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Cancer in Banana Plantation Workers in Costa Rica

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Background. Costa Rica has population and disease registries with potential value for epidemiological research. Pesticides have been intensively used on banana plantations, for example dibromochloropropane (DBCP). This study was planned to examine the quality of the cancer and civil registries and the feasibility of record linkages, and to explore cancer patterns among a highly exposed group.

Methods. A retrospective cohort study was carried out. Workers on the payrolls of banana companies, as reported to the Social Security System at any time between 1972 and 1979, were followed up in the cancer registry between 1981 and 1992: 29 565 men and 4892 women for 407 468 person-years. The observed cases of cancer were compared to the expected values, derived from the national incidence rates.

Results. We identified 368 cancer cases, 292 among men (standardized incidence ratio [SIR] = 76, 95% confidence interval [CI] 67–84) and 76 among women (SIR = 116, 95% CI : 90–142). Among men increased SIR were observed for melanoma (SIR = 197, 95% CI : 94–362) and penile cancer (SIR = 149, 95% CI : 55–324); among women for cervix cancer (SIR = 182, 95% CI : 122–241) and leukaemia (SIR = 274, 95% CI : 86–639). Risk estimates for lung cancer were elevated among male workers with the longest time of employment.

Conclusions. Follow-up was difficult due to deficient identification variables in the cancer registry and to easier identification of the living compared to the deceased in the civil registry at the end of the observation period. The various systematic errors in this study are likely to produce an underestimation of the relative risk estimates. This study contributes to improvements of the registries and increases the potential for cancer epidemiology in Costa Rica and other developing countries.

Keywords: cohort study, registries, cancer, pesticides, DBCP, developing country, banana workers, agriculture

High cancer risk has been reported among agricultural workers. Skin and lip malignancies have been associated with ultraviolet radiation exposures during outdoor farming and leukaemia with viral zoonosis. Increased occurrence of soft tissue sarcomas, various lymphohaematopoietic cancers, and cancer of the brain, testis, stomach and prostate have been observed among pesticide exposed populations.[1,2]

Particularly high exposures to pesticides occur in developing countries. Despite constraints to conducting research in the third world,[3] epidemiological cancer studies are increasing, mainly of the case-control type.[4–6] Cohort studies, however, are almost non-existent, because of scarce population-based cancer registries and limited possibilities to follow populations over time.

Working conditions in Costa Rica are insufficiently controlled. Banana production is labour intensive and pesticide use has been excessive for decades. The use of dibromochloropropane (DBCP) in the 1970s caused the sterilization of approximately 1500 banana workers.[7] DBCP is classified by IARC as a possible human carcinogen, and has caused multiple site cancers in various types of test animals.[8] Other potential carcinogens used on bananas are maneb,[8,9] mancozeb,[9] benomyl,[9] chlorothalonil,[8] and formaldehyde.[8]

In Costa Rica, high exposures co-exist with nationwide population and disease registries. Knowledge about the functioning and quality of these registries was insufficient but, in theory, several of them permitted the identification of exposed populations and health outcomes. A retrospective cohort study was planned among workers of banana plantations with the objective of gaining insight into the quality of the cancer and civil registries, to evaluate the possibility of record linkages, and to explore cancer patterns among a group highly exposed to pesticides. The hypothesis that DBCP exposure may be associated with an increase in cancer incidence is of particular concern.

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MATERIALS AND METHODS

The study population included all workers on the payrolls of banana companies, as reported to the Social Security between 1972 and 1979. This population was followed up in the cancer registry from 1981, the first year considered to have a reliable and complete national coverage, up to 1992, the last year for which data were available.

Employers report their payrolls to the Social Security of Costa Rica (CCSS) on a monthly basis for health care and pension purposes. Since 1969, the payrolls are kept on computer tapes which include a code for economic activity, a number for each employer, and identification variables for the workers. The tapes corresponding to the time period of DBCP use (1969–1979) were made available to us by CCSS.

Only the computer tapes for the years 1972–1979 were usable. The code for banana production included, besides plantations, other types of banana related enterprises which needed to be excluded. The employer's number is considered confidential by CCSS and did not allow the identification of plantations. In banana regions job turnover is extremely high and workers appear on the payrolls of many companies over time. Therefore, using various sources, we composed a list of names and ID numbers of workers who had been sterilized by DBCP on banana plantations during the 1970s, and linked these to the employer's numbers. All companies with one or more sterilized worker on their payrolls were considered plantations.

The database of selected companies contained roughly 150 000 records between 1972 and 1979, one for each worker per employer per year (Table 1). There were countless mistakes and missing data in the identification variables. To integrate these records into one individual record per worker, a computer program was designed which summarized the variables and corrected errors in the names, IDs and social security numbers. For difficult instances visual selection was used, but many uncertainties remained.

These difficulties determined the need for additional cleaning to obtain the correct identification for the cohort members before performing a record linkage with the cancer registry. Only records with an identification number were considered; records with numbers indicating foreign nationality or work permission for children were not allowed into the cohort (n = 4153). The remaining 38 000 records were linked with the Civil Registry to locate the subjects at the end of follow-up (Table 1).

A version of the Electoral Roll (ER) was made available to us which contained demographic information concerning all approximately 1.8 million Costa Rican citizens over 18 years alive in December 1992. The ER data base was linked to the CCSS data base. To consider records as pertaining to the same person they must have identical or almost identical IDs and names, according to previously established criteria. The correct identification variables of 33 482 workers alive in December 1992 were established (Table 1).

A subset of the data base of the Mortality Registry (MR) was provided to us with demographic information of the deceased population from 1972 (n = 204 984). Those banana worker records that were not identified through ER, were linked to MR. The correct identification variables of 887 deceased workers were established (Table 1).

The standardized mortality ratio (SMR) for all causes of death based on those observed so far was 53 for men and 56 for women for the entire observation period, and even lower for the earlier years (10 and 19 for males and females, respectively, in 1981). This indicated a severe problem in the identification of the deceased

TABLE 1 *Process of defining the study base and cancer identification*

I Identification of the study population from the payrolls of banana companies, 1972–1979	
150 000	Records on the payrolls reported to the Social Security by selected companies between 1972–1979
42 073	Records with ID numbers after integration into one individual record per worker
4153	Ineligible records: foreigners and children with work permissions
33 482	Workers identified on the Electoral Roll
887	Workers identified in the Mortality Registry
617	Workers identified in the Birth Registry
529	Excluded workers (year of birth unknown, year of birth after 1964, deceased before 1981)
2934	Records without identification (7.7%)
34 457	Total number of identified workers included in the cohort
II Follow-up at the National Tumor Registry, 1981–1992	
46 607	Incident cases, all cancer sites
13 251	Ineligible cancer records (basocellular skin cancers, *in situ* cervix cancers, born after 1964, without information on age)
33 356	Selected cancer sites, cases born before 1965
6430	Records not identified in the Civil Registry (19%)
26 926	Subset used in the analyses

banana workers in MR and the need for further identification.

The event of death is also annotated in the books at the Birth Registry (BR). The archives of BR are organized by ID number, and for the purpose of this study the remaining 3551 unidentified CCSS records with an ID number were reviewed manually. This process permitted us to establish the identity of an additional 617 workers, 515 deceased and 102 alive in December 1992 (Table 1). After the BR review, the SMR for all causes of death increased to 68 for males and 78 for females for the entire observation period with similar numbers for the earlier years.

Finally we corrected the gender and age variables of the members of the cohort according to the Civil Registry. We excluded those workers whose year of birth was missing both in the CCSS data base and in the Civil Registry and those who were born after 1964 (n = 223).

Thus, the final study population consisted of 34 457 cohort members with fully confirmed identification variables. Cohort members contributed to person-time experience from 1981 to 1992 or up to the year of occurrence of cancer diagnosis or death, for a total of 407 468 person-years.

To identify cancer cases in the study base, the CCSS data base of banana workers was linked to the National Tumor Registry (NTR).

The NTR was created in 1977 and became nationwide in 1980.[10] Being a relatively recent registry in a developing country NTR has faced limitations which were evident during this study. The NTR has improved its data base and performed a search for duplicates before the final linkage with the CCSS data base. However, this is an ongoing process.

Computerized record linkages of NTR with ER and MR, and a manual search of unmatched ID in BR were carried out as described for the CCSS payrolls. Matched ID numbers and names were corrected in NTR according to the Civil Registry, to improve linkage with the cohort.

During the observation period, NTR collected 46 607 incident cases. We excluded basal skin cancers and *in situ* cervix cancers, cases born after 1964, and a small number of cancers without any information on age. The remaining 33 356 records were eligible for linkage with the cohort. The proportion of unidentified individuals in this subset of NTR was 19% (Table 1).

Differences in cancer morbidity among banana workers as compared to the general population were assessed by comparing the observed numbers of all cancers and specific sites with the expected numbers. The 19% unidentified subjects in NTR cannot contribute to the number of cases among the banana workers. Therefore, to make the reference population comparable to the exposed population, we only used the identified subset in NTR to generate incidence rates among the general population. The expected numbers were derived for sex and 5-year age-specific strata from the person time in the cohort and the national incidence rates. The standardized incidence ratio (SIR) was calculated as the ratio of the observed to expected numbers of cases.[11] The 95% confidence intervals (CI) were calculated with the normal approximation of the Poisson distribution. For observed numbers below 20 the exact method was used.

As main exposure indicator we used categories of number of months of employment. Because of underreporting to CCSS by the companies, high job turnover within the region, and intermittent migration patterns to and from other parts of the country, we also categorized the number of years in which the workers appeared on the payrolls, independent of the number of months within each year. In addition, we grouped the workers according to first year of employment (1972–1975 versus 1976–1979), assuming that workers of the first time period are more likely to be workers with long-term pesticide exposure.

RESULTS

We identified 368 cases of cancer in the cohort during the observation time, 292 among men and 76 among women, with SIR for all cancer sites of 76 (95% CI : 67–84) and 116 (95% CI : 90–142) respectively (Table 2).

In men the SIR for melanoma was 197 and for penile cancer 149, the latter based on only six cases (Table 2). The SIR for all cancers of the lymphohaematopoietic system was close to unity (SIR = 102, 95% CI : 70–133), but there was a small increase for Hodgkin's disease and multiple myeloma; also two cases of malignant histiocytosis were observed.

Among women, a high risk was detected for invasive cervix cancer which counted for almost half of the cases. Excluding cervix, the risk for all other cancers combined diminished considerably (SIR = 87, 95% CI : 60–115). For most other sites the SIR were close to unity or based on only a few cases. An elevated risk was observed for lymphohaematopoietic cancers, particularly leukaemia with an SIR of 274 (Table 2).

The SIR for age-specific strata for all cancer sites showed a declining tendency with increasing age for the male workers. This decrease was consistent over different time periods in NTR and was also observed for the SMR for all causes of death (Table 3). For many

TABLE 2 *Cancer risk for all sites combined and selected sites (at least five observed cases); workers of banana plantations in Costa Rica, 1981–1992*

Cancer site (ICD-9)	Observed	SIR[a]	95% CI[b]
Men			
All sites (140–199)	292	76	67–84
Oral cavity (141–149)	8	64	27–125
Oesophagus (150)	5	72	23–167
Stomach (151)	79	75	59–92
Colon (153)	10	77	37–141
Rectum (154)	8	77	33–152
Liver (155)	6	55	20–121
Pancreas (157)	5	47	15–109
Larynx (161)	6	77	28–167
Lung (162)	30	107	69–146
Skin, non-melanoma (173)	6	46	17–101
Melanoma (872–879)	10	197	94–362
Prostate (185)	20	61	37–95
Testis (186)	6	59	22–129
Penile cancer (187)	6	149	55–324
Brain (191)	10	90	43–166
Hodgkin's disease (965–966)	9	117	54–223
Non-Hodgkin lymphoma (959–964, 969, 975)	10	78	38–144
Leukaemia (980–994)	14	97	53–164
Multiple myeloma (973)	6	121	44–264
Other and non-specified sites	23	51	30–72
Women			
All sites (140–199)	76	116	90–142
Stomach (151)	5	93	30–218
Breast (174)	10	70	33–128
Cervix (invasive) (180)	36	182	122–241
Leukaemia (980–994)	5	274	89–639

[a] Standardized incidence ratio.
[b] Confidence interval.

TABLE 3 *Risk for all cancer sites and for all causes of death, in relation to gender and age categories; workers of banana plantations in Costa Rica, 1981–1992*

I National Tumor Registry	Observed	SIR[a]	95% CI[b]
Men, all cancer sites	292	76	67–84
<40 years	57	93	69–117
40–59	123	83	68–97
≥60	111	63	51–75
Women, all cancer sites	76	116	90–142
<40	28	108	68–148
40–59	40	122	84–160
≥60	8	114	49–225
Women, all sites minus cervix	40	87	60–115
<40	12	80	42–141
40–59	22	89	52–126
≥60	6	98	36–214
II Civil Registry	**Observed**	**SMR[c]**	**95% CI[b]**
Men, all causes of death	1004	68	64–72
<40	293	87	77–97
40–59	389	77	69–84
≥60	322	51	45–57
Women, all causes of death	79	78	61–95
<40	27	88	55–121
40–59	39	89	61–117
≥60	13	49	26–83

[a] Standardized incidence ratio.
[b] Confidence interval.
[c] Standardized mortality ratio.

specific sites (colorectal, larynx, penile, and all lymphohaematopoietic cancers) SIR were considerably higher for male workers aged <50 compared to older workers; only for melanoma and lung cancer were the SIR clearly higher for workers aged ≥50. Such a tendency was also observed for the SMR of the female workers but not for the SIR. For the entire observation period, excluding cervix cancer, SIR increased with age.

A time window exposure analysis showed higher SIR for all cancers combined among the workers appearing on the payrolls for the first time between 1972 and 1975 as compared to those between 1976 and 1979, for both genders and different age categories (Table 4). This was also true for melanoma and penile cancer in men and for cervix cancer and leukaemia in women. The results of the analysis of number of months of employment as exposure indicator showed an increase in the risk estimates with length of employment for melanoma, penile, lung and brain cancer among the male workers, and for leukaemia among the female workers but based on small numbers. The SIR decreased or showed inconsistent patterns for all types of lymphohaematopoietic cancers among the males. The results of the analyses using the number of years on the payroll independently of the number of months of employment were rather similar (data not shown).

DISCUSSION

One main virtue of this study is the effort *per se* which has permitted a better understanding of the registries involved. This allows improvements and increases the potential for cancer epidemiology in Costa Rica, and other developing countries. Our most relevant findings were increased risk estimates for melanoma and penile cancer in men, and cervix cancer and leukaemia in

TABLE 4 *Cancer risk for all sites combined and for selected sites in relation to number of months of employment and category of first year of employment; workers of banana plantations in Costa Rica, 1981–1992*

	No. of months of employment									First year of employment					
	1–12			13–36			≥37			1972–1975			1976–1979		
	Cases	SIR[a]	95% CI[b]	Cases	SIR	95% CI	Cases	SIR	95% CI	Cases	SIR	95% CI	Cases	SIR	95% CI
Men															
All sites	111	73	60–87	99	72	57–86	82	85	67–104	154	82	69–95	138	70	58–81
Lung	7	68	27–140	11	106	53–190	12	165	85–288	18	129	77–205	12	86	44–175
Melanoma	3	147	30–431	3	166	34–485	4	323	88–828	5	207	68–233	5	188	60–233
Penile cancer	2	123	15–444	2	140	17–507	2	204	25–736	3	154	32–461	3	144	29–417
Brain	2	44	5–161	2	50	6–181	6	231	85–503	8	157	67–309	2	33	4–120
Hodgkin's disease	6	175	64–381	2	76	9–275	1	62	2–347	3	92	19–267	6	136	50–297
Leukaemia	7	114	46–235	6	120	44–261	1	31	1–173	5	79	25–233	9	113	51–214
Women															
All sites	37	107	72–141	26	155	96–215	13	92	49–158	52	143	104–182	24	82	49–115
Cervix	17	157	92–252	13	257	137–439	6	152	56–332	25	234	142–325	11	121	60–216
Leukaemia	1	99	2–551	2	438	53–1582	2	561	68–2025	5	529	180–1297	0	0	–

[a] Standardized incidence ratio.
[b] Confidence interval.

women. The quality and the organization of the data in the various registries required complex and tedious procedures to make them usable for linkages. Systematic errors might have been introduced at different stages of the investigation.

The main problem was the 19% of cancers in the NTR which could not be identified. Besides inaccurate reporting to NTR, shortcomings in the computerized data base of the MR can explain this difficulty. After our review of unidentified records of the cohort in BR, the SMR for all causes of death increased from 53 to 68 for the male workers and from 56 to 78 for the female workers. These SMR are still low and it is apparent that the underdetection of deaths is concentrated in the older workers (Table 3). To avoid a follow-up bias because of this we considered internal comparisons but the number of cases in the exposure categories (Table 4) were too small to permit age control.

To make the exposed and unexposed populations comparable, we excluded the unidentified subset of cancer cases among the reference population. Still, it is possible that inaccurate case reporting to NTR or missing data in MR occurred more frequently in remote areas like the Atlantic Region, where a majority of the members of our cohort were living during the follow-up period. This gives rise to a misclassification of disease which covaries with the exposure and a bias in the direction of the null may be the result.

The payrolls did not allow distinction between companies with high and low DBCP exposure, or between workers with different degrees of exposure by means of job titles. The inclusion of personnel with little or no occupational exposures to pesticides in this cohort of plantation workers gives rise to a non-differential misclassification with a dilution of the risk estimate towards the null. Also pesticide exposure among the reference population might be substantial. Not only do our cohort members contribute to the incidence rates among the general population, but practically 100% of the agricultural workers in the country use pesticides to various degrees,[12] which leads to a further dilution.

About 8% of the records eligible for inclusion in the study population were not identified and followed up (Table 1). Deceased workers might have been selectively excluded, with a high proportion of the deceased, possibly because of cancer, remaining among the unidentified records.

It appears most likely that the risk estimates for the exposed populations are underestimated rather than overestimated. In addition, the size of the cohort, especially of the subset of male workers, is large. Therefore, the positive findings are less likely to be due to bias or chance.

Geographical distribution of penile and cervix cancer show similarities globally; sexually transmitted viral infections, specifically human papilloma viruses, have been suggested as a common risk factor for both diseases.[13] Previous studies found high incidence rates of cervix,[14,15] and penile cancer[16] in the coastal regions of Costa Rica, where the banana plantations are located. Our findings could be due to confounding by high prevalence of sexual and reproductive risk factors and low economic status in these areas.[15] However, occupational exposures should be considered potential risk factors. Dermal contact with pesticides is a hypothesis to be considered for penile cancer. One study reported an increased risk for cancer of the cervix among female agricultural workers in California.[17] Exposure to organic solvents has been associated with cancer of the cervix and animal experiments have shown accumulation and biotransformation of these compounds in the cervical epithelium.[18] Our results suggest a need to orient research to include pesticide exposure.

The increased risk for malignant melanoma among male workers is consistent with other reports in the literature of increased risk for skin cancer among farmers[1,2,13] and has been associated with exposure to sunlight. The majority of the members of our cohort, however, are dark skinned and work in the shade. Eight of the ten cases of melanoma were located on the lower limbs, where contact can occur with liquid formulations of pesticides, specifically DBCP and paraquat.

A high SIR for leukaemia was observed for women. All women work at the packing plant areas where formaldehyde has been used as a disinfectant. Formaldehyde has been associated, among other sites, with leukaemia,[19,20] Hodgkin's disease,[20] and pharyngeal cancers.[19–21] In this study, among females, there were two cases of Hodgkin's disease (SIR = 403, 95% CI : 49–1455) and two cases of cancer of the pharynx (SIR = 1122, 95% CI : 136–4052).

Lung cancer is of special concern. DBCP causes lung cancer in experimental animals by inhalation.[8] Two studies have suggested an increased risk for respiratory cancers among DBCP exposed workers.[22,23] There was a slight excess for lung cancer in the higher age category of the men (SIR age >50 = 115, 95% CI : 72–159), despite the selection bias for the elderly. Confounding because of heavier smoking by banana workers as compared to the general population is possible. However, the cases seemed to occur more frequently among the workers employed for the longest time (Table 4). Differences in smoking habits

between the various categories of banana workers are not likely.

In conclusion, this study indicates that banana workers may be at increased risk for certain cancers, particularly melanoma in men and cervix cancer in women. In addition penile cancer, leukaemia, and lung cancer may also be elevated. In the case of cervix cancer socioeconomic confounding is a plausible explanation. If pesticides are involved, DBCP is one likely candidate.

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