Relationship of Age at Death to Calendar Year of Estimated Maximum Leukemia Mortality Rate

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A FALL IN LEUKEMIA mortality around the year 1940 was first discerned among white infants of the United States (*1*). A subsequent analysis of the secular trends in U.S. children by Slocumb and MacMahon (*2*) showed that with passing time the decline had also begun to affect successively older children. By 1959, a decline apparently had occurred in the mortality for 3-year-olds (*2*). More recently, Fraumeni and Miller (*3*) reported that the once increasing leukemia mortality rates among U.S. whites between the ages of 1 and 74 years had begun to decline. This latest observation suggested that the wave effect in the mortality rates (the increase and subsequent decrease occurring later in time with in-

creasing age at death) observed by Slocumb and MacMahon (*2*) has tended to continue. It further suggested that such an effect might possibly also be found in the mortality data for children of England and Wales and those for U.S. nonwhite children.

There are a number of alternative ways in which mortality data might be examined to test the hypothesis. One possibility would be the use of 3-year moving averages. From a purely descriptive point of view, this method would at least have the advantage of smoothing out the chance fluctuations in mortality rates computed on an annual basis. Its use would not be appropriate in the present instance, however, since the statistical validity of the results would be difficult to evaluate. What is needed is a single estimate of the maximum leukemia rate whose reliability can in turn be estimated. The procedure adopted, therefore, was to fit a quadratic equation, by means of regression, to the annual mortality rates for each age group and to estimate the points in time at which any decline might have begun by calculating the first derivatives. The assumption is made that the equation will relate to the interval of time

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examined. The extent to which it fits rates before and beyond this interval is problematical; obviously, at some stage a second-degree equation becomes totally inadequate.

Results

The estimated years of maximums in the leukemia mortality rates for U.S. white children (4–6), U.S. nonwhite children (4–6), and children of England and Wales (7) are compared in table 1. The children of England and Wales and U.S. nonwhite children, like U.S. white children, appear to exhibit the phenomenon of a time sequence in the estimated maximums that is closely associated with increasing age. Each sequence, moreover, has its own order in time and, for any age, the years of maximums for the three populations tend to occur in the same order.

To some extent the validity of these conclusions rests upon the interpretation of a certain amount of indeterminateness in the results. In several instances, the maximums were calculated as being beyond the actual range of the data and, therefore, they can be accepted only with caution. (These maximums apparently would have been within the data range, however, if a 3-year moving average had been used.) For the nonwhite children, there were also instances (among 3-year-olds and in the age group 5–9 years) in which the F value for the contribution made by the second-degree term was not conventionally significant. Nevertheless, the maximums were calculated since, when the levels of probability (0.13 and 0.12) were considered along with the remaining results, it seemed more likely than not that a similar wave effect was also a feature of the leukemia

Table 1. Years of estimated maximum in the secular trends of death rates from leukemia among various age groups of U.S. white, U.S. nonwhite, and British children, 1933–67

Age at death (years)	Year of estimated maximum			F for contribution made by $2°$ term [1]		
	U.S. whites	U.S. nonwhites	England and Wales	U.S. whites	U.S. nonwhites	England and Wales
0–..	41.8	49.1	48.8	13.87	11.72	6.25
1–..	46.5	54.5	51.7	30.23	3.88	6.24
2–..	49.8	55.5	52.6	122.57	12.80	21.14
3–..	52.9	65.4	53.3	90.21	1.31	56.02
4–..	59.8	(2)	65.1	30.17	.01	6.94
5–9..	65.8	3(91.0)	3(72.1)	45.27	1.50	4.42
10–14..	63.0	3(71.6)	67.0	28.45	3.28	4.71
0–14............................	55.1	62.3	58.1	290.89	16.42	69.95

[1] The degrees of freedom were 1 and 32.
[2] In all instances but this one the second degree regression coefficient was negative.
[3] Maximum estimated beyond actual data.

Table 2. Years of estimated maximum in the secular trends of death rates from leukemia among adults 15–49 years-of-age in the United States (whites and nonwhites separately) and England and Wales, 1933–67

Age at death (years)	Year of estimated maximum			F for contribution made by $2°$ term [1]		
	U.S. whites	U.S. nonwhites	England and Wales	U.S. whites	U.S. nonwhites	England and Wales
15–19..	57.0	66.1	57.9	57.95	7.24	11.01
20–24..	56.2	60.4	58.7	19.60	5.22	12.74
25–29..	54.4	(2)	66.5	41.11	0.00	3.01
30–34..	54.8	60.1	63.8	36.46	6.65	5.63
35–39..	57.9	64.1	67.2	33.00	2.79	10.29
40–44..	57.5	58.3	66.1	18.07	14.32	4.53
45–49..	56.8	62.0	60.0	67.30	17.66	22.72
15–49............................	56.9	62.4	61.0	193.48	36.12	53.30

[1] The degrees of freedom were 1 and 32.
[2] No reliable estimate.

mortality rates for this population of nonwhite children. Confidence bands around the maximums were not calculated because the method that was used does not take into account the hypothesized order of the maximums (8).

In the rates for nonwhite U.S. adults, in contrast to the almost general decline in the rates for whites—and for adults in England and Wales are served a general leveling off, a tendency which was also apparent for adults in England and Wales. The estimated years of maximums in the leukemia mortality rates for the period 1933–67 for U.S. adults 15–49 years—whites and non-whites—and for adults in England and Wales are compared in table 2. The three maximums in the rates for adults 15–49 years occur in the same order as was observed in the children's rates, al-

though such an order is not a regular feature when the data are examined by 5-year age groups. In addition, there is little evidence to suggest that, within each of the three populations, the maximums for adults advance with increasing age.

The leukemia mortality rates for children in the three populations over the period 1933–67 (4–7) that were used to generate the results in table 1 are shown in tables 3–5. For the same period, tables 6–8 show the rates (4–7) relevant to the results for adults (table 2).

Discussion

In their consideration of the beginning of the wave effect in the rates for U.S. white children, Slocumb and MacMahon (2) pointed out that the

Table 3. Mortality rates per million from leukemia among U.S. white children, by single years of age, 1933–67

Calendar year 19—	Age at death (years)							
	0–	1–	2–	3–	4–	5–9	10–14	0–14
67	22.2	25.8	36.1	49.9	57.4	41.5	25.9	35.5
66	20.1	32.4	36.4	46.5	60.5	38.0	23.7	33.9
65	22.1	28.7	37.2	48.7	68.0	37.5	25.1	34.9
64	21.3	25.3	41.6	54.2	61.0	39.0	22.3	34.5
63	27.1	30.1	43.3	67.2	77.6	42.0	24.0	38.8
62	23.0	29.4	43.2	68.4	67.1	41.5	23.3	37.5
61	27.0	33.8	50.6	63.2	74.0	43.2	26.2	40.2
60	27.8	33.6	53.5	82.6	71.3	40.4	27.7	41.3
59	28.4	29.0	43.7	81.1	71.1	42.5	26.2	40.5
58	24.2	35.8	55.3	65.2	78.1	40.7	25.8	40.2
57	29.0	36.6	52.2	73.0	81.2	39.6	25.1	40.8
56	20.9	41.0	62.1	68.0	68.3	41.8	21.7	40.0
55	28.1	35.7	54.5	78.9	66.9	38.4	23.0	39.5
54	31.0	40.1	62.1	78.3	63.4	37.9	24.9	40.8
53	36.2	36.0	51.1	76.4	64.3	36.0	22.6	38.7
52	35.4	37.1	62.6	75.8	75.3	37.2	22.4	41.1
51	34.2	42.8	64.5	82.5	66.6	36.8	23.2	42.1
50	40.1	39.6	73.5	73.3	62.2	33.6	25.5	41.5
49	43.7	43.7	61.8	80.1	52.8	36.1	21.6	40.0
48	50.1	31.2	68.3	68.5	48.5	29.6	21.7	36.2
47	43.1	43.1	59.1	73.7	63.1	33.8	22.0	39.2
46	47.2	44.2	55.2	63.7	57.8	28.4	21.0	35.9
45	50.3	46.8	57.3	58.8	60.3	30.4	18.0	35.7
44	55.3	47.3	60.5	54.7	45.1	28.7	19.8	34.7
43	47.5	41.6	58.6	57.6	45.6	26.4	18.4	32.2
42	58.0	42.3	56.8	47.0	48.6	25.4	17.9	31.4
41	47.7	45.8	66.2	59.7	43.5	25.6	19.0	32.2
40	54.4	45.2	54.6	58.0	45.6	27.1	17.6	31.6
39	37.3	47.0	43.2	50.5	39.3	21.8	13.9	25.8
38	39.4	44.3	49.3	39.2	39.9	19.9	15.6	25.2
37	42.9	39.0	52.1	43.8	36.4	20.3	14.7	25.0
36	38.5	36.1	33.8	40.7	40.3	19.5	15.6	23.5
35	30.2	30.3	38.1	46.0	28.4	20.0	13.7	22.1
34	47.7	35.4	36.6	32.4	32.1	19.3	14.4	22.7
33	30.4	24.7	27.9	35.6	31.2	15.2	12.1	18.6

SOURCE: References 4–6.

Table 4. Mortality rates per million from leukemia among U.S. nonwhite children, by single years of age, 1933–67

Calendar year 19—	Age at death (years)							
	0–	1–	2–	3–	4–	5–9	10–14	0–14
67	19.8	24.2	3.1	19.9	24.4	20.1	12.5	17.1
66	12.8	21.8	21.4	13.8	27.4	18.9	14.7	17.9
65	18.6	16.8	22.9	18.3	25.7	16.4	16.0	17.8
64	21.3	29.0	27.4	24.2	22.7	18.8	23.6	22.5
63	18.7	38.8	24.6	36.4	48.3	20.7	18.3	24.7
62	21.2	33.8	21.5	34.9	31.4	24.1	19.3	24.5
61	16.5	11.3	21.1	18.6	33.7	18.1	16.1	18.3
60	22.5	24.3	22.0	18.5	35.2	18.7	16.7	20.3
59	30.8	23.7	30.4	37.0	23.3	15.5	15.6	20.8
58	16.8	17.0	24.4	21.7	35.4	18.9	19.1	20.5
57	13.5	30.4	23.3	31.1	25.4	19.2	15.1	18.9
56	26.7	31.5	18.5	37.2	24.3	21.3	15.3	22.2
55	20.4	27.2	27.1	16.2	14.2	19.1	12.1	18.0
54	33.2	26.7	32.1	30.2	12.9	16.1	13.6	19.9
53	35.3	30.1	24.0	27.7	26.3	12.8	15.3	19.9
52	45.8	32.5	35.9	30.3	16.1	18.5	15.3	23.2
51	17.7	30.2	19.3	15.9	28.3	13.0	14.6	17.2
50	40.3	33.3	20.2	14.0	23.1	19.2	11.6	19.8
49	44.7	28.6	16.7	11.8	11.6	12.8	13.4	17.0
48	26.5	40.7	35.5	17.1	17.5	10.6	12.0	17.4
47	43.7	24.0	8.7	11.6	23.1	10.9	15.6	16.7
46	24.9	16.6	11.8	14.4	21.1	12.1	4.9	11.7
45	23.7	23.6	14.7	21.1	15.9	13.1	8.4	13.9
44	27.6	10.1	12.3	19.2	13.3	12.5	10.5	13.2
43	30.7	14.4	19.6	10.0	13.6	8.2	9.2	11.8
42	21.7	23.1	17.2	10.2	3.4	8.9	9.2	11.0
41	34.7	44.4	14.1	10.4	10.8	10.4	15.0	15.8
40	24.7	24.8	14.3	25.5	14.4	11.1	3.6	11.6
39	20.6	12.6	11.4	10.9	18.8	8.8	8.6	10.6
38	20.7	22.1	15.2	3.8	.0	12.4	4.3	9.4
37	17.5	13.2	3.9	4.0	3.9	7.9	7.8	8.0
36	26.0	4.5	8.3	15.8	7.7	4.2	2.8	6.2
35	4.4	9.3	12.3	19.3	3.8	6.3	5.7	7.2
34	41.1	18.2	8.0	7.7	22.7	9.0	4.3	10.4
33	8.8	26.4	4.0	7.6	11.3	6.9	5.8	7.9

SOURCE: References 4–6.

Table 5. Mortality rates per million from leukemia among children of England and Wales, by single years of age, 1933–67

Calendar year 19—	Age at death (years)							
	0–	1–	2–	3–	4–	5–9	10–14	0–14
67.............................	21.7	18.0	36.6	51.2	38.8	27.5	25.6	29.1
66.............................	14.3	29.4	29.7	50.8	55.6	31.4	20.0	29.7
65.............................	23.5	33.1	33.8	40.7	59.1	37.2	22.7	33.0
64.............................	27.3	20.5	39.4	44.9	51.1	36.0	18.4	30.7
63.............................	24.0	35.7	43.5	36.3	65.8	37.4	23.7	34.2
62.............................	21.1	29.4	52.4	51.7	47.6	28.4	22.2	30.5
61.............................	28.0	25.6	65.5	54.6	53.6	35.0	20.2	33.3
60.............................	25.6	31.3	53.1	50.7	55.6	39.7	21.8	34.5
59.............................	20.4	28.0	49.2	63.1	63.7	40.2	23.8	35.7
58.............................	30.5	18.8	52.4	52.8	56.3	34.4	21.3	32.2
57.............................	23.0	31.3	30.9	80.3	51.9	27.5	22.2	30.8
56.............................	16.2	43.1	45.3	59.4	57.4	36.4	20.7	33.9
55.............................	18.4	43.7	65.3	58.8	36.3	27.9	20.0	30.9
54.............................	34.3	18.2	57.1	63.3	46.8	30.2	17.6	31.0
53.............................	30.1	46.2	64.5	64.1	50.1	29.2	23.6	35.1
52.............................	30.5	35.8	68.2	62.5	55.7	32.4	22.6	36.2
51.............................	31.2	23.1	56.7	67.1	50.2	29.8	22.3	34.0
50.............................	20.1	33.1	46.3	61.6	43.7	29.3	18.0	30.8
49.............................	30.1	38.5	67.3	51.1	49.8	20.8	23.0	32.0
48.............................	21.7	37.0	55.5	61.7	40.4	28.0	16.2	30.0
47.............................	27.5	31.3	47.9	56.5	56.3	30.7	16.3	31.1
46.............................	25.7	19.2	37.1	53.6	43.3	22.3	22.2	27.1
45.............................	31.9	32.3	53.5	51.8	31.4	21.8	17.2	26.8
44.............................	26.1	23.3	41.4	44.6	33.6	24.8	16.3	24.9
43.............................	27.6	27.5	35.3	49.4	29.3	23.0	19.1	25.3
42.............................	33.9	24.0	38.7	43.0	32.8	20.7	18.5	24.6
41.............................	27.4	28.2	29.3	39.6	31.9	19.9	14.6	21.9
40.............................	24.1	34.1	32.5	65.0	28.6	17.5	14.0	22.7
39.............................	21.8	30.8	33.3	35.7	38.0	19.8	12.2	21.1
38.............................	21.9	31.5	35.7	36.2	31.4	20.0	11.2	20.5
37.............................	36.1	26.6	43.3	35.1	21.7	17.0	12.8	18.0
36.............................	34.9	19.8	23.9	25.3	26.1	15.8	13.0	18.0
35.............................	21.2	20.1	36.0	24.3	23.7	17.0	15.2	18.8
34.............................	14.4	26.9	34.7	28.7	30.4	18.7	11.7	18.6
33.............................	14.0	20.6	30.3	16.8	21.9	15.7	14.9	17.0

SOURCE: Reference 7.

Table 6. Mortality rates per million from leukemia among U.S. white adults 15–49 years, 1933–67

Calendar year 19—	Age at death (years)							
	15–19	20–24	25–29	30–34	35–39	40–44	45–49	15–49
67.............................	23.9	17.8	17.7	21.3	27.8	36.0	50.1	27.4
66.............................	23.1	19.0	18.3	23.5	28.3	35.2	47.6	27.5
65.............................	21.1	18.9	18.8	21.5	27.1	31.9	44.0	25.9
64.............................	22.6	17.5	19.3	23.6	29.1	35.8	49.7	28.0
63.............................	21.9	18.4	19.3	24.9	27.5	35.3	49.8	27.9
62.............................	22.7	19.8	17.6	19.7	25.0	36.6	49.1	27.1
61.............................	23.7	20.1	21.3	23.3	27.8	34.7	50.5	28.7
60.............................	24.3	17.4	21.3	24.9	28.4	37.1	51.6	29.2
59.............................	20.7	19.5	20.4	23.0	28.2	36.8	49.2	28.1
58.............................	27.5	17.6	16.7	21.3	32.1	35.0	45.1	27.9
57.............................	25.0	19.4	21.2	25.6	31.5	37.9	52.1	30.3
56.............................	23.4	18.9	21.2	26.6	28.0	37.6	47.4	28.9
55.............................	24.7	20.8	23.0	23.2	29.8	39.7	49.7	29.9
54.............................	21.6	19.1	20.0	24.9	25.1	36.9	53.0	28.3
53.............................	21.8	19.1	19.8	23.1	28.7	37.3	51.6	28.4
52.............................	26.6	20.3	19.9	23.3	27.2	39.0	49.1	28.8
51.............................	25.1	19.1	21.0	25.1	27.5	41.5	52.6	29.6
50.............................	22.7	16.5	24.5	24.4	29.5	38.5	46.1	28.3
49.............................	22.6	20.4	20.8	22.4	27.0	32.3	48.3	27.0
48.............................	22.3	18.1	18.6	22.2	27.6	30.4	50.2	26.2
47.............................	22.7	15.3	15.9	24.2	25.1	35.9	47.2	25.7
46.............................	19.6	16.0	18.4	24.6	25.9	30.1	45.8	25.1
45.............................	20.2	24.7	22.1	26.0	26.0	34.7	40.7	27.5
44.............................	22.7	19.1	20.9	24.6	27.1	28.7	41.9	26.1
43.............................	18.6	17.3	18.2	19.9	23.5	33.3	45.8	24.4
42.............................	20.0	17.4	17.8	21.4	25.0	29.3	42.8	24.0
41.............................	18.8	15.4	16.4	17.7	24.9	26.4	42.9	22.3
40.............................	17.4	14.9	15.5	19.3	24.4	31.8	44.3	22.8
39.............................	16.6	12.6	16.3	19.6	22.7	30.6	41.0	21.7
38.............................	15.3	11.0	15.3	19.2	20.6	30.3	36.6	20.2
37.............................	16.5	15.4	12.0	18.7	19.4	25.1	35.1	19.6
36.............................	13.8	11.7	12.8	14.3	18.6	29.8	37.0	18.7
35.............................	14.8	9.4	16.9	15.6	17.8	28.1	32.4	18.5
34.............................	12.5	13.8	11.4	15.4	19.1	26.7	29.1	17.5
33.............................	11.9	11.8	9.8	17.7	21.1	25.8	29.5	17.4

SOURCE: References 4–6.

Table 7. Mortality rates per million from leukemia among nonwhite U.S. adults 15–49 years of age, 1933–67

Calendar year 19—	Age at death (years)							
	15–19	20–24	25–29	30–34	35–39	40–44	45–49	15–49
67...........................	19.0	20.5	25.2	22.3	21.8	31.7	47.0	25.5
66...........................	19.2	13.3	10.9	20.0	33.7	40.2	48.3	25.0
65...........................	20.4	16.7	14.1	29.0	26.8	35.1	43.1	25.4
64...........................	14.3	13.6	24.1	22.0	26.7	26.3	46.3	23.4
63...........................	18.9	18.1	22.2	23.3	35.0	38.9	47.0	27.9
62...........................	19.4	11.7	21.5	17.7	17.5	30.8	47.1	22.7
61...........................	14.8	19.8	17.7	20.0	33.2	39.8	44.2	26.0
60...........................	14.7	19.5	21.4	22.1	23.1	34.7	51.9	25.6
59...........................	20.8	15.3	18.4	25.1	23.9	45.2	41.0	26.3
58...........................	21.5	17.8	23.9	32.3	30.1	35.9	48.0	29.1
57...........................	12.9	22.7	18.6	18.3	29.9	32.5	45.7	24.8
56...........................	19.7	10.9	23.3	23.4	24.9	40.3	56.4	27.1
55...........................	16.6	17.2	9.3	19.2	29.3	32.0	46.3	23.2
54...........................	23.5	14.4	14.7	27.0	28.0	32.5	47.1	25.8
53...........................	17.2	18.5	18.4	19.2	24.9	42.2	50.6	26.0
52...........................	14.3	11.9	16.6	22.9	33.1	32.3	44.1	23.9
51...........................	18.1	17.0	16.4	30.1	20.3	40.6	40.9	25.1
50...........................	15.1	11.2	13.3	18.3	27.8	39.4	40.1	22.3
49...........................	16.1	16.9	16.7	22.5	28.1	33.9	36.1	23.3
48...........................	14.3	14.6	13.7	20.1	18.1	34.5	40.4	20.9
47...........................	12.0	15.5	10.0	22.1	19.3	23.8	30.7	18.1
46...........................	15.8	12.5	17.8	14.3	20.4	23.2	44.6	19.9
45...........................	12.1	14.5	20.4	20.6	19.7	24.8	27.1	19.2
44...........................	12.0	14.9	12.2	19.4	28.2	36.1	27.7	20.5
43...........................	11.1	17.9	10.0	10.4	15.0	30.1	38.7	17.5
42...........................	9.5	7.2	10.8	19.0	22.7	22.6	36.8	16.8
41...........................	5.1	11.1	13.3	14.3	17.2	23.0	25.5	14.5
40...........................	9.5	14.4	10.0	17.3	14.5	33.9	37.1	17.7
39...........................	7.4	12.9	16.1	12.5	17.7	21.6	25.1	15.1
38...........................	8.9	11.3	12.9	11.3	19.2	17.1	21.2	13.8
37...........................	8.3	7.2	9.6	15.8	27.2	25.7	27.4	15.7
36...........................	7.7	8.0	10.5	7.4	12.0	17.0	23.7	11.3
35...........................	9.3	10.4	13.1	12.0	9.1	17.0	21.3	12.4
34...........................	6.3	8.0	12.2	17.9	17.1	17.0	21.7	13.3
33...........................	4.7	5.6	11.2	5.9	13.7	13.6	9.4	8.7

SOURCE: References 4–6.

Table 8. Mortality rates per million from leukemia among adults of England and Wales 15–49 years of age, 1933–67

Calendar year 19—	Age at death (years)							
	15–19	20–24	25–29	30–34	35–39	40–44	45–49	15–49
67..............................	18.6	14.4	17.3	17.1	28.6	29.4	34.3	22.6
66..............................	22.0	15.8	17.7	22.3	28.0	30.8	39.7	25.1
65..............................	22.0	18.6	19.7	20.1	23.9	29.1	35.9	24.1
64..............................	18.6	18.2	19.8	19.4	28.2	34.9	40.3	25.5
63..............................	21.3	20.0	19.4	26.2	26.2	31.5	41.1	26.5
62..............................	23.7	19.5	17.7	23.2	26.7	35.4	43.6	27.3
61..............................	24.0	18.4	19.3	21.2	28.3	28.6	40.2	26.0
60..............................	20.6	20.2	17.9	22.1	28.6	36.7	39.7	26.8
59..............................	23.3	19.4	21.0	20.5	28.1	41.3	32.3	26.7
58..............................	15.8	18.0	20.7	19.5	28.9	29.3	38.7	24.8
57..............................	21.2	17.8	20.1	22.0	25.7	36.3	41.3	26.8
56..............................	26.1	21.4	23.6	21.4	23.7	30.4	41.3	27.1
55..............................	21.6	18.8	19.4	19.5	25.6	33.8	43.4	26.4
54..............................	24.4	20.1	16.5	19.5	28.4	33.7	39.3	26.2
53..............................	20.4	15.9	16.3	15.3	30.9	35.8	38.1	25.0
52..............................	23.2	17.6	16.9	17.7	24.0	29.0	37.0	23.8
51..............................	19.5	17.7	21.6	20.6	23.2	34.2	35.0	24.9
50..............................	23.4	18.0	20.0	16.4	19.9	26.2	40.5	23.5
49..............................	25.7	16.6	14.7	23.7	19.7	27.4	37.3	23.4
48..............................	17.6	15.2	10.7	13.6	20.5	28.9	34.3	20.2
47..............................	17.4	13.0	13.4	19.3	18.8	26.3	34.4	20.6
46..............................	20.0	15.5	15.3	19.2	19.7	23.7	40.0	22.1
45..............................	22.8	15.2	14.7	21.0	27.0	20.2	28.3	21.9
44..............................	16.0	14.0	15.8	17.1	17.8	25.9	28.7	19.8
43..............................	13.9	16.9	16.0	15.2	17.3	21.4	29.3	18.7
42..............................	17.1	15.0	17.0	18.3	17.8	23.7	31.0	20.1
41..............................	19.3	13.5	13.2	14.7	16.7	16.9	19.1	16.3
40..............................	14.8	15.0	14.5	13.7	20.1	20.7	28.7	18.0
39..............................	13.2	16.2	12.9	16.0	13.3	18.7	25.2	16.2
38..............................	15.5	14.5	14.1	14.1	14.7	26.5	24.1	17.3
37..............................	12.9	8.9	15.7	11.2	17.9	19.0	18.9	14.7
36..............................	17.7	15.0	12.5	13.7	12.2	21.3	26.7	16 6
35..............................	14.6	13.8	13.6	12.0	11.1	17.2	24.3	14.9
34..............................	12.1	9.0	12.5	12.8	12.4	24.3	21.0	14 4
33..............................	13.7	10.1	10.2	11.8	9.8	17.7	17.6	12.7

SOURCE: Reference 7.

lengths of time between the apparent peaks in the rates for the successively older children were too great to be totally explained by factors affecting successive birth cohorts. They thought the wave effect more likely resulted from improved therapy (2). This explanation would certainly be compatible with the rather dramatic improvement in the average duration reported for childhood leukemia in recent years (9, 10). In the series reported by Zuelzer and Flatz (9), the mean survival time rose from 8.1 months to 13.0 months between the 5-year periods 1950–54 and 1955–59. An acknowledged difficulty with this explanation, however, is that the decline in the leukemia rates for white infants predated the introduction of antimetabolites (2).

Perhaps, as Hewitt (11) has suggested, this early secular decline in the leukemia rates for infants can be explained by fatal anemia gradually being less often incorrectly diagnosed as leukemia. An alternative ancillary explanation would be that there has been a shift toward an increased age at onset of leukemia, possibly as a result of a decreased rate of exposure to some leukemogenic agent whose nature may or may not have been infectious. A recent epidemiologic investigation has implicated an infectious process in the precipitation of childhood lymphoblastic leukemia (12). Any contribution made by an increasing average age at onset could probably be assessed by an examination of data on hospital admissions or insurance claims.

A feature of the results which seems particularly noteworthy is the similarity in the estimated calendar years of the maximums for children under 15 years considered together and for adults 15–49 years. This similarity suggests that those unknown factors which might, in general, explain the rise and subsequent fall in the leukemia mortality rates operated at essentially the same time in children as in adults and that the wave effect observed in the rates for children was probably due to the combined effect of supplementary factors such as improved treatment, better diagnoses, and decreased exposure to some leukemogenic agent. If this conclusion is correct, then the instances in which the maximums were estimated to lie beyond the range of the data become less important.

Further investigation of the estimated maximum leukemia mortality rates might be rewarding if attention were to be concentrated upon the differences in calendar time between the maximums of the different populations (the differences between the maximums for U.S. whites and nonwhites being the most enigmatic). The inaccessibility of relevant vital statistics prevented testing, for other countries, the hypothesis that among children under 15 years the calendar year of the estimated maximums tends to advance with an inceasing age at death. Over the period 1956–67, however, leukemia mortality rates for children under 15 years in a number of countries were available from publications of the World Health Organization (13, 14), and these rates are shown

Table 9. Mortality rates per million from leukemia among children aged 0–14 years in various countries, 1956–67

Country	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967
Australia	34.3	33.3	42.5	44.4	38.4	37.5	39.0	34.1	35.9	35.1	36.5	34.1
Austria	26.9	35.0	39.6	45.2	39.0	33.8	37.2	38.6	34.9	38.5	37.3	29.2
Belgium	40.8	29.0	31.2	40.1	39.0	39.0	47.3	40.2	34.0	29.2	34.3	29.7
Canada	35.9	34.9	32.3	41.6	35.0	35.2	35.4	37.8	36.2	36.7	32.5	33.4
Denmark	32.9	43.8	45.8	45.3	34.6	48.2	43.4	49.0	56.0	38.8	39.4	38.1
Finland	43.3	40.7	33.5	31.9	37.1	27.8	27.5	42.0	42.6	37.6	31.7	41.1
France	43.5	40.7	41.4	41.5	40.1	36.1	39.5	36.1	36.1	33.7	34.1	31.4
German Federal Republic	34.8	33.2	34.5	36.2	35.0	35.1	33.6	38.4	35.9	37.7	33.8	38.5
Hungary	27.6	25.6	30.8	30.9	28.7	27.4	27.3	34.2	35.7	35.1	28.5	34.6
Israel	38.0	43.6	45.2	28.0	60.9	32.8	31.7	28.1	28.7	36.4	29.6	29.7
Japan	25.8	24.6	28.8	27.6	29.6	29.1	32.3	31.5	30.8	32.9	32.5	31.1
Netherlands	31.8	36.8	38.6	38.7	38.9	31.0	41.0	37.2	39.9	42.0	36.1	33.3
Northern Ireland	17.1	24.8	27.2	39.4	29.3	26.6	21.7	31.2	33.2	25.8	30.2	31.5
Norway	44.6	43.9	35.8	31.3	44.2	44.4	55.5	30.5	35.9	36.9	49.6	39.6
Portugal	20.4	27.8	20.7	34.4	29.8	30.1	29.8	28.8	35.4	37.3	39.6	36.4
Scotland	27.1	30.8	32.1	30.3	35.3	30.0	31.0	26.3	28.5	27.6	29.1	25.2
Sweden	33.4	44.8	46.2	44.5	44.2	36.9	43.6	31.0	38.5	34.6	36.7	37.6
Switzerland	42.3	46.0	44.1	47.0	37.9	35.2	45.0	42.4	32.8	31.3	36.3	31.3

SOURCE: References 13 and 14.

in table 9. For some countries, such as Finland, the German Federal Republic, Hungary, and Portugal, no diminution in rates is apparent.

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SPIERS, PHILIP S. (University of North Carolina): *Relationship of age at death to calendar year of estimated maximum leukemia mortality rate. A study of three populations. HSMHA Health Reports, Vol. 87, January 1972, pp. 61–70.*

A regression analysis of the mortality rates from leukemia in England and Wales and in whites and nonwhites of the United States revealed a tendency for the calendar year of the estimated maximums to advance with an increasing age at death among children under 15 years in all three populations. In addition, each sequence of maximums had its own order in time. Adults under 50 years exhibited the same ordering of the three populations with respect to the estimated maximums, but there was little change with increasing age in the maximums for the rates by 5-year age groups.

The close similarity between the maximums for the age groups 0–14 years and 15–49 years suggests that some unknown factors, acting upon children and adults at the same time, may have produced the rise and subsequent fall in the leukemia mortality rates. Thus the association in children between the calendar year of the estimated maximums and the age at death could probably be explained as being a supplementary effect of such factors as improved treatment.