

FAX COVER SHEET

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Paul Merrell & Carol Van Strum

From:

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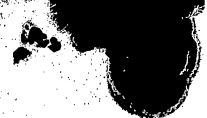
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9 pages (including this cover sheet)

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Comment:

In case you don't have this -- it's the
"Monson" article that Zack/Suskind cite.



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NOV-17-1994 19:54 FROM E.R.F.

TO ERF

P.81

COMPUTERS AND BIOLOGICAL RESEARCH 7, 325-332 (1974)

Analysis of Relative Survival and Proportional Mortality*

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Received August 21, 1973

A computer program utilizing cause-age-time-sex-race-specific mortality or incidence rates is described. The program is used to determine the expected number of deaths or expected to have died of each cause can be calculated using proportional mortalities. Mortality rates based on United States vital statistics have been assembled for 57 causes of death for white males, white females and non-white males for each five-year age and time period from 1925 through 1969. Proportional mortalities and proportional cancer mortalities have been calculated. Incidence rates from the Connecticut Cancer Registry are available. The computer program is general and can be modified to use other sets of rates in determining the expected number of deaths in any study population.

Two dissimilar epidemiologic techniques, the estimation of relative survival and proportional mortality, share a common ground: each is dependent upon a standard set of deaths. In relative survival, standard death rates are calculated and are used to compute the expected number of total deaths in a cohort. In proportional mortality the number of deaths due to a specific cause is divided by the number of total deaths and this proportion is used to compute the expected number of cause-specific deaths among a group of deceased persons.

This paper describes a computer program developed to analyze cohort studies using relative survival and its analogues and to analyze studies using proportional mortality. These techniques have been fully described and illustrated by other authors (1-3). The standard death rates and proportional mortalities are based on cause-age-time-sex-race-specific data for the population of the United States from 1925 to 1967.

CALCULATION OF STANDARD RATES

Standard population. For each year from 1925 to 1967, the enumerated or estimated age-specific population of the United States death registration area was

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abstracted (4, 5). For the years 1925-34, the population was grouped in 10-year age groups (0-4, 5-14, . . . , 85+). For succeeding years, the population was grouped in five-year age groups (0-4, 5-9, . . . , 85+). For each age group, the average population during each five-year period (1925-29, 1930-34, . . . , 1965-67) was calculated for white males, white females and non-white males.

Standard deaths. For each year from 1925 to 1967, the numbers of persons dying from selected causes of death were abstracted from United States Vital Statistics (5), specific for age, sex and race. To date, information on 23 categories of cancer and 34 categories of other causes have been abstracted. Prior to 1933 the data are derived from the states included in the death registration area. The age-time breakdown corresponds to that for the standard population. The average number of age-specific deaths per year within each five-year time period was calculated. For each cause a cause-of-death code was assigned according to the Seventh Revision of the International Classification of Diseases (6). Since codes and coding procedures change with time, causes from different times were grouped according to title of cause of death rather than according to ICD code.

Standard rates. For each age-time period for each race and sex the number of deaths per 1000 population per year was calculated. For some five-year periods the

TABLE 1

MORTALITY RATES FOR ALL CAUSES FOR WHITE FEMALES IN UNITED STATES ACCORDING TO AGE AND YEAR OF DEATH, EXPRESSED AS NUMBERS OF DEATHS PER 1000 POPULATION PER YEAR

Age at death	Year of death									
	1925-	1930-	1935-	1940-	1945-	1950-	1955-	1960-	1965-	
0-	15.9	13.0	12.1	9.7	7.4	5.6	5.0	4.4	3.8	
5-	1.6	1.3	1.2	0.8	0.6	0.5	0.4	0.4	0.3	
10-	1.6	1.3	1.0	0.7	0.3	0.4	0.3	0.3	0.3	
15-	2.9	2.1	1.5	1.0	0.9	0.6	0.5	0.5	0.5	
20-	2.9	2.1	2.1	1.5	1.1	0.7	0.6	0.6	0.6	
25-	4.0	3.2	2.6	1.7	1.3	0.9	0.7	0.7	0.7	
30-	4.0	3.2	3.0	2.2	1.6	1.2	1.0	1.0	1.0	
35-	5.8	4.8	3.7	2.9	2.3	1.7	1.5	1.5	1.5	
40-	5.8	4.8	5.0	3.9	3.2	2.7	2.4	2.3	2.4	
45-	10.1	9.0	7.0	5.7	4.8	4.1	3.7	3.6	3.7	
50-	10.1	9.0	9.9	8.6	7.4	6.4	5.7	5.5	5.6	
55-	21.0	19.6	14.7	12.9	11.0	9.7	8.1	8.1	8.3	
60-	21.0	19.6	22.4	19.6	17.2	15.2	13.7	12.3	12.4	
65-	49.2	45.4	34.9	30.7	26.7	24.2	22.6	20.9	22.5	
70-	49.2	45.4	54.2	51.1	45.3	40.4	36.6	34.0	33.4	
75-	118.2	107.9	92.5	81.2	74.6	66.8	62.6	57.3	55.0	
80-	118.2	107.9	141.7	131.9	114.3	109.0	105.4	100.4	94.4	
85+	283.1	244.7	227.2	220.5	208.9	191.4	196.0	195.8	200.0	

RELATIVE SUR

numbers of deaths for certain are assumed to be those of p are based on deaths from 11 causes for white females are for purposes of presentation.

Proportional mortalities. 7 number of deaths due to all c specific cause. The proportio ing to the age-time distributi

Proportional cancer mortal is the number of deaths due to a specific cancer. Proporti according to the age-time di

DATA A1

For each member of the s race, age at entry, year of deceased or lost to follow-up

The steps in the computer table has the format of Tabl upon the program option se tables to be printed.

Step 1. The death rate:
Step 2. The age-year-of five-year groupings.

Step 3. The age-time-sj
A person is assumed midpoint of the age assumed to have occi available to consider alive until the comm leaving in the same live withdrawal is wit or July 1. As an exa entered the study in survival would be di program is less preci days of survival are essentially no error many partial years c

[REDACTED]

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numbers of deaths for certain causes are not published; the rates during these periods are assumed to be those of preceding or succeeding periods. The rates for 1965-69 are based on deaths from 1965-67 only. As an example, total death rates for all causes for white females are presented in Table 1. (The rates have been truncated for purposes of presentation.)

Proportional mortalities. The denominator of a proportional mortality is the number of deaths due to all causes. The numerator is the number of deaths due to a specific cause. The proportional mortalities for each cause were calculated, according to the age-time distribution presented in Table 1.

Proportional cancer mortality. The denominator of a proportional cancer mortality is the number of deaths due to cancer. The numerator is the number of deaths due to a specific cancer. Proportional cancer mortalities were calculated for each cancer, according to the age-time distribution presented in Table 1.

DATA ANALYSIS USING RELATIVE SURVIVAL

For each member of the study cohort, the following information is needed: sex, race, age at entry, year of entry, years of survival, status at end of study (live, deceased or lost to follow-up) and cause of death, where appropriate.

The steps in the computer program are described below. Except for step 8, each table has the format of Table 2. The data may or may not be calculated, depending upon the program option selected. Also, options are available as to the number of tables to be printed.

Step 1. The death rate matrix is read.

Step 2. The age-year-of-entry distribution of the study cohort is determined in five-year groupings.

Step 3. The age-time-specific person-years of the study cohort are calculated.

A person is assumed to have entered on July 1 of the year of entry and at the midpoint of the age of entry. If a person is lost to follow-up, withdrawal is assumed to have occurred on July 1 of the year of withdrawal. (Options are available to consider lost persons to have died at the time of loss or to be alive until the common closing date of the study.) A person entering and leaving in the same year contributes 0.25 person-years. A person who is a live withdrawal is withdrawn at the common closing date, usually January 1 or July 1. As an example, consider the person described by Hill (7). He entered the study in 1952 at age 23 and left in 1962. His person-years of survival would be distributed as shown in Fig. 1. The method used in this program is less precise for an individual than Hill's method, since the exact days of survival are not computed. For the total population, however, essentially no error should be introduced, since persons who are given too many partial years of survival are counterbalanced by those with too few.

The total person-years in a study of survival following carcinoma of the endometrium (8) are distributed as illustrated in Table 2.

Step 4. The age-time distribution of the observed deaths is determined. The observed rates are calculated by dividing the observed deaths by the person-years of survival.

Step 5. The age-time-specific expected deaths are calculated by multiplying the age-time-specific standard death rates by the age-time-specific person-years of follow-up.

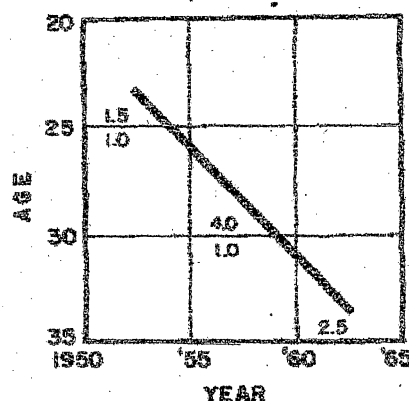


FIG. 1. Person-years experienced by a person entering at age 23 in 1952 and leaving in 1962.

Step 6. Mortality ratios are calculated by dividing each observed number of deaths by each expected number of deaths.

Step 7. The probability that the observed number of deaths differs significantly from the expected numbers of deaths is calculated using a modification of the Mantel-Haenszel procedure (9). A Mantel-Haenszel χ^2 is calculated for each marginal ratio as well as for the total observed/expected ratio. The Poisson approximation is made in determining the variance of the expected deaths, that is, the variance is assumed to be equal to the mean of the expected deaths. The resultant χ^2 is conservative, that is, it is less than the corresponding χ^2 calculated using the binomial variance.

Step 8. The relative survival life table is calculated (1). The standard errors are estimated according to the method of Greenwood (10). For each year of survival, the following numbers are calculated, as illustrated in Table 3 (the data in Table 3 are limited to the first ten years of follow-up): LX, number starting each interval; WX, number of live withdrawals; UX, number lost to follow-up; OBS(DX), observed deaths; EXP(DX), expected deaths; OBS/EXP, observed/expected ratio; SURV, crude interval survival (1 + 1); RSR, relative

RELATIVE SURVIVAL

(+ 1); RSR, relative CSURV, crude cumu survival; SECRSR, st

PERSON-YEARS OF SURVIVAL IN CARCINOMA OF THE

Age	1920-	1925-	1930-
25-			
30-			0.5
35-			9.5
40-	3.5	1.5	4.5
45-	11.3	14.0	6.3
50-	10.5	40.8	47.8
55-	14.0	53.3	82.3
60-	5.8	51.3	96.0
65-	4.0	26.3	63.8
70-	0.8	19.3	45.3
75-		2.3	19.0
80-		1.5	1.0
85+			1.5
Sum	49.8	210.0	377.3

RELATIVE SURVIVAL RATIOS FOR ENDOMETRIUM

Year	LX	WX	UX	OBS(DX)	EXP
0	761	1	0	91	14
1	669	0	0	60	11
2	609	1	0	40	12
3	568	1	0	28	11
4	539	0	0	18	11
5	521	2	0	22	11
6	497	5	0	11	11
7	481	12	0	10	12
8	459	24	0	11	12
9	424	20	0	11	12
10	296	0		465	26

$i+1$); RSR, relative interval survival; SECSR, standard error of RSR; CSURV, crude cumulative survival (0 to $i+1$); CRSR, relative cumulative survival; SECSR, standard error of CRSR.

TABLE 2

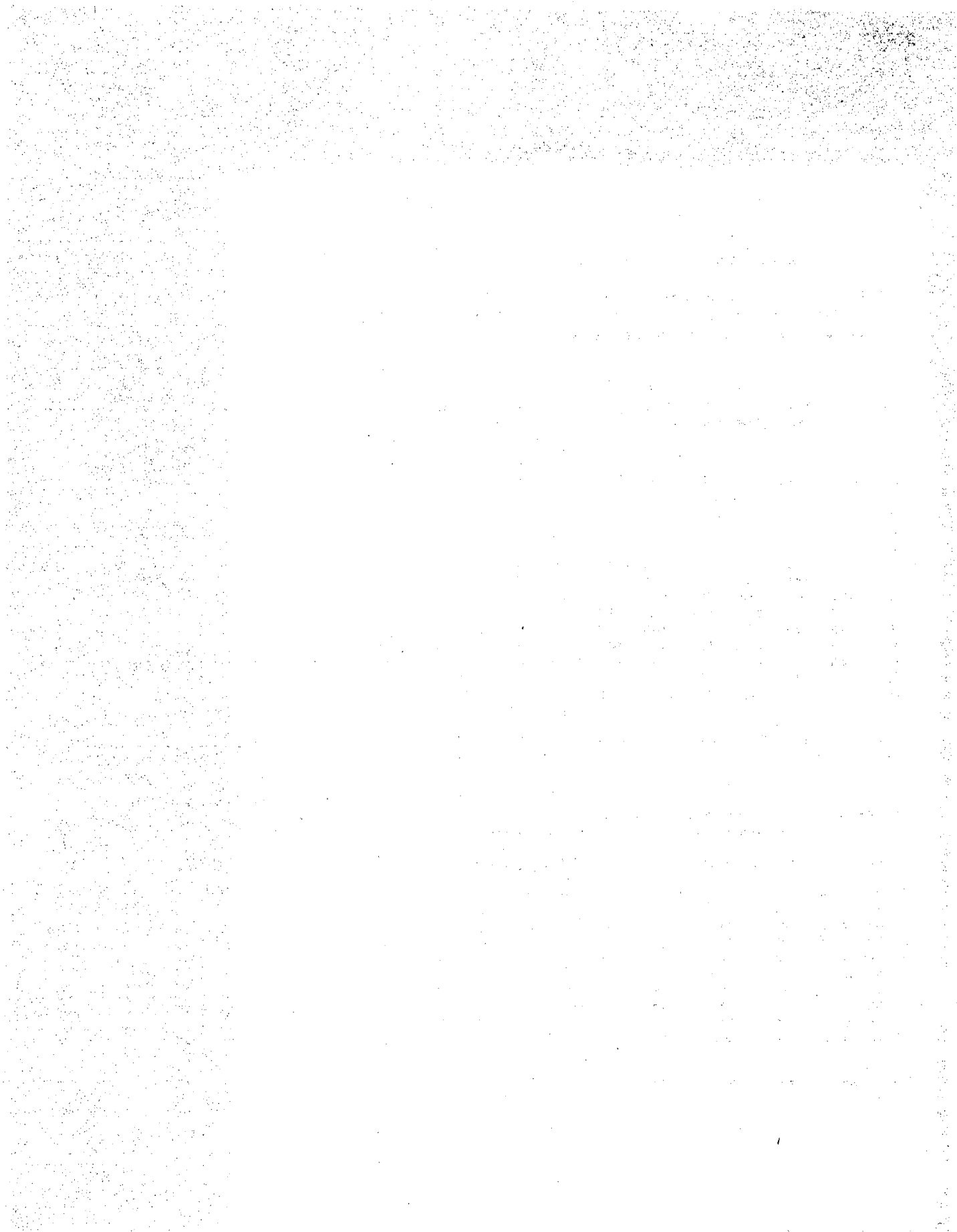
PERSON-YEARS OF SURVIVAL IN A COHORT OF 761 WHITE FEMALES FOLLOWING TREATMENT FOR CARCINOMA OF THE ENDOMETRIUM ACCORDING TO AGE AND YEAR

Age	Year										Sum
	1920-	1925-	1930-	1935-	1940-	1945-	1950-	1955-	1960-	1965-	
25-					3.5	1.5	3.5	4.0	1.0		13.5
30-			0.5	2.5	0.3	7.5	5.5	13.0	10.0	0.5	39.8
35-			9.5	4.5	6.0	9.0	19.5	10.5	19.0	3.5	81.5
40-	3.5	1.5	4.5	17.0	18.5	20.0	37.0	38.5	14.0	4.5	159.0
45-	11.3	14.0	6.3	15.8	54.0	71.8	69.3	90.0	55.5	3.5	391.3
50-	10.5	40.8	47.8	38.3	82.3	132.0	120.5	129.5	112.0	15.5	729.0
55-	14.0	51.3	82.3	104.8	95.8	178.5	256.0	237.8	165.0	27.5	1214.8
60-	5.8	51.3	96.0	123.8	166.8	159.0	295.8	346.0	263.5	36.0	1543.8
65-	4.0	26.3	63.8	112.5	117.8	204.3	208.8	343.3	347.0	49.0	1536.5
70-	0.8	19.3	45.3	52.8	100.3	161.5	209.0	203.5	329.5	64.5	1186.3
75-		2.3	19.0	31.3	37.5	90.0	141.5	185.8	158.0	37.0	702.3
80		1.5	1.0	12.3	17.5	21.5	63.8	93.5	106.0	14.5	332.0
85+			1.5	0.5		7.0	12.5	43.0	65.0	11.5	142.5
Sum	49.8	210.0	377.3	515.8	760.0	1063.5	1442.5	1740.3	1645.5	267.5	8672.0

TABLE 3

RELATIVE SURVIVAL RATIOS FOR 761 WOMEN FOLLOWING TREATMENT FOR CARCINOMA OF THE ENDOMETRIUM (SEE TEXT FOR DESCRIPTION OF DATA)

Year	LX	WX	UX	OBS(DX)	EXP(DX)	OBS/EXP	SURV	RSR	SECSR	CSURV	CRSR	SECSR
0-	761	1	0	91	14.4	6.3	.38	.90	.01	.38	.90	.01
1-	669	0	0	60	12.8	4.7	.91	.93	.01	.80	.83	.02
2-	609	1	0	40	12.7	3.2	.93	.95	.01	.75	.80	.02
3-	568	1	0	28	11.8	2.4	.95	.97	.01	.71	.77	.02
4-	539	0	0	18	11.5	1.6	.97	.99	.01	.69	.76	.02
5-	521	2	0	22	11.5	1.9	.96	.98	.01	.66	.75	.02
6-	497	5	0	11	11.7	0.9	.98	1.00	.01	.64	.75	.02
7-	481	12	0	10	12.7	0.8	.98	1.01	.01	.63	.75	.02
8-	459	24	0	11	12.7	0.9	.98	1.00	.01	.62	.75	.02
9-	424	20	0	11	12.0	0.9	.97	1.00	.01	.60	.76	.02
i												
Sum	—	296	0	465	263.6	1.8	—	—	—	—	—	—



Steps 9-11. These steps are similar to steps 4-6. However, the person-years for each person are not distributed diagonally, as in Table 2, but horizontally according to age at entry into the cohort.

Steps 12-14. These steps are similar to steps 9-11. The person years are distributed horizontally according to year of entry into the cohort.

MODIFICATIONS OF RELATIVE SURVIVAL

The numbers of cause-specific deaths expected in a cohort can be obtained if cause-specific mortality rates are substituted for total mortality rates in step 1. This technique has been used by others to determine whether excess mortality due to cancer has occurred in an industrial population (11, 12). Steps 1-14 are followed, with the only modification being in step 8. Persons dying from causes other than that being investigated are treated as live withdrawals in the year of their death. Thus, the total person-years of survival by the cohort is unchanged. However, only persons dying from the cause of interest are included in the observed deaths. The relative survival therefore is cause-specific.

If incidence rates are substituted for death rates in step 1, the expected number of incident cases of disease is obtained. Currently, the incidence rates of the Connecticut Cancer Registry from 1935-1962 are available (13).

DATA ANALYSIS USING PROPORTIONAL MORTALITY

For each member of the study group, the following information is needed: sex, race, age, year and cause of death.

The steps in the computer program follow.

Step 1. The proportional mortality data matrix is read.

Step 2. The age-year-of-death distribution of all deaths in the study population is determined in five-year groupings.

Step 3. The age-time distribution of the observed deaths is determined.

Step 4. The age-time-specific expected deaths for each cause are calculated by multiplying the proportional mortality matrix times the age-time distribution of total deaths.

Step 5. Proportional mortality ratios are calculated by dividing the observed ratios by the expected ratios.

Step 6. The Mantel-Haenszel χ^2 is calculated as described in step 7 above.

This procedure has been used in a study of the cause of death among alcoholics (14).

SOME TECHNICAL FEATURES

During one computer run, many causes of death may be evaluated in one cohort; one cause of death may be evaluated in many cohorts, or both. Several options

exist as to the detail of calculation screened against all causes of death of survival are determined. Then years matrix to obtain the expected observed deaths according to each all deaths, is screened against each calculated and printed.

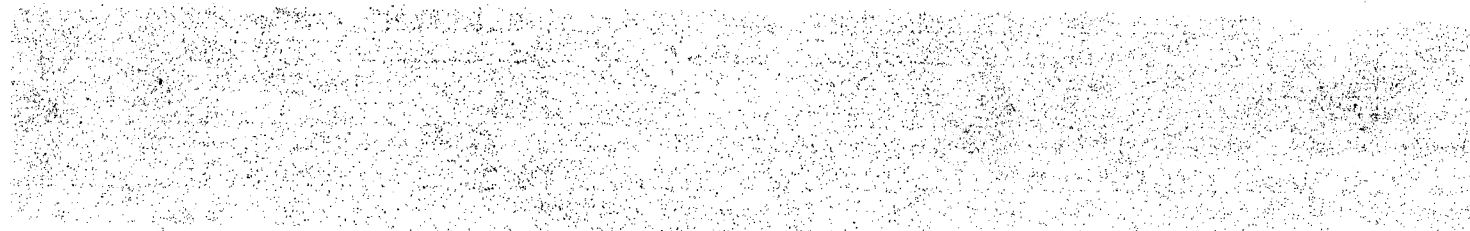
The program is written in Fortran 370/165 at the MIT-Harvard Computer Center and is called as a subprogram for each run to describe the selections to be made. In addition, further characteristics of the cohort

The major advantage of using comparison group need be extended back many years, this based on a large number of deaths.

The use of standard population of the study population which accounts for the standard population account only of age, time, sex and rates. The effects of this problem standard population which is selected (3). An estimate of the variables can be made (1, 15). This is to study them in diverse groups to conduct cohort studies using

Another disadvantage arises in standard population. If relevant two study groups, inferences made by comparing their expected for example, if relative survival different age distributions, age-specific second possibility is to compare the standard population and it available in the program.

The primary disadvantages of rates are not obtained. A proportion



exist as to the detail of calculation and output desired. When a single cohort is screened against all causes of death, the cohort data is read once and the person-years of survival are determined. Then each death rate matrix is multiplied by the person-years matrix to obtain the expected numbers of cause-specific deaths. Also, the observed deaths according to each cause are counted. When a single cause, usually all deaths, is screened against many cohorts, only the relative survival table is calculated and printed.

The program is written in Fortran IV and currently is in operation on the IBM 370/165 at the MIT-Harvard Computing Center. Most of the program has been compiled and is called as a subroutine. A short program (5-20 lines) must be written for each run to describe the input characteristics of the study cohort and any selections to be made. In addition, several control cards are needed to describe further characteristics of the cohort and to select the various options described above.

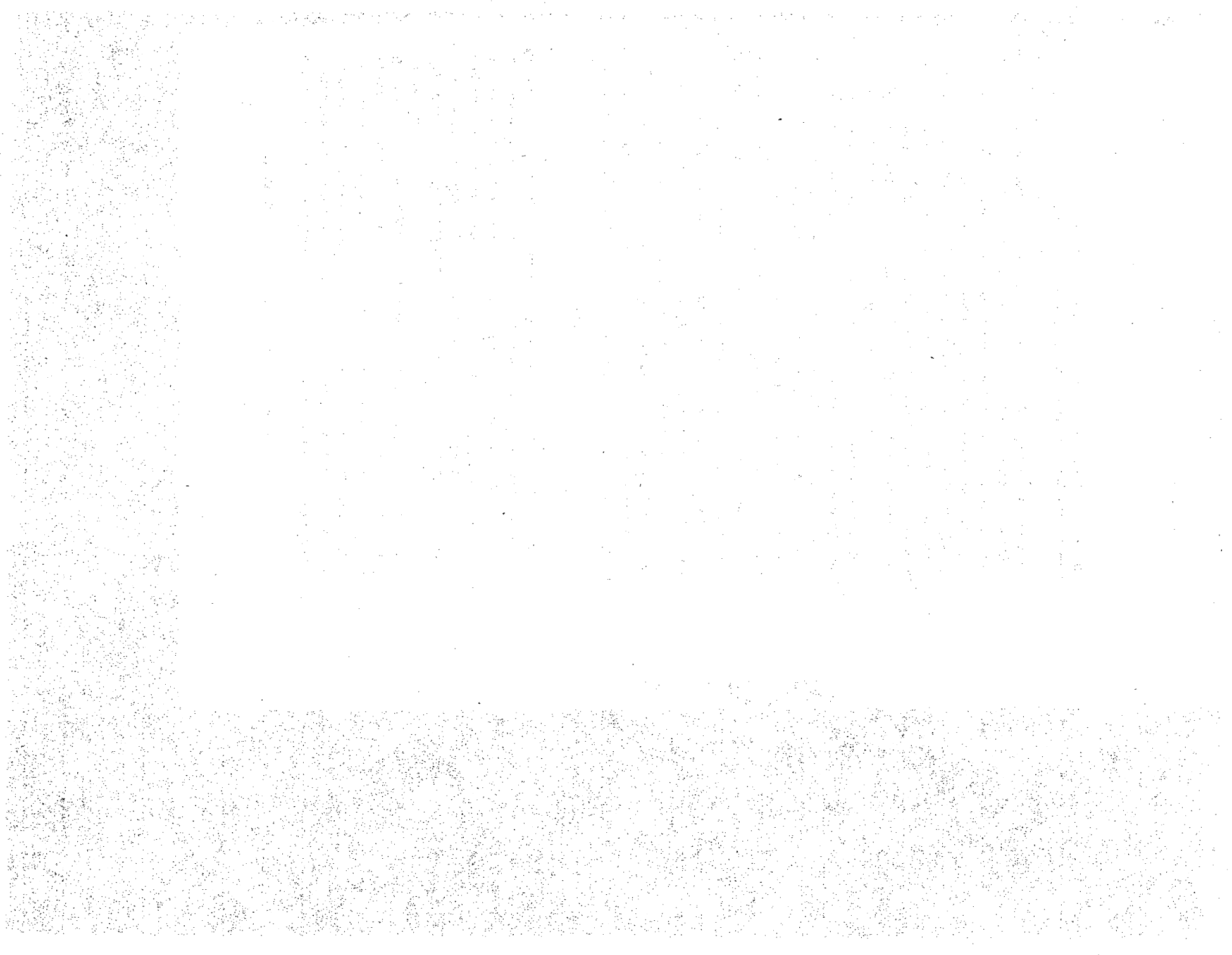
COMMENTS

The major advantage of using rates from a standard population is that no formal comparison group need be assembled. In the case of retrospective cohort studies extending back many years, this is difficult. Further, since the standard rates are based on a large number of deaths, the rates are relatively stable.

The use of standard population rates has several disadvantages: characteristics of the study population which are related to death (or disease) may be different from those of the standard population. The procedures described in this paper take account only of age, time, sex and race differences. No account can be made, for example, of the effect of cigarette smoking on differences in observed and expected rates. The effects of this problem may be studied in several ways. If available, a standard population which is relatively similar to the study population may be selected (3). An estimate of the maximum impact of confounding due to confounding variables can be made (1, 15). The best way to evaluate suspected causal relationships is to study them in diverse groups using diverse standard populations, or, if possible, to conduct cohort studies using a formal comparison group.

Another disadvantage arises if two or more study cohorts are compared to the standard population. If relevant demographic characteristics differ between the two study groups, inferences comparing the two groups may not necessarily be made by comparing their experience relative to the standard population (16, 17). For example, if relative survival is a function of age, and if two study cohorts have different age distributions, age-adjusted relative survival rates must be calculated. A second possibility is to compare the two groups directly, by using one group as the standard population and the other as the study population. This option is available in the program.

The primary disadvantages of studies using proportional mortality is that disease rates are not obtained. A proportional mortality greater than one may result from a



high disease-specific death rate or a low death rate from other causes. However, a proportional mortality study is very economical in terms of time and money and may serve as a preliminary test of a causal hypothesis (3, 14). If suggestive results are obtained, a cohort study (retrospective or prospective) may be designed to provide a more definitive test of the hypothesis.

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Experiments carried out on the aid of a mathematical model of the concepts of both "resting" per hour, and quiescent cells w

We found that cell loss was populations. In most experiment phase. The mean generation time state) increased from about 20 mean duration of the G₁ phase We have also shown how it results to error or uncertainty i

Until recently, most kinetic active tracer techniques were primitive mathematical metho tions for which little or no jus parameter values to an unkno Although such methods are of more sophisticated experin for collecting and analyzing k gation of cell population d demonstrated that by combin

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NOU-17-1994 20:02 FROM E.R.F.

TO ERF

P.08

FAX COVER SHEET**To:****Paul Merrell & Carol Van Strum****From:****Peter Montague****Environmental Research Foundation****(410) 263-1584 (voice)****(410) 263-8944 (fax)****4 pages (including this cover sheet)****Sent on 17-Nov-94 at 20:38****Comment:****Comments on the missing cohort, which is
no longer missing.**

November 17, 1994

Hi, Carol,

I have looked over the memo entitled "Chloracne Cases Not Related to 1949 TCP Accident." Here are my page-by-page comments. I will refer to pages by your hand-written page-number scheme. The memo begins on pg. 22.

Page 22:

Listed: 22 Active
13 deceased
4 unknown mortality status
39 TOTAL individuals

Noteworthy about this page:

Illegible names: 11 (but SS #s are legible)
Year of death provided for only 12 of 13 deceased; need year for 1 individual.
Cause of death code is given for 12 of 13 deceased, but 4 of the codes are illegible; therefore need code for 5 individuals.
2 names are crossed out (line through them) -- why?
Date of birth missing for 6 individuals.

Page 23:

Listed: 27 active
9 deceased
3 unknown mortality status
39 TOTAL individuals

Noteworthy about this page:

Cause of death code given for 9 deceased persons, but 2 are illegible; therefore need code for 2 individuals.
Date of birth missing for 1 individual

Page 24:

Listed: 18 active
14 deceased
6 unknown mortality status
1 no data on mortality status (not even a U)
39 TOTAL individuals

Year of death provided for only 13 of 14 deceased; need year for 1 individual.

Cause of death code is given for 13 of 14 deceased; therefore need code for 1 individuals.

Date of birth missing for 18 individuals.
SS # missing for 1 individual

Page 25:

Listed: 7 active
17 deceased
7 unknown mortality status
5 no data on mortality status (not even a U)
36 TOTAL individuals

Noteworthy about this page:

Cause of death code given for 15 of 17 deceased; therefore, need
code for 2 individuals.
Date of birth missing for 11 individuals.
One record crossed out (line through it) -- why?
SS # missing for 6 individuals.

Page 26:

Listed: 17 active
8 deceased
7 unknown mortality status
5 no data on mortality status (not even a U)
37 TOTAL individuals

Noteworthy about this page:

Date of birth missing for 8 individuals.
One individual crossed out (line through name) -- why?
SS # missing for 4 individuals.

Page 27:

Listed: 7 active
8 deceased
7 unknown mortality status
15 no data on mortality status (not even a U)
37 TOTAL individuals

Noteworthy about this page:

Year of death is given for 7 of 8 individuals, and 1 more is
given but with a question mark after it; therefore, need year
for 1 individual.

Cause of death code given for only 2 of 8 individuals; therefore,
need code for 6 individuals.
Date of birth missing for 15 individuals.

2 names are illegible & their social security numbers are illegible as well, so they will be hard to identify without a cleaner copy of the memo. It is conceivable that there is a 3rd illegible name at the very end of the list; if this were true, it would bring the total number of individuals to 228. SS # missing for 4 individuals & illegible for 2 individuals.

SUMMARY

Data is given on 227 individuals:

98 active
69 deceased
34 unknown mortality status
26 no data on mortality status (not even a U)
227 TOTAL individuals

In sum, there are 60 individuals for whom mortality status is missing or is listed as "U" (presumably meaning Unknown).

Cause of death code is missing or illegible for 16 individuals (in addition to the 60 individuals for whom mortality status is unknown);

Year of death is missing or illegible for 3 individuals (in addition to the 60 individuals for whom mortality status is unknown).

Data of birth missing for 59 individuals.

SS # is missing for 15 individuals

Conclusion: This DOES appear to be the missing cohort (!).



PS: Date of birth is needed for everyone in the cohort; see article by Monson cited by Zack/Suskind as their source for their computer program. Pg. 327 says "years of survival" are needed.

If we could get SS # for each of these individuals, perhaps Fingerhut would let loose of her data on these individuals exclusive of their names; I feel sure she has it all, but she won't give out the information, claiming privacy rights for the living persons. Just a thought.

PPS: I'll see Clapp on Saturday & will ask him how best to get info on these individuals.

