Research and Development

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Project Summary

Correlations Between Age-Adjusted Mortality Rates for White Males and Females in the United States, by County: 1968-1972

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This study was undertaken to test the suitability of the User-Prompted Graphics Data Evaluation (UPGRADE) computer system for use in environmental health studies. All possible pairs of correlation (2400 in all) between county mortality rates for about 50 causes of death were systematically investigated, using nearly all of the nation's 3082 counties in each calculation. The causes of death with the highest correlations were determined and their geographic variations mapped.

The strongest correlations were found between diseases that are closely associated with population density. In some cases, diseases affecting related organs were strongly correlated, but in many cases they were not correlated. The common practice of combining death from diseases affecting related organs may thus obscure rather than clarify associations with environmental or other variables.

The distribution of county mortality rates was shown to be neither normal nor log-normal. Thus the interpretation of the absolute values of the correlation coefficients is uncertain; however, their relative rankings may be more trust-worthy.

The UPGRADE computer system used to perform the calculations was shown to be useful in providing easy access to a valuable data base, but was also shown

to lack certain features that would have made the calculations more efficient and cost-effective.

This Project Summary was developed by EPA's Office of Monitoring Support and Quality Assurance, Washington, D.C., to announce key findings of the research project that is fully documented in a separate report of the same title (see Project Report ordering information at back).

Introduction

A flexible computer graphics and analysis system that can provide simultaneous access to environmental and health data bases would be helpful in environmental health studies. The United States Environmental Protection Agency has partially supported the development of such a system: User-Prompted Graphics Data Evaluation (UPGRADE). As an early test of the system's capabilities, a study was undertaken of correlations between county mortality rates.

A knowledge of correlations between causes of death is useful for several reasons:

 Strong correlations may imply common factors in the development of the disease. Conversely, weak correlations may be a warning that the diseases are not closely related and that they should not be combined

- or otherwise associated in epidemiological studies.
- Differences or similarities of correlations between sexes or races may indicate genetic or occupational factors of importance in tracing disease etiology.
- 3) Negative correlations may indicate competing causes of death.

The objective of the study was to evaluate use of the UPGRADE system to calculate all possible correlations, determine the strongest correlations, record them for future use by interested researchers, and investigate the geographical variation of the strongly correlated diseases.

Experimental Procedure.

The data base used in the study consisted of county-level, age-adjusted mortality rates averaged over the fiveyear period 1968-1972. The rates were calculated by Herb Sauer of the University of Missouri, using the detailed mortality records provided by the National Center for Health Statistics (NCHS), All deaths were recorded between 1968 and 1971, but only every other death in 1972. Thus, some sampling error could exist for the less common diseases. Death rate calculations were based on each county's 1970 population. About 50 causes of death were studied for white males and females (Table 1).

Because the 3082 mortality rates for almost any cause of death contained some 10-30 extraordinarily high rates, due often to confounding factors such as the existence of a major institution (Indian reservation, regional hospital, prison) in the county, and because these rates could exert undue influence on the Pearson correlation coefficient, such outliers were eliminated by use of a scatterplot screening technique. Visual inspection of the scatterplots suggested reasonable upper and lower bounds for county mortality rates to be included in the correlation calculations. Varying these limits provided an indication of the sensitivity of the calculations to the number of counties included: only about a 10-15% variation in the most significant correlations was observed.

A stringent significance criterion of p <.0001 was chosen to lessen the likelihood of error in identifying significant correlations. Even so, of the approximately 1200 possible correlations for each sex, 152 correlations were significant for white females and 136 correlations were significant for white males at the p <.0001 level.

Table 1. UPGRADE Variables Used in This Study with Corresponding ICDA Codes

	·	•
UPGRADE CODE	<i>VARIABLE</i>	ICDA CODES (8th Revision)
071	Tuberculosis, All Forms	010-019
072	Other Infective Disease	000-009, 020-136
073	Ca Buccal Cavity, Pharynx	140-149
074	Cancer of Esophagus	150
075	Cancer of Stomach	151
076	Cancer of Intestine	152, 153
077	Cancer of Rectum	154
078	Ca Liver, Gall B., Ducts	155, 156
079	Cancer of Pancreas	157
080	Other Digestive Cancer	158, 159
081	Cancer of Resp. System	160-163
082	Cancer of Breast	174
083	Cancer of Cervix	180
084	Cancer of Uterus	181, 182
085	Ca Prost, Other Female Ca	183, 184, 185
086	Cancer of Bladder	188
087	Cancer of Kidney, Etc.	189
088	Cancer of Central Nervous System (CNS)	191, 192
089	Residual Cancer	170-3, 183, 186-7, 190, 194
090	Cancer, III-Def. & Sec.	195-199
091	Lymphosarcoma, Etc.	200
092	Hodgkin's Disease	201
093	Multiple Myeloma	203
094	Leukemia	204-207
095	Other Lymphatic	202, 208, 209
096	Neoplasms, Benign & Unspecified	210-239
097	Diabetes	250
098	Alcoholism	303
099	Rheumatic Heart Dis.	390-398
100	Hypertension	400-404
101	Acute Ischemic Heart Dis.	410, 411
102	Chronic Ischemic Heart	412, 413
103	Other Heart Disease	420-429
104	Cerebrovascular Disease	430-438
105	Arteriosclerosis	440
106	Aortic Aneurysm	441
107	Other Arteries, Etc.	442-448
108	Veins, Etc.	450-458
109	Influenza and Pneumonia	470-486

(continued)

Table 1.	(Continued)	
UPGRADE CODE	VARIABLE	ICDA CODES (8th Revision)
110	Chronic Resp. Dis.	490-493, 517-519
111	Cirrhosis of Liver	<i>571</i>
112	Chronic Nephritis, Etc.	<i>582-584</i>
113	Infections of Kidney	590
114	Congenital Heart & Circ.	746, 747
115	Other Congenital	740-745, 748-759
116	Other Early Infancy	760-778
117	Symptoms, III-Defined	780-796
126	Major CV Diseases	390-448
127	Cancer, All Sites and Forms	140-209

Table 2. Correlation Coefficients for the Top Twenty Correlations

White Females

Disease Title	Scatterplot Method	Exclusion/ Filter Method
1. Cancer of the Respiratory System - Cirrhosis	.224	.206
2. Cancer of the Intestine - Cancer of the Breast	.211	.161
3. Chronic Ischemic - Cancer, All Forms	.189	.238
4. Chronic Ischemic - Cirrhosis	.182	.198
5. Cancer of the Intestine - Cancer of the Rectum	.180	.145
6. Cancer of the Cervix - Major CV	.180	.189
7. Other Heart Disease - Symptoms, III-Defined	.179	.203
8. Rheumatic Heart Disease - Chronic Ischemic	. 175	.193
9. Chronic Ischemic - Other Heart	172	201
10. Acute Ischemic - Cerebrovascular	.171	.173
11. Cancer of the Rectum - Rheumatic Heart	.170	.143
12. Aortic Aneurysm - Cirrhosis	.170	.152
13. Cancer of the Esophagus - Cirrhosis	.169	.118
14. Cancer of the Rectum - Chronic Ischemic	.167	.151
15. Rheumatic Heart - Cirrhosis	.166	.164
16. Diabetes - Major CV	.166	.210
17. Rheumatic Heart - Aortic Aneurysm	.161	.141
18. Cancer of the Rectum - Cancer of the Breast	.159	.155
19. Cirrhosis - Cancer, All Forms	.150	.194
20. Major CV - Cancer, All Forms	.146	.149

The top 30 of these correlations for each sex were further examined. If outliers were suspected, a new modified regression was run using different boundaries for excluding counties. (In most cases, fewer than 1% of all counties were excluded). This procedure resulted in some changes of order among the top correlations, but few sharp changes in the magnitudes of the correlation coefficients.

Results and Discussion

From the procedures discussed above, a final list of the 20 strongest correlations was obtained (Tables 2 and 3). No fewer than eleven correlations appear in both tables, and only two pairs of diseases for each sex were not strongly correlated in the other sex (Table 4). Thus, sex is not a strong factor in the co-variation of mortality rates for most diseases.

However, population density is very clearly an important factor in the most strongly correlated disease pairs, as can be seen by comparing those causes of death most strongly associated with county population to those most strongly correlated with each other. For white females, six of 48 causes of death investigated showed a strong (p <.0001) increase in mortality rates in the more populous counties (Table 5). Four of these six appear most often in the strongest 20 correlations for females. Similarly, nine of 46 causes of death investigated for white males showed a strong (p <.0001) increase with county population (Table 6). Six of these nine appear most often in the strongest 20 correlations for white males.

The strongest negative correlations are dominated by the "miscellaneous" categories of "Other Heart Disease" and "Symptoms, Ill-defined" (Table 7). These categories probably "compete" with other causes of death in the sense that inexperienced or untrained county medical officers are more likely to classify difficult cases in the miscellaneous category. However, the frequent appearance of rheumatic heart disease in this table does not appear to be explainable in the same way. Rheumatic heart disease appears only for white females and only in association with diseases that have higher mortality rates in rural regions. This phenomenon seems worthy of further study.

The Pearson product-moment correlation coefficient calculation assumes a normal distribution. However, the distribution of county mortality rates was cal-

Table 3. Correlation Coefficients for the Top Twenty Correlations

White Males

Disease Title	Scatterplot Method	Exclusion/ Filter Method
1. Other Heart Disease - Symptoms, Ill-Defined	.286	.256
Cancer of the Respiratory System - Major Cardiovascular	.286	.302
3. Chronic Ischemic Heart Disease - Aortic Aneurysm	.268	.201
4. Chronic Ischemic - Cirrhosis of the Liver	.263	.221
5. Chronic Ischemic - Cancer, All Forms and Sites	.250	.217
6. Cirrhosis - Aortic Aneurysm	.246	.146
7. Cirrhosis - Cancer, All Forms	.243	.249
8. Cancer of the Respiratory System - Chronic Ischemic	.242	.223
9. Cancer of the Rectum - Cancer of the Intestine	.242	.168
10. Cancer of the Rectum - Chronic Ischemic	.241	.205
11. Major CV - Cancer, All Forms	.239	.220
12. Acute Ischemic Heart Disease - Cerebrovascular	.235	.301
13. Cancer of the Buccal Cavity, Pharynx - Cancer of the Respiratory System	.233	.170
14. Cancer of the Esophagus - Cirrhosis	.231	.186
15. Cancer of the Respiratory System - Chronic Respiratory	.231	.203
16. Cancer of the Respiratory System - Aortic Aneurysm	.226	.173
17. Aortic Aneurysm - Cancer, All Forms	.214	.178
18. Cancer of the Rectum - Cirrhosis	.205	.161
19. Cancer of the Respiratory System - Cancer III-Defined and Unspecified	.202	.175
20. Cancer of the Respiratory System - Cirrhosis	.201	.183

Table 4. Correlations That Are Strong For One Sex But Not The Other

		Correlation Coefficie		
Rank (WF)		WF	WM	
11	Cancer of the Rectum - Rheumatic Heart Disease	.170	.130	
16	Diabetes - Major CV Diseases	.166	.098	
Rank (WM)				
1	Cancer of the Resp. System - Major CV Diseases	.084	.286	
13	Cancer of the Resp. System - Ca. Buccal Cavity	.074	.233	

culated for six causes of death for each of three race-sex groups and not one of the 18 data sets passed chi-square tests for normality. In every case, the distributions were more strongly clustered toward the mean and simultaneously more dispersed in the tails than the normal distribution. Such distributions are termed kurtic. The 18 distributions were then plotted on logarithmic probability paper but failed to display log-normal behavior. (Figure 1 provides an example of the nonlinear shape of the distribution). When a more homogenous set of counties is selected, the distribution of mortality rates may more nearly approach log-normality. For example, lung cancer death rates for white males in 234 mostly urban counties were much closer to a log-normal distribution than the rates from all 3082 counties (Figure 2).

Thus we are uncertain of the interpretation to be given to the absolute values of the Pearson product-moment correlations calculated in Tables 2 and 3, although the relative values may be more trustworthy. For this reason, we have considered only correlations with p <.0001. Nonparametric statistics would have been preferable, but because of the large number of counties involved, it was not feasible to calculate Spearman or Kendall correlation coefficients.

It should also be noted that the lack of normality of the county mortality rate distributions probably decreases the allowed range of negative correlations. (For example, two log-normally distributed variables have a minimum r of -0.369, although the positive limit remains at +1.0.) Thus, a negative r is probably indicative of a stronger relationship than a positive one of the same magnitude.

Geographic variations were studied using bivariate color maps created by the Domestic Information Display System (DIDS). Rates for each disease were categorized in quartiles, and colors assigned to each of the 16 cells of the resulting 4×4 matrix. Geographic characterizations of six disease pairs showing high correlations for both white males and white females were prepared. An example is given in Table 8.

Two other studies have used similar programs for investigating correlations between diseases. Sauer¹ has grouped the same basic mortality data (1968-72) by state and by state economic area; thus, the present study of county data can be viewed as complementary to Sauer's work. Wellington, MacDonald

Table 5. Variation in Mortality Rate with County Population
(Age-Adjusted Mortality Rate per Million at Risk (1968-72)—White Males)

1970 White Male County Population (in thousands)

	1970 White Male County Population (in thousands)					
Cause of Death	O-5	5-10	10-25	25-100	>100	P*
Tuberculosis, All Forms	25	30	32	31	35	
Other Infective Disease	64	65	56	56	<i>53</i>	_
CA Buccal Cavity, Pharynx	45	44	47	54	64	.02
Cancer of Esophagus	26	29	<i>33</i>	<i>38</i>	46	.0001
Cancer of Stomach	94	95	92	92	107	_
Cancer of Intestine	152	157	162	175	208	.0001
Cancer of Rectum	39	46	56	62	<i>72</i>	.0001
Cancer of Liver, Gall B., Ducts	31	28	28	29	35	
Cancer of Pancreas	110	105	108	108	111	_
Other Digestive Cancer	7	8	8	7	8	_
Cancer of Resp. System	512	<i>529</i>	566	600	645	.0001
Cancer of Breast	3	2	3	3	3	_
Cancer of Prostate	202	195	200	200	198	
Cancer of Bladder	61	<i>55</i>	59	70	78	_
Cancer of Kidney, Etc.	44	43	43	47	46	_
Cancer of CNS	47	47	49	47	<i>51</i>	_
Residual Cancer	77	77	72	70	68	_
ymphosarcoma, Etc.	38	36	40	41	43	
Cancer III-Def. and Sec.	109	109	111	113	118	_
łodgkin's Disease	22	22	21	20	21	
/lultiple Myeloma	24	24	24	25	24	_
eukemia	108	96	97	92	91	
Other Lymphatic	25	26	26	25	24	
leoplasms, Benign and Unspec.	23	20	22	25	26	_
Diabetes	170	166	171	174	173	_
Ncoholism	24	26	27	25	26	_
Rheumatic Heart Disease	<i>55</i>	61	65	72	<i>83</i>	.0001
lypertension	117	133	129	121	104	
Noute Ischemic Heart Dis.	3,006	3,004	3,019	2,860	2,629	.0001
Chronic Ischemic Heart	1,223	1,300	1,445	1,682	1,930	.0001
Other Heart Disease	376	321	293	247	190	.0001
Cerebrovascular Disease	1,207	1,229	1,252	1,166	1,056	.0003
Arteriosclerosis	198	198	202	199	180	_
Nortic Aneurysm	90	92	102	125	129	.0001
nfluenza and Pneumonia	415	403	397	387	393	
Chronic Resp. Disease	403	376	<i>395</i>	423	<i>397</i>	_
Cirrhosis of Liver	115	116	128	<i>15</i> 8	219	.0001
Chronic Nephritis	44	45	43	47	<i>35</i>	_
nfections of Kidney	50	46	49	44	<i>39</i>	-
Congenital Heart & Cir.	42	44	44	42	41	_
Other Congenital	48	45	47	45	42	_
Other Early Infancy	237	234	228	216	199	.02
Major Cardiovascular Diseases	6,355	6,416	6,587	6,549	6,311	_
Cancer, All Sites and Forms	1,777	1,774	1,848	1,926	2,071	.0001

^{*}Probability that the increase (decrease) in rates is due to chance (Pearson product-moment correlations applied to all counties)

and Wolf² considered cancer mortality between 1950 and 1969 on a statewide basis. Comparisons with results from both works reveals considerable agreement, although different choices of disease groups makes detailed comparisons impossible.

References

1. Sauer, H.I., Geographic Patterns in the Risk of Dying and Associated Fac-

tors: U.S. 1968-72, National Center for Health Statistics, U.S. Dept. of Health & Welfare, Wash. D.C. 1979.

 Wellington, MacDonald, and Wolf, Cancer Mortality: Environmental and Ethnic Factors, Academic Press, New York, 1979.

Table 6. Variation in Mortality Rate with County Population (Age-Adjusted Mortality Rate per Million at Risk (1968-72)—White Females)

1970 White Female County Population (in thousands)

	1970 White Female County Population (in thousands)					
Cause of Death	0-5	5-10	10-25	25-100	>100	P*
Tuberculosis, All Forms	9	10	10	10	10	
Other Infective Disease	56	<i>52</i>	46	42	40	.03
Cancer of Buccal Cavity, Pharynx	16	15	16	17	19	
Cancer of Esophagus	9	8	9	9	12	.03 -
Cancer of Stomach	50	46	48	45	52	_
Cancer of Intestine	143	147	156	160	173	.002
Cancer of Rectum	28	29	34	38	40	.002
Cancer of Liver, Gall B., Ducts	37	31	31	32	32	.002
Cancer of Pancreas	61	62	64	64	66	_
Other Digestive Cancer	8	6	6	6	6	
Cancer of Resp. System	85	90	97	107	126	.0001
Cancer of Breast	212	219	228	249	279	.0001
Cancer of Cervix	52	59	61	61	50 50	.0007
Cancer of Uterus	42	46	46	44	46	_
Other Female Cancer	81	40 84	91	95	99	.007
Cancer of Bladder	20	1 <i>7</i>	19	22	23	.007
Cancer of Bladder Cancer of Kidney, Etc.	20 22	21	13 21	22 21	23 21	_
Cancer of Kluney, Etc. Cancer of CNS	31	32	33	30	32	_
		32 44				
Residual Cancer	<i>46</i>		<i>43</i>	40	<i>39</i>	
Lymphosarcoma, Etc.	23 25	24 07	26	28	28	_
Cancer III-Def. and Sec.	85	97	91	89	92	_
Hodgkin's Disease	11	12	11	12	13	
Multiple Myeloma	17	<i>15</i>	16	17	17	_
Leukemia	58	59	59	56	<i>57</i>	
Other Lymphatic	16	16	16	15	16	_
Neoplasms, Benign and Unspec.	20	21	18	20	21	_
Diabetes	192	180	187	186	175	_
Alcoholism	6	5	5	6	7	-
Rheumatic Heart Disease	<i>51</i>	<i>50</i>	<i>55</i>	67	82	.0001
Hypertension	104	111	112	97	86	.05
Acute Ischemic Heart Dis.	1,197	1,212	1,202	1,161	1,114	.01
Chronic Ischemic Heart	900	938	1,026	1,179	1,263	.0001
Other Heart Disease	214	195	175	148	137	.003
Cerebrovascular Disease	1,000	978	996	962	899	.009
Arteriosclerosis	162	162	164	168	149	
Aortic Aneurysm	28	26	28	<i>33</i>	34	
Influenza and Pneumonia	264	252	243	233	225	.04
Chronic Resp. Disease	89	88	89	95	94	_
Cirrhosis of Liver	<i>51</i>	50	<i>57</i>	74	101	.0001
Chronic Nephritis, Etc.	28	29	29	25	22	_
Infections of Kidney	47	41	42	37	34	_
Congenital Heart & Circ.	<i>33</i>	<i>35</i>	<i>35</i>	34	<i>33</i>	_
Other Congenital	43	41	45	<i>43</i>	40	
Other Early Infancy	172	161	164	154	143	.04
Major Cardiovascular Diseases	3,712	3,723	3,813	3,869	3,815	_
Cancer, All Sites and Forms	1,153	1,178	1,227	1,254	1,359	.0001

^{*}See note to Table 5.

 Table 7.
 Strongest Negative Correlations

,			WF	WM
Chronic Ischemic	vs.	Other Heart Disease	172	197
Ca. Rectum	vs.	Other Heart Disease	10 5	146
Aortic Aneurysm	vs.	Other Heart Disease	086	101
Ca. Breast	vs.	Other Heart Disease	1 3 7	NA
Ca. Intestine	vs.	Other Heart Disease	*	1 30
Acute Ischemic	vs.	Other Heart Disease		097
Ca. Intestine	vs.	Other Heart Disease	125	
Ca., All Forms	vs.	Other Heart Disease	123	
Acute Ischemic	vs.	Symptoms, III-Defined	118	196
Chronic Ischemic	vs.	Symptoms, Ill-Defined	137	1 55
Major CV	vs.	Symptoms, III-Defined	114	1 23
Ca. Rectum	vs.	Symptoms, III-Defined	<i>083</i>	1 25
Ca. All Forms	vs.	Symptoms, III-Defined	1 39	
Ca. Breast	vs.	Symptoms, III-Defined	122	
Ca. Intestine	vs.	Symptoms, III-Defined	123	
Other Heart Disease	vs.	Rheumatic Heart Disease	141	
Infections of Breast	vs.	Rheumatic Heart Disease	137	
Symptoms, Ill-Defined	vs.	Rheumatic Heart Disease	125	
Acute Ischemic	vs.	Rheumatic Heart Disease	118	
Cerebrovascular	vs.	Rheumatic Heart Disease	092	
Chronic Isch. Heart Disease	vs.	Cerebrovascular	141	093
Ca. Rectum	vs.	Cerebrovascular		082

^{*}Blanks indicate correlations that were not significant at $p \le .0001$ for the particular sex.

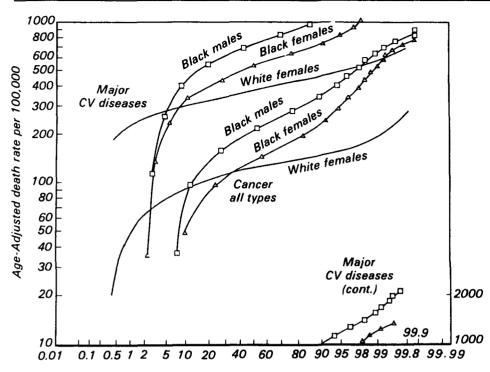


Figure 1. Cumulative frequency distribution of mortality rates: (1968-72).

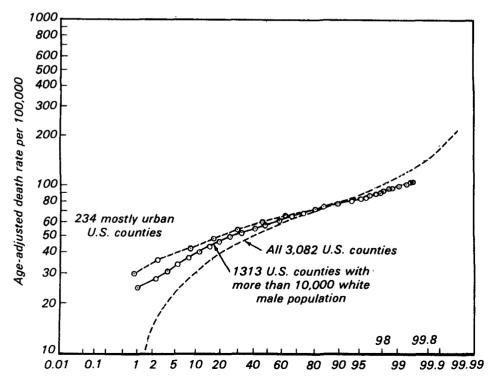


Figure 2. Cumulative frequency distribution of lung cancer mortality rates—white males (1968-72)

Table 8. Respiratory Cancer vs Cirrhosis of Liver

Respiratory Cancer	Cirrhosis of Liver	Sex Geographic Location
HIGH	HIGH	WM New England, California, Florida WF New England*, California, Florida, Nevada, Arizona, New Mexico, Washington (Seattle-Tacoma-Everett), Gulf Coast, Alaska
LOW	LOW	WM Tennessee, Kentucky, Virginia WF West**, Southeast
HIGH	MIXED	WM Georgia, South Carolina, Lower Mississippi River
LOW	HIGH	WM West, Southwest * * *

^{*} Particularly CONNECTICUT, MASSACHUSETTS, SOUTHERN VERMONT AND NEW HAMPSHIRE, EASTERN NEW YORK STATE, COASTAL PARTS OF MAIN, MOST OF NEW JERSEY

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The complete report, entitled "Correlations Between Age-Adjusted Mortality Rates for White Males and Females in the United States, by County: 1968-1972," (Order No. PB 82-224 114; Cost: \$10.50, subject to change) will be available only from:

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