Incidence and Mortality Rates for Leukemia and Lymphoma

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THE VARIOUS FORMS of leukemia and lymphoma are generally considered progressive and uniformly fatal. It may therefore be expected that, in any given population, incidence rates for these diseases will be close to the corresponding mortality rates. However, as shown by Shimkin (*1*) and others, this is not generally true. Table 1 shows the incidence rates for leukemia and lymphoma reported by two large-scale cancer surveys and one cancer register and compares them with mortality rates reported in the same areas and for the same years. All three incidence rates for leukemia and two of the three rates for lymphoma were substantially higher than the corresponding mortality rates.

An incidence-mortality ratio of, for example, 1.50 (equivalent to a mortality-incidence ratio of 0.67) seems to imply that one-third of the patients reported to have leukemia or lymphoma are not dying of these diseases. This is not necessarily true. For chronic disease registers receiving both case reports and death certificates, there are several ways in which a person could be included in incidence data for any given disease but could be omitted from the corresponding mortality data, or vice versa.

1. Factors that might inflate the incidence-mortality ratio:

(*a*) Some patients may be cured of the disease. This does not apply to patients with leukemia or lymphoma.

(*b*) Death may be due to a concomitant but unrelated cause.

(*c*) The physician attending a patient with the disease in question may incorrectly attribute death to some other cause.

(*d*) The diagnosis of the disease may be changed after the case is reported, but the patient may not be omitted from subsequent registry tabulations.

2. Factors that might deflate the incidence-mortality ratio:

The central registry may have data showing the death certificate to be incorrect in attributing death to the disease under study.

3. Factors that might operate in either direction:

(*a*) The decedent may have moved into or out of the study population between the time of diagnosis and death.

(*b*) There may be errors in abstracting, coding, or processing the data.

(*c*) The registration system and the vital statistics system may use incompatible definitions in classifying various diseases, such as leukemia or lymphoma.

In the absence of any of these factors there may still be differences between incidence and mortality rates because of changes in the frequency or distribution of the disease, or changes in the size or composition of the population. These differences arise because incidence and mortality rates for any given time period refer,

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in general, to two different groups of patients, since there is often an interval of one to several years between diagnosis and death. One may expect the average effect of random variations in numbers of cases or numbers of deaths to be small, but when there are rapid changes, real or spurious, in the incidence of newly diagnosed cases, as there are for both lymphoma and leukemia, or when there are changes in the population, observed changes in mortality rates may lag several years behind the corresponding changes in incidence rates. Similar considerations account for the fact that in the United States the birth rate is approximately 2.5 times as great as the death rate, although each person must eventually die. The introduction of new therapeutic methods which prolong life, even though they do not improve ultimate survival rates, may also change the ratio of incidence rates to mortality rates by causing a temporary decrease in numbers of deaths.

By comparing original registry or survey reports for cancer patients with death certificates for the same individuals, it is possible to eliminate the effect of changes in the population or in the occurrence of the disease and to examine and evaluate directly many of the other sources of difference between incidence and mortality data. Such a comparison has been made for 1,653 patients reported to the Connecticut Tumor Registry as having leukemia or lymphoma. The cases studied include all Connecticut residents reported to the registry as having an original diagnosis of leukemia or lymphoma made in the time period 1939–41 or 1949–51. The registry receives reports on neoplasms from nearly all Connecticut hospitals and, in addition, is sent copies of all death certificates for State residents which mention malignant neoplasms. Because of this reporting system, all cases included in the official mortality tabulations for Connecticut should be reported to the registry, although they are omitted from the registry tabulations if they do not meet all the criteria for inclusion. Cases reported to the registry by death certificate only are included or excluded by the same criteria as those that are reported by hospitals.

Table 1. Comparison of incidence and mortality rates [1] for leukemia and lymphoma

Disease	Incidence	Mortality	Incidence-mortality ratio
Survey of 10 urban areas, 1947–48:			
Leukemia	75	54	1.39
Lymphoma	94	51	1.84
Iowa cancer survey, 1950:			
Leukemia	120	90	1.33
Lymphoma	82	43	1.91
Connecticut Tumor Registry, 1951:			
Leukemia	107	73	1.47
Lymphoma	71	70	1.01

[1] Per million population.

SOURCE: References 1–4.

Of the original group of patients, 1,523 (92.1 percent) are known to have died. For all but six of these patients, copies or abstracts of the death certificates were obtained. Most of these included the code rubrics under which the deaths were tabulated in official mortality publications. For cases for which the code rubics were not included, the death certificates were divided into four groups according to the reported cause of death: those attributed to leukemia, to lymphoma, to other malignant neoplasms, or to nonmalignant diseases. Although detailed coding of cause of death is recognized as a difficult procedure requiring considerable training and experience, it was thought that this four-way classification could be made without serious error.

Table 2 compares the original cancer registry reports with the subsequent death certificates or other followup data for the cases studied. Of the original group, 103 patients were still living at the time of the most recent followup report, 1,523 patients were followed until death, and 27 had been reported to the registry by error. The magnitude of over-registration may be greater than is indicated by the small number of cases labeled "duplicate records," since this line shows only those cases for whom both reports gave a date of diagnosis within one of the time periods studied.

There was some shifting of cases from leukemia in the registry tabulations to lymphoma in the official mortality classifications and vice versa. Part of this shifting was due to the well-known changes in pathological characteristics of leukemia and lymphoma as they pro-

gress from early to late stages and part is due to differences between coding practices in the Connecticut Tumor Registry and practices specified for use in vital statistics offices (Fourth, Fifth, and Sixth Revisions of the Manual of the International List of Causes of Death). These coding differences are explained in the footnotes to table 2.

The 240 death certificates coded to diseases other than lymphoma or leukemia (table 2) are of particular interest here. Death certificates for 130 of these cases mentioned one of the two neoplasms studied, but under the coding rules in force at the time of death, the deaths were assigned to some other category. These cases are significant in showing that the certifying physician was aware of the presence of leukemia or lymphoma but thought that death was due to some other cause. Of the remaining 110 death certificates (last 2 lines in table 2), 60 were coded to some form of cancer. Seven of these were coded to unspecified sites, 1 was coded "secondary or unspecified malignant neoplasm of lymph nodes," and the remaining 52 were coded to 18 specific primary sites. Review of the registry records shows that many of these patients probably died of leukemia or lymphoma, but that the physician giving the

Table 2. Coded cause of death for patients reported to have leukemia or lymphoma, Connecticut, 1939–41 and 1949–51

	Disease [1] and year of diagnosis				
	1939–41		1949–51		Total
	Leukemia	Lymphoma	Leukemia	Lymphoma	
Total cases reported	293	242	618	500	1,653
Registration errors:					
Duplicate records	5	10	6	2	23
Other	1	0	1	2	4
Patient living at time of last report	1	11	23	68	[2] 103
Patient dead, cause of death not available	1	2	1	2	6
Coded cause of death: [3]					
Leukemia	232	[4] 16	422	15	685
Lymphoma	[5] 21	[6] 157	[7] 83	331	592
Other (leukemia noted on death certificate):					
Coded to cancer [8]	5	0	3	1	9
Not coded to cancer	11	0	35	1	47
Other (lymphoma noted on death certificate):					
Coded to cancer [8]	2	[9] 19	1	15	37
Not coded to cancer	4	3	11	19	37
Other (neither disease noted on death certificate):					
Coded to cancer [8]	2	17	9	32	60
Not coded to cancer	8	7	23	12	50

[1] As coded by Connecticut Tumor Registry. Includes cases reported only by death certificate. Excludes localized lymphomas coded by the Connecticut Tumor Registry to specific sites—55 cases in 1939–41, and 56 cases in 1949–51.

[2] 91 patients known to have been living in 1957 or later; 12 patients lost for periods of 2 to 18 years.

[3] In all years multiple myeloma and plasma cell myeloma were coded as leukemia by the Connecticut Tumor Registry and as lymphoma by the bureau of vital statistics, Connecticut State Department of Health.

[4] 10 deaths specified as due to Hodgkins' disease; in 1939 deaths from this cause were coded as leukemia.

[5] 17 deaths were due to Hodgkins' disease (see footnote 3).

[6] In 1940–48 deaths from Hodgkins' disease were coded with a residual category of infectious diseases; in 1939–48 deaths from all lymphomas except Hodgkins' disease were coded with a residual category of malignant neoplasms. All deaths coded to either of these residual categories, regardless of the specific cause of death, are included here as lymphoma.

[7] 72 deaths were due to Hodgkins' disease (see footnote 3).

[8] Includes all deaths coded to malignant neoplasms of any site other than leukemia or lymphoma. Deaths coded as benign neoplasms or as neoplasms of unspecified malignancy are included under "not coded to cancer."

[9] By coding rules in force 1939–48 deaths from lymphomas of any type specified to be limited to a particular site were coded with other neoplasms of that site rather than with generalized lymphomas; 16 deaths coded to specific sites of cancer under this rule.

cause of death was not fully informed of the preceding medical history. Some of the 50 deaths not coded to cancer, such as those coded to pneumonia, hemorrhage or anemia, or suicide, may also have been related to leukemia or lymphoma.

By omitting from table 2 all patients who are still living and those whose death certificates are not available, one can construct incidence-mortality ratios for Connecticut which are roughly comparable to those in table 1 but which do not reflect the changing frequency of leukemia and lymphoma. Thus, for the first time period there would remain 291 reported leukemia patients to be compared with reported leukemia deaths among patients with one or the other of the two diseases studied; there were 248 such deaths if the usual vital statistics definitions are used, or 255 if the deaths are classified by the Tumor Registry code (see footnotes to table 2). Incidence-mortality ratios calculated in this way are compared with ratios calculated directly from the published 1951 data in table 3.

It appears from table 3 (first column) that, when deaths are coded by the vital statistics definitions the 1949–51 ratios are close to the ratios calculated directly from published inci-

Table 3. Incidence-mortality ratios calculated from published rates and from death certificates as coded by the Connecticut bureau of vital statistics and the Connecticut Tumor Registry

Disease and date	Ratio calculated from published rates [1]	Death certificates coded by definition of—					
		Connecticut bureau of vital statistics			Connecticut Tumor Registry		
		Incidence [2]	Mortality [3]	Ratio	Incidence [2]	Mortality [4]	Ratio
1939–41							
Leukemia	----------	291	248	1. 17	291	255	1. 14
Lymphoma	----------	229	178	1. 29	229	171	1. 34
1949–51							
Leukemia	1. 47	594	437	1. 36	594	509	1. 17
Lymphoma	1. 01	430	414	1. 04	430	342	1. 26

[1] 1951 only (from table 1).
[2] Case reports coded to the specified disease, regardless of subsequent cause of death.
[3] Death certificates coded to specified disease, regardless of original case report.
[4] Death certificates which would have been coded to specified cause under Connecticut Tumor Registry rules regardless of original case report or code rubric assigned by the Connecticut bureau of vital statistics.

Table 4. Deaths of patients with leukemia or lymphoma not coded to either cause

Age (years)	Leukemia						Lymphoma					
	1939–41			1949–51			1939–41			1949–51		
	Total deaths	Other causes [1]		Total deaths	Other causes [1]		Total deaths	Other causes [1]		Total deaths	Other causes [1]	
		Number	Percent		Number	Percent		Number	Percent		Number	Percent
Under 30	61	3	5	95	5	5	51	6	12	47	7	15
30–49	55	8	15	85	3	4	59	9	15	102	13	13
50 and over	169	21	12	407	74	18	109	31	28	277	60	22
All ages	285	32	11	587	82	14	219	46	21	426	80	19

[1] All deaths coded to causes other than leukemia or lymphoma.

dence and mortality rates for 1951. There is a substantial difference between incidence and mortality for both diseases and in both time periods when the same definitions are used for the registration and vital statistics data. However, because the published registration and mortality data are not based on the same definitions, the difference for leukemia in the most recent time period is artificially increased, while the difference for lymphoma is nearly eliminated.

It is reasonable to expect some age differences in the proportion of deaths coded to leukemia or lymphoma, since mortality rates for other causes of death vary with age. The proportions of deaths not coded to one or the other of the two diseases studied are given in table 4. It seems that increasing age is in fact associated with an increasing proportion of deaths attributed to causes other than leukemia or lymphoma, but even among young patients the proportion of such deaths is not negligible.

The relative importance of the time lag between incidence and mortality rates cannot be evaluated directly, but it is probably rather small. For instance, if annual incidence rates for leukemia are assumed to rise at a constant proportion of 5 percent per year, if survival rates are similar to those reported for males with leukemia (*4*), and if all patients are assumed to have died from leukemia, then the incidence-mortality ratio for any given year will be about 1.05. This difference does not depend on whether the observed changes are real or are artifacts due to changing diagnostic methods and criteria, so long as the incidence and mortality data are affected equally.

Table 1 shows that the survey of 10 urban areas and the Iowa cancer survey each showed a very large excess of incidence over mortality for lymphomas, although the excess in Connecticut was trivial. For leukemia the excess was about the same in the three areas. The reason for this discrepancy in incidence-mortality ratios for lymphoma is not clear, but it does not seem to be related to differences in definitions of sites as used in the two surveys and in the corresponding vital statistics publications. For each survey, data are available (table 5) showing the number of deaths occurring among registered patients during the study year and 6 months thereafter, and the number of deaths coded to various sites of cancer. In the 10-city study the Sixth Revision of the International List was used in coding primary site by both case report and cause of death. In the Iowa survey the Sixth Revision of the International List was also used, except that in the incidence

Table 5. Cancer site recorded on case report and on death certificate

Primary cause recorded on case report	Total deaths tabulated [1]	Primary cause recorded on death certificate [2]					Death certificate not available
		Cancer			Not cancer		
		Leukemia	Lymphoma	Other types	Cancer noted	Cancer not noted	
10-city survey, 1947–48	31, 148	1, 001	962	25, 595	353	1, 059	2, 178
Leukemia	1, 105	975	10	8	5	22	85
Lymphoma	1, 128	16	842	108	16	33	113
Other	28, 915	10	110	25, 479	332	1, 004	1, 980
Iowa survey, 1950	5, 628	281	158	4, 609	240	150	190
Leukemia	313	273	11	5	13	3	8
Lymphoma	157	2	126	16	5	4	4
Other	5, 158	6	21	4, 588	222	143	178

[1] Based on cancer cases seen or treated during the study year, with followup through 6 months following the study year. For the 10-city survey, primary cause of death was coded by the survey staff according to the sixth revision of the International List. For the Iowa survey coding was done by the division of vital statistics of the Iowa State Department of Health and verified by the National Office of Vital Statistics.

[2] Includes cases reported by death certificate only.

NOTE: Unpublished data supplied by William Haenszel and Dr. Sidney Cutler, Biometry Branch, National Cancer Institute, National Institutes of Health, Public Health Service. (See references 2 and 3.)

data all malignancies of the spleen were coded with leukemias, and lymphomas reported as arising in a specific site were coded to that site. Among patients dying during the study interval and for whom death certificates were available, the incidence-mortality ratios (table 5) were:

	Incidence	*Mortality*	*Ratio*
10 urban areas, 1947–48:			
Leukemia	1, 105	1, 001	1. 10
Lymphoma	1, 128	962	1. 17
Iowa, 1950:			
Leukemia	313	281	1. 11
Lymphoma	157	158	. 99

While these ratios might be changed by the collection of death information over a longer period of time, by tabulating cause of death for cases without death certificates, or by restricting the analysis in each area to newly diagnosed resident cases rather than all cases seen or treated during the study year, it is unlikely that these refinements would reconcile the differences between the ratios given here and those in table 1. These differences remain unexplained. It would be interesting to compare current incidence-mortality ratios with those for these two surveys, both conducted more than 10 years ago.

Summary and Conclusions

For both leukemia and lymphoma, reported incidence rates may be substantially higher than reported mortality rates in the same populations. These differences seem to be due mainly to four factors: errors in certifying cause of death, errors in registration of incidence data, differences in definitions used in reports on cancer incidence and mortality, and deaths that were in fact not related to lymphoma or leukemia. The use of mortality data as a substitute for incidence data, or the reverse, can lead to significant errors in estimating the hazards to health associated with the various forms of leukemia and lymphoma.

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American Industrial Hygiene Conference

The American Industrial Hygiene Conference will be held May 13–17, 1962, at the Sheraton-Park Hotel in Washington, D.C. Conference sponsors are the American Industrial Hygiene Association and the American Conference of Governmental Industrial Hygienists.

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