

FLUORIDATION AND CANCER  
AGE-DEPENDENCE OF CANCER MORTALITY RELATED  
TO ARTIFICIAL FLUORIDATION

by

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**SUMMARY:** Data indicating a more rapid increase in cancer death rate in fluoridated than in nonfluoridated cities were analyzed to determine to what extent the net increase observed in fluoridated cities could be attributed to age, race, or sex. Between 1952 and 1969, no significant fluoridation-linked increase in cancer death rate could be observed in populations 0-24 and 25-44 years of age. In populations 45-64 years of age, a fluoridation-linked increase in cancer death rate of 15/100,000 population was observed ( $P < .02$ ); in populations 65+ years of age, an increase of 35/100,000 was observed ( $P < .05$ ). The fluoridation-linked increase in cancer death rate could not be ascribed to changes in the racial or sex compositions of the fluoridated and nonfluoridated populations.

Tumorigenic effects of low levels of fluoride have been reported by Herskowitz and Norton (1) who were able to induce tumors in 5-90% of the fruit flies exposed to 20 to 50 ppm fluoride with a dose-dependent effect. Taylor and Taylor (2) observed a 13-17% increase in tumor growth rate in cancer-prone mice fed 1 ppm fluoride in the drinking water.

A number of other papers have demonstrated mutagenic effects of fluoride (3-15). Most recently, reports that low levels of fluoride added to the drinking water of mice can cause chromosomal damage have aroused more concern (16). As little as 1 to 5 ppm fluoride given to mice fed low-fluoride diets produced a significant dose-dependent increase in the rate of chromosomal aberrations in the testes and bone marrow of mice within 3 to 6 weeks (17). It is generally agreed that the mutagenic activity of a substance in such systems could be a warning of its possible cancer-causing activity.

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The purpose of this paper is to present a detailed analysis of the cancer death rates of residents of fluoridated and nonfluoridated cities to see if the implications and observations concerning the carcinogenicity of fluoride observed under controlled laboratory conditions with animals could be confirmed epidemiologically in humans.

### Methods

The ten largest fluoridated cities\* in the United States were taken as the experimental group. In 1953, the year closest to the initiation of fluoridation for which cancer death rate data from the National Center for Health Statistics are available, the cancer death rate of each of these cities was above 155 cancer deaths per 100,000 inhabitants. The ten largest cities in the United States not fluoridated as of 1969 but with a 1953 cancer death rate greater than 155 per 100,000 per year were taken as the control group (Table 1).

Total cancer deaths for each of the cities for 1940-50 and 1953-69 were obtained from *Vital Statistics of the U.S.* for those years. City data were not reported in *Vital Statistics* for 1951 and 1952. Total cancer deaths for Boston were not reported for 1953-4 and 1956-8. These figures were estimated by linear interpolation.

Annual resident cancer deaths from 1952 to 1969 by age (0-24, 25-44, 45-64, and 65+) for Philadelphia, Cleveland, Pittsburgh, New Orleans, Seattle, Cincinnati, Atlanta, Columbus, Newark, and Portland were provided by the respective state health departments. Similar data for Baltimore, Milwaukee, and Boston were provided through the respective city health departments or their annual reports. Data for Washington, D.C. were obtained through *Vital Statistics* and data for St. Louis, Kansas City, San Francisco, Los Angeles, and Chicago\*\* were obtained through the respective state health departments or their annual reports and in part through their city health departments. Buffalo data were supplied by the Erie County Health Department. Similar data for race and sex (where available) were obtained through the same sources. Missing data for Philadelphia and Pittsburgh in 1952 and Buffalo in 1968 were supplied by means of linear extrapolation and interpolation. Cancer death rates by site were obtained from *Vital Statistics of the U.S.* published by the National Center for Health Statistics. Age-, race-, sex-specific population estimates for these cities were obtained by linear interpolation of census figures.

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\*According to the 1960 census, "cities" as used in this manuscript refers to central cities.

\*\*For Chicago, occurrence cancer deaths for 1952-8 for each age group were normalized to resident cancer deaths; for Kansas City, residence-occurrence deaths for 1952-9 for each age group were normalized to residence cancer deaths.

Table 1

Selection of Cities			
	Fluoridated Before 1960	CDR Greater Than 155/100,000 in 1953	Date Fluoridated
1 Chicago	x	x	1956
2 Philadelphia	x	x	1954
3 Baltimore	x	x	1952
4 Cleveland	x	x	1956
5 Washington	x	x	1952
6 Milwaukee	x	x	1953
7 St. Louis	x	x	1955
8 San Francisco	x	x	1952
9 Pittsburgh	x	x	1952-3
10 Buffalo	x	x	1955
	Not Fluoridated as of 1969	CDR Greater Than 155/100,000 in 1953	Date Fluoridated
New York		x	1965
1 Los Angeles	x	x	—
Detroit		x	1967
Houston	x		—
2 Boston	x	x	—
Dallas			1966
3 New Orleans	x	x	*
San Antonio	x		—
San Diego	x		—
4 Seattle	x	x	*
5 Cincinnati	x	x	*
Memphis	x		—
6 Atlanta	x	x	*
7 Kansas City (Mo.)	x	x	—
8 Columbus (O.)	x	x	*
Phoenix	x		—
9 Newark	x	x	—
10 Portland	x	x	

\*December 1969 or thereafter

To study the effects of artificial fluoridation, calculations of the total cancer death rate were made year-by-year prior to fluoridation of the experimental group, 1940 to 1950, and after fluoridation of the experimental group but before any fluoridation of the control group, 1953-1969. In addition, linear regression analysis of cancer death rates of each of the age groupings 0-24, 25-44, 45-64, and 65+ were made from 1952 to 1969. All averages of cancer death rates are unweighted averages. Age-adjusted cancer death rates were also computed by the direct method using a reference population with an age distribution intermediate between the control and experimental groups.

Census figures were obtained from *Census of the U.S. Population* 1940, 1950, 1960, and 1970 and from Special Report PC (3) 1D, published by the U.S. Bureau of the Census.

Data regarding fluoridation status of experimental and control cities were obtained from *Fluoridation Census 1969*, published by the Division of Dental Health, U.S. Public Health Service.

### Results

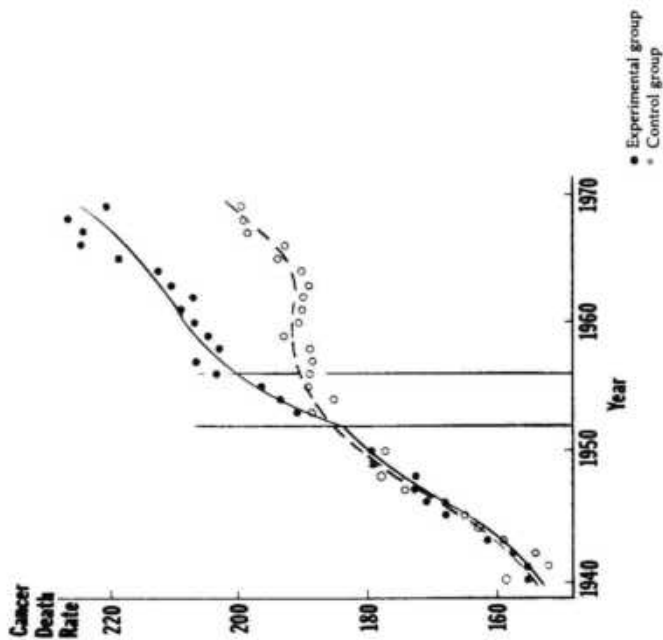
The crude cancer death rates of both groups of cities had a strikingly similar trend between 1940 and 1950 (Figure 1). Subsequent to fluoridation however, an equally striking divergence could be observed that was maintained through 1969, the last year of study. This increase in crude cancer death rate could be observed in virtually all of the fluoridated cities when compared to the control cities, indicating that the difference in averages was not due to the sharp increase in cancer death rate of only one or two of the fluoridated cities (Table 2). Figure 2 indicates the increase in deaths due to cancers of various tissues.

Since cancer death rates are dependent on the age distribution of a population, the age distributions of both groups of cities were compared for 1950, 1960, and 1970 (Table 3). The trends in age distribution for the two groups of cities are similar; however, a slightly more rapid increase in the age of the population of the fluoridated cities as compared to that of the nonfluoridated cities was observed.

To determine whether this slight age differential might account for the divergence in crude cancer deaths following fluoridation, year-by-year cancer death rates were computed for each of the age groups 0-24, 25-44, 45-64, and 65+ for both the fluoridated (Table 4) and nonfluoridated (Table 5) groups of cities; year-by-year averages of cancer death rates for both groups were also computed. Linear regression analysis of the year-by-year averages (Table 6a) indicates a significant decrease in the cancer death rates in both groups of cities in the 0-24 age group and a less significant decrease in the 25-44 year age group.

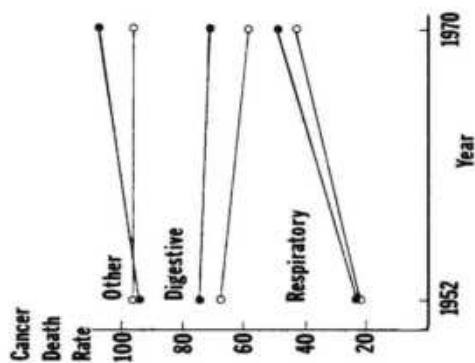
In populations 45 and over, an increase in cancer death rate was observed in

Figure 1



Vertical lines at 1952 and 1956 contain the period during which fluoridation of the experimental group began. All figures represent crude cancer death rates.

Figure 2



Lines represent a linear regression of year-by-year deaths due to cancers as listed above.

Table 2

## Cancer Death Rates (CDRs) Before and After Fluoridation

	Average 5-Year		
	CDR Before Fluoridation	CDR After Fluoridation	
<b>Cities Fluoridated in 1952</b>			
Baltimore	171	195	+24
Washington	157	178	+21
San Francisco	193	214	+21
10 Control Cities	177*	188	+11
<b>Cities Fluoridated in 1953</b>			
Milwaukee	176*	187	+11
Pittsburgh	177*	219	+42
10 Control Cities	178*	188	+10
<b>Cities Fluoridated in 1954</b>			
Philadelphia	187	205	+18
10 Control Cities	182*	190	+08
<b>Cities Fluoridated in 1955</b>			
St. Louis	201	223	+22
Buffalo	193*	212	+19
10 Control Cities	184*	190	+06
<b>Cities Fluoridated in 1956</b>			
Chicago	188*	196	+08
Cleveland	188*	199	+11
10 Control Cities	188*	190	+02

\*1951 and/or 1952 data missing from Vital Statistics.

Table 3

## Age Distribution (as %) of Fluoridated &amp; Nonfluoridated Populations

	Age Distribution (as %) of Fluoridated & Nonfluoridated Populations	
	Fluoridated	Nonfluoridated
	0-24	
	35.71	36.15
1950	39.78	41.03
1960	42.94	44.80
1970		
	25-44	
	32.83	32.17
1950	26.40	26.20
1960	22.74	23.19
1970		
	45-64	
	23.30	22.73
1950	23.27	22.14
1960	22.42	20.82
1970		
	65+	
	8.16	8.94
1950	10.54	10.63
1960	11.91	11.17
1970		

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Table 4 Year-by-Year Cancer Death Rates by Age Group — Fluoridated Cities

Year	Under Age 25										Age 25 To 44										Age 45 To 64										Age 65 & Over												
	Chicago	Philadelphia	Baltimore	Cleveland	Washington	Milwaukee	St. Louis	San Francisco	Pittsburgh	Buffalo	Average	Chicago	Philadelphia	Baltimore	Cleveland	Washington	Milwaukee	St. Louis	San Francisco	Pittsburgh	Buffalo	Average	Chicago	Philadelphia	Baltimore	Cleveland	Washington	Milwaukee	St. Louis	San Francisco	Pittsburgh	Buffalo	Average										
1952	15	9	9	8	8	8	10	8	9	9	346	350	380	357	326	309	313	315	351	350	1043	1056	1022	1084	973	1192	905	1067	1094	1018	1045	1030	1057	992	1044	923	1086	947	990	1061	1042	1017	
1953	12	9	10	7	11	12	8	9	12	10	345	353	362	355	342	311	318	316	391	333	1030	1057	992	1044	923	1086	947	990	1061	1042	1017	1034	1046	1082	1047	932	1129	923	989	1094	1053	1033	
1954	11	9	9	7	10	8	7	11	8	9	341	339	359	348	309	320	327	339	389	345	1034	1046	1082	1047	932	1129	923	989	1094	1053	1033	999	1044	1079	1094	987	1108	944	981	1167	1079	1048	
1955	15	8	7	10	9	8	10	7	12	11	360	372	395	357	344	317	358	326	380	357	1007	1090	1077	1060	1088	1169	980	1033	1119	1010	1063	53	51	52	53	48	37	45	42	53	42	48	
1956	11	8	8	8	11	9	6	12	6	12	353	374	403	354	382	302	337	337	372	354	1007	1090	1077	1060	1088	1169	980	1033	1119	1010	1063	53	52	49	47	47	41	58	42	48	49	49	
1957	12	9	9	6	10	11	6	11	8	9	338	346	371	364	382	317	351	321	334	357	1028	1101	1044	1089	1090	1092	1029	1075	1158	1027	1073	1957	53	52	49	47	47	41	58	42	48	49	
1958	12	8	9	6	10	11	6	11	8	9	336	366	364	368	364	290	376	321	348	305	1028	1101	1044	1089	1090	1092	1029	1075	1158	1027	1073	1958	55	50	56	49	51	41	55	43	53	44	50
1959	9	8	7	6	9	8	5	11	7	11	331	351	373	360	370	285	386	361	327	369	1028	1101	1044	1089	1090	1092	1029	1075	1158	1027	1073	1959	48	48	54	46	55	46	54	39	40	65	50
1960	10	8	5	10	7	8	6	9	5	10	349	374	380	357	369	277	379	321	348	305	1006	1051	1079	1048	1010	920	1003	874	1050	1081	1012	1960	49	48	68	50	58	40	54	44	43	54	51
1961	9	8	7	12	7	7	8	7	10	9	335	361	360	350	364	268	361	328	388	366	1045	1062	1097	1145	916	867	1017	1035	1070	1140	1039	1961	50	47	52	50	48	30	46	39	47	51	46
1962	8	9	6	7	7	7	7	7	7	7	336	366	364	368	364	290	376	320	388	366	1045	1062	1097	1145	916	867	1017	1035	1070	1140	1039	1962	50	50	56	51	45	41	60	44	45	52	49
1963	9	9	7	7	10	8	7	11	8	12	335	342	386	359	368	290	376	320	388	366	1015	1034	1099	1200	963	1019	961	1012	1045	1068	1033	1963	45	51	58	46	55	37	61	38	41	41	47
1964	8	7	8	8	8	6	9	8	7	9	345	362	375	341	369	316	357	337	413	365	1015	1034	1099	1200	963	1019	961	1012	1045	1068	1033	1964	50	48	55	46	51	42	51	33	46	39	46
1965	9	9	8	7	7	7	6	11	10	8	348	359	413	339	406	316	364	361	404	344	1047	1090	1032	1194	945	1058	974	1056	1069	1110	1058	1965	50	49	56	48	54	35	54	45	45	53	52
1966	8	8	7	9	9	9	7	7	9	4	348	367	404	374	383	272	399	322	413	406	1047	1090	1032	1194	945	1058	974	1056	1069	1110	1058	1966	51	48	55	46	51	42	51	33	46	39	46
1967	9	8	6	5	10	9	5	9	6	8	361	369	404	402	375	309	396	327	430	351	1066	1117	1096	1204	1062	1064	1086	1025	1155	1117	1098	1967	47	48	46	46	46	47	45	60	39	60	50
1968	8	7	8	10	7	6	8	9	8	7	365	378	392	425	413	323	416	362	436	374	1066	1117	1096	1204	1062	1064	1086	1025	1155	1117	1098	1968	49	48	55	39	46	62	38	55	34	52	48
1969	7	7	6	8	4	6	7	10	6	11	369	393	406	373	390	328	402	356	459	360	1066	1117	1096	1204	1062	1064	1086	1025	1155	1117	1098	1969	46	43	47	49	54	46	58	55	31	36	44

Table 5 Year-by-Year Cancer Death Rates by Age Group — Nonfluoridated Cities

Year	Los Angeles	Boston	New Orleans	Seattle	Cincinnati	Atlanta	Kansas City	Columbus	Newark	Portland	Average	Los Angeles	Boston	New Orleans	Seattle	Cincinnati	Atlanta	Kansas City	Columbus	Newark	Portland	Average
1952	10	9	9	9	8	16	6	11	12	10	10	274	345	394	275	332	383	276	259	391	265	319
1953	10	9	9	8	14	9	12	8	8	9	9	281	328	359	274	355	370	313	288	405	322	330
1954	8	12	8	10	9	15	8	8	8	9	12	285	354	367	276	365	431	289	344	386	258	335
1955	10	6	17	7	9	7	12	7	11	11	10	291	298	382	341	358	379	302	312	385	261	332
1956	10	7	9	14	9	9	10	4	9	8	9	295	349	402	296	336	378	297	305	377	277	333
1957	8	5	8	12	8	7	7	7	7	10	5	277	344	364	286	336	338	304	317	392	282	334
1958	8	6	10	8	11	8	7	6	10	5	8	290	347	342	410	306	348	378	317	348	295	359
1959	8	7	17	8	7	8	7	7	7	12	9	308	346	342	304	351	342	309	326	415	273	332
1960	8	9	14	6	6	8	8	8	8	9	14	279	399	387	278	365	318	314	335	381	319	337
1961	8	9	10	10	6	9	9	11	9	9	9	296	358	371	310	352	321	316	321	383	261	329
1962	9	9	13	7	5	9	6	7	5	6	8	289	358	341	284	373	315	277	315	379	308	334
1963	9	8	13	11	7	6	8	7	5	7	8	286	368	382	269	365	384	339	327	388	288	342
1964	8	8	7	9	9	9	5	7	9	11	8	300	365	388	296	379	345	308	315	359	291	335
1965	8	8	11	7	7	8	5	6	7	7	7	292	378	361	304	346	377	311	304	424	283	338
1966	9	8	8	8	8	9	5	11	4	7	5	284	365	383	296	361	383	311	330	433	291	344
1967	9	7	7	7	7	8	5	6	8	10	6	287	370	405	300	409	368	341	299	427	326	353
1968	9	6	8	7	6	6	9	9	7	14	8	304	341	402	274	416	369	349	343	346	340	348
1969	8	7	5	6	8	9	5	8	10	11	8	300	347	409	318	435	363	349	343	355	300	352
Age 25 To 44																						
1952	39	39	47	46	44	70	45	36	46	34	45	900	1113	998	911	1040	1048	969	942	1156	832	991
1953	44	38	55	36	52	65	47	53	49	35	47	895	1088	1013	968	972	902	968	1028	1174	825	963
1954	42	46	43	48	44	61	49	44	44	44	47	844	1249	879	969	1008	877	943	969	1171	874	978
1955	43	47	42	42	49	70	38	46	42	44	48	859	1219	1004	1010	1066	961	898	937	1038	837	963
1956	44	39	55	44	50	65	33	46	46	47	47	914	1075	1018	1028	1050	855	1052	866	1052	806	954
1957	38	44	48	36	45	63	33	36	48	38	43	939	1198	1055	974	1039	872	858	959	1148	878	992
1958	45	45	47	42	63	62	41	39	59	48	48	863	1106	1089	986	996	746	909	1067	1038	889	969
1959	42	43	51	47	59	53	43	42	42	51	50	904	1030	984	1000	1035	913	876	1030	1123	815	971
1960	38	45	53	36	67	50	46	42	43	41	46	900	1092	952	964	1032	788	948	927	926	846	938
1961	39	54	55	40	59	68	44	29	49	50	47	896	1108	991	969	996	834	852	960	1178	845	963
1962	44	46	61	49	49	43	39	38	43	37	45	865	1218	1058	920	1059	827	931	1023	1168	959	987
1963	43	43	51	34	44	41	41	45	53	49	44	861	1185	959	869	951	881	874	991	1078	913	962
1964	42	43	58	40	56	51	44	45	41	44	44	895	1104	1008	905	1053	903	875	995	1078	920	975
1965	48	53	50	34	49	49	54	44	48	50	28	844	1127	1092	964	1091	934	879	1014	1093	901	999
1966	44	53	50	37	55	58	45	44	45	24	45	947	1084	1008	947	1007	871	961	1006	1040	828	970
1967	36	41	59	36	56	45	44	37	53	44	45	931	1016	940	916	1062	899	1038	962	1106	920	979
1968	37	27	52	49	54	49	46	46	49	38	42	940	1017	1016	1032	1134	808	1004	932	1135	833	987
1969	38	38	55	30	50	45	29	33	55	44	42	937	1135	978	931	1168	803	899	982	1123	918	987
Age 65 & Over																						
1952	39	39	47	46	44	70	45	36	46	34	45	900	1113	998	911	1040	1048	969	942	1156	832	991
1953	44	38	55	36	52	65	47	53	49	35	47	895	1088	1013	968	972	902	968	1028	1174	825	963
1954	42	46	43	48	44	61	49	44	44	44	47	844	1249	879	969	1008	877	943	969	1171	874	978
1955	43	47	42	42	49	70	38	46	42	44	48	859	1219	1004	1010	1066	961	898	937	1038	837	963
1956	44	39	55	44	50	65	33	46	46	47	47	914	1075	1018	1028	1050	855	1052	866	1052	806	954
1957	38	44	48	36	45	63	33	36	48	38	43	939	1198	1055	974	1039	872	858	959	1148	878	992
1958	45	45	47	42	63	62	41	39	59	48	48	863	1106	1089	986	996	746	909	1067	1038	889	969
1959	42	43	51	47	59	53	43	42	42	51	50	904	1030	984	1000	1035	913	876	1030	1123	815	971
1960	38	45	53	36	67	50	46	42	43	41	46	900	1092	952	964	1032	788	948	927	926	846	938
1961	39	54	55	40	59	68	44	29	49	50	47	896	1108	991	969	996	834	852	960	1178	845	963
1962	44	46	61	49	49	43	39	38	43	37	45	865	1218	1058	920	1059	827	931	1023	1168	959	987
1963	43	43	51	34	44	41	41	45	53	49	44	861	1185	959	869	951	881	874	991	1078	913	962
1964	42	43	58	40	56	51	44	45	41	44	44	895	1104	1008	905	1053	903	875	995	1078	920	975
1965	48	53	50	34	49	49	54	44	48	50	28	844	1127	1092	964	1091	934	879	1014	1093	901	999
1966	44	53	50	37	55	58	45	44	45	24	45	947	1084	1008	947	1007	871	961	1006	1040	828	970
1967	36	41	59	36	56	45	44	37	53	44	45	931	1016	940	916	1062	899	1038	962	1106	920	979
1968	37	27	52	49	54	49	46	46	49	38	42	940	1017	1016	1032	1134	808	1004	932	1135	833	987
1969	38	38	55	30	50	45	29	33	55	44	42	937	1135	978	931	1168	803	899	982	1123	918	987

Table 6a  
 Linear Regression of Year-By-Year Average Cancer Death Rates (N = 18)

Age Group	Cities	Sample Size	Correlation Coefficient	Slope	Cancer Death Rate-1952	Cancer Death Rate-1969	CDR Increase 1952-1969	P
0-24	Fluoridated	18	-0.8802	-0.1414	9.70	7.30	-2.40	$< 10^{-5}$
	Nonfluoridated	18	-0.7954	-0.1465	9.69	7.20	-2.49	$< 10^{-4}$
25-44	Fluoridated	18	-0.4754	-0.1651	49.96	47.15	-2.81	$< .05$
	Nonfluoridated	18	-0.4127	-0.1569	47.33	44.67	-2.66	$< .10$
45-64	Fluoridated	18	0.8375	2.165	336.3	375.1	36.8	$< 10^{-5}$
	Nonfluoridated	18	0.7826	1.395	323.5	347.2	23.7	$< 10^{-4}$
65+	Fluoridated	18	0.4901	2.186	1032.8	1069.9	37.1	$< .05$
	Nonfluoridated	18	0.0678	0.1920	974.4	977.6	3.2	NS

P value tests  $r \neq 0$  with 100 (1-P)% certainty NS - not significant

all cases with the exception of the nonfluoridated 65+ age group. Linear regression analysis of year-by-year cancer death rates from individual city data (Table 6b) confirms these findings.

In addition, the increases in cancer death rates for both 45-64 and 65+ age groups are greater for the fluoridated group of cities than for the nonfluoridated group of cities, whereas no significant differential in cancer death rate trends in the 0-24 and 25-44 year age groups are evident. To test the significance of these differences, a linear regression analysis of year-by-year differences of the average cancer death rates of the fluoridated group of cities minus the average cancer death rates of the nonfluoridated group of cities was performed (Table 7). No significant difference in the cancer death rate of either the 0-24 or 25-44 year age group could be observed; however significant increases were observed in fluoridated cities in populations 45 and over: an increase of 15.2 cancer deaths per 100,000 population ( $P < .02$ ) in the 45-64 year age group and an increase of 35.4 cancer deaths per 100,000 population ( $P < .05$ ) in the 65+ age group. The differences observed are quite similar to the differences that would be computed from Tables 6a and 6b (Table 8).

Whereas the cancer death rate in the fluoridated cities is clearly increasing faster than in the nonfluoridated cities, it might still be argued that the age intervals chosen were too large and that the 45-64 year age group in the fluoridated cities is growing older faster than the same age group in the nonfluoridated cities, and similarly for the 65+ age group. Table 9 shows that the age distribution trends within these age groups are virtually identical and dispels such an objection.

Age-corrected cancer death rates were calculated by using a reference population with an age distribution intermediate between those of the fluoridated and nonfluoridated populations of 1952 and 1969 (Table 3 and Table 10).

The age-corrected cancer death rates appear on Table 11 and reflect 8-9 more cancer deaths per 100,000 population per year in the fluoridated cities than in the nonfluoridated cities.

There is a greater increase in the percentage of nonwhites in the fluoridated group of cities than in the nonfluoridated group. Most of this increase occurs in the 0-24 and 25-44 year age groups, with smaller increases observed in the 45-64 and 65+ age groups (Table 12). To determine whether this relative increase in nonwhite population could account for the increase in cancer death rate observed in fluoridated cities, a regression analysis of increase in age-adjusted cancer death rate against increase in % nonwhite population was performed for each city. No significant correlation could be obtained. Similarly, since the most significant increase in cancer death rate of fluoridated cities in excess of that of nonfluoridated cities occurred in the 45-64 age group, a linear regression of increase in cancer death rate of cities for this group as a function of increase in % nonwhite population was performed. Again no significant correlation could be observed.

Table 6b

## Linear Regression of Year-By-Year Cancer Death Rates for Each City (N = 180)

Age Group	Cities	Sample Size	Correlation Coefficient	Slope	Cancer Death Rate-1952	Cancer Death Rate-1969	CDR Increase 1952-1969	P
0-24	Fluoridated	180	-0.3792	-0.1388	9.57	7.08	-2.49	$\leq 10^{-4}$
	Nonfluoridated	180	-0.3097	-0.1416	9.67	7.12	-2.55	$< 10^{-4}$
25-44	Fluoridated	180	-0.0857	-0.1123	49.42	47.40	-2.02	NS
	Nonfluoridated	180	-0.1026	-0.1673	47.39	44.38	-3.01	$< .20$
45-64	Fluoridated	180	0.3722	2.257	337.2	377.9	40.7	$< 10^{-5}$
	Nonfluoridated	180	0.1603	1.341	324.5	348.6	24.1	$< .05$
65+	Fluoridated	180	0.1790	2.246	1031.9	1072.4	40.5	$< .02$
	Nonfluoridated	180	0.0109	0.2100	974.2	978.0	3.8	NS

P value tests  $r \neq 0$  with 100 (1-P)% certainty

NS - not significant

Table 7

Linear Regression of Year-by-Year Differences in Average Cancer Death Rates

Age Group	Sample Size	Correlation Coefficient	Slope	Difference* in CDR		Increase in CDR F-NF from 1952 - 1969	P
				F-NF 1952	F-NF 1969		
0-24	18	0.1443	0.0227	-0.1929	+0.2157	+0.41	NS
25-44	18	0.0196	0.0093	+2.212	+2.370	+0.16	NS
45-64	18	0.5294	0.8916	+12.98	+28.13	+15.2	<.02
65+	18	0.4338	2.0815	+57.36	+92.75	+35.4	<.05

P value tests  $t > 0$  with 100 (1-P)% certainty.

\*The difference in cancer death rate obtained by linear regression of the year-by-year differences in the average cancer death rate of the ten fluoridated cities minus the ten nonfluoridated cities. NS - not significant

Table 8

Increase in the Difference in Cancer Death Rate (per 100,000) of Fluoridated Cities and Nonfluoridated Cities by Age from 1952 to 1969

Method*	Age Group			
	0-24	25-44	45-64	65+
6a	+0.09	-0.15	+13.1	+33.9
6b	+0.06	+0.99	+16.4	+36.7
7	+0.41	+0.16	+15.2	+35.4
	(NS)	(NS)	(P < .02)	(P < .05)

Table 9

Age Distribution Within Age Groups 45-64 and 65+ for Fluoridated (F) and Nonfluoridated (NF) Cities

	1950	1960	1970
F (55-64/45-64)	.43	.45	.48
NF (55-64/45-64)	.43	.45	.47
F (75+/65+)	.29	.31	.37
NF (75+/65+)	.29	.34	.38

Table 10

	Age Distribution of Reference Population			
	0-24	25-44	45-64	65+
1952	36.72	31.55	22.88	8.86
1969	43.47	23.45	21.69	11.39

This table was obtained by taking an average of the values for 1950 and 1970 on Table 3 and interpolating to obtain an age distribution exactly between the fluoridated and nonfluoridated cities for 1952 and 1969.

Table 11

	Age-Adjusted Cancer Death Rates (per 100,000) of Fluoridated and Nonfluoridated Cities		
	1952	1969	Increase*
<b>Fluoridated Cities</b>			
6a	188.25	217.46	29.21
6b	187.69	218.31	30.63
<b>Nonfluoridated Cities</b>			
6a	178.83	200.26	21.43
6b	179.08	200.50	21.43
<b>Difference</b>			
6a	9.42	17.20	7.78
6b	8.61	17.81	9.20
7	8.68	17.32	8.64

\*As calculated by the methods described in Tables 6a, 6b, and 7.

Table 12

	% Nonwhite in Fluoridated and Nonfluoridated Cities for 1950, 1960 & 1970				
	Total	0-24	25-44	45-64	65+
<b>1950</b>					
Fluoridated	15.9	18.36	17.50	12.56	8.07
Nonfluoridated	15.3	17.27	18.61	12.64	9.28
Difference	0.6	1.09	-1.11	-0.08	-1.21
<b>1960</b>					
Fluoridated	25.7	31.50	27.81	18.92	11.95
Nonfluoridated	20.7	24.59	22.45	16.27	11.29
Difference	5.0	6.91	5.36	2.65	0.66
<b>1970</b>					
Fluoridated	35.4	42.79	37.39	27.13	18.72
Nonfluoridated	28.6	34.17	29.02	22.76	16.29
Difference	6.8	8.62	8.37	4.37	2.43
Net Increase in F-NF from 1950 to 1970	6.2%	7.53%	9.48%	4.45%	3.64%

While nationally the cancer death rate of nonwhites is increasing faster than the cancer death rate of whites, we have been unable to observe such a trend in central cities. When the cancer death rate of nonwhites was plotted as a function of the proportion of nonwhites living in central cities to total nonwhites living in the U.S. ( $NW_{cc}/NW_{u.s.}$ ) for 1920, 1930, 1940, 1950, 1960, and 1970, correlation coefficients of .902, .952, and .982 were observed for age groups 45-54, 55-64, and 65-74, respectively. When the same data were tabulated for whites, it was found that whites and nonwhites at similar degrees of urbanization experience similar cancer death rates.

From 1952 to 1969, the proportion of males 45-64 and 65+ decreased faster in the fluoridated group of cities than in the nonfluoridated group of cities (Table 13).

Table 13

Sex Composition of Fluoridated and Nonfluoridated Populations		Males per Total Population		
		1950	1960	1970
Total	Fluoridated	.486	.482	.471
	Nonfluoridated	.482	.478	.471
0-24	Fluoridated	.481	.480	.491
	Nonfluoridated	.493	.494	.492
25-44	Fluoridated	.481	.475	.483
	Nonfluoridated	.481	.489	.491
45-64	Fluoridated	.495	.469	.461
	Nonfluoridated	.482	.472	.463
65+	Fluoridated	.473	.431	.403
	Nonfluoridated	.429	.418	.406

### Discussion

According to the National Cancer Institute, the total U.S. age-adjusted cancer mortality rate (per 100,000) for white males has increased from 165.3 in 1950-4 to 182.5

in 1965-9. Similarly, the cancer death rate of highly urbanized counties has increased accordingly during the same period (18). Thus, during this period, there has been a real increase in cancer death rate that cannot be explained by either age or urbanization.

It has been strongly suggested that the addition of chemical carcinogens to the environment is a major cause of this increase in cancer (19).

"... the U.S. population ... is being continually exposed to a wide range of known and identified chemical carcinogens in their air, water, and food, besides, in all likelihood, to a greater range still of unknown or untested carcinogens."

Furthermore, the inability to detect the carcinogenicity of a substance epidemiologically does not demonstrate that that substance is not carcinogenic:

"... it is generally considered that epidemiological techniques are unlikely to detect weak carcinogens unless there are sharp differentials in exposure of the general population, as with cigarette smoking; even with smoking, the single largest cause of cancer deaths, several decades of investigation were required before causality could be established. For widely dispersed agents ... , human experience is unlikely to provide any meaningful indication of safety or hazard" (19).

In this context, it is not surprising that both negative and positive findings concerning a link between fluoridation and cancer have been reported. In most of these reports (20, 21, 22, 23), no study of cancer death rates before and after fluoridation was made.

Only recently have before-and-after studies been performed.

In November 1975 the NCI released a report (24), later published in its Journal (25), indicating no excessive increase in cancer death rate after fluoridation as compared to before fluoridation. The shortcomings of this study have already been described elsewhere (26).

Yiamouyiannis and Burk earlier reported a substantial increase in crude cancer death rate following fluoridation (26) and subsequently reported preliminary findings indicating that this increase occurred in white as well as nonwhite and occurred exclusively within 45-64 and 65+ age groups (27).

The present study shows that the increase in cancer death rates in fluoridated cities is significantly higher in people aged 45 and over than in nonfluoridated cities.

Age-corrected cancer death rate figures confirm earlier indications using crude cancer death rates that the cancer death rate in fluoridated cities is increasing at a faster rate than the cancer death rate of nonfluoridated cities.

Within central cities, the cancer death rate of nonwhites is not increasing faster than the cancer death rate of whites. The disagreement of these findings with national figures is due to the greater urbanization trends of nonwhites. Since this study considered central cities only, the urbanization-related increase in cancer death rate among nonwhites was eliminated.

In fact, looking at increases in age-adjusted cancer death rates of the 20 cities as a function of increase in the % population nonwhite, no significant correlation could be observed.

All other things being equal, there is no reason to expect that "nonwhite" cancer death rate should be increasing at a faster rate than "white" cancer death rate. In the deep south states where urbanization among whites and nonwhites is comparable (about 50%), there is no significant difference in cancer death rates between the two groups. Only in northern states, where 70% of the whites and 95% of the nonwhites live in urban areas, is the cancer death rate among nonwhites greater than the cancer death rate among whites.

Nationally, the cancer death rate of males is higher than that of females in populations 45+ years of age (28). Age-sex corrected cancer death rates indicate 9-10 more cancer deaths per 100,000 per year in the fluoridated group of cities than in the nonfluoridated group of cities.

The unreliability of the SMR (Standardized Mortality Ratio) used in a number of studies of the fluoridation-cancer link has been discussed elsewhere (29) but also deserves mention here. Consider Table 14 of two hypothetical populations in which one population serves as a control and the other population is fluoridated at the end of 1950. The increase in the crude cancer death rate for the fluoridated population ( $279 - 204 = 75$ ) exceeds the increase in the crude cancer death rate for the nonfluoridated population ( $258 - 204 = 54$ ); however the increase in SMR for the fluoridated population ( $1.24 - 1.00 = 0.24$ ) is less than the increase in SMR for the nonfluoridated population ( $1.26 - 1.00 = 0.26$ ). Comparison of the two populations in Table 14 shows that the fluoridated population has, in every age group, a cancer death rate increase equal to or greater than that of the nonfluoridated population.

In this illustrative case, the crude death rate indicated (in part) a true (greater) increase in cancer death rate in the fluoridated population relative to the nonfluoridated population, whereas the SMRs indicated an untrue (lesser) increase in cancer death rate in the fluoridated population relative to the nonfluoridated population.

Table 14

Age Group (years)	Nonfluoridated — 1950		Prefluoridated — 1950		Reference Population
	Population	Cancer Deaths	Population	Deaths	
0-	300,000	24	300,000	24	8
25-	300,000	120	300,000	120	40
45-	300,000	900	300,000	900	300
65+	100,000	1000	100,000	1000	1000
All ages	1,000,000	2044	1,000,000	2044	204
Expected SMR		2044		2044	
		1.00		1.00	

Age Group (years)	Nonfluoridated — 1970		Fluoridated — 1970		Reference Population
	Population	Cancer Deaths	Population	Deaths	
0-	300,000	24	350,000	28	8
25-	300,000	210	300,000	210	70
45-	300,000	1350	200,000	900	450
65+	100,000	1000	150,000	1650	1100
All ages	1,000,000	2584	1,000,000	2788	279
Expected SMR		2044		2248	
		1.26		1.24	

The unreliability of the SMR is further evident from the findings of Taves (30) who reported a mere 2% increase in cancer death rates in large cities from 1950 to 1970 as compared to the NCI figure of approximately 13% (18) and our figure of approximately 14% during the same period of time. Using the same data, Taves was also able to observe that by using different reference populations, he could get results indicating a positive or negative relationship which depended only upon the reference population he was using, clearly indicating that his results were artefacts of the method itself.

Considering other demographic variables, only one remained that might indicate an alternative explanation for the increased cancer death rate observed in the fluoridated group of cities. In the fluoridated group, most of the cities experienced a decrease in population, whereas among the nonfluoridated cities, most experienced an increase in population. Comparison of the cancer death rate of fluoridated cities whose population decreased with the cancer death rate of nonfluoridated cities whose population decreased still indicated a higher cancer death rate in the fluoridated group of the same magnitude, 8 per 100,000 per year.

This study was confined to large cities for the following reasons: 1) Fluoridated water comprises only part of the fluoride intake. Food products and beverages such as infant formulas, soft drinks, beer, spaghetti, salad dressings, jellies, etc. that are made with water will contain more or less fluoride depending on whether or not the water in that area is fluoridated. People living in large cities are more likely to consume products made in that area than are people living in smaller cities. This means that in larger cities fluoride intake will be more directly related to water fluoride content than in smaller cities. 2) Each city provides a large enough sample size to justify the use of unweighted averages. 3) Highly urbanized areas are compared to highly urbanized areas. 4) Data for large cities in the detail necessary for the present study are more readily available. 5) Using city rather than county or SMSA (Standard Metropolitan Statistical Area) data allows a study involving areas that are either completely fluoridated or completely nonfluoridated.

In a preliminary survey, the 1970 cancer death rates of all cities east of the Mississippi with population 10,000 and over were compared, state by state, for fluoridated and nonfluoridated cities. For each state, the percent difference in the cancer death rate of the fluoridated cities and the nonfluoridated cities was determined, weighted by the square root of the product of the state's population in cities 10,000 and over that were fluoridated and the state's population in cities 10,000 and over that were not fluoridated ( $\sqrt{P(F) \times P(NF)}$ ); these values were added for all states east of the Mississippi. Again an excess in cancer death rate similar to that reported herein was found.

**Animal Studies:** The increase in the incidence in melanotic tumors in fruit flies exposed to low levels of fluoride originally reported by I. Rapaport (31) was

confirmed by Herskowitz and Norton who showed a dose-dependent increase in tumor incidence with increasing levels of fluoride (1).

Taylor and Taylor (2) reported that 1 ppm fluoride in the drinking water of DBA strain mice implanted inguinally with RC mammary adenocarcinoma experienced a 13-17% increase in tumor growth rate, although a dose-dependent relation in this case was not observed. Both control (n=203) and experimental (n=184) groups of mice were fed a mixed grain diet containing negligible amounts of fluoride. An increase in the incidence of mammary cancer has been reported in C<sub>3</sub>H and DBA female mice fed 1 ppm fluoride in their drinking water (32), but no significant difference was found in CD-1 strain mice fed "10 ug/ml fluorine as sodium-fluoride" in their drinking water (33).

From our results, it is not possible to determine whether the fluoridation-linked increases in cancer death rate were due to increased incidence, or increased mortality of persons who already had cancer.

Studies of the relationship of nonwater-borne fluorides and cancer have reported positive correlations between food fluoride levels and stomach cancer (34) and a possible correlation between air-borne fluorides and lung cancer (35 and 36).

In addition, *in vivo* and *in vitro* experiments indicating that 1 ppm fluoride interferes with DNA repair (37) and that low levels of fluoride can alter the G/C ratio of RNA (38) provide one explanation of how the carcinogenic and mutagenic effects of fluoride may be mediated.

### Conclusions

In view of animal studies showing that low levels of fluoride are tumorigenic and that 1 ppm fluoride increases tumor growth rate, interferes with DNA repair *in vitro* and *in vivo*, and is mutagenic, it is not surprising that this study has found an increase in human cancer death rate in fluoridated areas. Furthermore, it perhaps would not have been surprising to have found that the carcinogenic effects of fluoride would be swamped out by the variation in cancer death rates of individual cities due to other variables. According to current dogma, 20-30 years must pass before a substance will begin to affect cancer death rate. In this context, the two most powerful results of this paper are 1) that a large part of the increase in cancer death rate occurred in a relatively short time (5 years) and 2) that increase plus additional increases were sustained during the entire period of study. Another premise of the current dogma is that all carcinogens exhibit a dose-dependent relationship. In the case of fluoride, it appears that a chronic low-level exposure to fluoride would be optimal for producing metabolic aberrations conducive to producing a cancerous cell (1) or selectively stimulating the growth rate of cancerous cells (2) and that higher concentrations do not enhance these effects and may, in fact, lead to cell stasis or death.

We expect that the value of the fluoridation-linked increase reported herein is low since we do not believe that the increase in cancer death rate in fluoridated vs. nonfluoridated cities is a linear function of time. Thus fitting our data to a straight line would tend to minimize the increase. Also, because of the movement of people and fluoride-containing food products in and out of the cities studied, we believe the effects observed were diluted and that, had the populations and food products been confined to their areas, a larger fluoridation-linked increase in cancer would have been observed.

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### Discussion

- Prof. Burgstahler: From your unadjusted curves it almost seems that something ceased to occur in the cities that did not fluoridate after 1950. I realize, of course, that the pre-1950 increases in cancer death rates might have tapered off without something ceasing to occur, but I wonder what comment you might care to make on this.
- Dr. Burk: The way I like to draw the curves is as differences in cancer death rates plotted against time. In this way one can see clearly that the effect showed up right after the start of fluoridation and that the differences have continued to grow even to the present. Although corrections for small differences in age and race between the two sets of cities make the rate differences less than the unadjusted ones, adjustment for the "mixing" factor arising from the use of fluoridated foods and beverages in nonfluoridated cities would doubtless show that the true differences are much larger. In England, because tea drinking is so widespread, it would probably be impossible to detect differences such as we have found.
- Dr. Moolenburgh: Can you explain why the standard mortality ratio (SMR) approach seems to show no increase in cancer death rate with fluoridation (or even some "protection" from it), while your data show just the opposite?
- Dr. Burk: That is because SMR calculations are arbitrary, fictitious, and hypothetical; they depend strictly on what figures are used as a standard. SMR calculations are useful in certain types of statistical analyses but not here. Even the National Cancer Institute SMR figures for fluoridated versus nonfluoridated cities differ significantly from those calculated by Dr. Taves.
- Dr. Oelschlager: How do your data compare with those of other countries such as India and England? Do they have any bearing on specific cancer sites, such as the 7-fold higher esophageal cancer rate in England?
- Dr. Burk: Direct comparison of these cancer death rates with those of other countries is not possible. There are too many demographic, climatological, environmental, dietary, and other differences. Only by comparing an extremely large number of people in comparable circumstances, as in our ten largest fluoridated and nonfluoridated U.S. cities, can such a comparison be meaningful.
- Dr. Teotia: This paper is very exciting, but I believe other factors such as increasing air pollution, growth in industrialization, and differences in smoking habits must be considered and ruled out before the differences which you report can be attributed to fluoridation.

Dr. Burk: What you say is true, but by taking the ten largest cities in each group throughout the United States, these factors tend to be equalized. With such large numbers of people involved it is highly unlikely that there would be appreciable differences in such factors as smoking habits or even the amount and effects of air pollution.

FLUORIDE-INDUCED CHANGES IN 60 RETIRED ALUMINUM WORKERS

by

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SUMMARY: Orthopedic, radiological and analytical examinations were performed in a group of 60 retired disabled workers of an aluminum factory. Occupational disease had previously been recognized in this group because of disturbances in the respiratory and circulatory systems. The age of those examined averaged 49.6 years; the duration of exposure averaged 16.9 years; 88.3% had worked in the electrolysis department.

In the majority of cases orthopedic examination showed changes of a generalized character in locomotion, differing in the degree of intensity. Exostoses and ossification of the interosseous membranes and muscle attachments were the most frequently detected radiological changes. Generalized sclerosis and periosteal reactions occurred less frequently. No major variations from the norm were noted in the levels of serum calcium, phosphorus, acid and alkaline phosphatase.

Expansion of the industrial uses of fluoride compounds accounts for an ever-increasing pollution of the environment. The halogen emanates into the environment during industrial exploitation of minerals containing fluoride (cryolites, apatites, phosphorites) in aluminum and fertilizer factor-

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