New Approaches for Epidemiologic Studies of Mortality Statistics[1]

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Finding and analyzing multiple causes of death—rather than single causes—has major epidemiologic advantages. Besides helping to reveal the magnitude of the causes or morbid conditions leading to death, it also demonstrates that deaths are usually the result of several simultaneous or sequential causes. This article reviews ways that multiple cause of death data have been analyzed in order to improve our knowledge of these causes and other relevant health factors.

The results of the Inter-American Investigation of Mortality relating to adults (1) convinced us in the late 1960s that a new approach to analyzing causes of death was desirable. Certain kinds of deaths—such as those caused by infectious diseases, malignant neoplasms, and violence—could usually be attributed to a single underlying cause. However, in classifying many other kinds of deaths, the medical referees (Drs. Percy Stocks and Darío Curiel) found it difficult to select one underlying cause in accordance with international rules (2). Indeed, as a consequence of selecting and assigning one underlying cause, valuable information on death certificates was being discarded. One of the recommendations of this investigation was that a system for recording and analyzing multiple causes of death in accordance with international standards should be established.

During the subsequent Inter-American Investigation of Mortality in Childhood (3), it was found necessary to engage in experiments using modern computer techniques in order to study the epidemiology of diseases not as isolated entities but as combinations of pathologic states. In addition to multiple causes, multiple factors such as maternal age, birth order, and birthweight were found to have an important bearing on the infant death rate. In a similar vein, recent analyses by the National Center for Health Statistics (4, 5) have shown that two other factors, weight gain and smoking in pregnancy, affect the outcome of pregnancy and thus infant mortality.

Data from these two investigations of mortality have shown the great value of adopting such approaches to mortality statistics. It should be noted, however, that the multiple cause approach is not new, and that several statisticians have previously pointed out its value (6, 7). Indeed, suitable methods of handling multiple cause data have been devised in the United States, and informative tabulations are currently being provided for use in health planning and studies of disease epidemiology. In addition, the National Center for Health Statistics (8), Israel (9–11), and others (12–15) are presenting US data in order to illustrate

these new dimensions in cause of death statistics.

Recent programs for matching birth and infant death certificates in the United States (4, 16), New York City (17), and Chile (18) have greatly extended our knowledge of the multiple causes of death and the multiple factors involved for purposes of health planning, reduction of infant mortality, and improvement of babies' condition at birth and their survival. At the same time, the emergence of new health problems such as sudden infant death syndrome, AIDS, certain other sexually transmitted diseases, and drug addiction among others have been making investigations and analyses of multiple causes and factors leading to death and their interrelationships especially important.

Right now, the challenges facing vital and health statisticians seeking to explore these new approaches for developing and using mortality statistics are considerable. A few examples will be given here of information derived from studies of multiple causes of death in the United States among infants and subjects of all ages. Some of the results are already being used, but much more needs to be done to obtain and utilize such findings in programs for the prevention of illness and death throughout the world.

MULTIPLE CAUSES OF DEATH IN ADULTS

The problem of assigning the underlying causes of death in the Inter-American Investigation of Mortality (1) was especially difficult when the deaths studied involved diabetes, hypertension, arteriosclerosis, and diseases of the heart. The WHO definition of underlying cause states that this is "the disease or injury which initiated the train of morbid events leading directly to death." But which

cause started the chain of events? And what about health planning as it relates to diseases and conditions not considered serious enough to lead to death? Could such diseases and conditions be prevented by appropriate measures?

The synergistic relationship of infectious diseases and nutritional deficiency has been shown by various studies (19–21). Among the works cited, in 1968 Scrimshaw, Taylor, and Gordon (21) provided a comprehensive review of the interaction of nutrition and infection. Also, our data from the Inter-American Investigation of Mortality in Childhood (3) illustrated the synergistic relationship involved and indicated the frequencies with which immaturity and nutritional deficiency occurred as associated causes of death.

An analysis of multiple causes of death in adults was conducted using 1962–1964 data obtained by the Inter-American Investigation of Mortality from hospital, clinical, and autopsy records as well as from death certificates. One of the Investigation's medical referees, Dr. Darío Curiel, coded the multiple causes of death for two cities studied in the investigation, San Francisco (USA) and Bristol (England). The work dealt with those deaths among people 35–74 years old for which both death certificates and hospital, clinical, and autopsy records were available—38% (1,569) of the deaths in Bristol and 52% (1,937) of those in San Francisco. The resulting analysis, published in 1970 (22), included the following points:

Diabetes mellitus, a disease of particular concern to the Investigation, was classified as the underlying cause of death on only 18 of the 1,937 San Francisco death certificates; but it was cited as one of the multiple causes on 61 death certificates (3.4 times as many) and was reported in 134 (7.4 times as many) on hospital, clinical, or autopsy records (Table 1). As may

Table 1. Diabetes mellitus as underlying or one of multiple causes on death certificates and on hospital, clinical, or autopsy records of adults 35–74 years of age, San Francisco (USA) and Bristol (England), 1962–1964.

City	Death certificates with diabetes			Hospital, clinical, or autopsy records with diabetes as a cause	
	Underlying cause	One of multiple causes	Ratio (Col. 2 to Col. 1)	No.	Ratio (Col. 4 to Col. 1)
San Francisco	18	61	3.4	134	7.4
Bristol	17	41	2.4	86	5.1

Source: Deaths from natural causes with hospital, clinical, or autopsy records; Inter-American Investigation of Mortality (22).

be seen, these ratios were lower among the 1,569 Bristol decedents, though it seems clear that diabetes was a frequent contributory cause of death. However, the true role of the disease as a contributory cause of death was only revealed by the multiple cause approach and intensive investigation.

Similarly, the use of sources other than death certificates revealed large apparent increases in deaths due to a few specific causes in San Francisco. These causes included tuberculosis of the respiratory system (the increase was from 1.1 to 5.1 per 100 deaths), alcoholism and alcoholic psychosis (from 0.6 to 14.5 per 100 deaths), avitaminosis and other metabolic diseases (from 0.3 to 3.5 per 100 deaths), and anemias (from 0.1 to 3.3 per 100 deaths). Arteriosclerotic and degenerative heart disease (categories 420–422 in the Seventh Revision of the *International Classification of Diseases—2*) increased from 34.4 to 55.3 per 100 deaths, indicating that these were contributory causes of over half the deaths studied.

These results indicate that if the true frequencies of causes leading to death are desired, intensive study—such as the studies performed in the Inter-American Investigations of Mortality in adults and in children under five years of age—is necessary, utilizing all available hospital, clinical, and autopsy records.

The findings also raise questions regarding the quality and completeness of data on death certificates. Among other things, the training of physicians completing these certificates may vary from one country to another and also within the same country. Also, the instructions on medical certificates regarding both contributing and underlying causes of death need to be considered.

Despite such concerns, however, the time has come to extend tabulations and analyses so as to improve our understanding of important health problems and provide a sound basis for various actions. As Israel et al. have asserted (*11*), analyses of mortality statistics must begin to shift their emphasis away from sole reliance on the underlying cause of death and to complement underlying cause of death statistics with multiple cause of death statistics.

MULTIPLE CAUSES OF DEATH IN ALL AGE GROUPS

The provision of multiple causes of death in the United States has a long history dating back to 1917 (see Israel et al., *10* and *11*). However, routine production and publication of multiple cause of death information is much more recent, commencing with a 1984 number of the *Monthly Vital Statistics Report* that pre-

Table 2. Fourteen selected causes of death with rates per 100,000 population of underlying and reported causes, with ratios of reported to underlying causes (United States, 1984).

Causes of death	Category numbers[a]	Underlying causes[b]		Reported causes[b]		Ratio of reported to underlying causes
		Deaths	Rate	Deaths	Rate	
Hypertension	401, 403	7,774	3.3	88,571	37.5	11.4
Nutritional deficiencies	260–269	2,600	1.1	25,452	10.8	9.8
Anemias	280–285	3,527	1.5	30,243	12.8	8.6
Septicemia	38	15,028	6.4	82,603	34.9	5.5
Nephritis, nephrotic syndrome, and nephrosis	508–589	20,126	8.5	104,587	44.2	5.2
Arteriosclerosis	440	24,462	10.3	120,639	51.0	4.9
Diabetes mellitus	250	35,787	15.1	144,548	61.1	4.0
Pneumonia and influenza	480–487	58,894	24.9	168,615	71.3	2.9
Bronchitis, emphysema, and asthma	490–493	20,372	8.6	46,837	19.8	2.3
Tuberculosis, all forms	010–018	1,729	0.7	3,858	1.6	2.2
Cerebrovascular disease	430–438	154,327	65.3	262,508	111.0	1.7
Accidents	E800–E949	92,911	39.3	149,579	63.2	1.6
Diseases of the heart	390–398, 402, 404–429	765,114	323.5	1,163,586	492.0	1.5
Malignant neoplasms	140–208	453,492	191.8	514,837	217.7	1.1

Source: US Department of Health and Human Services, National Center for Health Statistics, *Public Use Data Tape Documentation, Multiple Cause of Death for ICD-9, 1984 Data* (23).
[a]From the Ninth Revision of the *International Classification of Diseases* (24).
[b]Based on 72 cause list and recorded axis multiple cause table.

sented data for 1978 (8). (Computer tapes with data on multiple causes of deaths for the years 1968 through 1983 have also been released.)

The present article makes use of selected United States data from a document[3] of the National Center for Health Statistics provided by Israel entitled *Public Use Data Tape Documentation, Multiple Cause of Death for ICD-9, 1984 Data* (23). Available data on underlying causes of death and all reported causes of death are used to illustrate the value of this new approach in mortality statistics.

Table 2 indicates the roles played by 14 selected causes of death as underlying and reported causes in the United States in 1984. The three leading underlying causes of death (diseases of the heart, malignant neoplasms, and cerebrovascular disease) remained the three leaders when total reported causes were considered. However, the fourth leading underlying cause, accidents, dropped to fifth place in reported causes—below pneumonia and influenza, which were stated more frequently as reported causes on death certificates. It should also be noted that the seven causes listed first in Table 2 had much higher death rates as reported causes than as underlying causes of death.

The ratio between these two frequencies, shown graphically for the 14 selected causes in Figure 1, demonstrates that many important contributory causes occur frequently. For example, hypertension (categories 401 and 403 of the Ninth Revision of the *International Classification*

Figure 1. Ratios of reported to underlying causes of 14 selected causes of deaths, United States, 1984.

Ratio

Source: US Department of Health and Human Services, National Center for Health Statistics, *Public Use Data Tape Documentation, Multiple Cause of Death for ICD-9, 1984 Data,* Hyattsville, Maryland, 1986.

of Diseases—24) was reported 11.4 times more often than it was named as an underlying cause (88,571 times as reported and 7,774 as underlying cause). Hypertension, a contributory cause of death from heart and renal diseases, is receiving major attention in preventive programs.

Similarly, nutritional deficiencies were reported on 9.8 times as many death certificates as those on which they were assigned as the underlying cause. Again, the prevention of nutritional deficiency is an important health problem that merits effective action in the maternal and child

health programs of Latin America. Although the problem is recognized as affecting infants and children in Latin America, it could also be a serious problem for other age groups such as preadolescents and adolescents. In addition, nutritional deficiency may be a contributory cause of maternal mortality and excessive numbers of low and deficient birthweights.

Nutritional deficiency can also be a problem for the elderly. For instance, in the United States the multiple cause approach (8) has revealed that nutritional deficiency was the tenth leading reported

cause of death among those 65 years of age and over. Therefore, adequate health planning in many areas of the world requires knowledge of nutritional deficiency in all age groups. Clearly, provision of multiple causes would contribute to this process.

Anemias, likewise, were reported 8.6 times as often on death certificates as assigned as the underlying cause. (Early diagnosis and treatment of anemias are important, especially for women in the reproductive period.)

The ratios of reported causes to underlying causes for arteriosclerosis and diabetes were 4.9 and 4.0, respectively, indicating that the multiple cause approach can make a valuable contribution to our knowledge regarding the extent of these problems.

Although tuberculosis is no longer a major cause of death in the United States, it has been making a significant contribution to the fatal outcome of other diseases and conditions. For example, while it was the underlying cause of only 1,729 of the deaths covered in Table 2, it was listed as a contributory cause of 2,129 others. In other countries where tuberculosis is a greater menace, the rates may be much higher and, likewise, its role as a contributory cause of death could also be much greater.

The two leading causes of death, diseases of the heart and malignant neoplasms, had low ratios (1.5 and 1.1). This was to be expected, as these diseases are commonly assigned as underlying causes. However, in the United States diseases of the heart have emerged as the second leading reported cause of death in children 1–4 years and 5–14 years of age, and in adults 25–44 years of age. Thus, preventive programs are probably needed early in life.

In São Paulo, Laurenti (26) analyzed multiple causes of death among a sample of people dying in hospitals during the period March 1971–February 1972 utilizing death certificates and employing additional information from medical records to complete corrected death certificates. For five causes of death classified by the Eighth Revision of the *International Classification of Diseases* (25), the ratios of reported to underlying causes were as follows:

Diabetes mellitus (category 250)		2.1
Avitaminoses and other nutritional deficiency	(260–269)	17.1
Anemias	(280–285)	28.5
Hypertensive disease	(400–404)	6.2
Pneumonias	(481–486)	6.2

As may be seen, the ratios found for avitaminoses and other nutritional deficiencies, anemias, and pneumonias were much higher in São Paulo than in the United States, suggesting that the frequencies of these diseases may be higher in São Paulo. In this vein, practices relating to diagnosis and reporting of diseases and conditions on clinical records and death certificates presumably vary in different areas, a matter that will need to be considered in evaluating differences. Overall, it is expected that further studies of multiple causes of death will have important implications for health planning in Latin America.

For measurement of progress of health programs over a given period of time, utilization of rates and ratios obtained through the multiple cause approach is advisable. However, in order to make effective comparisons over an extended period, knowledge of the many changes introduced in the revisions of the *International Classification of Diseases* is necessary.

For example, the Eighth Revision (ICDA-8) provides fourth-digit subdivisions for hypertension (conditions in 400–404) within the categories for ische-

mic heart disease (410–414) and cerebrovascular disease (430–438). In the Ninth Revision (ICD-9), however, these fourth-digit subdivisions are not used. Thus, as Israel (11) stated, "As a result, where for 1978 the multiple cause tabulation indicates about 7,000 deaths with mention of ICDA-8 code 401 (essential benign hypertension), for 1979 the multiple cause tabulation indicates over 77,000 with mention of ICD-9 code 401 (essential hypertension)." Hence, for effective comparison of multiple causes coded by the Eighth and Ninth Revisions, the combined categories with hypertension would need to be included.

This divergence provides a good example of how changes in the revisions affect both underlying and contributory causes of death and why caution is advisable in seeking sound comparisons of mortality over time.

For the period when the Eighth Revision was in use, Manton (13) and Wing and Manton (14) analyzed changes in multiple causes of death in 1968 and 1977 in the United States. Manton (13) provided age-race-sex standardized death rates for underlying and multiple causes of death for certain diseases. One subject of concern in this period—when ischemic heart disease as an underlying cause of death declined by 23% and cerebrovascular disease declined by 32%—was changes in death rates from hypertensive disease and arteriosclerosis as reported causes. Examination of multiple cause of death data revealed a 48% decline in the death rate from generalized arteriosclerosis as a cause of death, and a 29% decline in the rate from hypertensive disease.

Wing and Manton (14) presented age-specific and age-adjusted rates for all deaths in the population 35 and over where hypertension was mentioned as a cause during the years 1968 and 1977. Compared to 1968 data, the 1977 figures for white males showed a 25% decline in

hypertension as a cause of death—from 186.8 deaths per 100,000 population in 1968 to 139.8 in 1977. The death rates for white females were lower in both years (164.0 and 114.3 deaths per 100,000, respectively), while the percentage reduction (30%) was somewhat greater. Among nonwhite males and females the death rates from hypertension were higher but the reductions were 30% and 33%, respectively. As Wing and Manton note: "These results strongly suggest that there has been a major reduction in the contribution of hypertension to mortality in the US over the 10-year period 1968–1977."

This analysis of death rates from hypertension provides an excellent example of the value that multiple cause of death analysis can have for planning and evaluating health programs. According to reports of the United States Department of Health and Human Services (27, 28), age-adjusted mortality from heart disease declined by 28% in 1970–1984, and mortality from stroke fell by 50% in the same period. Thus, progress is being made in the prevention of deaths from these diseases.

In addition to the principal causes of death, the multiple cause approach enables study of less common diseases and conditions which may not often be assigned as the underlying cause of death. For example, multiple cause analysis has helped to show the magnitude of one of the problems of the elderly, Alzheimer's disease. Specifically, Aubert and co-workers (15) studied the frequency with which Alzheimer's has been included as one of the causes of death in the United States. Using age- and sex-standardized death rates, they observed a five-fold increase in this frequency—from a rate of 2.7 per 100,000 population in 1979 to an estimated 14.9 in 1983—this latter being nearly 19 times the frequency recorded in 1968.

At this time, with the increasing incidence of cases and deaths from acquired immunodeficiency syndrome, AIDS analysis and study of multiple causes of death are of special importance. The immune system of those infected with the human immunodeficiency virus becomes ". . . vulnerable and defenseless against infectious diseases and some cancers. Some infected people suffer less profound weakening of the immune system and develop other, usually less severe diseases, called 'AIDS-related conditions' " (29). The provision of the interrelationships of causes of death due to AIDS as well as of many other causes will contribute to ongoing research and health planning.

As these examples demonstrate, the current analysis of multiple causes of death in the United States is yielding a wealth of material for planning and evaluating health programs. In particular, the National Center for Health Statistics, under the leadership of Israel and others, deserves our congratulations for achieving this very valuable extension of mortality statistics and in this manner improving understanding of disease epidemiology.

MULTIPLE CAUSES OF DEATH IN INFANCY AND CHILDHOOD

A principal goal of the Inter-American Investigation of Mortality in Childhood (3) was to make an in-depth exploration of the multiple causes of death, and also of interrelationships between these causes and multiple factors, that were responsible for the excessive infant and childhood mortality in Latin America. The resulting research succeeded in providing a greater understanding of many causes and factors and proved to be an exciting and rewarding experience.
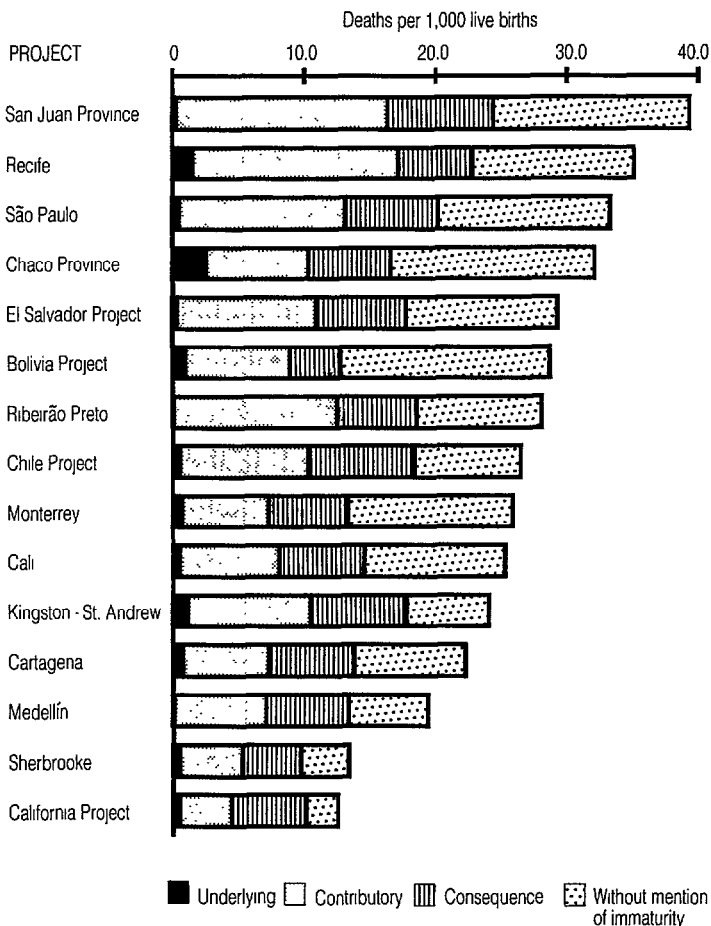
Immaturity

The Seventh Revision of the *International Classification of Diseases* (2) defined immaturity as follows: "For the purpose of this classification, an immature infant is a liveborn infant with a birth weight of five and a half pounds (2,500 grams) or less, or specified as immature." Immaturity was assigned as a cause of death in the neonatal period whenever a birthweight of 2,500 grams or less or a clinical diagnosis of immaturity or prematurity was recorded. However, according to the rules for assignment of underlying causes, it was not to be assigned if any other cause of perinatal mortality was reported. Usually it was assigned as an associated cause.

Efforts were made during the 15-project Investigation to establish the cause-and-effect relationships involved— that is, to determine whether immaturity was a consequence of another cause or whether it contributed to the fatal outcome. This research revealed that immaturity was a very serious problem in many areas of Latin America, and that it could be considered the most important factor in vulnerability to disease and death in the neonatal period.

Figure 2 shows neonatal mortality in each of the 15 projects—divided into those in which immaturity was considered the underlying cause, those in which it appeared to be a contributory cause or a consequence, and those in which immaturity was not mentioned. The rates for immaturity as an underlying or associated cause ranged from 9.8 and 9.9 per 1,000 live births in the Sherbrooke (Canada) and California (USA) projects, respectively, to 23.0 and 24.7 in the Recife (Brazil) and San Juan (Argentina) projects—the latter rates being over 2.3 times as high. Immaturity was considered an associated cause in

Figure 2. Immaturity as underlying or associated cause of neonatal mortality in 15 projects.

Source: *Patterns of Mortality in Childhood* (3).

57.5% of the 12,674 neonatal deaths. In nearly a quarter (23.7%) it was considered a consequence and in one-third (33.9%) a contributory cause. The ratio of deaths in which immaturity was mentioned (as an underlying or associated cause) to those in which it was assigned as the underlying cause was very high (17.6 to 1).

For several maternal conditions—such as conditions that occurred before the pregnancy, conditions of the placenta, and certain complications of pregnancy such as premature rupture of membranes, immaturity was considered a consequence. However, the frequency with which immaturity was considered a contributory cause was much higher in all the Latin American projects than it was in the California project. Several factors, such as the frequency of low birthweights and the quality of medical services, could account for these differences.

As reported in *Patterns of Birthweights* (30), these high death rates from immaturity in Latin America led to study of birthweights. At present five countries in Latin America are known to include birthweight on the birth certificate or birth record.

Differences were noted in neonatal death rates in which immaturity was an underlying or associated cause, with higher rates in rural than in urban areas of two projects. Similar differences were noted with regard to nutritional deficiency. Therefore, the possibility exists that low birthweights are more common in rural areas than in urban areas, owing to the unfavorable nutritional status of mothers in rural areas and insufficient access to prenatal care.

Nutritional Deficiency

The findings of the Inter-American Investigation of Mortality in Childhood (3) also clarified the role of nutritional deficiency in children under five years of age in Latin America. To measure the impact of this important health problem, study of the associated as well as underlying causes of death was necessary.

According to the rules of the Eighth Revision of the *International Classification of Diseases* (ICD-8, 25), if an infectious disease was cited on the death certificate, it would take precedence over a state of nutritional deficiency. And since measles or diarrheal disease often initiated the train of events leading to death, nutritional deficiency was assigned as an associated rather than the underlying cause of death.

For the first time, however, this 1965 Revision (ICD-8) included a group of categories (260–269) under the heading "Avitaminoses and other Nutritional Deficiency." (Earlier revisions had been organized so that some of the deaths due to nutritional deficiency were assigned to nutritional maladjustment—category 772 of the Seventh Revision in the section "Certain Diseases of Early Infancy." The new grouping brought together in one section all deaths from these important causes and thus facilitated measurement of the size of the problem. In the Investigation only 15 deaths were found to be due to a specific vitamin deficiency, and thus in our report the group has been more properly named "Nutritional Deficiency."

Both nutritional deficiency and immaturity reflect deficits in growth and development. However, the Investigation made only one assignment, either immaturity (category 777) or a nutritional deficiency (within categories 260–269), and thus the total number of infants and young children who died with either one of these two conditions was obtained. Of the 35,095 deaths among children under five years of age in the 15 projects, 19,994 (57.0%) involved one of these conditions as an underlying or associated cause. Indeed, in several areas around two-thirds of the deceased children showed evidence that at least one of these conditions had increased their vulnerability to disease and risk of death.

Figure 3 shows overall mortality among children under five in each of the 15 projects and indicates the rates in which nutritional deficiency or immaturity was assigned as an underlying or associated cause. The large differences in mortality involving nutritional deficiency or immaturity (the combined rates ranged from 19.5 per 1,000 population in Recife and 16.6 in the El Salvador Project to 2.4 in the California Project and 2.0 in Sherbrooke) indicated serious problems in these areas of Latin America and the Caribbean. Indeed, even the lowest rates found in the Latin American and Caribbean areas (7.2 per 1,000 population in the Chile Project and 6.1 in the Kingston-St. Andrew Project) were much higher

Figure 3. Mortality from all causes and nutritional deficiency and immaturity as underlying or associated causes in children under five years of age in 15 projects.
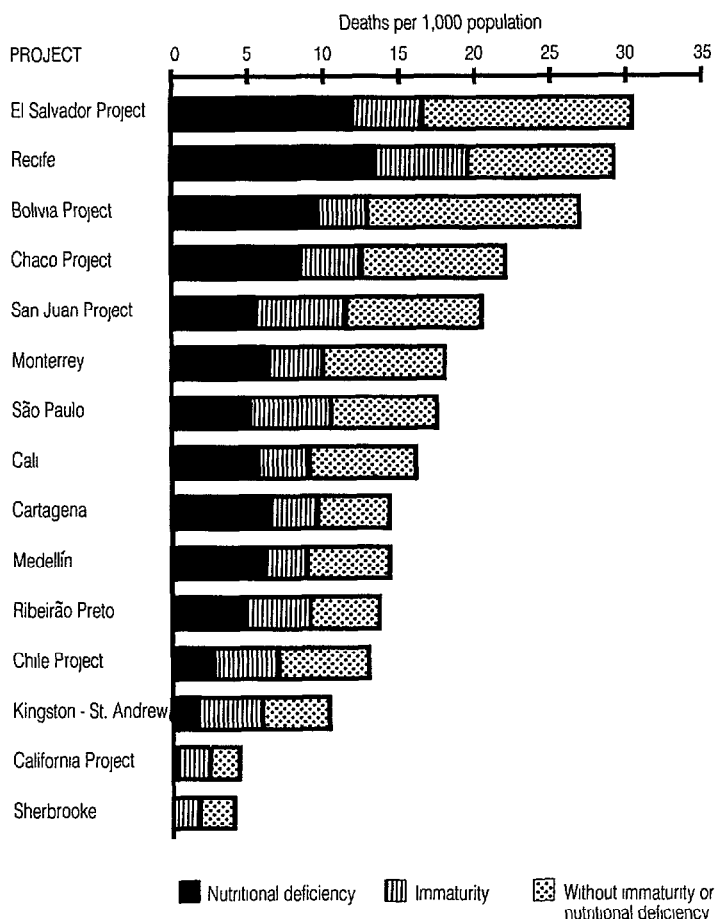
Source: *Patterns of Mortality in Childhood* (3).

than the rates found in the North American projects.

In the Latin American projects, nutritional deficiency was assigned as an underlying or associated cause in over half (52.4%) of the deaths among children under five years of age (excluding neonatal deaths). Table 3 provides more specific data by age group. This finding—that nutritional deficiency was an underlying or associated cause of over half the postneonatal deaths among children un-

Table 3. Deaths under five years of age (excluding neonatal deaths) from all causes and from nutritional deficiency as an underlying or associated cause in 13 Latin American projects.

Age group	Total deaths	Nutritional deficiency No.	%
Postneonatal	14,633	7,300	49.9
1 year	4,308	2,589	60.1
2–4 years	3,010	1,625	53.9
Total	21,951	11,512	52.4

Source: Inter-American Investigation of Mortality in Childhood (3).

der five—has been projected to other regions of the world, including Africa and Asia, to help assess the nutritional deficiency problem in those regions (31). Meanwhile, as reported by Daza (32), many Latin American countries have made tremendous progress in providing supplemental food.

In general, the value for health planning of these data derived from study of mortality in childhood in the Americas has been demonstrated. However, much more can be learned through greater use of the multiple cause approach, and the role of nutritional deficiency in mortality of persons of all ages needs to be determined.

Measles and Other Infectious Diseases

When data from all 13 of the Investigation's Latin American projects were combined, the synergistic action of infectious diseases and nutritional deficiency became clear. As indicated in Figure 4, nutritional deficiency was found to be an associated cause in 60.9% of the deaths from infectious diseases, as compared to only 32.7% of the deaths from other causes. These findings are in accordance with previous research, as reported by Scrimshaw et al. (21), indicating the importance of the host's nutritional state in development of disease.

Specifically regarding measles, the Investigation's study of causes associated with fatalities in which measles was the

Figure 4. Nutritional deficiency as an associated cause of deaths due to infectious diseases and other causes in children under five years of age (excluding neonatal deaths) in 13 Latin American projects combined.
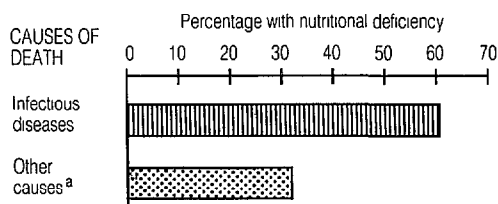
a Respiratory diseases and other causes combined

Source: Figure 95, p. 184, *Patterns of Mortality in Childhood* (3).

underlying cause demonstrated important relationships. As indicated in Table 4, pneumonia was reported as an associated cause of 1,691 (80.3%) of the 2,106 deaths assigned to measles in the 13 Latin American projects. In all but two of these deaths pneumonia was designated a consequence rather than a contributory cause. Despite the fact that this cause-and-effect relationship between measles and pneumonia is well known, however, pneumonia is often stated as the cause of death—a circumstance noted especially in the Investigation's Recife Project.

In contrast, nutritional deficiency (assigned as an associated cause in 62.3% of the measles deaths) usually occurred before the onset of measles and thus was a contributory cause in all but 65 deaths.

Regarding diarrheal disease, an associated cause in 52.9% of the measles

Table 4. Number and percent of 2,106 measles deaths with pneumonia, nutritional deficiency, and diarrheal disease as associated causes (contributory or consequence) in 13 Latin American projects.

Associated cause	Contributory		Consequence		Total	
	No.	%	No.	%	No.	%
Pneumonia	2	0.1	1,689	80.2	1,691	80.3
Nutritional deficiency	1,248	59.3	65	3.1	1,313	62.3
Diarrheal disease	53	2.5	1,061	50.4	1,114	52.9

Source: Inter-American Investigation of Mortality in Childhood (3).

deaths, this resembled pneumonia in that it was nearly always a consequence of measles rather than a contributory cause.

Scrimshaw et al. (33), reporting on a study of measles, diarrhea, and nutritional deficiency in rural Guatemala, have provided a good description of the various interactions of these diseases.

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These examples from the Inter-American Investigation of Mortality in Childhood (3) amply demonstrate the value of analyzing multiple causes of death. However, the Investigation's approach with regard to associated causes has been very different from that adopted in presenting data on multiple causes of death in the United States. Nevertheless, the total reported causes of death in our Investigation can be obtained by adding the underlying and associated causes—which are provided for each project in Appendix 2 of *Patterns of Mortality in Childhood* (3).

With regard to nutritional deficiency, the ratio of total reported causes of death to underlying causes was 11.1. The use of the previously mentioned computer tapes—providing data on multiple causes of death in the United States—will enable study of many interrelationships between causes, and new approaches in this field will prove of great benefit to studies of the epidemiology of diseases.

It is true that the availability of data on multiple causes on death certificates depends in part on the quality of medical certification. Not all diseases and conditions present at death will be stated. In our investigations, the data presented were obtained from hospital, clinical, and autopsy records as well as from death certificates. On the other hand, Israel (11) has pointed out that once the usefulness of the data has been established, it will be easier to implement programs for educating medical certifiers.

MULTIPLE FACTORS

In addition to multiple causes of death, several other factors need to be studied in order to provide an adequate basis for preventive programs. As Serrano pointed out in a paper on multiple causes of death (34), the interrelationships and associations between maternal, fetal, delivery, and postneonatal factors constitutes an extremely interesting field for analysis. These factors need to be considered in combination with the underlying and associated causes of death in order to provide a sound basis for preventive actions.

Fortunately, great progress has been made recently in the study of infant mortality. Some of the multiple factors involved in infant mortality have been known since classic studies in the United States provided data for early 1950 and 1960 (35, 36). However, Taffel and Keppel recently discovered and documented additional factors responsible for excessive mortality in early life (4, 5). Thus, a broader approach has been indicated for epidemiologic studies of mortality statistics.

The findings of the Inter-American Investigation of Mortality in Childhood have been analyzed with respect to the three important determinants of infant mortality: birthweight, maternal age, and birth order (37). Infant mortality was lowest among products of mothers 25-29 years of age and much higher among those of the youngest mothers. Infant death rates increased with increasing birth order and were highest among infants of fifth and higher birth orders.

Matching infant death certificates with those of live births provides excellent data for studying multiple factors as well as causes of death and their relation to
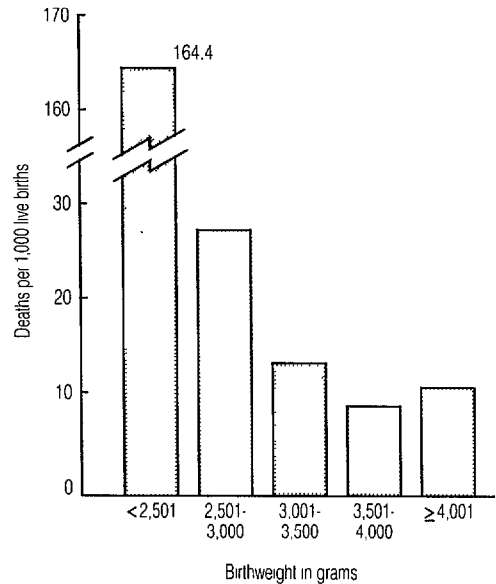
these factors. Kessner et al. (*17*) carried out a valuable study of 142,017 live births registered with the New York City Department of Health in 1968. Infant death certificates were matched with birth certificates and analyzed. The infant death rate was found to be lowest (5.6 per 1,000 live births) for those babies weighing 3,501–4,000 grams at birth.

In Chile, infant death and live birth certificates have been matched each year beginning in 1976 (*18*). To help illustrate the important relationship between infant mortality and birthweight, Table 5 provides the infant death rates for five birthweight groups in Chile (1982) and New York City (1968). In both cases the rates were lowest for those weighing 3,501–4,000 grams at birth and highest for the low-weight group—those weighing less than 2,501 grams at birth.

The birthweight group of 2,501–3,000 grams has been termed a "deficient" weight group because the death rate in this group is usually two to three times higher than among newborns weighing 3,501–4,000 grams. This pattern is illustrated in Figure 5, which shows 1982 infant mortality in Chile in five birthweight groups.

Mardones Santander (*37*), who considered many related factors using matched 1976 birth and infant death certificates, made the first thorough analysis of

Figure 5. Infant mortality in five birthweight groups in Chile, 1982.

Source: Patterns of Birthweights (30).

Table 5. Infant deaths per 1,000 live births in five birthweight groups in Chile (1982) and New York City (1968).

Birthweight (in grams)	Chile	New York City
< 2,501	164.4	140.5
2,501–3,000	27.2	12.1
3,001–3,500	13.3	7.7
3,501–4,000	8.9	5.6
≥ 4,001	11.0	8.0
Total	25.3[a]	21.9

Sources: Mardones-Restat (*18*) and Kessner et al. (*17*).
[a]Without correction for underregistration of births.

birthweights at the national level in Chile. As he pointed out, and as the records proved, the maternal nutrition factor was fundamental—making it imperative for peremptory measures to be included in the national plan designed to confront the problem of infant mortality. Two actions were proposed: (a) an increase in the recommended weight gain during pregnancy—from nine to 12.5 kilograms for well-nourished mothers; and (b) an increase in the complementary food allotment for the national program.

The use to which this analysis has been put provides a fine illustration of the value of mortality statistics for health planning. Since then, Mardones-Restat (*39, 40*) has released several papers utilizing analyses of infant mortality according to birthweight, maternal educational level, birth order, provision of supplementary food, etc. Chile's infant death rate declined sharply—from 54.0 deaths

per 1,000 live births in 1976 to 20.6 in 1984 (30).

Keppel and Taffel (4) of the US National Center for Health Statistics also made an outstanding contribution to the study of infant mortality using data from the US 1980 National Natality Survey/National Death Index Match. As Figure 6 shows, they found the infant death rate for newborns of married mothers who gained less than 21 pounds (9.5 kg) was nearly three times the death rate for newborns of mothers who gained 21 pounds or more (22.2 and 7.8 deaths per 1,000 live births, respectively). They analyzed two factors, weight gain and smoking in pregnancy, and found that for babies of mothers who gained 21 pounds or more, the infant death rate was 11.5 per 1,000 live births if the mother smoked, as compared to only 6.6 if she did not. In this way the authors demonstrated the value of combining these two determinants, weight gain and smoking in pregnancy.

Knowledge of these important factors influencing the survival of newborns should be widely used by health and medical educators and health planners around the world. The Director-General of the Ministry of Health of Thailand (41) has stated that often mothers have simply not understood the importance to health of a proper diet during pregnancy; and in Brazil a class of nurses had to be shown that the best age to have a baby in terms of the infant's survival was not 18 years.

Of course, many of the factors and causes involved are interrelated and operate together. For example, the teenage mother usually has less education, lower weight gain in pregnancy, and (often) repeated pregnancies. As shown by Taffel (5), weight gains decline with successive pregnancies. Although poverty has been reported as the cause of excessive infant mortality, underlying circumstances such as weight gains in pregnancy and the need for supplemental food are probably contributing factors.

In the United States, the National Infant Mortality Surveillance (NIMS) project has been established to address the issue of infant mortality and infant

Figure 6. Infant deaths per 1,000 live births of US mothers according to weight gain in pregnancy and smoking (National Natality Survey/National Death Index Match), United States, 1980.
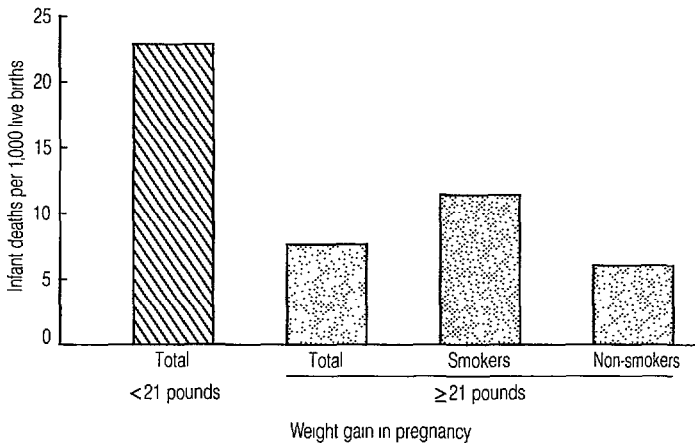
Source: K.G. Keppel and S.M. Taffel, National Center for Health Statistics (4).

health. The procedures used in matching birth and infant death certificates have been described in contributions to *Public Health Reports* (16).

One of these papers included an analysis of the causes of infant deaths by birthweight (42). As expected, the death rates were excessive for the low birthweight newborns of 500–1,499 g and 1,500–2,499 g. However, even the rate for those weighing 2,500–3,999 g was higher than the rate for those who weighed 4,000 g or more. One factor presumably contributing to this high rate in the 2,500–3,999 g group is the fact that it included the deficient weight group of 2,500–2,999 g. The study also found a surprisingly high infant death rate from sudden infant death syndrome—which could be partly accounted for by several factors including maternal age, the quality of certification, etc.

The maternal and child health directors of state health departments in the United States (43) have already explored the use of linked birth and infant death records for health planning and evaluation. One recent article published by the Massachusetts Medical Society (44), under Perspectives in Disease Prevention and Health Promotion, includes the following statement: "A national system that links infant death and birth records is essential to the effective monitoring of trends and identification of high-risk populations." In this same vein, the standard birth certificate recommended for use in the United States beginning in 1989 has sections for entering medical risk factors and other risks for the pregnancy—including use of tobacco and alcohol as well as weight gain during pregnancy. Thus, current matching of birth and infant death certificates and inclusion of important risk factors on birth certificates is making a wealth of information available for development of new approaches in infant mortality statistics.

In many areas of the Americas, data could be collected and analyzed to help convince health authorities of the importance of reducing teenage pregnancy, promoting satisfactory weight gains during pregnancy, and eliminating smoking during pregnancy. In cities, counties, or states, local analyses could be made of prevailing risk factors in relation to birthweight through follow-up studies of neonatal and infant deaths. The inclusion of birthweights on birth certificates in all countries would be a progressive forward step that could be followed by matching birth and infant death certificates to make greater use of this excellent source of valuable data for understanding the epidemiology of diseases and relevant health conditions of infancy. In this regard, the Pan American Health Organization is promoting use of a simplified clinical record in hospitals that provides essential information for the study of birthweights, weight gains during pregnancy, maternal age, smoking, and other risk factors.

In Chile, where birth and infant death certificates have been matched since 1976, progress in reducing infant mortality and low and deficient birthweights has been monitored by determining the proportions of infant deaths in which immaturity and nutritional deficiency were underlying and associated causes of death (18). Thus, in considering new approaches for epidemiologic studies based on mortality statistics, Mardones-Restat has demonstrated the value of combined examination of multiple causes and multiple factors through analysis of matched birth and infant death records. This approach can likewise be used to analyze multiple causes of death in many countries by using linked birth and infant death certificates.

In summary, use of the multiple cause approach in mortality statistics not only permits measurement of the magnitude

of the causes or morbid conditions leading to death but also demonstrates that deaths are usually the result of several simultaneous or sequential causes. In contrast, the single cause approach disregards the significant effect of associated causes—both preexisting and additional causes. Also, it has been shown that the synergistic effect of preexisting or additional causes, as well as other factors, increases a person's vulnerability, and so knowledge of these causes and factors provides a better understanding of events leading to death.

In this article various examples wherein multiple causes of death and multiple factors involved in mortality statistics are analyzed. The approaches used to study multiple causes have differed, and use of many different approaches can be expected to contribute to greater understanding of diseases leading to death. With respect to infants, by combining linked birth and infant death certificates and analyses of multiple causes and factors, the mortality statistics of the future should make a major contribution to the planning and evaluation of health programs. Likewise, in other age groups combined analysis of causes and factors will make a valuable contribution to epidemiologic studies derived from mortality statistics. The preventive implications of these analyses of combinations of causes and factors should be taken into account in planning health actions.

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WHO Studies Health Effects of Climate Change

In recent years, scientific and public concern has been growing over gases released into the atmosphere as a result of man's activities. Some, such as carbon dioxide and methane, may lead to a rise in average temperatures as they accumulate by trapping more heat close to the earth. Others, such as chlorofluorocarbons, deplete the protective ozone layer, causing more ultraviolet radiation to reach the earth's surface.

Through its Environmental Health Division, the World Health Organization has undertaken to assess the potential health effects associated with these changes with the aim of publishing an expert report and providing input on health to the specialized working group of the Intergovernmental Panel on Climate Change (IPCC), established under the auspices of the World Meteorological Association and the United Nations Environmental Program. WHO's initial expert discussion in this field was convened in Geneva from 12 to 16 June 1989. At the conclusion of the meeting, a report was drafted and sent for comments to Member States. It is anticipated that a Task Group will finalize the report at a meeting early in 1990. WHO will provide continuous input to IPCC over the next year in preparation for that panel's presentation of a comprehensive report to the World Climate Conference, planned for late 1990, on the impact of climate change and strategies to mitigate it.

Source: World Health Organization, Press Release WHO/25, Geneva, 16 June 1989.