

Fluoridated Drinking Water and the Occurrence of Cancer¹

Robert N. Hoover, M.D.,² Frank W. McKay,² and Joseph F. Fraumeni, Jr., M.D.^{2, 3}

ABSTRACT—A recent report by the National Health Federation, a private agency, related cancer mortality patterns in the United States to fluoridation of water supplies, triggering much public health concern and some political response. To clarify the issues raised, we studied cancer mortality and incidence statistics for U.S. counties, 1950–69. No trends could be ascribed to the consumption of water that is artificially or naturally fluoridated.—*J Natl Cancer Inst* 57: 757–768, 1976.

A recent report in the Congressional Record (1) linked cancer mortality patterns in certain counties of the United States to artificial fluoridation of water supplies. Because of the medical and public health concerns raised by this finding, we analyzed cancer mortality trends in counties where the water supply has been artificially or naturally fluoridated to see if we could uncover similar trends—after taking into account the demographic variables known to affect cancer incidence and mortality.

If fluoride does affect cancer mortality, one would expect a change in cancer risk in both sexes subsequent to the artificial fluoridation of communities. If the pattern resembles that for carcinogenic exposures generally, there should be a time lag between artificial fluoridation and the change in risk (latent period) and variations in risk within naturally fluoridated areas in a manner suggesting a dose-response relationship.

These issues were evaluated by two studies: 1) a comparison of cancer mortality in areas using water containing various levels of natural fluoride and 2) an analysis of mortality trends in areas in which the water has been artificially fluoridated.

NATURAL FLUORIDATION STUDY

Methods

The measures of exposure to natural fluorides were obtained from a special listing provided by the Division of Dentistry (DHEW), wherein communities and their natural fluoride content as published in a census of natural fluoridation (2) are arranged by county. The natural fluoridation study was conducted in Texas, since the number of counties in this State is large and a substantial population is exposed to markedly varying levels of natural fluoride. A similar study could be done for the entire United States, with adjustment for geographic region. Confining our study to Texas permitted a meaningful comparison without further "regional" adjustment. A county was included as a "fluoride county" if more than two-thirds of the inhabitants (1960 census) resided in communities exposed to 0.7 ppm or more (the minimum value reported in the natural fluoridation census). We calculated estimates of the relative amount of fluoride to which the population was exposed by using the level of fluoridation reported for each community multiplied by the proportion of the total population of all naturally fluoridated communities in

the particular county. Given these estimates, counties were classified as intermediate (0.7–1.2 ppm), high (1.3–1.9 ppm), or very high (2.0+ ppm) exposure counties. Control counties were those Texas counties in which no community was listed in the natural fluoridation census. Counties with artificially fluoridated water were excluded. Since the data on fluoridation were restricted to community water supplies, the study was restricted to those counties listed as at least 50% urban (1960 census definition). Appendix table 1 lists the counties included in each group.

Demographic, social, and economic characteristics of counties were ascertained from the 1960 census of the population. The following measures previously shown to be related to cancer mortality were used: percent urban, median number of years of schooling completed by the population over the age of 25, percent nonwhite, and percent foreign stock.

Age-, race-, and sex-specific numbers of cancer deaths, coded according to the International Classification of Diseases, were provided by the National Center for Health Statistics for each county of the United States from 1950 through 1969. The county specified was the usual residence of the decedent. Age-, race-, and sex-specific population estimates for these counties were obtained by linear interpolation of census figures. Age-standardized death rates from cancer of 35 sites (Appendix table 2) were calculated among white males and females for the entire 20-year period, 1950–69. The analyses were limited to whites because the population estimates were more reliable. The standard used was the age distribution of the entire 1960 U.S. population (5-yr age groups through ages 74, 75–84, and 85+).

Cancer incidence rates for two metropolitan areas—Birmingham, Alabama, and Denver, Colorado—were obtained from the Second (1947–48) and Third (1969–71) National Cancer Surveys (3, 4). The data for Denver from the Third Survey were divided from the reported statewide data for Colorado by special tabulation.

Throughout this report, cancer sites are considered in two groups—those under suspicion of being related to fluoride and those for which there is no a priori suspicion. Those sites under suspicion are the ones identified in the National Health Federation report (1) and two other sites (thyroid and bone) that others thought might be related to fluoride on biologic grounds (5). In most

ABBREVIATIONS USED: SMR=standardized mortality ratio; SMSA=standardized metropolitan statistical area; RR=relative risk.

¹ Received December 2, 1975; accepted April 2, 1976.

² Environmental Epidemiology Branch, National Cancer Institute, National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare (DHEW), Bethesda, Md. 20014.

³ We thank K. Beckwith, F. Favali, M. Harren, N. Jones, and R. Weil for technical assistance; D. Peterson for manuscript preparation; and Drs. W. Blot, D. Byar, T. Mason, R. Miller, and M. Schneiderman for advice and critical review.

tables, the sites examined with a priori suspicion are listed first and separated from the other sites by a dotted line.

Statistical Analyses

When controlling for urbanization and socioeconomic class, we used the SMR as the measure for comparison. To compute SMR's, all those counties in a particular stratum of the covariables were identified (e.g., high social class-high urbanization). The age-specific mortality rates in each stratum were then applied to the appropriate person-years in each fluoride-exposure group. This gives an "expected number" of cases. For each group, the expected values in each stratum were then summed and compared to the total number of actually observed deaths. The ratio of the observed-to-expected deaths is the SMR. Where appropriate, 95% confidence intervals for an SMR were computed (6). If the 95% confidence interval does not include 1.0 (SMR=1.0 when the observed number is the same as the expected), then the SMR would be considered significantly different from the expected ratio at the 5% level (i.e., $P < 0.05$).

Weighted regression analyses were also used that related cancer mortality (the age-adjusted rate by sex in each county) to various explanatory variables. These variables were the measures of demographic and socioeconomic characteristics for each county described above and a measure of fluoridation. The measure of fluoride was the midpoint in ppm of the group to which a county belonged (2.8 was used for the 2.0+ group—its median). For each county, the weighting factor used was directly proportional to the square root of the total county population, and hence inversely proportional to the standard error of the mortality rates. We attempted to account for the variation in mortality in two ways: 1) how much variation can be accounted for by all these demographic variables and 2) how much can be accounted for by these variables plus a "fluoride" variable. If the total accounted for is significantly increased (F -test) by the addition of the fluoride variable, then we can conclude that fluoride has a significant association with cancer mortality (7). The measure of strength of the association is the regression coefficient associated with the fluoride variable.

The measure of the relative difference between the incidence rates in the two areas used from the National Cancer Surveys is the maximum likelihood estimate of the summary relative risk, obtained after stratification on a control variable (age). The methods used to obtain this estimate and its confidence intervals are described by Gart (8) and incorporated in a computer program by Thomas (9).

Results

The Texas counties, after having been classified by level of natural fluoride, were subdivided further by percent urbanization and socioeconomic categories. The urbanization groups ($\geq 71\%$ urban and $< 71\%$ urban) were categorized further by socioeconomic class

groups based on the median number of years of school completed by the adult population of each county (≥ 10.2 yr and < 10.2 yr). We then calculated the expected values for each grouping of counties according to fluoride level, controlling for urbanization and socioeconomic class. The resulting SMR's and numbers of observed deaths are given in table 1. If a grouping of counties by fluoride category contained less than 5 deaths, it was added, when possible, to another category in table 1.

If natural fluoridation does affect cancer risk, we should see a steady increase in the SMR's with increasing levels of fluoride. The SMR's for all sites combined in white males and females were remarkably uniform (1.0 for each fluoride level up to the highest level, where the SMR falls to only 0.9 for both sexes). Little variation by fluoride level was seen for any cancer site. Among the sites previously linked to fluoride, two sites (mouth and throat, and esophagus) in men showed a consistent linear trend in SMR's. The trends, however, were opposite from what was expected, going down rather than up with increasing fluoride level. Among women, there was no equivalent trend for mouth and throat cancer, but the pattern for esophagus cancer was similar to that in men, namely, in the reverse direction from what was expected. Among other cancers, two sites (rectum, bone) showed peculiarities, but again the lowest SMR's were in the highest fluoride level. The figures for bone cancer were based on small numbers, with confidence limits around both SMR's including 1.0, and showed little evidence of any trend. On the other hand, the figures for rectal cancer were based on substantial numbers, with the 95% confidence limits not including 1.0 for the males (extending to 1.2 for females) and showed a downward trend with increasing fluoride concentration.

In four instances (3 sites), the SMR for the controls was below 1.0, but the upper bounds of the 95% confidence intervals included 1.0.

For cancer sites not under a priori suspicion, one cancer (skin) showed a consistent linear trend. The trend ran in the opposite direction to fluoride exposure and was limited to women. Although the lowest SMR for skin cancer was in the highest fluoride category among men also, there was no evidence of a trend. In addition, the SMR's in the last category for men and in the last two for women were based on small numbers and the 95% confidence intervals all included 1.0.

Four other sites showed extreme SMR's (either largest or smallest) in the highest fluoride category among males and females. In three instances—"other endocrine" cancers, connective-tissue cancers, and Hodgkin's disease—the 95% confidence limits included 1.0, and no trend was found (i.e., SMR for controls being ≥ 1.0 in 5 of 6 site-sex comparisons). For cancers of the brain and other parts of the nervous system, the lowest SMR was in the highest fluoride category for both sexes (0.7 in both) and the highest SMR (1.2) for both sexes occurred in the control counties. The lower bound of the SMR for the control counties was 1.0 for both sexes. The upper bound for the low SMR in the highest fluoride grouping

TABLE 1.—Site- and sex-specific SMR's and observed number of cancer deaths (1950-69) in counties in Texas grouped according to natural fluoride levels

Site	Sex	Levels of natural fluoride ^a				Site	Sex	Levels of natural fluoride ^a			
		Control	Inter-mediate	High	Very high			Control	Inter-mediate	High	Very high
All sites combined	♂	1.0(4,467)	1.0(10,721)	1.0(2,960)	0.9(1,174)	Nose and nasal sinuses	♂	1.1(15)	1.1(36)	0.8(10)	
	♀	1.0(3,707)	1.0(9,517)	1.0(2,385)	0.9(994)		♀	1.2(7)	0.7(10)	2.0(9)	
Mouth and throat	♂	1.1(123)	1.0(280)	0.8(58)	0.7(20)	Larynx	♂	1.1(65)	1.1(198)	0.6(25)	1.3(22)
	♀	1.0(33)	1.0(89)	1.2(26)	0.9(8)		♀	0.7(5)	1.1(28)	1.1(7)	
Esophagus	♂	1.1(87)	1.0(203)	0.9(46)	0.8(18)	Lung	♂	1.0(999)	1.0(2,534)	1.0(761)	0.8(257)
	♀	1.2(48)	1.0(95)	1.0(20)	0.6(5)		♀	0.9(192)	1.0(551)'	1.0(140)	1.0(57)
Stomach	♂	1.0(375)	1.0(914)	1.1(239)	1.1(112)	Cervix	♀	0.9(247)	1.1(859)	1.0(204)	0.9(74)
	♀	1.0(236)	1.0(583)	1.0(122)	1.0(55)		Uterus	♀	1.0(187)	1.0(448)	1.1(111)
Colon	♂	1.0(306)	1.0(724)	1.0(195)	0.9(75)	Prostate		♂	1.0(507)	1.0(930)	1.0(226)
	♀	1.1(430)	1.0(809)	1.0(239)	1.0(107)		Testis	♂	0.9(21)	1.1(83)	0.7(16)
Rectum	♂	1.1(102)	1.0(242)	1.0(63)	0.6(18)	Melanoma		♂	1.0(62)	0.9(127)	1.2(66)
	♀	1.0(85)	1.1(213)	0.9(51)	0.8(20)		♀	0.9(50)	1.0(113)	1.2(44)	1.0(16)
Kidney	♂	1.1(121)	1.0(235)	1.2(84)	0.6(19)	Other skin	♂	1.0(79)	1.0(138)	1.0(41)	0.9(17)
	♀	1.0(68)	1.0(163)	1.0(46)	1.2(23)		♀	1.1(40)	1.0(74)	0.8(13)	0.7(5)
Bladder	♂	1.0(120)	1.0(331)	1.1(88)	1.0(36)	Eye	♂	1.5(13)	0.9(19)	1.0(7)	
	♀	0.9(65)	1.0(162)	1.2(46)	0.7(12)		♀	1.3(10)	0.7(7)	1.6(7)	
Thyroid	♂	0.8(8)	1.2(22)	1.1(7)		Brain	♂	1.2(125)	1.0(329)	1.0(114)	0.7(32)
	♀	0.6(9)	1.3(74)	0.7(12)			♀	1.2(102)	1.0(234)	1.1(85)	0.7(22)
Bone	♂	1.0(40)	1.0(118)	1.2(39)	0.6(8)	Other endo- crine	♂	1.0(9)	0.9(22)	1.4(15)	
	♀	0.9(27)	1.1(70)	0.9(14)	0.8(5)		♀	1.0(5)	0.9(13)	1.6(8)	
Breast	♀	1.0(567)	1.0(1,589)	1.0(429)	1.0(186)	Connective tis- sue	♂	1.0(14)	0.9(43)	1.5(20)	1.8(7)
Ovary	♀	1.1(239)	1.0(544)	1.0(155)	0.9(56)		♀	0.9(12)	1.1(43)	0.9(11)	1.9(8)
Lip	♂	1.1(8)	0.9(19)	0.9(5)	2.4(5)	Hodgkin's dis- ease	♂	1.0(57)	1.1(141)	0.7(30)	1.4(24)
	♀	(Total of only 6 cases among women)					♀	1.1(30)	1.1(84)	0.6(16)	1.4(14)
Salivary gland	♂	0.9(15)	1.2(43)	0.9(10)		Other lym- phoma	♂	0.8(109)	1.1(351)	1.0(97)	0.9(38)
	♀	1.1(8)	1.0(18)	1.5(7)			♀	1.0(99)	1.0(237)	1.1(73)	1.1(31)
Nasopharynx	♂	1.8(16)	0.9(22)	0.9(8)		Multiple mye- loma	♂	1.2(51)	0.9(103)	1.2(40)	0.7(10)
	♀	1.2(16)		0.5(2)			♀	0.9(23)	0.9(59)	1.5(27)	1.7(13)
Liver and bile duct	♂	1.0(162)	1.1(410)	0.8(69)	0.8(30)	Leukemia	♂	1.0(252)	1.0(676)	1.0(186)	1.0(82)
	♀	0.9(160)	1.1(528)	0.7(78)	0.9(39)		♀	1.0(202)	1.1(485)	0.9(119)	0.9(54)
Pancreas	♂	1.0(280)	1.0(638)	1.1(198)	1.1(85)	Other and un- specified	♂	1.0(319)	1.0(774)	1.0(211)	0.9(83)
	♀	1.1(199)	1.0(465)	0.9(108)	1.2(60)		♀	1.0(318)	1.0(854)	0.9(170)	0.9(73)

^a Numbers of deaths are in parentheses.

was 1.0 for the males and 1.1 for the females.

To gain better control for urbanization, socioeconomic class, and other relevant variables, weighted multiple regression analyses were performed. We tried to explain sex- and site-specific cancer mortality by considering the percent urban, median school years completed by the adult population, percent of the total population who were nonwhite, and percent of the white population who were of foreign stock (first and second generation). As a second step, the weighted average fluoride concentration for each county was included as a possible "explanatory" model and its effect tested for statistical

significance. For total cancer, the fluoride variable was negatively related with the age-adjusted mortality rate (regression coefficient = -3.01 for males and -1.50 for females). This negative association did not approach statistical significance (at the 0.05 level). In four sex-site breakdowns, the fluoride variable significantly increased the amount of variation that could be explained; these were rectal cancer in males, ovarian cancer in females, and brain cancer in males and females. In each instance the association was reversed—higher fluoride concentrations associated with lower mortality rates. In 64 independent tests of significance, we might expect 3

to occur by chance alone (at the 0.05 level). The association with brain cancer might be worth looking into, however, since it occurs for both sexes and is consistent with the SMR analyses.

ARTIFICIAL FLUORIDATION STUDY

Methods

To study the effects of artificial fluoridation, calculations were made of the proportion of the population in each U.S. county, by 5-year interval, residing in communities where the water supply was artificially fluoridated. We did these calculations by hand using the published census of artificial fluoridation (10). Since the emphasis here is on time trends, counties were included for study when communities comprising at least two-thirds of the total county population (1960 census) were first fluoridated in one of three time intervals (1950-54, 1955-59, or 1960-64). Control counties were those in which no communities artificially fluoridated their water supply before 1970. Counties with communities having naturally fluoridated water systems were not eliminated from either exposed or control group. Such an exclusion was not necessary, since the natural fluoridation study, which was done first, revealed essentially no effect of natural fluoridation on cancer risk. Even if there were such an effect, it would be constant and thus controlled for by our study design, which was a trend analysis of differences in risk over time related to the onset of artificial fluoridation. Appendix table 3 lists the counties in each grouping.

The sources of data for deaths and populations at risk were the same as those described for the natural fluoridation study. However, since this analysis was based on time trends, age-adjusted rates were also calculated for the 5-year intervals (pentads) 1950-54, 1955-59, 1960-64, and 1965-69 for each grouping of counties.

The measure of association used was the ratio of the age-adjusted rates in the several groupings of fluoridated counties to that in the control counties. Summary SMR's were also calculated for 5-year intervals before, during, and after fluoridation. The method of calculation of these SMR's was the same as that described for the natural fluoridation study, only in this instance the control variable on which the data were stratified was calendar time, in the 5-year intervals used. The standard set of age-specific rates used to generate the expected values were those prevailing in the control counties in each calendar time grouping.

A regression analysis similar to that used in the natural fluoridation study was also used to reanalyze the report in the Congressional Record (1). However, since this involved only artificial fluoridation, the fluoride variable was dichotomous ("1" for a fluoridated county and "0" for a nonfluoridated one). Since this analysis also involved large urban areas throughout the United States, two additional demographic variables were taken from the U.S. census—percent of the employed engaged in manufacturing industries and geographic region of the county.

Results

The effect of artificial fluoridation was evaluated by the difference in mortality rates between counties in which no community was artificially fluoridated in the 20-year period and counties that underwent rapid and massive fluoridation in one of the first three pentads. This comparison made possible the calculation of ratios of rates in fluoridated counties to those in nonfluoridated counties in various time intervals before, during, and up to 15 years after fluoridation. Since all but one of the fluoridated counties were greater than two-thirds urban (the exception being 60% urban), comparison was made with nonfluoridated counties that were at least two-thirds urban in 1960. (In addition, ratios were calculated for all nonfluoridated counties and yielded results consistent with those presented here.)

The percent of the population exposed to fluoridation in the 5-year interval for each group of counties was: 86% in 1950-54, 84% in 1955-59, and 74% in 1960-64.

If fluoridation increases cancer risk, then the ratios of age-adjusted cancer deaths in fluoridated to nonfluoridated counties should increase with time after fluoridation. This trend was not seen for men or women (table 2). The rates for both men and women in the counties fluoridated in 1950-54 were 10% greater than those in the nonfluoridated counties in 1950-54, and in each successive 5-year interval. The results for counties fluoridated in 1955-59 and 1960-64 were similar and established the consistency of the ratios 5 and 10 years before the fluoridation. It is important to note that for counties fluoridated after 1954 (i.e., counties for which we have prefluoridation and postfluoridation data), the rates were higher before fluoridation than in the control counties.

The summary line of table 2 gives SMR's for each 5-year grouping. These SMR's control for calendar time differences in giving summary estimates for each of the fluoridation-related time periods. For all sites combined, these estimates showed no important variation in risk over time—the same observation noted in the detail of table 2.

Table 3 presents these summary SMR's with the total numbers of observed deaths for each cancer site in men and women. Except for some rare sites, most comparisons were based on large numbers of deaths and provided stable estimates.

The uniformity of the SMR's over time is striking. For the 11 sites chosen because of a priori suspicion, three showed an SMR in both sexes 15 years after fluoridation that was different from the one 5 years before fluoridation (stomach, colon, and bone); but in each instance the SMR was lower after fluoridation. However, for colon cancer in both sexes and bone cancer among women, the postfluoridation SMR's were the same as those computed for the 5-year period when fluoridation took place.

The SMR's for sites without a priori suspicion also showed only small changes with time. Specific attention was given to sites in which 1) the SMR's 15 years after

TABLE 2.—Ratios of age-adjusted cancer mortality rates (all sites) in fluoridated counties to those in control counties in 5-year intervals (pentads), by pentad of fluoridation and sex^a

Pentad of fluoridation	Prior to fluoridation		Ratio in pentad of fluoridation	After fluoridation		
	10 yr	5 yr		5 yr	10 yr	15 yr
Males:						
1950-54			1.11	1.12	1.11	1.10
1955-59		1.17	1.15	1.16	1.12	
1960-64	1.02	1.03	1.02	1.03		
Summary SMR	1.01	1.16	1.12	1.13	1.11	1.10
	(3,123)	(36,873)	(76,858)	(83,697)	(82,583)	(47,111)
Females:						
1950-54			1.10	1.10	1.09	1.09
1955-59		1.13	1.13	1.13	1.12	
1960-64	1.01	1.05	1.02	1.06		
Summary SMR	1.01	1.13	1.11	1.11	1.10	1.09
	(2,873)	(32,864)	(69,985)	(73,168)	(71,688)	(41,166)

^a Summary SMR's for each interval are also provided based on total numbers of deaths (in parentheses).

fluoridation were above or below the SMR's for the pentads before and during fluoridation, and 2) the variation was in the same direction for both sexes. Three sites showed a slight upward trend, and three a slight downward trend. A detailed breakdown is given in table 4. In every instance there was no evidence of a trend that was consistent between the three study groups of fluoridated counties.

Further analysis was made of counties in which communities containing 80% or more of the population were fluoridated in one of the 5-year periods specified. This examination was confined to counties fluoridated in 1950-54 and in 1955-59, since only one small county was 80% fluoridated in 1960-64. The weighted average population receiving fluoridated water in the 1950-54 group was 95%. The weighted average for the group fluoridated in 1955-59 was 96% of the population.

The ratios for all sites combined are given in table 5. The ratios did not increase over time as would be expected if fluoride exposure increased cancer risk. Three of the 11 a priori selected sites showed a trend in both sexes among the counties fluoridated in the early 1950's—mouth and throat, colon, and kidney. The ratios of the age-adjusted rates for these cancers are given in table 6. The trend was upward for mouth and throat cancers and downward for colon and kidney cancers, but the differences were minimal. In most instances the data from counties fluoridated in 1955-59 did not show a similar trend. None of the other sites analyzed gave any consistent evidence of either a positive or negative correlation with fluoridation.

Incidence data, although sparse, might uncover a trend before its appearance in mortality statistics. Some use can be made of information from the Second and Third National Cancer Surveys. The Second Survey was conducted in 1947-48 in ten metropolitan areas in the United States, and the Third Survey in seven metropolitan areas and two States in 1969-71. There were seven areas included in both surveys. Birmingham was chosen as the control area for our comparison; it was the only location remaining largely unfluoridated in the years after the Second Survey (only 3.2% of the 1970 SMSA

was fluoridated by 1970). Denver was chosen as the fluoridated area most likely to uncover an effect on cancer risk; it was not fluoridated in 1947-48, but by 1955, 66% of the 1970 SMSA had been fluoridated. All of the other areas common to both surveys had undergone significant fluoridation by 1970, but Denver had the most massive fluoridation immediately after the Second Survey. Ratios of rates in Denver versus Birmingham are presented in table 7. There were 22 comparisons made for the sites chosen with a priori suspicion; in 9 instances the ratio went up, in 8 it went down, and in 5 it remained the same. The ratio moved in the same direction in both sexes for only 2 tumors—up for esophagus and down for bone. For the 22 comparisons made for other sites, in 10 instances the ratio went up, in 11 it went down, and in 1 it remained the same. Table 8 gives the estimate of the summary relative risk (Denver relative to Birmingham) after stratification on age for all cancers combined (minus skin). The point estimates changed very little. In addition, the relative risks for the Third Survey fell well within the confidence limits of the Second, indicating no statistically significant differences. Also, there were no significant differences for sites in which both sexes showed similarities in trends (esophagus, bone, small intestine, liver, lung, Hodgkin's disease, "other lymphomas," and leukemia), or for the sexual and reproductive sites.

DISCUSSION

This study provides no support for recent claims that the fluoridation of water supplies in the United States has increased the risk of cancer. No significant excess mortality from cancer could be detected up to 15 years after fluoridation in areas where 95% of the population were abruptly and then continuously exposed.

The possibility that a latent period longer than 15 years may be involved was evaluated by a study of communities long exposed to natural fluoride at various levels. The risk of cancer was not elevated in these areas, in accord with findings from the United Kingdom (5, 11). Since both artificial and natural fluoridation exposures reduce the risk of dental caries, it seems likely that

TABLE 3.—SMR's and number of deaths in fluoridated counties in 5-year intervals (pentads) related to pentad of fluoridation^a

Site	Sex	Prior to fluoridation		Ratio in pentad of fluoridation	After fluoridation		
		10 yr	5 yr		5 yr	10 yr	15 yr
Mouth and throat	♂	1.1(100)	1.3(1,228)	1.3(2,581)	1.3(2,695)	1.3(2,654)	1.3(1,491)
	♀	1.3(25)	1.0(195)	1.1(509)	1.1(622)	1.0(673)	1.1(454)
Esophagus	♂	1.0(80)	1.7(1,444)	1.5(2,619)	1.4(2,546)	1.4(2,335)	1.3(1,244)
	♀	0.7(15)	1.1(252)	1.1(571)	1.1(609)	1.1(641)	1.1(382)
Stomach	♂	1.0(352)	1.3(4,509)	1.2(8,053)	1.2(6,971)	1.2(5,597)	1.0(2,454)
	♀	0.9(205)	1.2(2,630)	1.2(5,143)	1.1(4,340)	1.1(3,655)	1.0(1,671)
Colon	♂	1.2(320)	1.3(3,695)	1.3(7,519)	1.3(8,199)	1.2(8,037)	1.2(4,497)
	♀	1.0(342)	1.2(4,092)	1.1(8,604)	1.2(9,733)	1.2(9,433)	1.1(5,368)
Rectum	♂	1.2(185)	1.4(2,179)	1.3(4,241)	1.3(4,095)	1.3(3,463)	1.2(1,673)
	♀	1.0(123)	1.2(1,532)	1.2(3,040)	1.2(2,979)	1.1(2,556)	1.2(1,390)
Breast	♀	1.1(556)	1.2(6,403)	1.1(13,833)	1.2(14,986)	1.1(14,631)	1.1(8,331)
Ovary	♀	1.1(186)	1.2(2,202)	1.1(4,568)	1.2(5,096)	1.1(4,969)	1.1(2,802)
Kidney	♂	1.1(76)	1.1(785)	1.2(1,796)	1.2(1,946)	1.1(1,889)	1.1(1,009)
	♀	1.2(44)	1.3(517)	1.1(991)	1.1(1,142)	1.0(1,072)	1.0(633)
Bladder	♂	1.0(134)	1.2(1,589)	1.1(3,211)	1.2(3,411)	1.1(3,116)	1.1(1,649)
	♀	1.0(55)	1.2(678)	1.2(1,448)	1.2(1,472)	1.1(1,374)	1.2(839)
Thyroid	♂	1.4(13)	1.2(118)	1.1(210)	1.3(222)	1.2(197)	1.1(93)
	♀	0.8(13)	1.1(185)	1.3(468)	1.2(417)	1.0(332)	1.1(191)
Bone	♂	0.9(28)	1.2(351)	1.1(642)	1.1(597)	1.1(499)	1.0(269)
	♀	1.1(23)	1.1(216)	1.0(438)	1.1(413)	1.1(358)	1.0(173)
Lip	♂	0.8(7)	1.0(91)	0.8(138)	1.1(128)	0.9(67)	1.2(41)
	♀	0.0(0)	0.6(5)	0.8(13)	0.9(13)	1.1(12)	1.3(6)
Salivary gland	♂	0.6(5)	1.0(88)	1.2(214)	1.3(242)	1.1(200)	1.1(96)
	♀	0.7(4)	0.9(52)	1.1(132)	1.1(136)	1.1(136)	1.0(63)
Nasopharynx	♂	1.0(6)	1.3(87)	1.2(190)	1.2(220)	1.1(207)	1.2(117)
	♀	1.8(4)	1.0(24)	1.3(68)	1.0(64)	1.1(72)	0.9(32)
Liver and bile duct	♂	0.9(105)	1.2(1,316)	1.1(2,578)	1.1(2,481)	1.1(2,168)	1.2(1,126)
	♀	1.0(135)	1.3(1,745)	1.2(3,288)	1.2(3,071)	1.2(2,683)	1.1(1,278)
Pancreas	♂	1.1(171)	1.1(1,797)	1.1(3,946)	1.1(4,506)	1.0(4,475)	1.0(2,580)
	♀	0.9(100)	1.1(1,287)	1.1(2,811)	1.1(3,282)	1.1(3,502)	1.0(1,980)
Nasal sinus	♂	0.7(6)	1.1(100)	1.1(199)	1.1(193)	1.0(173)	1.0(97)
	♀	1.4(9)	1.0(67)	0.9(116)	1.1(126)	1.1(114)	1.0(65)
Larynx	♂	1.0(49)	1.3(700)	1.3(1,429)	1.2(1,475)	1.2(1,411)	1.2(785)
	♀	1.3(6)	1.0(45)	1.1(119)	1.0(115)	1.1(149)	1.1(94)
Lung	♂	1.0(525)	1.1(6,682)	1.1(15,280)	1.1(19,605)	1.1(21,781)	1.1(13,555)
	♀	1.1(110)	1.2(1,256)	1.1(2,672)	1.0(3,282)	1.0(4,162)	1.1(2,961)
Melanoma	♂	0.9(24)	0.7(202)	0.8(508)	0.9(614)	0.9(698)	0.9(424)
	♀	1.0(20)	0.8(169)	0.9(447)	0.9(479)	0.9(539)	0.9(361)
Skin	♂	1.1(35)	0.8(233)	0.8(529)	0.9(562)	0.9(473)	1.0(253)
	♀	1.2(22)	0.8(155)	1.0(387)	0.9(324)	1.0(288)	1.0(155)
Eye	♂	0.9(4)	1.4(66)	0.9(86)	1.1(99)	1.1(89)	1.3(52)
	♀	1.3(5)	1.2(47)	1.2(105)	1.1(95)	1.1(92)	1.0(51)
Brain and other parts of nervous system	♂	1.2(91)	1.1(892)	1.1(1,903)	1.1(2,081)	1.1(2,042)	1.1(1,207)
	♀	1.0(52)	1.2(671)	1.1(1,356)	1.1(1,534)	1.0(1,519)	1.0(909)
Other endocrine glands	♂	0.6(5)	0.8(69)	1.0(168)	1.0(169)	1.1(151)	0.8(61)
	♀	0.5(2)	1.1(48)	1.0(94)	1.0(105)	1.1(112)	1.0(55)

TABLE 3.—Continued

Site	Sex	Prior to fluoridation		Ratio in pentad of fluoridation	After fluoridation		
		10 yr	5 yr		5 yr	10 yr	15 yr
Connective tissues	♂	0.9(10)	0.8(89)	1.0(239)	1.0(280)	1.1(313)	1.2(222)
	♀	1.1(9)	0.9(77)	1.1(214)	1.0(251)	1.0(275)	1.0(165)
Hodgkin's disease	♂	0.9(41)	1.0(467)	1.0(1,011)	1.1(1,063)	1.0(923)	1.1(569)
	♀	1.3(35)	1.1(320)	1.0(635)	1.0(697)	1.2(764)	1.1(386)
Other lymphomas	♂	0.9(70)	1.1(890)	1.1(2,050)	1.1(2,382)	1.1(2,426)	1.1(1,332)
	♀	0.8(39)	1.2(653)	1.2(1,533)	1.1(1,799)	1.1(2,052)	1.1(1,246)
Multiple melanoma	♂	0.9(22)	0.9(258)	1.0(632)	1.0(748)	1.0(811)	1.1(527)
	♀	1.0(17)	1.0(192)	1.2(556)	1.1(699)	1.0(708)	1.0(432)
Leukemia	♂	1.1(166)	1.1(1,635)	1.0(3,335)	1.1(3,860)	1.1(3,817)	1.0(2,108)
	♀	1.2(129)	1.1(1,208)	1.1(2,737)	1.1(2,947)	1.0(2,879)	1.1(1,777)
Other	♂	1.0(203)	0.9(1,923)	1.0(4,436)	1.0(4,682)	1.1(5,173)	1.2(3,400)
	♀	0.8(184)	0.9(2,042)	1.0(4,844)	1.0(4,871)	1.1(5,383)	1.2(3,678)
Cervix	♀	1.1(235)	0.9(1,889)	1.0(4,490)	1.0(4,101)	1.1(3,563)	1.1(1,824)
Corpus uteri	♀	1.0(169)	1.2(2,010)	1.1(3,755)	1.2(3,368)	1.2(3,000)	1.0(1,414)
Prostate	♂	0.9(275)	1.1(3,143)	1.0(6,565)	1.1(7,104)	1.1(6,896)	1.1(3,933)
Testis	♂	0.5(9)	1.0(174)	1.2(425)	1.1(375)	1.2(391)	0.9(175)

^a Number of deaths are *in parentheses*.

TABLE 4.—Ratios of age-adjusted cancer mortality rates in fluoridated counties to those in control counties in 5-year intervals (pentads), by pentad of fluoridation and sex for 6 cancer sites^a

Site	Pentad of fluoridation	Prior to fluoridation		Ratio in pentad of fluoridation	After fluoridation		
		10 yr	5 yr		5 yr	10 yr	15 yr
Males:							
Lip	1950-54			0.95(94)	1.00(82)	0.87(39)	1.18(41)
	1955-59		1.08(83)	0.62(39)	1.24(43)	1.01(28)	
	1960-64	0.79(7)	1.08(8)	1.15(5)	0.92(3)		
Pancreas	1950-54			1.06(1,867)	1.05(2,173)	1.02(2,341)	1.04(2,580)
	1955-59		1.05(1,578)	1.09(1,867)	1.12(2,096)	1.08(2,134)	
	1960-64	1.10(171)	1.16(219)	0.99(212)	1.00(237)		
Testis	1950-54			1.15(228)	1.10(206)	1.18(206)	0.88(175)
	1955-59		1.01(153)	1.26(183)	1.18(154)	1.27(185)	
	1960-64	0.53(9)	1.21(21)	0.89(14)	0.84(15)		
"Other and unspecified"	1950-54			1.05(2,397)	1.11(2,583)	1.19(2,913)	1.20(3,400)
	1955-59		0.89(1,728)	0.95(1,823)	0.90(1,803)	1.01(2,260)	
	1960-64	0.98(203)	0.92(195)	0.94(216)	1.09(296)		
Females:							
Lip	1950-54			1.00(10)	0.97(8)	0.96(7)	1.36(6)
	1955-59		0.67(5)	0.50(3)	0.91(5)	1.43(5)	
	1960-64	— (0)	— (0)	— (0)	— (0)		
Pancreas	1950-54			1.06(1,358)	1.01(1,603)	1.05(1,850)	1.01(1,980)
	1955-59		1.12(1,141)	1.07(1,329)	1.10(1,509)	1.11(1,652)	
	1960-64	0.90(100)	1.06(146)	0.79(124)	0.96(170)		
Cervix uteri	1950-54			1.04(2,525)	1.03(2,384)	1.04(2,181)	1.08(1,824)
	1955-59		0.86(1,681)	0.93(1,714)	0.94(1,532)	1.07(1,382)	
	1960-64	1.13(235)	1.03(208)	1.33(251)	1.19(185)		
Corpus uteri	1950-54			1.06(2,054)	1.11(1,790)	1.08(1,626)	1.03(1,414)
	1955-59		1.20(1,867)	1.22(1,556)	1.23(1,444)	1.31(1,374)	
	1960-64	1.01(169)	1.01(143)	1.07(145)	1.07(134)		
"Other and unspecified"	1950-54			1.04(2,737)	1.15(2,849)	1.18(3,077)	1.25(3,678)
	1955-59		0.86(1,799)	0.97(1,872)	0.86(1,730)	1.03(2,306)	
	1960-64	0.81(184)	1.12(243)	1.00(235)	1.06(292)		

^a Total number of deaths on which the rates in the fluoridated counties are based are *in parentheses*.

other biologic effects would be similar (12). Of possible importance was the reduced mortality from cancers of the brain and nervous system in communities with high levels of natural fluoride. This finding might be due to chance, because of the multiple comparisons made in this analysis, but additional observations in other areas seem indicated.

Since demographic factors such as urbanization, socioeconomic class, and ethnicity affect cancer rates, we attempted to control for them by various multivariate techniques, including cross-classification and regression analyses. In addition, we made comparisons involving the same area before and after fluoridation. These methodologies cannot exclude the influence of all variables affecting cancer risk, particularly when one is dealing with heterogeneous and dynamic populations. For example, when the same area before and after fluoridation is compared to a control area, changes in other potential risk factors may have occurred differentially

TABLE 5.—Ratios of age-adjusted cancer mortality rates (all sites) in heavily fluoridated counties to those in control counties in 5-year intervals (pentads), by pentad of fluoridation and sex^a

Pentad of fluoridation	5 yr before fluoridation	Ratio in pentad of fluoridation	After fluoridation		
			5 yr	10 yr	15 yr
Males:					
1950-54		1.17 (27,369)	1.19 (29,806)	1.16 (30,315)	1.16 (31,144)
1955-59	1.18 (11,095)	1.18 (11,929)	1.17 (12,311)	1.16 (12,523)	
Females:					
1950-54		1.13 (25,766)	1.15 (26,582)	1.13 (26,514)	1.14 (27,176)
1955-59	1.11 (9,951)	1.13 (10,383)	1.12 (10,494)	1.10 (10,591)	

^a Total number of deaths on which the rates in the fluoridated counties are based are in parentheses.

TABLE 6.—Ratios of age-adjusted cancer mortality rates in heavily fluoridated counties to those in control counties in 5-year intervals (pentads), by pentad of fluoridation and sex for 3 cancer sites^a

Site	Pentad of fluoridation	5 yr before fluoridation	Ratio in pentad of fluoridation	After fluoridation		
				5 yr	10 yr	15 yr
Males:						
Mouth and throat	1950-54		1.37(967)	1.37(1,020)	1.44(1,055)	1.51(1,049)
	1955-59	1.43(407)	1.46(438)	1.39(406)	1.42(394)	
Rectum	1950-54		1.43(1,672)	1.43(1,617)	1.30(1,345)	1.30(1,183)
	1955-59	1.41(686)	1.34(622)	1.37(568)	1.41(510)	
Kidney	1950-54		1.19(617)	1.23(687)	1.06(647)	1.14(669)
	1955-59	0.99(206)	1.18(264)	1.07(263)	1.26(296)	
Females:						
Mouth and throat	1950-54		1.24(196)	1.19(220)	1.20(258)	1.30(327)
	1955-59	1.09(68)	0.88(64)	1.09(93)	1.15(117)	
Rectum	1950-54		1.26(1,244)	1.28(1,212)	1.17(1,043)	1.23(941)
	1955-59	1.24(480)	1.31(490)	1.18(419)	1.05(320)	
Kidney	1950-54		1.13(337)	1.14(391)	1.04(380)	1.04(410)
	1955-59	1.25(147)	1.06(141)	1.23(180)	0.97(147)	

^a Total number of deaths on which the rates in the fluoridated counties are based are in parentheses.

over time in these areas also. However, the ratios of urbanization, socioeconomic, and ethnic variables in the group fluoridated in 1950-54 to those in the control group varied by 8% or less between the 1950 and 1970 censuses. However, these confounding variables might be responsible for the small differences in risk yielded by certain analyses in this study. In addition, the task of relating community fluoridation measures to total

TABLE 7.—Direction of change^a in the ratios of the age-adjusted, site-specific cancer incidence rates in Denver, Colorado, and Birmingham, Alabama

Site	Males	Females
All sites	0	+
Buccal cavity	+	0
Esophagus	+	+
Stomach	-	+
Large intestine	0	+
Rectum	0	-
Breast		0
Ovary		-
Kidney	+	-
Bladder	-	+
Thyroid	-	+
Bone	-	-

Small intestine	-	-
Liver	-	-
Pancreas	+	+
Larynx	-	+
Lung	-	-
Uterus		0
Vagina		+
Prostate	-	
Other male genital	+	
Brain and nervous system	-	+
Hodgkin's disease	+	+
Other lymphoma	-	-
Leukemia	+	+

^a From Second National Cancer Survey (1947-48) to Third National Cancer Survey (1969-71). + indicates a greater ratio in the Third Survey than in the Second; - indicates a lesser ratio in the Third than in the Second; 0 indicates no change. Those sites listed above the dotted line indicate those sites with a priori suspicion.

TABLE 8.—Age-adjusted RR and its 95% confidence intervals (95% CI) of cancer incidence in the Denver, Colorado, SMSA to that in the Birmingham, Alabama, SMSA, in 2 time periods, all sites combined^a

Sex	Second National Cancer Survey (1947-48)		Third National Cancer Survey (1969-71)	
	RR	95% CI	RR	95% CI
M	1.04	0.92-1.19	0.97	0.92-1.03
F	1.02	0.91-1.15	1.07	1.02-1.13

^a Except skin cancer.

TABLE 9.—Regression coefficients (β) and F values associated with a fluoride variable entered into a regression analysis to predict sex- and site-specific cancer mortality rates in 20 counties^a with and without control^b for demographic risk factors

Site	Sex	Without control		With control	
		β	F ^c	β	F ^d
Mouth and throat	♂	1.14	2.6	-0.78	0.8
	♀	-0.16	1.9	-0.13	0.9
Esophagus	♂	2.55	25.0	0.57	1.2
	♀	-0.08	0.5	-0.29	2.6
Stomach	♂	5.02	19.7	2.31	11.6
	♀	2.22	11.1	0.79	7.4
Colon	♂	5.47	23.1	0.64	0.3
	♀	3.57	13.3	-0.31	0.1
Rectum	♂	3.72	21.5	1.12	1.1
	♀	1.50	17.5	0.22	0.2
Breast	♀	3.85	16.1	0.76	0.2
Ovary	♀	1.18	9.8	0.69	2.3
Kidney	♂	0.44	7.2	0.11	0.2
	♀	0.21	8.2	0.07	0.7
Bladder	♂	1.49	13.1	0.84	1.3
	♀	0.36	8.9	0.26	2.2

^a Same 20 counties used in another study (1).

^b In the without control group, the fluoride variable was the only one entered. In the with control group, the fluoride variable was entered in the second step of an analysis in which the following variables were entered in the first step: population density, median number of years of schooling of the adult population, percent non-white, percent foreign stock, percent employed in manufacturing, and geographic section of the country.

^c F (1, 18 degrees of freedom), approximate values where P=0.05 is 4.41.

^d F (1, 10 degrees of freedom), approximate value where P=0.05 is 4.96.

county populations was complicated by the varying definitions of "community," the small size of many water districts, and the propensity of some communities to purchase their water from others, making it difficult to identify "exposed" and "unexposed" counties for the entire country. There may be other areas in the country that would meet our criteria for either fluoridated or

control counties. However, we did not select the study counties by virtue of their cancer experience or anything correlated with it, so it is likely that as a group these counties are representative of all U.S. counties that could meet our criteria for fluoridated or control areas.

The report of a positive association between fluoridation and cancer that appeared in the Congressional Record (1) also utilized U.S. cancer mortality statistics. That report based many of its conclusions on a comparison of counties containing the 10 largest fluoridated cities to counties containing the 10 largest nonfluoridated cities. No attempt was made to take into account the demographic variables known to affect cancer mortality. Table 9 shows the gross differences that can occur if these factors are not considered. We analyzed the cancer mortality data for the same 20 study counties and the 9 cancer sites reported to be correlated with fluoridation, using the same weighted regression technique as in our earlier analyses. When only the fluoride variable (0 or 1) was used to predict the cancer mortality rate, it was a highly significant predictor, being positively associated with most of the sex-site groupings. However, after the other demographic variables were taken into account, the presence or absence of fluoride made no statistically significant contribution for any site, other than stomach cancer. Stomach cancer is known to develop excessively in certain ethnic groups (13). Regression analyses for stomach cancer that allowed for control of the high-risk ethnic groups yielded a nonsignificant F value of 0.02 for females and a value of 6.9 for males (P<0.05). Thus almost all the elevated cancer mortality rates previously described (1) for artificially fluoridated areas can be traced to confounding demographic risk factors.

APPENDIX

APPENDIX TABLE 1.—Texas counties allocated to natural fluoride groupings

Level of natural fluoride			
Control	Intermediate	High	Very high
Bastrop	Brooks	Calhoun	Andrews
Bowie	Cameron	Ector	Brewster
Brazos	Crockett	Garza	Dallam
Brown	El Paso	Hansford	Dawson
Coleman	Galveston	Hutchinson	Jim Hogg
Crane	Gray	Moore	Midland
Dimmit	Hardeman	Potter	Ochiltree
Jones	Hidalgo	Randall	Pecos
Llano	Howard	Reagan	Presidio
Montague	Lubbock	Reeves	Yoakum
Palo Pinto	Maverick	Upton	
Sutton	McCulloch	Ward	
Uvalde	Navarro		
Val Verde	Webb		
Victoria	Winkler		
Zavala			

APPENDIX TABLE 2.—Site combinations used in county analysis

Site	ICD No. ^a
Lip	140
Salivary gland	142
Nasopharynx	146
Mouth and throat:	
Tongue	141
Floor of mouth	143
Other parts of mouth; and mouth, unspecified	144
Oral mesopharynx	145
Pharynx, unspecified	148
Esophagus	150
Stomach	151
Colon (large intestine, except rectum)	153
Rectum	154
Hepatobiliary (biliary passages and liver stated to be primary site or unspecified)	155
Pancreas	157
Nasal sinuses (nose, nasal cavities, middle ear, and accessory sinuses)	160
Larynx	161
Lung:	
Trachea, bronchus and lung specified as primary	162
Lung and bronchus, unspecified as to whether primary or secondary	163
Breast	170
Cervix uteri	171
Corpus uteri	172
Other parts of uterus, including chorionepithelioma	173
Uterus, unspecified	174
Ovary (including fallopian tube and broad ligament)	175
Prostate	177
Testis	178
Kidney	180
Bladder (including other urinary organs)	181
Melanoma of skin	190
Other skin	191
Eye	192
Brain (including other parts of nervous system)	193
Thyroid gland	194
Other endocrine glands	195
Bone (including jaw bone)	196
Connective tissue	197
Hodgkin's disease	201
Non-Hodgkin's lymphoma:	
Lymphosarcoma and reticulosarcoma	200
Other forms of lymphoma (reticulosis)	202
Mycosis fungoides	205
Multiple myeloma (plasmacytoma)	203
Leukemia and aleukemia	204
Other (all ICD's not previously listed)	147, 152, 156, 158, 164, 165, 176, 179, 198, 199
All malignant neoplasms	140-205

^a From (14).

APPENDIX TABLE 3.—Counties or cities used in artificial fluoridation study

Specification	State	County or city	
Controls"	Arizona	Maricopa, Pima, Santa Cruz	
	Arkansas	Sebastian	
	California	Kern, Marin, Orange, Riverside, Sacramento, San Bernardino, San Diego, San Joaquin, Santa Barbara, Yolo	
	Colorado	El Paso, Pueblo	
	Florida	Broward, Duval, Escambia, Hillsborough, Pinellas, Sarasota	
	Georgia	Bibb, Chatham, Glynn, Muscogee	
	Idaho	Bannock, Bonneville	
	Indiana	Fayette, Vigo	
	Iowa	Woodbury	
	Kansas	Barton, Finney, Pratt, Scott, Seward, Sherman	
	Louisiana	Caddo, Calcasieu, East Baton Rouge, Iberia, Orleans, Ouachita	
	Massachusetts	Berkshire, Hampden, Nantucket, Suffolk	
	Michigan	Dickinson, Gogebic	
	Mississippi	Forrest, Harrison, Warren, Washington	
	Missouri	Boone, Buchanan, Greene, Jackson, Pettis	
	Montana	Cascade, Lewis and Clark, Missoula, Powell, Silver Bow, Yellowstone	
	Nebraska	Adams, Box Butte, Hall, Lancaster	
	Nevada	Clark, Washoe	
	New Hampshire	Hillsborough	
	New Jersey	Bergen, Camden, Cumberland, Essex, Gloucester, Hudson, Passaic	
	New Mexico	Bernalillo, Chaves, Curry, Eddy, Hidalgo, Lea, Los Alamos, Luna, Otero	
	New York	Rockland	
	Ohio	Allen, Clark, Montgomery, Richland, Stark	
	Oklahoma	Comanche	
	Oregon	Multnomah	
	Pennsylvania	Montgomery	
	South Carolina	Charleston	
	South Dakota	Lawrence, Minnehaha, Pennington	
	Texas	Andrews, Bexar, Brazos, Brewster, Brooks, Brown, Cameron, Childress, Comal, Crane, Crockett, Dallam, Ector, El Paso, Galveston, Garza, Gray, Harris, Hidalgo, Howard, Hutchinson, Jim Hogg, Kleberg, Lubbock, McLennan, Maverick, Midland, Ochiltree, Potter, Randall, Reagan, Reeves, Scurry, Sutton, Tom Green, Travis, Val Verde, Victoria, Webb, Wilbarger, Winkler, Zavala	
		Utah	Davis, Grand, Iron, Salt Lake, Utah, Weber
		Washington	Asotin, Franklin, Spokane, Walla Walla
	Wisconsin	Douglas	
	Wyoming	Laramie, Natrona, Sweetwater	
Fluoridation of water supply during 1950-54	Arkansas	Pulaski	
	California	San Francisco	
	Colorado	Denver	
	District of Columbia	Washington	
	Georgia	Dougherty	
	Indiana	Allen, Howard, Marion	
	Iowa	Dubuque, Linn, Scott	
	Kansas	Douglas	
	Kentucky	Jefferson	
	Maryland	Baltimore, Baltimore City	
	Minnesota	Ramsey	
	Mississippi	Lauderdale	
	North Dakota	Cass	
	Oklahoma	Jackson, Oklahoma, Tulsa	
	Pennsylvania	Philadelphia	
	Rhode Island	Bristol	
	South Dakota	Brown, Codington, Davison	
	Texas	Nueces, Stephens	
	Virginia	Arlington, Chesapeake, James City	
West Virginia	Cabell, Ohio		
Wisconsin	Milwaukee, Winnebago		
Wyoming	Albany		
Fluoridation of water supply during 1955-59	Georgia	Ware	
	Illinois	Cook, Morgan	
	Iowa	Polk, Wapello	
	Kansas	Lyon, Shawnee	
	Missouri	Cape Girardeau, Marion, St. Louis City	
	Montana	Custer	
	New Mexico	Santa Fe	
	North Dakota	Burleigh, Grand Forks	
	Ohio	Cuyahoga, Lucas	
Texas	Nolan		

APPENDIX TABLE 3.—Continued

Specification	State	County or city
Fluoridation of water supply during 1960-64	Indiana	Vanderburgh
	Iowa	Des Moines, Pottawattamie
	Kansas	Wyandotte
	Missouri	Cole
	New Jersey	Mercer
	North Carolina	Durham
	Wisconsin	Kenosha

^a Only those $\geq 2/3$ urban counties are listed, since these were the counties used to produce the results presented.

REFERENCES

- (1) Congressional Record: House H7172-H7176, July 21, 1975
- (2) U.S. Public Health Service: National Fluoride Content of Community Water Supplies. Bethesda, Md., U.S. Department of Health, Education, and Welfare, Division of Dental Health, 1969
- (3) DORN HF, CUTLER SJ: Morbidity from Cancer in the United States. Public Health Monogr No. 56. Washington D.C., U.S. Govt Print Off, 1959
- (4) CUTLER SJ, YOUNG JL JR: Third National Cancer Survey, Incidence Data. Washington D.C., U.S. Govt Print Off, 1975
- (5) KINLEN L: Cancer incidence in relation to fluoride level in water supplies. *Br Dent J* 138:221-224, 1975
- (6) HAENSZEL W, LOVELAND DB, SIRKEN MG: Lung-cancer mortality as related to residence and smoking histories. I. White males. *J Natl Cancer Inst* 28:947-1001, 1962 (*see* Appendix Table C)
- (7) DRAPER NR, SMITH H: Applied Regression Analysis. New York, Wiley, 1966
- (8) GART JJ: Point and interval estimation of the common odds ratio in the combination of 2×2 tables with fixed marginals. *Biometrika* 57:471-475, 1970
- (9) THOMAS DG: Exact and asymptotic methods for the combination of 2×2 tables. *Comput Biomed Res* 8:423-446, 1973
- (10) U.S. Public Health Service: Fluoridation Census 1969. Bethesda, Md., U.S. Department of Health, Education, and Welfare, Division of Dental Health, 1970
- (11) NIXON JM, CARPENTER RG: Mortality in areas containing natural fluoride in their water supplies, taking account of socioenvironmental factors and water hardness. *Lancet* 2:1068-1071, 1974
- (12) McCLURE FJ, ed.: Fluoride Drinking Waters. Public Health Service Publication No. 825. Washington D.C., U.S. Govt Print Off, 1962
- (13) HOOVER R, MASON TJ, MCKAY FW, et al: Cancer by county: New resource for etiologic clues. *Science* 189:1005-1007, 1975
- (14) World Health Organization: Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, 6th revision, vol 1. Geneva, Switzerland, World Health Organization, 1948