmatches (Jaro, 1995) while potential matches were reviewed manually. Cases were further divided by anatomic subsite (gastric cardia vs. non-cardia), intestinal vs. diffuse and degree of differentiation at diagnosis.

2.2. Controls

For each case of stomach cancer diagnosed in the UFW cohort between 1988 and 2003, several controls from the remainder of the cohort (free of stomach cancer), were frequency matched on age, sex, and Hispanic ethnicity. Prior to control selection, deaths in the cohort were identified and removed from the roster by matching the UFW database with the California Death Certificate Master file (Mills et al., 2006). After eligible controls were identified, proof of residence in California up to the date of the corresponding cases' diagnosis was conducted by using several people locator resources including internet-based search engines, telephone directories and reverse directories.

2.3. Assessment of occupational history and pesticide use

The records for each UFW member included information on who employed the worker (grower), where he or she worked (county), and when he or she worked (month and year). The UFW had signed contracts with approximately 265 growers at the time the roster for this study was constructed; an expert reviewer at UFW headquarters determinined the primary crop/commodity produced by these growers and based on these reports, each worker was assigned a primary crop/commodity during their membership with the union. In addition, the state of California has maintained a pesticide-reporting program since the early 1970s for many restricted use chemicals and implemented full-use reporting in 1990 (California Department of Pesticide Regulation, 2000). Since union records indicate when and where workers were employed and grower contracts indicate in what crop/commodity the worker was involved, linkages with the DPR records were conducted to determine what pesticide(s) were applied to those crops in a given county/month and year.

2.4. Analysis

Descriptive analyses were completed by calculating frequencies for several variables including age, sex, date of first union affiliation, duration of union membership, and primary crop/commodity worked by UFW members. For 14 different chemicals including organochlorine, organophosphate, triazine, and phenoxyactic acetic acid herbicides, pounds of use of active ingredients applied on each crop in a given year/month and county were summed for individual cases and controls based on where, when and in which crop the cases/controls worked. Duration of exposure was incorporated into the construction of our exposure metric by multiplying the pounds of active ingredients of chemicals applied to a given crop in a given time, location by the time spent by the worker in the crop, location time and summing these pounds for all cases/controls. We then initially dichotomized these sums into zero pounds (unexposed) or greater than zero pounds (exposed). In addition, for each crop, we calculated the total number of months in which the worker was employed in that crop; for each of the pesticides we calculated the total number of pounds of active ingredients applied in the county/crop/year and month for all cases and controls and calculated age- and multivariate-adjusted OR for several categories of these summed pounds (rather than simple dichotomies of exposed vs. unexposed). In addition, we calculated the OR using zero (0) pounds as the reference as well as by using the lowest (non-zero) category of poundage as the reference. The distributions of the summed totals were examined. Many were skewed and were therefore transformed using the natural logarithm.

Age- and sex-adjusted OR were calculated after stratification on these variables using the method of Mantel and Haenszel (1959). Unconditional logistic regression (Breslow and Day, 1980) was then used to calculate multivariate-adjusted OR and 95% confidence limits for the 14 chemicals.

3. Results

Between 1988 and 2003, a total of 100 cases of gastric cancer were diagnosed among members of the UFW cohort (78 males, 22 females) (Table 1). Two hundred and ten controls were selected. Many cases were relatively short-term members of the union and most had first joined in the 1970s. Among the cases, 28% were in the gastric antrum and 14% in the gastric cardia region. Twenty-seven percent of the gastric cancers were either well or moderately well differentiated at diagnoses, while 63% were poorly differentiated or undifferentiated (10% unknown degree of differentiation). Sixty one percent of the cancers were classified as adenocarcinoma, not otherwise specified; the next largest group was comprised of signet ring cell carcinomas (15%). We considered diffuse gastric cancers to include those signet cell carcinomas (M8490) as well as linitis plastica tumors (M8142) and diffuse carcinomas (M8145). In total these comprised 19% of all the gastric cancers in this series. Intestinal type tumors included all others.

Gastric cancer was associated with the cultivation of citrus fruits (OR = 2.88; 95% CI = 1.02,8.12) (Table 2). No other crop or commodity was associated with gastric cancer.

Age- and multivariate-adjusted OR for 14 chemicals are presented in Table 3. Exposures were dichotomized and also examined in terms of increasing pounds of use of the chemicals. OR using the unexposed (zero pounds of use) and low-level exposed as the referent category are presented. Gastric cancer was associated with use of 2,4-D, and the OR were approximately twice as high in the second through fourth quartile of use compared to the non-exposed. The pattern was not seen when the low exposed group was used as the referent. The organochlorine chemical chlordane was associated with a three-fold increase in the OR for gastric cancer, again using the non-exposed as the referent. Use of the organophosphate insecticide malathion was associated with a doubling of the OR which was statistically significant when the low use group was used as the referent, while both of the fungicides maneb and mancozeb were associated with three-fold increases in the OR which were also statistically significant. Methyl bromide, a heavily used fumigant was associated with a two-fold increase in the OR for gastric cancer. The acaricide propargite was associated with three-fold elevations in the OR regardless of which reference group was used. Finally, use of the herbicide triflualin was associated with a two-fold increase in the OR for gastric cancer, which was statistically significant when using the non-exposed as the reference category.

Since previous studies have linked exposure to the herbicide 2,4-D with gastric cancer (Ekstrom et al., 1999), we evaluated this exposure by sub-categories (Table 4). The 2,4-D association was not modified by anatomic location or histology. However, the association between 2,4-D and cancer was much greater in well or moderately well differentiated tumors (OR = 12.83) than in poorly or undifferentiated tumors (OR = 1.13).

4. Discussion

In this analysis we found gastric cancer to be elevated in farm workers involved in cultivation of citrus fruits and in workers exposed to high levels of the herbicides 2,4-D and trifluran, the insecticides chlordane and malathion, the fungicides mancozeb, and maneb, the fumigant methyl bromide and the acaricide propargite. Four of the chemicals associated with elevated gastric cancer (i.e. chlordane, maneb, mancozeb, and propargite) are class B2 chemicals (probable carcinogens) as classified by the United States Environmental Protection Agency (U.S. Environmental Protection Agency, 2006), while trifluran and simazine are class C chemicals (possible carcinogen). These chemicals were used extensively in California agriculture and in one representative year (1980) the following pounds of pesticidal active ingredients were applied; 894,423 pounds of 2,4-D; 272,416 pounds of chlordane; 1,797,896 pounds of propargite; and 198,992 pounds of triflurin (State of California, DFA, 1980). (Table 5).

In another representative year (1986) the most frequently applied chemical used on citrus was methyl bromide (69,479 pounds) and an association with this chemical was present in our analysis.

The gastric cancer sub site distribution was approximately the same among the farm workers and Hispanic males in California, 1990–1994. Among the farm workers, 14% were of the gastric cardia; it was 18.7% in California Hispanic males (Perkins et al., 1997). Similarly, among the farm workers, 61% of the cancers were classified as adenocarcinoma, not otherwise specified while 64% of California Hispanic males were of this histologic type. The proportion of Signet ring cell carcinomas was the same in the farm workers and California Hispanic males (15%). The grade at diagnosis was also similar in farm workers and Hispanic males; among both groups, about 25% were either well differentiated (Grade I) or moderately well differentiated (Grade II).

Table 1
Characteristics of stomach cancer cases in the United Farm Workers of America (UFW), 1988–2003

Characteristic	No. cases ($N = 100$)
Gender	
Male	78
Female	22
Age at diagnosis	
⩽61	18
62–74	20
75–82	34
83+	28
Year of first union membership	
⩽1977	38
1978–79	32
1980+	30
Duration in months of union affiliation	
⩽3	40
4–17	24
18–63	19
64–315	17
Anatomic subsite	
Cardia, NOS	14
Fundus	5
Body	9
Gastric antrum	28
Pylorus	6
Lesser curvature	10
Greater curvature	3
Overlapping lesion	12
Stomach, NOS	13
Grade	
Well differentiated	5
Moderately (well) differentiated	22
Poorly differentiated	59
Undifferent/anaplasitc	4
Unknown	10
Histology (ICD-O2)	
Adenocarcinoma, NOS (8140)	61
Linitis plastica (8142)	2
Adenocarcinoma, intestinal type (8144)	4
Carcinoma, diffuse type (8145)	2
Carcinoid tumor (8240)	5
Signet ring cell carcinoma (8490)	15
Unknown	11

Table 2
Age-adjusted odds ratios for duration of work with crops and commodities and stomach cancer risk in the United Farm Workers of America (UFW)

Crop/length of work (months)	No. cases	No. controls	OR	95% CI
Citrus				
0	86	201	1.00	
1–261	9	72	2.88	1.02–8.12
Grapes				
0	54	121	1.00	
1–7	26	42	1.35	0.76–2.41
8–314	15	45	0.67	0.34–1.33
Horticulture				
0	92	187	1.00	
1–213	4	22	0.39	0.13–1.18
Mushroom				
0	92	198	1.00	
1–242	3	10	0.74	0.19–2.81
Strawberries				
0	93	201	1.00	
1–31	1	7	0.28	0.03–2.28
Vegetables				
0	60	135	1.00	
1–9	18	37	1.05	0.55–2.00
10–136	17	36	1.07	0.55–2.08

Table 3
Age- and multivariate-adjusted odds ratios (95%CI) for agricultural chemicals and stomach cancer risk in the United Farm Workers of America (UFW), by ever/never exposed and pounds of use, 1988–2003

Chemical	Ever/never use	Chemical (lbs)	No. cases	No. controls	OR_{age} (95% CI)	OR_{MV} (95% CI)[a]	
					No exposed as ref.	No exposed as ref.	Low exposed as ref.
2,4-D		2,4-D					
Odds ratio	1.85	0 lbs	58	139	1.00	1.00	
95% CI	1.05–3.25	1–14	17	24	1.55 (0.77–3.11)	2.16 (1.02–4.56)	1.00
		15–86	14	30	1.02 (0.50–2.10)	1.57 (0.71–3.51)	0.86 (0.32–2.3)
		86–1950	11	17	1.55 (0.68–3.50)	2.09 (0.87–5.05)	1.04 (0.37–2.93)
Chlordane		Chlordane					
Odds ratio	2.96	0 lbs	65	156	1.00	1.00	
95% CI	1.48–5.94	1–85	11	18	1.46 (0.65–2.48)	2.98 (1.15–7.76)	1.00
		86–318	13	18	1.65 (0.75–3.61)	3.95 (1.49–10.44)	1.06 (0.35–3.21)
		319–6574	11	18	1.44 (0.64–3.22)	2.43 (0.99–5.98)	0.63 (0.19–2.06)
DBCP		DBCP					
Odds ratio	1.28	0 lbs	78	166	1.00	1.00	
95% CI	0.60–2.73	1–5639	13	16	1.48 (0.66–3.30)	2.06 (0.83–5.11)	1.00
		5640–10,726	5	14	0.75 (0.27–2.14)	0.78 (0.24–2.50)	0.52 (0.13–2.06)
		10,727–18,657	4	14	0.59 (0.19–1.84)	0.80 (0.22–2.88)	0.48 (0.12–2.05)
Diazinon		Diazinon					
Odds ratio	1.54	0 lbs	38	80	1.00	1.00	
95% CI	0.87–2.71	1–43	15	44	0.63 (0.30–1.30)	0.95 (0.44–2.04)	1.00
		44–507	25	42	1.19 (0.63–2.26)	1.52 (0.76–3.05)	1.80 (0.80–4.02)
		508–4484	22	44	0.94 (0.48–1.85)	1.14 (0.57–2.30)	1.41 (0.61–3.25)
Dicofol		Dicofol					
Odds ratio	1.58	0 lbs	49	107	1.00	1.00	
95% CI	0.88–2.83	1–28	12	34	0.73 (0.34–1.55)	0.94 (0.42–2.11)	1.00
		29–202	17	35	1.02 (0.51–2.05)	1.33 (0.76–3.05)	1.29 (0.50–3.29)
		203–6811	22	34	1.32 (0.69–2.53)	1.63 (0.81–3.29)	2.14 (0.86–5.30)
Malathion		Malathion					
Odds ratio	1.43	0 lbs	34	76	1.00	1.00	
95% CI	0.84–2.44	1–11	14	48	0.50 (0.23–1.08)	0.72 (0.33–1.60)	1.00
		12–42	25	42	1.03 (0.52–2.01)	1.30 (0.62–2.72)	1.96 (0.88–4.38)
		43–8164	30	44	1.28 (0.67–2.44)	1.49 (0.76–2.90)	2.61 (1.18–5.76)
Mancozeb		Mancozeb					
Odds ratio	1.20	0 lbs	55	110	1.00	1.00	
95% CI	0.70–2.06	1–11	11	42	0.52 (0.25–1.10)	0.62 (0.28–1.36)	1.00
		12–132	8	25	0.66 (0.28–1.56)	0.70 (0.29–1.71)	1.47 (0.50–4.31)
		133–16,468	26	33	1.48 (0.80–2.76)	1.79 (0.91–3.53)	3.27 (1.37–7.84)
Maneb		Maneb					
Odds ratio	0.93	0 lbs	54	98	1.00	1.00	
95% CI	0.57–1.66	1–76	10	37	0.44 (0.20–0.97)	0.58 (0.25–1.31)	1.00
		77–360	8	38	0.37 (0.16–.85)	0.38 (0.16–0.91)	0.74 (0.25–2.18)
		361–29,212	28	37	1.24 (0.67–2.29)	1.26 (0.67–2.38)	3.01 (1.16–7.81)
Methyl bromide		Methyl Bromide					
Odds ratio	1.01	0 lbs	38	69	1.00	1.00	
95% CI	0.59–1.74	1–133	12	47	0.39 (0.18–.86)	0.56 (0.25–1.24)	1.00
		134–4856	23	48	0.77 (0.40–1.48)	0.99 (0.50–1.99)	1.93 (0.85–4.39)
		4857–280,130	27	46	0.98 (0.52–1.82)	1.33 (0.67–2.67)	2.38 (1.06–5.37)
Captan		Captan					
Odds ratio	1.00	≤30 lbs	52	117	1.00	1.00	
95% CI	0.59–1.72	31–262	19	31	1.38 (0.71–2.66)	1.80 (0.86–2.10)	1.00
		263–1916	20	31	1.45 (0.76–2.78)	1.93 (0.95–3.93)	1.15 (0.49–2.72)
		1917–132,364	9	31	0.65 (0.29–1.47)	0.57 (0.25–1.32)	0.47 (0.16–1.34)
Propane		Propane					
Odds ratio	1.13	0 lbs	49	101	1.00	1.00	
95% CI	0.66–1.94	1–7526	14	36	0.74 (.36–1.54)	0.98 (0.46–2.10)	1.00
		7257–46,313	21	37	1.06 (0.55–2.03)	1.42 (0.71–2.84)	1.59 (0.69–3.70)
		46,314–700,928	16	36	0.93 (0.47–1.84)	1.00 (0.49–2.08)	1.10 (0.46–2.63)

Table 3 (*continued*)

Chemical	Ever/never use	Chemical (lbs)	No. cases	No. controls	OR_{age} (95% CI)	OR_{MV} (95% CI)[a]	
					No exposed as ref.	No exposed as ref.	Low exposed as ref.
Propargite		Propargite					
Odds ratio	2.86	0 lbs	56	130	1.00	1.00	
95% CI	1.56–5.23	1–76	5	25	0.46 (0.16–1.26)	0.87 (0.29–2.63)	1.00
		77–495	20	29	1.59 (0.83–3.06)	3.21 (1.43–7.15)	4.19 (1.22–14.43)
		496–59,054	19	26	1.65 (0.84–3.25)	2.63 (1.24–5.56)	3.71 (1.10–12.49)
Simazine		Simazine					
Odds ratio	1.49	0 lbs	48	107	1.00	1.00	
95% CI	0.86–2.58	1–47	13	34	0.83 (0.40–1.73)	1.29 (0.58–2.88)	1.00
		48–333	19	35	1.06 (0.54–2.08)	1.60 (0.77–3.35)	1.50 (0.60–3.75)
		334–11,745	20	34	1.23 (0.63–2.39)	1.73 (0.83–3.60)	1.50 (0.62–3.63)
Trifluran		Trifluran					
Odds ratio	1.69	0 lbs	56	131	1.00	1.00	
95% CI	0.99–2.89	1–63	10	26	0.89 (0.40–1.97)	1.13 (0.49–2.58)	1.00
		64–177	13	27	1.09 (0.52–2.31)	1.25 (0.56–2.77)	1.05 (0.35–3.16)
		178–8921	20	26	1.76 (0.90–3.42)	2.34 (1.15–4.78)	1.99 (0.76–5.23)

[a]Adjusted for age, sex, length of union affiliation, and date of first union affiliation.

Table 4
Odds ratios[a] (95% CI) for herbicide 2,4-D and gastric cancer by anatomic subsite, histology and grade, UFW study

Category	No. cases	No. controls	OR (95% CI)
Non-cardia	86	179	1.80 (0.97–3.34)
Cardia	14	31	2.07 (0.47–9.16)
Intestinal	83	162	1.89 (1.00–3.58)
Diffuse	17	48	1.33 (0.34–5.28)
Grade I and II	27	60	12.83 (3.00–54.94)
Grade III and IV	73	150	1.13 (0.58–2.19)

[a]Adjusted for age, gender, date of first union affiliation and duration of membership.

Our findings of elevated stomach cancer associated with exposure to the herbicide 2,4-D were in agreement with results from Sweden where an OR of 1.70 (95% CI = 1.16–2.48) was observed (Ekstrom et al., 1999). Those results persisted after adjustment for several confounding factors including socioeconomic status, geographic area, and number of siblings, alcohol intake, and smoking. In the current study, we did not collect information on these variables. On the other hand, a population-based case-control study in Nebraska did not reveal any alterations in stomach cancer associated with several agricultural chemicals based upon interviews with 170 stomach cancer cases diagnosed, 1988–1993. However, because of poor survival in stomach cancer, 80% of the case interviews in that study were conducted with next-of-kin or proxy respondents (Lee et al., 2004). It is interesting to note that two of the chemicals judged to be "nitrosatable" in that study (i.e. able to react with nitrite to form N-nitroso derivatives that may increase gastric cancer risk) were associated with gastric cancer in our study, namely 2,4-D and triflurin. The association with 2,4-D did not differ among cardia and non-cardia gastric cancers, or by diffuse vs. intestinal cancers. A much stronger association, however, occurred in those tumors that were well differentiated.

In addition, stomach cancer may be related to pesticides in the atmosphere and the San Joaquin Valley is one of the most severely polluted areas of the U.S. Airborne contaminants, including pesticides may be swallowed and may act on the gastric cardia mucosa. By definition, these farm workers are employed outdoors and pesticides have been detected in the ambient air in California near agricultural fields (Majewski and Capel, 1995). In a case-control study in Sweden involving 262 cases of gastric cardia adenocarcinoma, work in "agriculture, horticultural, and livestock" industries was associated with an OR of 2.2 (95% CI = 0.8–6.0) for adenocarcinoma of the gastric cardia. In addition, in the same study high exposure to airborne pesticides was associated with an OR of 2.1 (95% CI = 1.0–4.6) (Jansson et al., 2006). It could be that the main route of exposure in the farm workers in this study is through inhalation of airborne pesticides. Previous studies of men working in dusty trades in California have found elevated PCIR for stomach cancer (PCIR = 1.3, 95% CI = 1.2–1.4) and those authors speculated that dust can enter the gastrointestinal tract via ingestion or indirectly by mucociliary clearance and swallowing (Wright et al., 1988). Propulsion of abrasive particulates through the stomach by peristalsis may disrupt mucosal barriers allowing either acid or mechanical damage, thereby allowing cellular contact with the swallowed carcinogens.

This study has several limitations. We did not collect information on dietary habits, family history, smoking, or alcohol consumption which may act as confounders. Many OR were calculated and some statistically significant results may have occurred by chance. Returning to Mexico for

Table 5
Summary of chemicals evaluated in this study, U.S. E.P.A. carcinogenic classification status and pounds applied in California in 1980

Chemical name	Chemical class and action	E.P.A. Classification	Pounds applied, 1980[a]
2,4-D	Phenoxyacetic acid, herbicide	Group D—not classifiable as to human carcinogenicity	894,423
Chlordane	Chlorinated cyclodiene, insecticide	Group B2—probable human carcinogen	272,416
DBCP	Fumigant	Group B2—probable human carcinogen	11,683
Diazinon	Organophosphate, insecticide	Not likely to be carcinogenic to humans	488,421
Dicofol	Organochlorine, araricide	Group C—possible human carcinogen	42,109
Malathion	Organophosphate, insecticide	Suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential	326,891
Mancozeb	Dithiocarbamate, Fungicide	Group B2—probable human carcinogen	0
Maneb	Dithiocarbamate, Fungicide	Group B2—probable human carcinogen	2,189,356
Methyl Bromide	Fumigant	Not likely to be a human carcinogen	6,064,629
Captan	Dicarboximide, Fungicide	Group B2—probable human carcinogen	790,344
Propane	Petroleum gas, flame cultivation	–	0
Propargite	Sulfite ester, acaracide	Group B2—probable human carcinogen	1,797,896
Simazine	Triazine, herbicide	Group C—possible human carcinogen	238,185
Triflurin	Trifluor-toluidine, herbicide	Group C—possible human carcinogen	189,992

[a]Pesticide Use Report, Annual, 1980. Department of Food and Agriculture, Pesticide Registration and Agricultural Activity, Sacramento, CA.

cancer diagnosis, treatment, or death may result in uncaptured UFW cancer cases. Given greater healthcare costs and language barriers, farm workers may be more likely to use Mexico's medical system. In a study of current agricultural workers in California, 18% of respondents who ever visited a doctor or clinic went to Mexico for the medical care (Villarejo et al., 2000). In addition, the return migration or "salmon bias" phenomenon has been shown to be a factor in the Hispanic paradox (Palloni and Arias, 2004), in which lower mortality rates in Hispanics appear to be limited to foreign born Mexicans who constitute a large proportion of the UFW membership.

Undoubtedly some misclassification of exposure status occurred. Our analysis was limited by having only county-level information on the growers. Our common-sense approach was that if a worker was known to have been working in a given crop (e.g. grapes) in a given month and year (e.g. July, 1983) in a certain county (e.g. Fresno) and the Pesticide Use Reports reveals that X pounds of a certain chemical were applied to the grapes in that month in that county, there is a fair likelihood the worker was present and "exposed", certainly in comparison to a worker in whom there is no evidence of work in that crop, in that month and county. In addition, if the misclassification was non-differential the overall impact would be to drive the point estimates towards the null.

The 265 growers included in this analysis represented a very small fraction of all growers in the state of California and the 139,000 farm workers in the UFW cohort represent a very small fraction of all farm workers in California, 1973–1996. (It is estimated that in any given year there are between 300,000 and 750,000 persons working in the agricultural industry in California.) The growers included in this analysis to a large degree are those growers that agreed to sign contracts with the UFW, primarily in the early organizing years of the union (late 1960s early to mid 1970s) and represent producers of those crops where the union concentrated its organizing efforts, particularly the grape, citrus, and vegetable industries. It is difficult to estimate how representative the growers and farm workers in this study are of all growers or all farm workers in California.

Our study was limited by a relatively small number of cases and controls and exposure assessment was somewhat ecological in nature; nevertheless, the exposure histories were not based on individual recall and occurred in the two decades prior to diagnosis of cancer. The chemicals included in this analysis are used extensively in California agriculture and have been found in detectable levels in the ambient atmosphere of the San Joaquin Valley where many farm workers are employed. These finding are similar to other studies of gastric cancer conducted in Europe and suggest that the elevated gastric cancer risk experienced by farm workers may be attributed to specific and avoidable workplace exposure.

Acknowledgments

The authors gratefully acknowledge the contributions of Douglas Blaylock, Administrator of the Robert K. Kennedy Farm Workers Medical Plan.

This research was supported by a grant from the National Cancer Institute to Dr. Paul K. Mills (5RO1CA101181-02).

The Institutional Review Board of the Public Health Institute, Oakland, CA, approved this research.

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