

Lung Cancer Mortality and Residential Proximity to Industry

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A potential causal relationship has been suggested by other studies between air pollution and lung cancer. To attempt to define the risk of lung cancer associated with residential proximity to industry by type in Louisiana, lung cancer deaths occurring between 1960 and 1975 in residents of 20 parishes were compared to controls matched on age, sex, year of death and parish of residence. The comparisons were limited to cases ($N = 1418$) and controls ($N = 1429$) with known length of exposure to and residing within 0.99 mile (exposed) and 1.0 to 3.0 miles (unexposed) radius of an industry type. Of the 13 industry types evaluated, the petroleum and chemical industries showed the highest consistent elevations in risk associated with closeness of residence to industry, whereas possible risks shown for food, grain, canning, and paper industries are less defined.

For the petroleum industry, the risk was demonstrated in the group with 10 or more years of residential exposure to the industry in question. For the chemical industry, the residential risk was found in people employed in low risk occupations, who were exposed to large individual industries and was independent of length of exposure as determined for less or more than ten years, ($RR = 4.5$). The results suggest that residential proximity to petrochemical industries may make a contribution to the lung cancer mortality in Louisiana.

Introduction

Lung cancer mortality and incidence in certain southern parishes of Louisiana are among the highest in the U.S. (1-3). There are certain unique industrial characteristics in Louisiana. Numerous petroleum refineries are situated along the Gulf Coast and in Louisiana. The petrochemical industry along the Mississippi River and related areas is about as concentrated as in any other region in the United States.

A potential causal relationship has been suggested by other studies between urban air pollution and lung cancer. A number of investigators have shown an urban-rural gradient in lung cancer mortality (4, 5). However, access to and availability of medical care, migration due to illness, cigarette smoking and occupation are factors associated with urban-

rural residence which may distort the ability to attribute such a gradient to air pollution. Even with the present access to medical care for residents of rural areas, this gradient persists (5). After controlling for cigarette smoking patterns, a number of studies in different populations have shown the gradient still to be present (6-12). Due to the limited employment of the population in occupations identified as contributing to the risk of lung cancer, occupational hazards could not completely account for the urban-rural gradient (5).

Correlation analyses have shown a relationship between lung cancer mortality, benzo[a]pyrene measurements, solid-fuel consumption, and total settled dust (4, 13). Commoner has demonstrated that certain samples of urban air in Chicago are mutagenic (14). Extrapolation of results from occupational exposure to polycyclic hydrocarbons, and specifically benzo[a]pyrene have led investigators to the conclusion that lung cancer mortality may be substantially increased by exposure to air pollution (15, 16). Lung cancer has been shown to be associated with the percentage of the population of a county employed in the petroleum, chemical, paper,

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and transportation industries (17). Lloyd's report of excess lung cancer mortality in a residential community downwind from a steel foundry further supports the potential effect of air pollution (18).

The present report details a mortality study using a case-control methodology in which the length of exposure is estimated and distances from exposure sources are calculated while controlling for occupational exposure and some demographic variables, which strongly suggests a lung cancer risk attributable to residential proximity to industry. Because of the short length of survival from the date of diagnosis of lung cancer, mortality data can be used to approximate incidence data, and the length of residence prior to death can be used to approximate exposure to effluents before onset of disease.

Materials and Methods

Study Population

Twenty parishes (counties) in Louisiana were selected for study based on 1% or more of the population being employed in the paper, chemical and petroleum industries, and/or high rates of mortality from lung cancer (1950-1969) (19).

Cases were primary lung cancer deaths identified from death certificates, (ICD 162.1, 163, 7th revision; 162.1, 8th revision) occurring between 1960 and 1975 with a verified minimum length of residence in the parish of residence at death (20). Controls were drawn from a sampling frame which excluded deaths due to neoplasms, and were matched on parish of residence, age (± 2 years), race, sex, and year of death.

Industry of Occupation

Usual industry of occupation and occupation were abstracted from death certificates and classified according to the definitions of the Census Bureau Classification, (21). For this report, industry of occupation was dichotomized into high and low risk (19). High risk industries of occupation for lung cancer included fishing, construction (including painting), metal equipment and transportation equipment manufacturing (including shipbuilding), petroleum refining, chemical, other manufacturing (U.S. Census Bureau Codes 119-138, 248-259, 299-319, 337-398) (including electrical equipment) and transportation.

Manufacturing Industries

Manufacturing industries in operation between 1942 and 1965 were identified using the Louisiana

Directory of Manufacturers (22). All the industries reported in the directories published between 1942 and 1975 were compiled in order to overcome the variability in reporting to individual editions. The type of industry, opening and closing dates, addresses, and average number of employees (size) were obtained. These industries were mapped on parish maps to the nearest 0.1 mile, and the location was transformed to a coordinate system.

Distance and Exposure

Place of usual residence was abstracted from the death certificate. Addresses of cases and controls were transformed by the same method as that used for industries. Information on length at residence was obtained by field workers surveying public utility records and town directories. The distances of cases and controls from an industry were calculated using the simple Pythagorean rule.

A subset of cases and controls was further defined according to known residential exposure to industrial effluents; that is, those with concurrent known dates of residence and dates of operation of the industry. Years of known exposure were calculated according to the years of overlap. This report is limited to cases and controls with known minimum years of exposure to specific types of industries prior to death. Exposure variables were considered separately rather than in combination as a single dose-response variable. Distance from industry was chosen as the primary response variable as it was the most accurately measured. Years exposure are minimum known years at residence of death during which the industry was in operation. Industry size (assumed to be proportional to effluents released) was estimated from the number of employees recorded as employed by the company.

Case-Control Comparison

In comparing case-control distributions on exposure variables, the comparison was limited to cases and controls residing within three miles of the specific industry type being evaluated. Each case could be identified with more than one industry and may appear in more than one analysis. Therefore, each industry study is a separate analysis, but not completely independent, from the others. The potential confounding from this source was limited by restricting the study to less urbanized parishes.

Exposure was defined as residence within 1.0 mile of an industry type; no exposure was defined as residence 1-3 miles from the industry under study. This arbitrary distance was selected because wind patterns were reported as too variable to define in this area and because particulate matter is

Table 1. Demographic comparison of cases and controls with verified length and location of residence.

Demographic characteristic	Cases		Controls	
	N	%	N	%
Age, years				
< 50	164	11.6	181	12.7
50-59	338	23.8	401	28.1
60-69	524	37.0	518	36.2
70	392	27.6	329	23.0
Race				
White	1113	78.5	1120	78.4
Other	305	21.5	309	21.6
Sex				
Male	1212	85.5	1222	85.5
Female	206	14.5	207	14.5
Year of death				
1960-63	175	12.3	172	12.0
1964-67	273	19.3	264	18.5
1968-71	391	27.6	421	29.5
1972-75	579	40.8	572	40.0
Total	1418	100.0	1429	100.0

reported to descend within one mile of exhaust depending upon the height of the stack, particle size, and density. Comparisons were limited to within 3 miles to control for the known urban-rural gradient in lung cancer mortality. This gradient is also associated with cigarette smoking, and socioeconomic status which was not examined in this study due to the already limited numbers available.

The same procedures were followed to obtain information for cases and controls. There were no significant differences in the numbers of located cases and controls by sex, race, age group, or parish.

Relative odds ($\hat{RR}$) were calculated by using maximum likelihood point estimates, and the exact conditional confidence limits were computed for the unadjusted risk estimates (23).

Control of potential confounding variables and the modifying effect of others was obtained by using a multiple logistic analysis, (24). Standard errors of the parameters were calculated by use of the variance-covariance matrix, and standard errors of the adjusted relative risks were calculated from a linear combination of the appropriate matrix elements. Approximate 95% confidence limits of the adjusted relative risks were based on these standard errors.

Results

In all, 3518 lung cancer deaths and 3518 control deaths were abstracted. Of these, information on residential location, and length at residence was available for 1418 (40.3%) cases, and 1429 (40.6%) controls.

Location and length of residence information was more complete on those who died during later years of the study, and more were male and white, compared to those with incomplete residence information.

The cases and controls with known residence information were compared on demographic characteristics using a log-linear model. Age was statistically associated with case-control status but differed on the average by only one year. This association was due to the priority system in matching on age, for which controls two years younger than the case were systematically sought first; mean age of the cases were 62.9 years and controls 61.7 years. Year of death, sex, and race were not associated with case-control status. Moreover, three way and higher order interactions were not found between age, race, sex, year of death and case-control status (Table 1).

Manufacturing industries identified as operating during the period 1942-1965 were classified into 30 different categories, which represented the complete study population. Those categories which either possessed a potential effect on the population based on earlier information, or had more than 40 individual plants in the category are shown in Table 2. These also represented most of the study population. The largest categories (> 100 individual plants) were lumber, grain, miscellaneous food, and printing. Those industry types with the largest average years in operation were paper (35.8 years), printing (33.8 years), chemical (30.8 years) and miscellaneous food (30.0 years). All industrial categories were in operation an average of more than 15 years, thus allowing an exposure period consistent with suspected latency periods for lung cancer. Only these

Table 2. Selected industries in operation between 1942 and 1965 in 20 Southern Louisiana parishes.

Industry type/(census code)	Specific industries (number)	Average years in operation
Lumber (107-9)	Logging, sawmills, miscellaneous wood products (163)	21.6
Cement (127-37)	Cement, concrete, gypsum, plaster, clay, and pottery (65)	18.4
Metal Mfg. (157-69)	Cutlery, hand tools, fabricated structural metal, screw machine, stamping and miscellaneous metal (63)	18.0
Machine Mfg. (177-98, 258)	Machinery (except electrical), ordnance (92)	23.6
Food (268-9)	Meat, dairy products, (71)	25.3
Canning (278)	Canning, preserving fruits, vegetables and seafood (84)	25.0
Grain (279)	Grain-mill products (107)	23.3
Bakery (287-9)	Bakery, confectionary, beverage and related products (89)	30.0
Misc. Food (297-8)	Miscellaneous and not specified food (102)	30.7
Paper (328-37)	Pulp, paper, paperboard mills and products (18)	35.8
Printing (338-9)	Newspaper and allied publishing and printing (100)	33.8
Chemical (347-9, 368-9)	Industrial chemicals, paints, varnishes, miscellaneous and not specified chemicals (67)	30.8
Petroleum (49, 377-8, 387)	Crude petroleum gas extraction, petroleum refining, coal and miscellaneous plastic products (47)	17.1

13 industry types will be considered in the analysis below (Table 3).

For the following industry types, there was no evidence of any increase in risk associated with residential proximity to the industry: lumber, cement, machine manufacturing, printing and miscellaneous food (Table 2). The food and grain industries showed slight elevations in risk for 10 or more years exposure; the paper industry only in the case of large industries. However, for these risks 1.0 was included in the confidence intervals.

Though metal manufacturing and canning industries showed an excess risk for large industries, the sample size was too small to provide meaningful estimates. The petroleum industry showed elevations in risk for 10 years or more exposure. Examining the petroleum industry without consideration of industry size resulted in a relative risk of 1.65 ($RR = 0.91$).

The chemical industry showed elevations in risk with exposure to large industries, regardless of length of exposure, this was 2.11 and 1.51 for < 10 years and 10+ years exposure, respectively. When combined the risk was 1.81 ($RR = 1.10$).

The resulting residential risk estimates for grain, petroleum, paper and chemical industries after controlling for age, race, sex, year of death and birthplace by using a logistic model were similar to the uncontrolled risk estimates, with the petroleum and chemical industries showing the highest risk for 10+ years exposure and large industries, respectively. This is likely to be due to the effectiveness of the matching procedure.

The modifying effect of industry of occupation on the residential risk for the petroleum and chemical industries is shown in Table 4. Inclusion of industry of occupation as an effect modifier in the logistic model resulted in a significantly elevated residen-

tial risk only for those with a low risk industry of occupation, in those with residential exposure to large chemical industries ($RR = 4.5$, $RR = 1.85$) $\chi^2 = 12.4$, $p < 0.001$, not confined to more than 10 years exposure. An elevated although not significant, residential risk was noted in the low and high risk occupational groups for those with 10 or more years exposure to the petroleum industry (low risk $RR = 1.34$, $RR = (0.41-4.330)$; high risk $RR = 1.61$, $RR = (0.55-4.76)$).

Except for proximity to large chemical industries, a comparison of overall residential and occupational risks revealed higher relative risk estimates for occupation than for residential exposure to either the petroleum or the chemical industry (Table 5). The residential risk was identifiable only for those with low risk occupations, and there was no evidence of synergism from exposure to both high risk occupation and residential proximity. Since the water source was controlled by matching on parish of residence, analysis of water source in cases and controls did not reveal any difference in potable water source, and an effect on residential risk by the type of potable water used (ground, surface) could not be studied. Exposure to more than one chemical or petroleum industry could not be validly evaluated due to small sample size of multiple exposures.

Discussion

This study describes a gradient of risk for lung cancer by length and/or amount of residential exposure for several selected industries, (food, canning, grain, paper, chemical and petroleum). As with any death certificate study, possible bias resulting from

Table 3. Relative risk estimates (RR) for lung cancer associated with known residential proximity to selected industry types by distance, size, and length of exposure

Industry type	Residential proximity, miles	< 100 employees						≥ 100 employees					
		0-9 yr exposure			≥ 10 yr exposure			0-9 yr exposure			≥ 10/yr exposure		
		Cases N	Controls N	RR	Cases N	Controls N	RR	Cases N	Controls N	RR	Cases N	Controls N	RR
Lumber	< 1.0	47	45	0.86	82	78	1.05	17	27	0.92	27	24	0.94
	≥ 1.0	34	28		26	26		11	16		12	10	
Cement	< 1.0	41	52	0.63	105	96	0.80	2	2	0.57	0	0	-
	≥ 1.0	44	35		37	27		7	4		1	1	
Metal Mfg.	< 1.0	26	34	0.58	81	82	0.87	8	10	1.08	1	2	-
	≥ 1.0	17	13		17	15		4	9		3	1	
Machine Mfg.	< 1.0	48	43	0.77	91	71	1.00	7	9	1.09	21	29	0.79
	≥ 1.0	32	22		36	28		5	7		11	12	
Food	< 1.0	55	71	1.06	93	116	1.30	6	10	0.30	57	64	1.29
	≥ 1.0	33	45		40	65		12	6		9	13	
Bakery	< 1.0	101	110	1.23	193	180	0.94	0	0	-	0	0	-
	≥ 1.0	62	83		50	44		0	0		0	0	
Miscellaneous Food	< 1.0	61	49	1.03	129	116	0.88	10	13	0.89	18	21	1.18
	≥ 1.0	46	38		38	30		13	15		21	29	
Printing	< 1.0	30	22	1.02	94	93	0.42	0	0	-	0	0	-
	≥ 1.0	8	6		17	7		0	0		0	0	
Canning	< 1.0	33	45	0.64	61	76	0.46	11	5	1.65	12	10	1.86
	≥ 1.0	15	13		28	16		8	6		5	7	
Grain	< 1.0	24	37	0.77	78	81	1.26	7	7	0.60	10	9	1.17
	≥ 1.0	21	25		13	17		15	9		19	20	
Paper	< 1.0	0	0	-	0	0	-	21	24	1.00	54	44	1.37
	≥ 1.0	1	1		0	0		27	31		60	67	
Chemical	< 1.0	24	31	0.60	20	20	0.69	16	11	2.11	55	35	1.51
	≥ 1.0	9	7		13	9		20	29		27	26	
Petroleum	< 1.0	11	16	0.63	11	5	1.47	17	17	0.68	32	24	1.65
	≥ 1.0	12	11		6	4		22	15		21	26	

Table 4. Modifying effect of industry of occupation, years of exposure or industry size on residential risk of lung cancer for selected industry types.^a

Industry type	Industry of occupation	Exposure time, yr		Adjusted residential estimate	
		Industry size		RR	RR
Petroleum ^b	Low risk	< 10 years		0.82	0.27-2.49
	Low risk ^d	≥ 10 years		1.34	0.41-4.33
	High risk	< 10 years		0.50	0.16-1.56
	High risk ^e	≥ 10 years		1.61	0.55-4.76
Chemical ^c	Low risk	< 100 employees		0.49	0.19-1.26
	Low risk ^f	≥ 100 employees		4.54	1.85-11.11
	High risk	< 100 employees		1.33	0.27-6.47
	High risk	≥ 100 employees		0.82	0.34-2.00

^aExcludes 21 cases and 18 controls exposed to chemical industry and 15 cases and 10 controls exposed to petroleum industry with unknown industry of occupation.

^bControlled for years of death, age, race, sex, and industry size.

^cControlled for year of death, age, race, sex and years of exposure.

^dDistance < 1.0 mile for 12 cases, 11 controls; distance ≥ 1.0 mile for 12 cases, 14 controls.

^eDistance < 1.0 mile for 22 cases, 11 controls; distance ≥ 1.0 mile for 13 cases, 12 controls.

^fDistance < 1.0 mile for 32 cases, 20 controls; distance ≥ 1.0 mile for 12 cases, 34 controls.

unmeasured exposures which may be related to distance from industry may be present, and have not been evaluated. No cigarette smoking history was obtained despite its known major contribution to lung cancer (8-11). However, the difference in observations resulting from the comparison of sev-

eral industry types suggests that the major observed effect is not likely to be due solely to cigarette smoking. Other unknown environmental exposures were controlled by limiting case-control comparison to within three miles of the industry under study. However, the degree of control that was obtained

Table 5. Occupational and residential risk estimates for the chemical and petroleum industries for lung cancer.

	Industry of occupation ^a	Residential proximity	Predicted risk ^b		Cases	Controls
			$\hat{R} \hat{R}$	RR		
Petroleum	+	+	2.27	1.04-4.92	36	23
	-	+	1.07	0.48-2.39	22	31
	+	-	2.52	1.12-5.66	34	20
	-	-	1.00		22	30
Chemical	+	+	2.56	1.27-5.16	41	26
	-	+	1.65	0.89-3.07	60	59
	+	-	2.72	1.27-5.81	33	19
	-	-	1.00		27	44

^aExcludes 23 cases and 20 controls exposed to chemical industry and 18 cases and 14 controls exposed to petroleum industry with unknown industry of occupation.

^bControlled for year of death, age, race, years of exposure and industry size.

by this method is unknown. Nevertheless, this methodology was selected, as it enabled a sufficiently large geographic area without many confounding industries, to be surveyed over a sufficient time period to acquire enough subjects from areas with limited population in which to examine residential risks. Deaths due to other neoplasms were excluded in the controls to avoid confounding as other cancers might also be associated with exposure to a particular industry in question, and interfere with the observation of a true risk.

Approximately 40% of cases and controls had quantitative information on residence. As these subjects had only minor demographic differences in comparison to those subjects with incomplete residence information, generalization of the results to the population under study seems justified. Within the set of subjects with complete information, cases and controls were comparable in their distributions of race, sex, and years of death. The age difference of less than two years between cases and controls was not felt to be a biasing factor in the risk estimates for this disease.

The combination of industries into type is based on the similarity of their raw materials and products, and on the assumption of a similarity in the type of effluent produced. Exposure to industry by type is examined for each subject for the time period during which the subject was in residence and the industry in operation. Effluent measurements by industry were not available for the residential areas for the time periods of interest.

Residence in proximity to multiple industries should be examined to determine whether cause of death may have been preferentially related to proximity to a combination of industries, rather than to a specific industry type. A crude exposure index could be constructed to represent a function of distance of residence from the plant, length of exposure, and size and type of the industry. This

could then be summed for all industrial exposures of a subject and used as a measure of total exposure to industrial effluents. This resulted in some positive results, but this approach precludes the identification, by type, of an industry particularly at high risk, and would be limited by the approximations used to combine industries by assuming similarities in products and effluents.

The duration of residence following exposure and prior to the onset of disease is unavailable from death certificate data. Date of diagnosis of disease is also unknown. For lung cancer, date of diagnosis and death are reasonable approximations of each other, and length of exposure to the time of death is an approximation of length of exposure to diagnosis. An assumption necessary for this study is that usual residence at death represents long-term residence at that address if it could have been validated. This assumption is warranted here due to the low mobility of the population in Louisiana, particularly in the parishes and age group selected for this study (1970 U.S. Census data).

The industries which did not produce elevated residential risk estimates, have not been reported to be associated with production of harmful effluents by others.

The cement and grain industries are known to release particulates (25). However, only for the grain industries was a slight elevation in residential risk, associated with 10 or more years exposure noted, and since only a small number of persons were available, no conclusions are warranted. In these parishes, grain industries have an average length of operation of five years longer than the cement industry. This suggests that the length of exposure to the cement industry may not be long enough to demonstrate a potential risk.

The slight elevation in residential risk for 10 or more years exposure to the food industry ($\hat{R} \hat{R} = 1.3$) is noteworthy, as a number of the industries in

this category are involved in the smoking of meats, which may result in a release of polycyclic hydrocarbons.

The kraft paper mill industry, which predominates in the southern states, releases a variety of sulfides into the surrounding atmosphere (26). A moderate elevation in residential risk to this industry was noted for large industries with longer exposure. This is somewhat supportive of the association between lung cancer mortality and county employment in the paper industry found by Blot and Fraumeni (17).

The industry groups involved with metals include the metal manufacturing, machine manufacturing and canning industries. While certain categories tended to show elevations in residential risk, both their inconsistency with respect to a causal hypothesis (decreasing risk with increasing exposure), and small sample size reduced the epidemiologic significance of these observations.

While both occupational and residential risk to lung cancer has been shown for certain primary metal foundries and smelters, (18, 27), none of these were represented among industries in this study.

The elevated residential risk to the petroleum industry (Table 3), for 10 or more years exposure, while not excluding 1.0 in the 95% confidence limit, is interesting in light of the variety and amount of hydrocarbons and gases released by these industries (28). The residential risk shown for this industry is shown for those with both low and high occupational risk, and long residential exposure (Table 4).

The strongest residential risk measured was for the chemical industry. Unlike that in the petroleum industry, the chemical industry risk was limited to large industries (approximately a twofold risk), regardless of length of exposure. A possible explanation for the differential risk in small and large industries is that only a limited number of the "small" industries were recorded as producing organic chemicals in the Directory of Manufacturers, while the majority of the "large" industries produce petrochemicals. Moreover, the aerial dispersion is likely to be more concentrated for "larger" industries. The observation of a residential risk to chemical industries at less than 10 years of exposure suggests that, in comparison to the petroleum effluents, a shorter period of exposure to these effluents may be sufficient for an effect.

The risk for residential exposure to the chemical industry was observed in those with only low risk occupational exposures. The 95% confidence interval of this 4.5-fold risk excluded 1.0. Therefore lower dose residential exposure for people in low risk occupations may result in a cumulative expo-

sure to chemical carcinogens similar to that of the high risk occupational group. Since a further increase in risk is not noted for those already exposed to high risk occupations, additional low level exposure may not be additive or synergistic. Therefore, it is reasonable that this effect would only be observable in those without occupational exposures. It is also possible that the high and low risk occupational groups differ with respect to variables not measured, e.g., cigarette smoking, amount of time spent at residence and distance of residence from industry.

The observation that length of exposure was not as important in the chemical industry as in the petroleum industry suggests an hypothesis on the mechanism of carcinogenesis. It is possible that short-term damage from chemical industry exposure can induce a lasting risk of lung cancer (like asbestos), while for the petroleum industry longer exposure is necessary for accumulation of carcinogenic agents (more similar to cigarette smoking).

It is unlikely that the risks observed for the petroleum and chemical industries are due to other confounding exposures likely to be found in all major industrial agglomerations, as these observations were not found to be associated with the several additional industries which were similarly examined.

That these observations result solely from other undefined socioeconomic factors is unlikely, as there is no reason to believe that these factors would be specific only to certain selected industries. Since the population under study is limited to deaths, some degree of care must be used in extrapolation to the general population due to differential factors in migration due to illness. Further studies to validate these results and obtain the necessary socioeconomic data should be through next-of-kin contact. Furthermore specific studies on those at risk to these industries need to be undertaken.

The overall residential risk to chemical or petroleum industries was lower than that found for occupation (Table 5). However, as the number of exposed individuals was approximately twice as high for residence than for occupation, the resulting attributable risk percent for occupation and residence is equal, at approximately 3-4%.

Thus, the findings of this study suggest that residential proximity to the petroleum, and chemical industries may be an important risk factor for lung cancer in Louisiana. The consistency of the data and corroboration of other studies, in terms of both positive and negative findings by industry types, lend validity to the observations. The importance of residential risk to industries on a national level is unknown, but could be far more significant in terms of the numbers of exposed individuals than

occupational exposure. Further research is required to validate the findings of this study, and to assess the true attributable risk percent, which is likely to be much higher than can be assessed through death certificate information where only the last usual residence is known, and information on other critical variables is unavailable.

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