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ORIGINAL ARTICLE: RESEARCH

Acute myeloid leukemia risk by industry and occupation

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Abstract

Acute myeloid leukemia (AML) is the most common type of leukemia found in adults. Identifying jobs that pose a risk for AML may be useful for identifying new risk factors. A matched case–control analysis was conducted using California Cancer Registry data from 1988 to 2007. This study included 8999 cases of AML and 24 822 controls. Industries with a statistically significant increased AML risk were construction (matched odds ratio [mOR] = 1.13); crop production (mOR = 1.41); support activities for agriculture and forestry (mOR = 2.05); and animal slaughtering and processing (mOR = 2.09). Among occupations with a statistically significant increased AML risk were miscellaneous agricultural workers (mOR = 1.76); fishers and related fishing workers (mOR = 2.02); nursing, psychiatric and home health aides (mOR = 1.65); and janitors and building cleaners (mOR = 1.54). Further investigation is needed to confirm study findings and to identify specific exposures responsible for the increased risks.

Keywords: Acute myeloid leukemia, industry, occupation, risk factors

Introduction

Acute myeloid leukemia (AML) is the most common type of leukemia found in adults. In 2012, an estimated 14 590 individuals were diagnosed with AML in the USA, constituting 0.9% of cancer diagnoses and 1.8% of cancer deaths [1]. Prognosis for AML is poor, with a 5-year survival rate of 25.7% [2]. Males are slightly more likely to develop AML than females [2].

The etiology of most cases of AML is unknown. Known and suspect occupational risk factors of AML include exposure to benzene [3–7], ionizing radiation [6,8,9], electric and magnetic fields (EMFs) [10,11], pesticides and fertilizers [5,12,13], infectious agents/viruses [12,14–16], alkylating

agents [17,18] and formaldehyde [19]. Unfortunately, information on such exposures is generally not available for cases of AML. Previous research has also found an increased risk for AML among semiconductor workers [20,21], dry cleaners [22–24], teachers [23,25], nurses [23,26,27], hairdressers [6], mechanics [23] and workers in the oil/gas industries [6,25]. In the absence of systematically collected exposure data, examining patterns of AML risk among workers using cancer registry data can identify specific industry and occupation categories at increased risk. In addition to providing clues about known leukemogens, identifying jobs that are associated with an increased risk for AML may be useful for identifying new risk factors that can be targeted for intervention.

The purpose of this analysis was to assess the risk for AML by longest-held job using data from the California Cancer Registry (CCR). Since this was a hypothesis-generating study, reported findings were not adjusted for multiple comparisons. We used a matched case–control methodology which adjusted for age, sex, race and year of diagnosis.

Materials and methods

California Cancer Registry

The CCR is a population-based cancer surveillance system that collects data on all cancers (excluding non-melanoma skin cancers and *in situ* cervical carcinoma) among California residents. Cancer reporting has been mandated by California law since 1985, and CCR has collected state-wide cancer data from doctors, hospitals and other medical facilities since 1 January 1988. Data collected by the CCR include demographics, cancer characteristics and cancer treatments. Information on the usual (i.e. longest-held) industry and occupation (I&O) held by each case is also collected in narrative form. CCR provided the National Institute for Occupational Safety and Health (NIOSH) with

cancer data collected from 1988 to 2007. NIOSH assigned detailed Bureau of the Census (BOC) 2002 codes to the I&O narratives. Because this study is a public health surveillance study with analyses conducted on anonymous data without link to personal identifiers, it did not require review by the NIOSH Institutional Review Board.

Study population and exclusion criteria

A matched case-control methodology was used. Cases and controls were between the ages of 18 and 97 and were selected from 1 366 268 individuals who were diagnosed with cancer in California between 1988 and 2007. This study included only adult subjects who had I&O information available. Since the aim of this study was to explore the association between longest-held job and AML, subjects who were homemakers, had never worked or had unknown or insufficient I&O narratives (e.g. narratives that mention only unemployed, disabled or retired) were excluded from analysis. Subjects in the military were also excluded because data reporting from military treatment facilities was considered incomplete.

Case selection/definition

Cases were subjects diagnosed with AML. They were identified using Surveillance, Epidemiology, and End Results (SEER) incidence site recode 35021. In order to study the effects of occupational exposure, individuals with AML who were previously diagnosed with a cancer before their AML diagnosis were excluded from this study, as they might have had treatment induced AML (tAML) [28]. Cases diagnosed with a subsequent cancer after their AML diagnosis were kept in the study.

Control selection/definition

Up to three controls were randomly matched to each case of AML based on age (5-year age groups), sex, race and year of diagnosis (5-year intervals). Controls were subjects who were diagnosed with colorectal (SEER incidence site recode = 21041 21042 21043 21044 21045 21046 21047 21048 21049 21051 21052 21060), breast (SEER incidence site recode = 26000) or low-grade localized prostate (SEER incidence site recode = 28010) cancers. Low-grade (i.e. latent) localized prostate tumors are well or moderately well differentiated and are confined to the prostate gland. Subjects with these cancers were chosen to serve as controls because these cancers are not known to be associated with occupational exposures. Because a study conducted by Koutros *et al.* [29] showed an association between pesticide exposure and aggressive prostate cancer, subjects with high grade prostate tumors [30] (i.e. poorly differentiated, undifferentiated or unknown differentiation) and tumors not confined to the prostate gland were excluded as controls. Subjects diagnosed with both an eligible control cancer (colorectal, breast or low-grade localized prostate cancers) and ineligible cancers were excluded. For cases and controls with multiple cancer records, the first recorded I&O was used in the analysis because I&O information from the earliest record was thought to give the best indication for longest-held/usual occupation.

Data analysis

Descriptive and analytical analyses were conducted using SAS[®] 9.2. For the purposes of this analysis, longest-held I&O category classifications were based on BOC 2002 codes. There are 21 broad industry and 23 broad occupation categories. Each broad category contains multiple BOC 2002 codes. To ensure adequate sample size, sample size restrictions were placed on certain analyses. This study looked at the association between AML and (1) broad I&O categories, (2) within broad I&O categories that showed an increased AML risk, specific BOC 2002 codes with at least 30 subjects (cases and controls), (3) I&O pairings (I&O combinations of BOC 2002 codes) with at least 10 cases of AML and (4) I&Os of interest based on findings from previous studies. The I&Os of interest based on previous findings included the semiconductor industry (e.g. electronic component manufacturing) [20,21], dry cleaners [22–24], protective services occupations (e.g. firefighters and police) [23], teachers [23,25], childcare workers [16], registered nurses [23,26,27], diagnostic related technicians [23,26], maids and housekeepers [27], hairdressers [6], barbers [6], radio and telecommunication workers [31], welding, soldering and brazing workers [31], automotive mechanics [23], tool and die makers [22], butchers [32,33], shoe makers [34] and workers employed in oil/gas/rubber I&Os (who may be exposed to benzene and its byproducts) [6,25].

The comparison group for any industry, occupation or I&O pairing was all other industries, occupations or I&O pairings. Conditional logistic regression was used to estimate the matched odds ratios (mOR) and 95% confidence interval (CI). Unless otherwise stated, all reported comparisons are significantly different at the $p < 0.05$ level. Adjustment for multiple comparisons was not done.

Results

A total of 8999 cases of AML were included in the analyses from among the 19 306 cases of AML available in the CCR database. Among the included cases of AML, the median age of diagnosis was 62 years, and most were male (65.6%) and white (71.2%) (Table I). Survival after initial diagnosis was poor. The overall 5-year survival rate was 11.9%, and was lower for males (10.3%) and for those aged 55 years or older (<10%). A total of 24 822 eligible controls with I&O data were randomly matched to the cases. Among cancer controls, 28% were diagnosed with breast cancer, 34% with low-grade localized prostate cancer and 38% with colorectal cancer. Compared to controls, cases were slightly but significantly older, and more likely to be male, and of Hispanic descent. Of the 10 307 excluded cases of AML, 9390 had missing I&O data, 12 had unknown race, 10 were identified as American Indian and 895 had possible tAML. This study found that compared to subjects included in the analyses, excluded subjects with colorectal, breast, low-grade localized prostate cancers or AML were more likely to be older (median age of 71 years), female (64%) and of Hispanic (13%) descent.

Table I. Demographics of cases of AML diagnosed in California 1988–2007.

	Cases (n = 8999)		Controls (n = 24 822)	
	n	%	n	%
Age of diagnosis				
Mean	60.3		59.5	
Median	62		61	
18–44	2015	22.4	5148	20.7
45–54	1374	15.3	4021	16.2
55–64	1660	18.5	4658	18.8
65–74	1841	20.5	5126	20.7
75–84	1638	18.2	4547	18.3
84+	471	5.2	1322	5.3
Sex				
Male	5900	65.6	15 538	62.6
Female	3099	34.4	9284	37.4
Race/ethnicity				
Non-Hispanic white	6406	71.2	17 901	72.1
Non-Hispanic black	454	5.1	1284	5.2
Hispanic	1376	15.3	3492	14.1
Asian/Pacific Islander	763	8.5	2145	8.6
Year of diagnosis				
1988–1992	2061	22.9	5394	21.7
1993–1997	2304	25.6	6294	25.4
1998–2002	2422	26.9	6862	27.6
2003–2007	2212	24.6	6272	25.3

AML, acute myeloid leukemia.

Industries

Using information on longest-held job, three broad industry categories were associated with an increased risk for AML: “agriculture, forestry, fishing and hunting”, “construction” and “manufacturing – non-durable goods” (Table II). Within the broad “agriculture, forestry, fishing and hunting” industry category, the specific industries “crop production” and “support activities for agriculture and forestry” were found to have an increased risk for AML. Within “manufacturing – non-durable goods”, the subsector “animal slaughtering and processing” had an elevated AML risk. The 2002 BOC classification does not include codes for specific construction industry subsectors.

Occupations

Using information on longest-held job, five broad occupation categories had an increased risk for AML: “healthcare support”, “building and grounds cleaning and maintenance”, “farming, fishing and forestry”, “installation, maintenance and repair” and “production” (Table II). Within “healthcare support”, the only specific occupation with an increased AML risk was “nursing, psychiatric and home aides”. Within

Table II. Industries and occupations (I&O) with statistically significant AML findings.

Industry code*	Industry text	Total	Cases	Controls	mOR†	95% CI
			(n = 8999) (% in I&O)	(n = 24 822) (% in I&O)		
Industries with significantly increased risk						
0170-0290	Agriculture, forestry, fishing, and hunting	871	291 (3.23)	580 (2.34)	1.32	1.14–1.53
0170	Crop production	560	197 (2.19)	363 (1.46)	1.41	1.18–1.69
0290	Support activities for agriculture and forestry	38	16 (0.18)	22 (0.08)	2.05	1.08–3.92
0770	Construction	2138	640 (7.11)	1498 (6.03)	1.13	1.03–1.25
1070-2390	Non-durable goods manufacturing	1248	378 (4.20)	870 (3.50)	1.19	1.05–1.35
1180	Animal slaughtering and processing	31	14 (0.16)	17 (0.07)	2.09	1.02–4.28
7690	Services to buildings and dwellings	283	96 (1.07)	187 (0.75)	1.39	1.08–1.78
Industries with significantly decreased risk						
7270-7490	Professional and technical services	2823	657 (7.30)	2166 (8.73)	0.84	0.77–0.92
7270	Legal services	461	99 (1.10)	362 (1.46)	0.78	0.62–0.97
7380	Computer systems design and related services	278	50 (0.56)	228 (0.92)	0.61	0.45–0.82
7570-7790	Management, administrative and waste services	1402	317 (3.52)	1085 (4.37)	0.78	0.69–0.89
7590	Business support services	354	32 (0.36)	322 (1.30)	0.29	0.20–0.41
7780	Other administrative and other support services	104	17 (0.19)	87 (0.35)	0.55	0.33–0.93
9370-9590	Public administration	2193	530 (5.89)	1663 (6.70)	0.89	0.80–0.98
9490	Administration of environmental quality and housing programs	43	5 (0.06)	38 (0.15)	0.35	0.14–0.90
Occupation code*	Occupation text	Total	Cases	Controls	mOR†	95% CI
Occupations with significantly increased risk						
3600-3650	Healthcare support occupations	344	118 (1.31)	226 (0.91)	1.53	1.22–1.91
3600	Nursing, psychiatric and home health aides	208	75 (0.83)	133 (0.54)	1.65	1.24–2.20
4200-4250	Building and grounds cleaning and maintenance occupations	964	304 (3.38)	660 (2.66)	1.26	1.09–1.45
4220	Janitors and building cleaners	480	173 (1.92)	307 (1.24)	1.54	1.28–1.87
6000-6130	Farming, fishing and forestry occupations	375	151 (1.68)	224 (0.90)	1.72	1.38–2.13
6050	Miscellaneous agricultural workers	280	116 (1.29)	164 (0.66)	1.76	1.37–2.26
6100	Fishers and related fishing workers	33	14 (0.16)	19 (0.08)	2.02	1.01–4.03
6200-6940	Construction and extraction occupations	1705	508 (5.65)	1197 (4.82)	1.11	0.99–1.24
6240	Carpet, floor and tile installers and finishers	40	18 (0.20)	22 (0.09)	2.04	1.09–3.84
6260	Construction laborers	378	128 (1.42)	250 (1.01)	1.32	1.06–1.64
6350	Electricians	214	78 (0.87)	136 (0.55)	1.53	1.15–2.03
7000-7620	Installation, maintenance and repair occupations	1073	348 (3.87)	725 (2.92)	1.29	1.13–1.47
7700-8960	Production occupations	2187	646 (7.18)	1541 (6.21)	1.14	1.04–1.26
7700	First-line supervisors/managers of production and operating workers	158	59 (0.66)	99 (0.40)	1.62	1.17–2.25
Occupations with significantly decreased risk						
2100-2150	Legal occupations	462	102 (1.13)	360 (1.45)	0.8	0.64–0.99
2100	Lawyers	325	70 (0.78)	255 (1.03)	0.77	0.59–0.99
9000-9750	Transportation and material moving occupations	2811	687 (7.63)	2124 (8.56)	0.85	0.78–0.93
9620	Laborers and freight, stock and material movers, hand	365	82 (0.91)	283 (1.14)	0.73	0.57–0.94

I&O, industry and occupation; AML, acute myeloid leukemia; mOR, matched odds ratio; CI, confidence interval.

*Bureau of the Census (BOC) 2002 codes were used.

†Matched on age, sex, race and year of diagnosis.

“building and grounds cleaning and maintenance”, the only occupation with increased AML risk was “janitors and building cleaners”. Within “farming, fishing and forestry”, the two occupations with increased AML risk were “miscellaneous agricultural workers” and “fishers and related fishing workers”. The “miscellaneous agricultural workers” occupation consists mostly of farm workers and farm laborers. Within “production occupations”, the only occupation with an increased AML risk was “first-line supervisors/managers of production and operating workers”. Within “installation, maintenance and repair” there were no specific occupations with a significantly elevated risk.

The broad occupation category “construction and extraction” had a slightly elevated, non-significant risk for AML. Under this broad category, we found three occupations with an increased AML risk: “carpet, floor and tile installer and finisher”, “construction laborer” and “electrician”.

I&O pairings

This study found 121 longest-held I&O pairs with at least 10 AML cases. Of these, there were 12 pairings that had a significantly elevated AML risk and one pairing that yielded no controls (produced mORs with an infinite value). Some of our paired I&O findings reflected our industry and occupation findings (reported above). For example, within the construction industry, an elevated AML risk was observed for two occupations: “construction laborers” and “electricians”.

Also, workers employed as janitors and building cleaners in both “services to buildings and dwellings” and “elementary and secondary schools” industries had increased risk. Moreover, the risk for AML was increased in the “nursing, psychiatric and home health aides” occupation for three industry subcategories: “outpatient care centers”, “hospitals” and “nursing care facilities”. Similarly, “other agricultural workers in crop production” and “fishers and related fishing workers in fishing, hunting and trapping” had increased AML risk (Table III).

Other I&O pairs with elevated AML risks were “actors employed in the motion picture and video industry”, “civil engineers employed in the architectural, engineering and related services industry” and “brick/block/stone masons in construction” (Table III). The pairing that yielded no controls was “travel agents employed in service industries incidental to transportation” ($n = 14$ cases).

I&Os with decreased risk for AML

Certain longest-held I&Os were also found to have a statistically significantly decreased risk for AML. These included three broad industry categories: “professional and technical services”, “management, administrative and waste services” and “public administration”. Within “professional and technical services”, the two specific industries with decreased risk were “legal services” and “computer systems design and related services”. Within the “management, administrative

Table III. Risk of AML with statistically significant findings by industry-occupation pairings.

Industry*	Industry text	Occupation*	Occupation text	Total	Cases ($n = 8999$) (% in I&O)	Controls ($n = 24\ 822$) (% in I&O)	mOR [†]	95% CI
Industry-occupation pairings with significantly increased risk								
0170	Crop production	6050	Other agricultural workers	237	99 (1.10)	138 (0.56)	1.78	1.35-2.33
0280	Fishing, hunting and trapping	6100	Fishers and related fishing workers	33	14 (0.16)	19 (0.08)	2.02	1.01-4.03
0770	Construction	6220	Brick masons, block masons and stone masons	21	10 (0.11)	11 (0.04)	2.48	1.05-5.84
770	Construction	6260	Construction laborers	369	126 (1.40)	243 (0.98)	1.34	1.07-1.67
770	Construction	6350	Electricians	147	56 (0.62)	91 (0.37)	1.63	1.16-2.28
6290	Services incidental to transportation	4830	Travel agents	14	14 (0)	0 (0)	7.85 [‡]	3.62-∞
6570	Motion pictures and video industries	2700	Actors	18	14 (0.16)	4 (0.02)	9.79	3.22-29.78
7290	Architectural, engineering and related services	1360	Civil engineers	278	92 (1.02)	186 (0.75)	1.37	1.06-1.76
7690	Services to buildings and dwellings	4220	Janitors and building cleaners	188	69 (0.77)	119 (0.48)	1.55	1.15-2.09
7860	Elementary and secondary schools	4220	Janitors and building cleaners	72	30 (0.33)	42 (0.17)	2	1.25-3.20
8090	Outpatient care centers	3600	Nursing, psychiatric, and home health aides	65	24 (0.27)	41 (0.17)	1.67	1.01-2.78
8190	Hospitals	3600	Nursing, psychiatric, and home health aides	73	27 (0.30)	46 (0.19)	1.78	1.10-2.86
8270	Nursing care facilities	3600	Nursing, psychiatric and home health aides	26	12 (0.13)	14 (0.06)	2.42	1.11-5.27
Industry-occupation pairings with significantly decreased risk								
7290	Architectural, engineering and related services	1300	Architects, except naval	80	13 (0.14)	67 (0.27)	0.53	0.30-0.97
7980	Business, technical and trade schools and training	3010	Dentists	113	15 (0.17)	98 (0.39)	0.41	0.24-0.71
8690	Drinking places, alcoholic beverages	4040	Bartenders	73	11 (0.12)	62 (0.25)	0.48	0.25-0.90

AML, acute myeloid leukemia; I&O, industry and occupation; mOR, matched odds ratio; CI, confidence interval.

*Bureau of the Census (BOC) 2002 codes were used.

[†]Matched on age, sex, race and year of diagnosis.

[‡]The exact conditional logistic regression method was used to calculate mOR because none of the 24 822 controls had this I&O pairing.

and waste services industry”, the specific industry with a decreased risk was “business support services”. Within “public administration”, the only industry with decreased AML risk was “administration of environmental quality and housing programs” (Table II).

Two broad occupation categories had a decreased risk for AML: “legal” and “transportation and material moving”. Within “legal”, “lawyers” was the specific occupation found to have a decreased risk for AML. Within “transportation and material moving”, the only occupation with a decreased risk was “laborers and freight, stock and material movers, hand” (Table II).

The longest-held I&O pairings analyses also found a decreased risk for AML for three I&O pairs: “architects (except naval) employed in architectural, engineering and related services”, “dentists employed in educational services” and “bartenders employed in drinking places (alcoholic beverages)” (Table III).

Other industries and occupations of interest

Semiconductor workers do not have a separate BOC 2002 occupation code. Instead they were lumped into the I&O pair consisting of two occupations (i.e. “electrical, electronic and electromechanical assemblers” and “miscellaneous assemblers and fabricators”) employed in the “electronic component and product manufacturing” industry. A non-significant association with AML was observed for this I&O pairing (nine cases, 23 controls; mOR = 1.15; 95% CI: 0.53, 2.49).

Statistically significant associations with AML were not found for other I&Os of interest, including laundry and dry cleaning workers (mOR = 1.17); firefighters (mOR = 1.14); police and sheriff’s patrol officers (mOR = 1.04); teachers (mOR = 0.95–1.6); childcare workers (mOR = 1.23); registered nurses (mOR = 1.07); diagnostic related technologists and technicians (mOR = 1.77); maids and house-keeping cleaners (mOR = 0.91); hairdressers, hairstylists and cosmetologists (mOR = 1.31); barbers (mOR = 0.66); radio and telecommunications equipment installers and repairers (mOR = 1.10); welding, soldering and brazing workers (mOR = 1.07); automotive service technicians and mechanics (mOR = 1.24); machinists (mOR = 1.31); tool and die makers (mOR = 1.69); butchers (mOR = 0.97); shoemakers (mOR = 0.76); and workers in I&Os with high potential benzene exposure (e.g. oil, gas, rubber, glue) (mOR = 0.78 to 1.91).

Discussion

Previous research found that established risk factors (e.g. benzene and ionizing radiation) explained only a small fraction of cases of AML. Therefore, identifying I&Os with an elevated AML risk is important for finding new potential risk factors. Using information on longest-held job, this study identified multiple I&Os with an elevated AML risk. We identified several longest-held I&Os that have not been previously reported to have an increased AML risk, such as farm workers, fishers and related fishing occupations, brick masons, and nursing and home health aides. Additionally,

some of the longest-held jobs found to have an increased AML risk were similarly identified by prior research, such as construction laborers, slaughter house workers and janitors.

A previous study used CCR data to examine the risk of leukemia (all major classes) among construction workers [35]. Although the study design had many similarities with our study (including the same age range and the same years of diagnosis), the earlier study examined construction workers only, selected dissimilar control cancers and used an older BOC classification system (i.e. 1990 I&O codes versus the 2002 codes). Both studies found significantly elevated AML risks for construction laborers, electricians and carpet installers. However, our study also found an increased risk for “brick, block and stone masons”. The potential exposure to benzene and other leukemogens may be responsible for the increased risk of AML among construction laborers and carpet installers [35]. However, it is not clear why brick, block and stone masons have an increased risk. It has been suggested that exposure to asbestos may be involved in the etiology of AML [36], and masons can have asbestos exposure (e.g. through contact with asbestos-cement products).

Some research suggests that workers in occupations with high exposure to viruses or other infectious agents (e.g. healthcare workers, teachers, child care workers and those who work with live animals) are susceptible to developing leukemia [23,27,37]. Since the hematopoietic system is involved with immunity and is the origin of AML, frequent exposure to viruses and infectious agents may initiate immune responses that promote hematopoietic malignancies [37]. Previous research has found that workers who work with living animals may be at risk for leukemia [23,32,33, 37–39]. Various livestock (e.g. cattle, poultry, pig and sheep) harbor retroviruses that may affect human cells. Exposure to these oncoviruses has been hypothesized to contribute to the development of AML [38–40]. Animal viruses that induce hematological tumors in animals include the bovine leukemia virus (cattle), the avian sarcoma leucosis virus (poultry) and the Marek disease virus (poultry) [33].

Interestingly, our study found an increased AML risk among individuals whose longest-held job was in the animal slaughtering and processing industry (within the broad category of non-durable goods manufacturing), but not among butchers working in grocery or specialty food stores, or among agricultural workers involved in animal production. This is consistent with a previous study by Bethwaite *et al.*, which found an increased risk for AML among workers employed in an abattoir [33], but not among butchers or meat packers who worked in retail or wholesale, nor among cattle, dairy or sheep farmers [33]. Furthermore, the Agricultural Health Study (AHS) did not find an elevated leukemia risk among farmers who worked with various types of livestock; however, findings specific for AML were not reported [41]. It should be noted that laboratory studies have found little evidence that animal viruses infect human cells [33,42]. As such, the role animal viruses’ play in the development of AML warrants additional investigation.

This study found that those whose longest-held jobs were as miscellaneous agricultural workers (i.e. farm workers) in

crop production, as opposed to animal production, had a higher risk for developing AML. Numerous studies, including the AHS, have found an association between pesticide exposure and leukemia [43,44]. Similarly, a systematic review found an increased risk for AML among those with occupational pesticide exposures [45]. However, specific pesticides associated with an elevated AML risk have not been identified [44]. Agriculture workers who work with crops may be more likely to be exposed to pesticides compared to those who work with animals. Although farms involved with animal production also often produce crops, these crops are typically forage crops (e.g. grain) that are highly mechanized. In contrast, workers employed in crop production are more likely to engage in hand labor activities, which increases the likelihood of contact with pesticide residues present on plants. In addition to pesticides, crop production workers are frequently exposed to solvents, oils, paints and welding fumes [46]. This differential exposure may influence AML development [37].

An association between AML and fishers/related fishing workers was also found. Fishers may have AML risk factors related to exposure to contaminants found in fish (e.g. pesticides) [45]. Fishers also experience stressful working and sleeping conditions, which may weaken their immune systems and increase their susceptibility to leukemogens [47].

Those whose longest-held jobs were as nursing aides, psychiatric aides and home health aides were found to be at increased risk for AML across three different healthcare industries (i.e. outpatient care centers, hospitals and nursing care facilities). These aides provide support to registered nurses by assisting patients with bathing, dressing, light housekeeping and administration of medication under supervision. Given these responsibilities and their close and prolonged contact with patients, healthcare support staff, compared to other healthcare workers, may have greater exposure to various viruses and other infectious agents found in bodily fluids such as saliva, vomitus and blood [27]. Nursing aides can also be exposed to biological material through accidental finger pricks when capping needles [48], and may be exposed to chemotherapeutic agents (an AML risk factor) [18] found in patients' urine, sweat and vomit [26]. Although teachers and childcare workers are more likely to be exposed to viruses compared to the general public, their risk for AML was not significantly elevated in this study.

Although exposure to high-dose ionizing radiation (γ) has been previously linked to AML [9], there is no conclusive evidence to support an association between AML and lower-dose radiation exposure (e.g. diagnostic imaging procedures, X-rays, mammograms) [49]. Our study also did not find an association between AML and longest-held employment as diagnostic related technologists and technicians (this group includes radiologic, X-ray, magnetic resonance imaging scan and computed tomography scan technologists).

Our study found that individuals whose longest-held job was being a janitor or building cleaner who provided services to buildings, dwellings and schools had a significantly elevated AML risk. Similarly, Blair *et al.* found an associa-

tion between leukemia and janitors/cleaners who worked for > 10 years [27]. Janitors are exposed to chemicals in cleaning products that may act as leukemogens, including acetone, formaldehyde, sodium hypochlorite, borates and morpholine [27,50]. In addition, janitors may be exposed to residues or fumes from pesticides applied to school buildings [27]. In contrast, maids and housekeeping cleaners were not found to have an elevated AML risk. One possible reason that janitors and not maids are at increased risk may be because the former are more likely to use chemical cleaners, solvents and acids [51].

Due to a recent cluster of lymphohematopoietic cancers among workers employed in the South Korean semiconductor industry [21], we were particularly interested in the relationship between semiconductor workers and AML. In addition to the Korean findings, research that examined the association between leukemia and semiconductor employment was conducted in the United States, the United Kingdom and Taiwan [20]. However, these studies reported a small number of cases, and their findings were inconsistent and therefore inconclusive [20]. Our study was also limited by the low number of subjects whose longest held jobs were classified as assemblers or fabricators in the electronic component and product manufacturing industry. When we examined the I&O text fields for those workers, only three (one case and two controls) appeared to have had semiconductor employment.

Surprisingly, we found evidence of increased risks for several longest-held jobs not likely to involve high levels of exposure to any known leukemogens, such as "first-line supervisors/managers of production and operation workers", "actors in motion picture and video industry", "travel agents in service industries incidental to transportation" and "civil engineers in architectural, engineering and related services industry." Although past studies have observed an association between the broad category of hematolymphopoietic malignancies (findings for AML were not reported) and engineers [22,23], to our knowledge, no previous studies reported an increased AML risk among travel agents, actors or supervisors of production. It is possible that these represent spurious results due to multiple comparisons, but we cannot rule out the possibility of hazardous exposures among these groups of workers. A table with findings from all I&O that were assessed is available online. Please see link at the end of the article. Approximately 5.8% of the industries and 4.8% of the occupations assessed had statistically significant elevations or decrements in risk.

I&Os we identified as having a significantly decreased risk for AML were generally in the professional, business or administrative industries. Laborers and freight, stock and material movers in the transportation and material moving occupation were also found to have a decreased risk.

Strengths

Since AML is a relatively rare cancer, many previous AML studies had small sample sizes, thus limiting the statistical power to detect associations. We examined 8999 cases of AML between 1988 and 2007, allowing us to both confirm previously reported associations and identify previously

undetected associations. By using the more up-to-date BOC 2002 codes, we could explore AML risk among relatively recent industry and occupation entrants to the US economy (e.g. software publishing industry, construction managers). Also, since previous cancer treatment is associated with the development of AML [28], we were able to exclude cases of tAML to reduce bias.

Limitations

This study has several limitations. First, I&O information captured by CCR was often incomplete. Between 1988 and 2007, a total of 19 306 cases of AML were identified by CCR, of which only 9916 (51%) had sufficient narrative information to code industry and/or occupation. Second, the I&O captured by the CCR may not represent the longest-held job. When I&O data are present in the medical record, they may be from an uncertain time frame (i.e. it may be the current and not usual industry and occupation). It is reassuring that analyses of a large representative sample of US workers found moderate-to-high levels of agreement between current/most recent job and longest-held job [52,53]. As such, even if current employment information is the only available I&O data, it can serve as a reasonable surrogate for longest-held job. Third, we did not have information on some potential AML risk factors, such as body mass index, alcohol consumption and smoking, and therefore could not control for these exposures. In addition, information on specific workplace exposures was not available. Fourth, error could occur if the distribution of patients with available I&O is biased toward specific I&Os and cancers, leading to misrepresentation of certain industries and occupations that fail to reflect the true I&O distribution in the case and control group [54]; however, we have no evidence to suggest the presence of this bias. Fifth, the control cancers (breast, colorectal and low grade prostate) were chosen because there is little evidence to suggest they are associated with occupational exposures. However, if in reality these cancers share similar exposure risks to those with AML, our results may be biased toward the null. Finally, because this was a hypothesis-generating study and did not adjust for multiple comparisons, we cannot rule out the possibility that some of our results were spurious due to the large number of comparisons that were performed.

Conclusions

Construction laborers, electricians, carpet installers, animal slaughtering and processing workers, nurses and home aides, crop production workers, brick masons and janitors showed an increased risk for AML. These findings suggest that chemicals used in construction, viruses and/or other infectious agents, pesticides and cleaning products may be important occupational contributors to AML risk. We also found evidence of increased AML risk among some I&Os without any clear potentially leukemogenic exposures. As AML has poor survival, efforts in AML prevention are needed. Our findings should be followed-up with studies that employ a more detailed exposure assessment of those I&Os with elevated risk.

Acknowledgements

The authors thank the following individuals for their review of earlier versions of this manuscript: Dr. Aaron Blair and Dr. David McLean. The collection of data used in this publication was supported by the California Department of Health Services as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; by the National Cancer Institute, National Institutes of Health, Department of Health and Human Services under Contract No. N01-PC-2010-00035; and grant number 1U58DP000807-3 from the Centers for Disease Control and Prevention.

Potential conflict of interest: Disclosure forms provided by the authors are available with the full text of this article at www.informahealthcare.com/lal.

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Supplementary material available online

Supplementary Tables showing further results available online at <http://informahealthcare.com/doi/abs/10.3109/10428194.2014.894189>.