

DRAFT

Proposal
Case-Control Study
Liver Cancer Among Chemical Workers
Kanawha Valley, West Virginia

Background

NIOSH and the Union Carbide Corporation (UCC) are cooperatively conducting a cohort mortality study of approximately 33,000 UCC employees in the Kanawha Valley from January 1, 1940 - December 31, 1978. Preliminary life table analyses have revealed a statistically significant excess of deaths due to liver cancer occurring during the period 1970 - 1978. Excessive deaths from liver cancer were seen under two NIOSH death categories, Category 11, "Biliary passages and liver," and Category 12, "Malignant neoplasm, liver, unspecified as to primary or secondary." The excess was virtually confined to individuals with over 20 years latency and duration of employment. Table 1 shows observed and expected deaths in these categories by 5 year interval, 1950 - 1978. Table 2 lists the year of each death and death certificate diagnosis.

Vinyl chloride, an agent known to cause angiosarcoma of the liver, has been produced and used in the study plants. From a preliminary look at data previously provided by UCC, it appeared that vinyl chloride was present in one process at the Institute plant from 1959 - 1963. It's production began at the South Charleston plant in the 1930's, where it was used in a number of departments to manufacture vinyl products. Five of the liver cancer deaths were listed as angiosarcomas on the death certificates. We are requesting confirmation of the diagnosis of all liver cancer deaths from hospital and pathology records.

We believe that timely investigation of the statistical excess in liver cancer mortality is called for. The excess is most striking in the 1975 - 1978 period (the last period in which data is available), and therefore may represent an ongoing problem.

Objective

1) To determine the extent to which the observed excess in liver cancer mortality among workers at UCC's Kanawha Valley plants is associated with prior employment in departments with potential vinyl chloride exposure. 2) To explore other possible etiologies by examining the frequency of case and control employment in individual departments and departments grouped by common exposures.

Methods

1. Literature review - We are currently conducting a review of the literature concerning 1) the epidemiology of angiosarcomas and the association with vinyl chloride and other agents, 2) the epidemiology of other hepatic tumors and known occupational and non-occupational risk factors and 3) the pathology and classification of liver tumors, and the accuracy of diagnosis on the death certificate.

UCC 099716

2. Selection of cases and controls - Cases will include all individuals whose cause of death is included in NIOSH death categories 11 and 12. Potential controls will be selected from individuals who survived the case, and are matched to the case by date of birth (plus or minus 1 year), date first employed (plus or minus one year) and race. A random selection of controls will be made from the pool of potential controls for each case. Ten controls will be selected for each case.
3. Coding of the detailed work histories - The detailed work histories will be coded jointly by NIOSH and UCC personnel. Currently, each individual's file should have an alpha and/or numeric code for each department in which he worked. Therefore, the primary data transcription task will be to complete the starting and ending dates for each assignment.
4. Decoding department codes - Accurate decoding of the alpha/numeric codes for departments is potentially a very time-consuming task. One possible way to streamline this process would be to construct a matrix of each unique department that has occurred and the years during which each worker was employed as the work histories are coded. All work histories would be included in the matrix irrespective of case-control status. At the end of data coding, the matrix would be condensed so that only the earliest starting year and latest ending year will be included. The next step would be to determine what process each department code represents during the relevant time periods.
- 5) Determinining exposures for each department - NIOSH and UCC personnel will jointly review the nature of the process and relevant exposures in each department during the periods relevant to the study. A short description of each process will be written, and potential chemical exposures will be coded for computer analysis. (We will investigate whether it would be desirable to use any standard method of coding in further analyses or whether it will be adequate to assign our own unique numeric code to each agent identified).
6. Determining exposure to vinyl chloride - Since vinyl chloride is a chemical of a priori interest, we will try to determine not only whether it was present in a department during a particular time interval but also the degree of potential exposure. Since it is unlikely that quantitative data will be available, we will try to look at degree of exposure on a low-med-high scale.
7. Analyses - This study has both hypothesis testing (association with vinyl chloride) and exploratory (identification of other agents) aspects. In the exploratory analyses, we will analyze frequency of employment in various departments as well as the frequency of exposures to groups of common chemicals. We might stratify the cases by the three or four major tumor types, if we believe that we have sufficient data to do this accurately. Odds ratios will be calculated using techniques for multiple strata. Conditional logistic regression will be used to model the data. The model would consider degree of exposure to vinyl chloride as well as any other risk factors identified in the exploratory analyses.

Budget:

Coding of the detailed work histories on site: \$1,500 travel

Completing the job-exposure matrix: \$1,000 travel

Keypunching the work histories: \$2,000

Computer funds: \$3,000.

Table 1

Observed and Expected Deaths from Liver Cancer, 1950 - 1978
 UCC Kanawha Valley Plants, by Five Year Intervals ;

YEAR	Category 11 "Biliary passages and liver"		Category 12 "Malignant neoplasm, liver, unspecified whether primary or secondary"	
	OBS	EXP	OBS	EXP
50-54	0	0.95	1	1.05
55-59	1	1.56	1	1.24
60-64	0	2.42	3	1.44
65-69	3	3.46	2	1.88
70-74	3	4.45	6	2.22
75-78	11	5.20	4	2.08
70-78	13	9.66	10	4.21

Total 1970 - 1978 Obs/Exp = 23/13.9 p = 0.02

Total 1950 - 1978 Obs/Exp = 34/27.9 p = 0.05

Table 2

Death Certificate Diagnoses - NIOSH Death Categories
11 and 12 :

Category 11

1970-1974

1970 Ca of Gallbladder
1972 Ca of Gallbladder

1975-1978

1975 Ca of Colon and Gallbladder
1975 Ca of Gallbladder
1976 Ca of Bile Duct
1976 Ca of Gallbladder
1976 Hepatic cell Ca
1976 Primary Hepatoma
1977 Ca of Gallbladder
1977 Primary malignancy of liver (notation of angiosarcoma)
1977 Ca of liver - Cholangiocarcinoma
1978 Colangiocarcinoma
1978 Primary liver ca - angiosarcoma

Category 12

1970-1974

1970 Ca of liver
1970 Ca of Liver
1972 Ca of Liver
1974 Ca of Liver
1974 Ca of Liver
1974 Angiosarcoma

1975-1978

1975 Undiagnosed Ca of Liver
1976 Angiosarcoma
1977 Ca of Liver
1978 Angiosarcoma

VCL (Draft)

— Too Vague
Stat Analysts

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NIOSH will provide us path findings