
The Accuracy of Liver Cancer as the Underlying Cause of Death on Death Certificates

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Synopsis

Studies of liver cancer mortality are subject to confusion attributable to the changes in categories by which liver cancer is identified in successive revisions of the

International Classification of Diseases. To determine the effects of these changes, diagnoses of 2,388 cases of primary liver cancer in the years 1973–80 were compared to the underlying causes of death recorded on the death certificates, using data from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. Results showed that only 53 percent of the deaths were attributed on death certificates to primary liver cancer.

In a reverse comparison of 2,977 death certificates from the years 1973–85 with an underlying cause of death of primary liver cancer, 83 percent had been diagnosed as liver cancer. However, among the certificates that specified cancer of the liver, not specified as primary or secondary, as the cause of death, only 40 percent had been diagnosed originally as liver cancer.

The mortality of liver cancer can be either underestimated or overestimated depending on which disease classification categories are used.

MORTALITY STATISTICS FOR CANCER of a specific site should reflect only deaths from primary cancer at that site. However, because of unclear or incomplete certification of cause of death on death certificates by physicians, mortality statistics may include cancers of a particular site when the cancer at that site is secondary or metastatic. The problem is more evident for the more common sites of metastases, such as the liver. Liver cancer has a 4.5 percent 5-year survival rate (1), so low that the mortality rate easily could be considered a surrogate for incidence in epidemiologic studies.

Liver cancer occurs more frequently in some parts of the world as well as in different ethnic groups (2) and appears associated with the hepatitis B virus or aflatoxins (3). Accurate comparisons of liver cancer incidence and mortality can be made only if the same categories or codes are used for comparing their statistics.

Confusion in studying mortality from cancer of the liver arises because there are several categories for cancer of liver in the World Health Organization's International Classification of Diseases (ICD). Changes in categories between the Eighth Revision (ICD-8) (4), which was used in the years 1969–78, and the Ninth

Revision (ICD-9) (5), which was used beginning in 1979, have compounded the confusion.

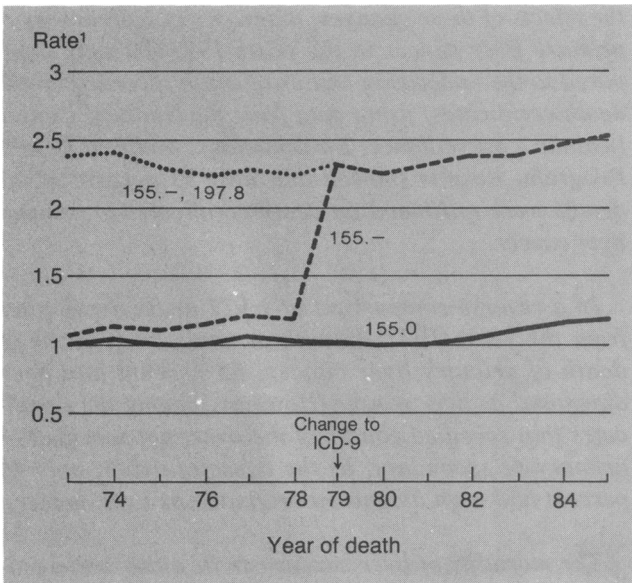
This study was undertaken to emphasize changes in the liver cancer categories between ICD-8 and ICD-9, to show the effect of rule changes made in ICD-9, and to study discrepancies in liver cancer statistics between the hospital diagnoses and the underlying cause of death shown on the death certificates.

Methods

Data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program were used (6) for the study. The SEER Program collects information on all cases of cancer (except superficial skin cancers) that have been diagnosed since 1973 in about the 10 percent of the total U.S. population that is contained in the five States of Connecticut, Hawaii, Iowa, New Mexico, and Utah and the four metropolitan areas of San Francisco-Oakland, Detroit, Seattle-Puget Sound, and Atlanta.

Most of the information is obtained from hospital records, including pathology and autopsy reports. The best possible information from all available sources is

Figure 1. The effect of changing from ICD-8 to ICD-9 on the observed secular trends in liver cancer mortality; United States, 1973-85



¹Age-adjusted rate per 100,000 (1970 U.S. Standard Million).
NOTE: 155.- is total liver cancer, excluding liver, NOS (197.8) before 1979. 155.0 is primary liver cancer.

Table 1. A comparison of possible classification categories for liver cancer in ICD-8¹, used 1969-78, and ICD-9², used 1979 to present

Term	ICD-8	ICD-9
Malignant neoplasm of:		
Liver and intrahepatic bile duct.....	155.-	155.-
Liver, primary (hepatocellular carcinoma, hepatoblastoma, etc.).....	155.0	155.0
Intrahepatic bile duct (cholangiocarcinoma).....	155.1	155.1
Liver, not specified as primary or secondary.....	197.8	155.2
Secondary malignant neoplasm of liver.....	197.7	³ 199.1

¹Reference 4.
²Reference 5.
³199.1 (unknown primary site) includes all secondary or metastatic sites of cancer including liver in ICD-9 as well as cancer without mention of primary site.

used to summarize and code the hospital diagnosis. Autopsy records are routinely reviewed. SEER uses the International Classification of Diseases for Oncology (ICD-O) (7) for coding the site (topography) and morphology of all cancers.

Since SEER collects cases and codes only by primary site (where the cancer originates), there is only one code for liver cancer, 155.-, under which is 155.0 for liver, primary, such as hepatocellular carcinomas and hepatomas, and 155.1 for intrahepatic bile duct carcinomas, including cholangiocarcinomas. (The fourth digit is replaced by a dash as an indication that four digits exist.) SEER does quality control for the topography and morphology coding by sample reabstracting

and recoding and computer edits. Unusual combinations of topography and morphology are reviewed by medical consultants.

To begin, we needed to know how accurately the death certificates reported liver cancer and how many patients diagnosed with primary liver cancer actually died of the disease. Part A of the study was set up to cover all patients with primary liver cancers, including intrahepatic bile duct of the liver, who were diagnosed in the SEER areas in the period 1973-80 and who died before 1986.

SEER follows all cases until the death of the patient. If a case is known to involve metastases of the liver, the case is not included as liver cancer and is coded according to the primary site of origin. When death is reported, death certificates or the equivalent are obtained. The certificates include the code for the underlying cause of death (UCD) as coded by the State health department. This information also appears on the SEER record. There may be some concern that the coding of the UCD by the State health department may differ from that by the National Center for Health Statistics (NCHS). For most States, NCHS accepts the coding of the State health department. Furthermore, quality control and independent studies have shown that there is very little difference between the two.

Certain categories of cases with a diagnosis of primary liver cancer (155.0) and intrahepatic bile duct cancer (155.1), diagnosed in the years 1973-80 and followed through 1985, were excluded from the part A analysis.

Reason for exclusion	Number	Percent
Total before exclusions.....	3,576	100.0
Alive.....	70	2.0
Multiple primaries.....	300	8.4
Death certificate only (no medical report mentioning this cancer was found except for a death certificate).....	122	3.4
Autopsy finding, not diagnosed before death.....	255	7.1
No death certificate.....	56	1.6
Not confirmed microscopically.....	385	10.8
Total remaining for study.....	2,388	66.7

Both a hospital or pathology diagnosis as well as a death certificate were needed on each case. Multiple cancers were excluded because of the impossibility of judging the accuracy of the UCD when the person was diagnosed as having multiple independent cancers. To ensure accuracy of the diagnosis of liver cancer, hospital diagnoses were included in part A only if they were confirmed by tissue examination by a pathologist.

Part B of the study used persons in the SEER file who died in the period 1973-85 of primary liver cancer or intrahepatic bile duct cancer (ICD categories 155.0

and 155.1), as well as liver cancer not specified as primary or secondary (ICD-8 category 197.8 or ICD-9 category 155.2), or secondary liver cancer (197.7, ICD-8 only). The UCD on the death certificate was compared with the original diagnosis or pathology report of the hospital. The exclusions for part B were as follows.

Reasons for exclusion	Number	Percent
Total before exclusions	8,187	100.0
Multiple primaries	758	9.3
Autopsy finding, not diagnosed before death	197	2.4
Death certificate only (no medical report mentioning this cancer was found except for a death certificate)	498	6.1
Total remaining for study	6,734	82.3

Results

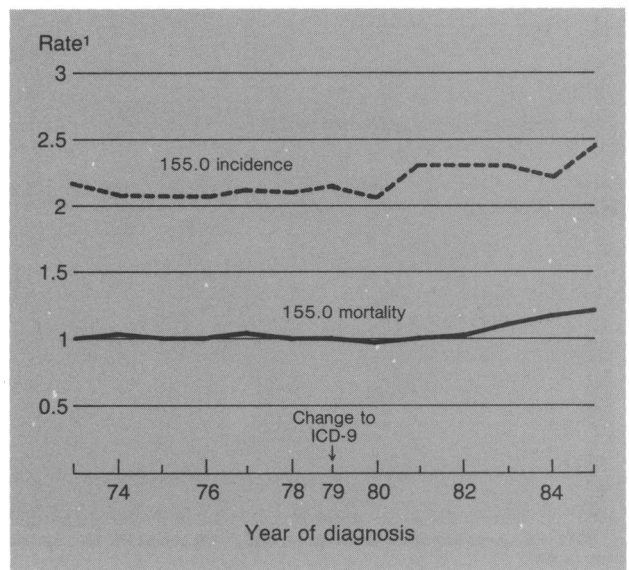
The impact of the change from ICD-8 to ICD-9 may be seen in table 1, which shows the categories that could be used in liver cancer mortality statistics and their code numbers under both revisions. The major changes are: (a) "Liver, not specified as primary or secondary," code number 197.8 in ICD-8, which became 155.2 in ICD-9; and (b) a new rule in ICD-9, which disallowed coding of secondary sites for UCD.

The first change, from 197.8 to 155.2, would seem to have little impact, since the content of the categories remained the same. If the category 155.0 (primary liver cancer), which is the same in both revisions, were to be used, there would be very little change in mortality rates. However, since mortality rates are usually calculated only on the first three digits, in this case 155.—, the effect was to double the figure for liver cancer mortality in the United States between 1978 and 1979 (figure 1).

The effect was so dramatic because the frequency of the diagnosis of liver, unspecified (ICD-8, 197.8), for U.S. mortality has always been about the same or slightly higher than that for primary liver cancer. If 197.8 is included with 155.— for the years in which ICD-8 was in effect, in order to balance the effect of the inclusion of ICD-9 category 155.2 (liver, not specified as primary or secondary) for the years in which ICD-9 was in effect, there is little change in liver cancer mortality for the entire period 1973–85 (figure 1).

The second change occurred because a basic rule for coding cancer deaths was changed when ICD-9 went into effect. In ICD-8, sites of metastatic cancer were allowed to be used to code the underlying cause of death, but under ICD-9 a site of secondary cancer was not allowed to be selected. Therefore, if the UCD is "metastatic carcinoma to the liver," it is coded to "unspecified site" (199.1) in ICD-9. Since ICD-9 category 199.1 contains all underlying causes of death from

Figure 2. Comparison of age-adjusted incidence (SEER) and U.S. mortality rates for primary liver cancer (155.0), 1973–85



¹Age-adjusted rate per 100,000 (1970 U.S. Standard Million).

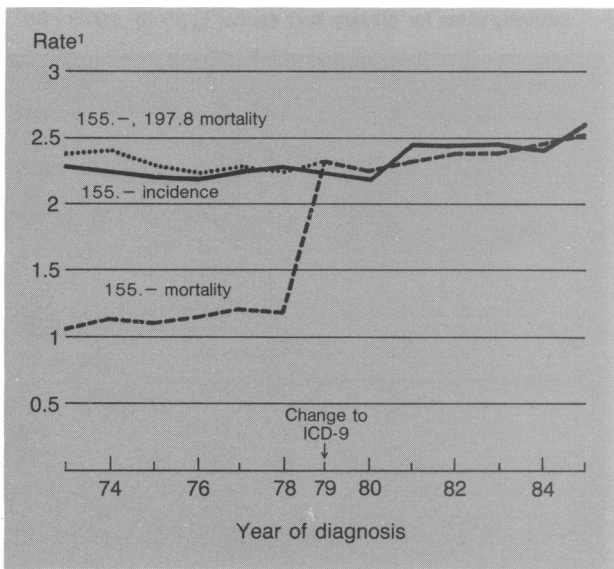
an unknown primary site as well as deaths for which only the metastatic site is given as the UCD, there is no way of telling how many deaths coded 199.1 actually have been secondary liver cancer since 1979, when ICD-9 went into effect. An estimate of about 3 percent can be obtained by using previous data coded by the rubrics of ICD-8.

To demonstrate further the effects of these changes and problems associated with the certification of liver cancer as primary, secondary, or not otherwise specified (NOS), the incidence data for primary liver cancer (155.0) are shown compared to the U.S. mortality data for 155.0 (figure 2) and for 155.— with and without ICD-8 category 197.8 (figure 3). Since SEER uses ICD-O for coding sites, there has been no change in the coding of the hospital diagnosis.

The topography code for ICD-O is based on the malignant neoplasm section of ICD-9. If only 155.0 (figure 2) is used, the age-adjusted incidence rate is about twice the mortality rate per 100,000 population for primary liver cancer. Since the survival rate for liver cancer is low, the mortality rate is being underestimated when only 155.0 is used. However, when one compares the incidence to the mortality line of 155.— and 197.8 in ICD-8, which includes liver, NOS, the incidence line is the same or slightly lower than the mortality (figure 3).

As a side issue, the mortality rate, represented by the dashed line for the years 1973–78 in figure 1, is slightly higher than that for 155.0 because it includes 155.1

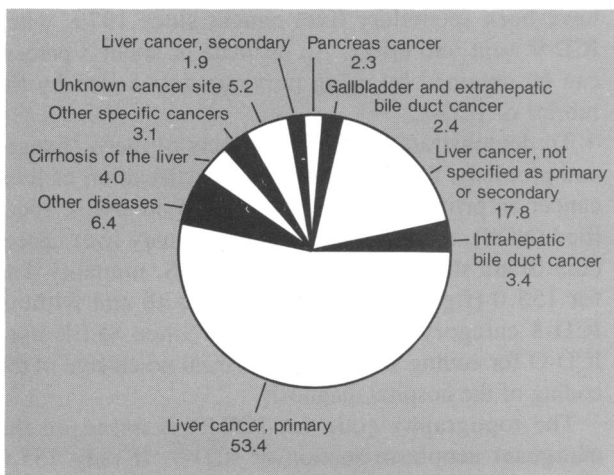
Figure 3. Comparison of age-adjusted incidence rates (SEER) and U.S. mortality rates for total liver cancer (155), 1973–85



NOTE: 155.- is total liver cancer, excluding liver, NOS (197.8), before 1979. 155.0 is primary liver cancer.

¹Age-adjusted rate per 100,000 (1970 U.S. Standard Million).

Figure 4. Cause of death recorded on death certificate for patients diagnosed with primary liver cancer, confirmed microscopically, in SEER areas, 1973–80 (percentages)



(intrahepatic bile duct of liver) as well as 155.0 (primary liver).

Part A. There were 2,232 microscopically confirmed primary liver cancer (hepatocellular carcinomas or hepatomas) cases diagnosed in the SEER registries for the years 1973–80 involving deaths before 1986. As figure 4 shows, only about half (57 percent) died of primary liver cancer, of which 3.4 percent were intrahepatic bile duct cancers of the liver. In addition, 18 percent

died of liver cancer, NOS, and about 2 percent of secondary liver cancer. Obviously, the certificates on the last two groups did not reflect accurately that the liver cancer was primary.

Since the survival time for liver cancer is so low, most of the patients who develop liver cancer die of their disease. About 25 percent of the deaths were attributed to other underlying causes, half from other cancers, and half from other noncancer diagnoses, such as cirrhosis of the liver. This illustrates that it would be unwise to compare primary liver cancer incidence solely with category 155.0 primary liver cancer mortality.

Although there were only 156 cases of cancer of the intrahepatic bile duct of liver (cholangiocarcinomas) diagnosed in the 8-year period, the causes of death recorded on the death certificates were interesting and disturbing. Only 24 percent of the patients had died with a recorded underlying cause of intrahepatic bile duct cancer of the liver (table 2). Another 24 percent were coded to some sort of liver cancer. However, 26 percent had died of extrahepatic bile duct cancer, which includes bile duct cancer, NOS. There is no way to separate bile duct, NOS, from extrahepatic bile duct in ICD-8, ICD-9, or ICD-O.

Because of the large proportion of liver cancer cases with a UCD of extrahepatic bile duct cancer, cases diagnosed as extrahepatic bile duct were examined even though they are not considered liver cancer. About six times as many cases of extrahepatic bile duct cancer were diagnosed in SEER as intrahepatic bile duct cancer (907 cases). Of these, only a very small number (60 deaths, or 7 percent) died with a UCD of intrahepatic bile duct cancer. In addition, 129 cases were diagnosed as cancer of the biliary tract, unspecified, and 17 percent of these died of some sort of liver cancer.

Part B. For this part of the study, the 6,734 death certificates of patients with a UCD of primary liver cancer (155.0), intrahepatic bile duct cancer (155.1), or liver cancer, NOS (197.8 or 155.2), in the SEER data set who died in the period 1973–85 were compared with their original diagnosis. The frequency results are shown in table 3. Only 56.6 percent (3,809 of 6,734) of these patients were actually diagnosed with liver cancer in the hospital. About 20 percent (1,330 of 6,734) had only a diagnosis of cancer of unknown primary site; most of these patients probably had cancers that had already metastasized to the liver when they entered the hospital. The remaining were diagnosed as having cancer of specific sites that probably metastasized to the liver and were improperly signed out on the death certificates.

When only the 2,977 death certificates with a UCD of primary liver cancer (such as hepatocellular car-

cinoma or hepatoma) were compared with the patients' hospital diagnoses, 83 percent were diagnosed as having liver cancer (figure 5). In other words, 17 percent had a different primary cancer site at diagnosis. If those showing a UCD of liver cancer, NOS, were followed back to their hospital diagnosis, only 37 percent were originally diagnosed as liver cancer, and 33 percent were cancer of unknown site, the rest being other specific sites of cancer.

Although there were only 537 deaths (table 3) from intrahepatic bile duct cancer, only 18 percent of the patients (99 of 537) were diagnosed with that in the hospital; 29 percent were diagnosed as having primary liver cancer in the hospital, and 28 percent were found to have extrahepatic bile duct cancers when originally diagnosed.

As mentioned previously, secondary liver cancers are not identifiable since ICD-9 went into effect. However, the 744 deaths of patients who died from secondary liver cancer before 1979 were compared with their original diagnosis. Only 7 percent were diagnosed as primary liver cancer; 25 percent were of specific sites of cancer, such as colon and rectum, pancreas, and lung; and 68 percent were of unknown primary site. These groups were probably metastatic when they originally entered the hospital.

Discussion

A study conducted in the early 1970s, based on data from the Third National Cancer Survey (8), showed liver cancer death certificates to be inaccurate (9). Our study is an update. Since the previous study was a limited survey, it did not allow for complete patient followup. The SEER Program is an ongoing data collection effort that has more complete followup. Since the selection of UCD provides for choosing only one cause, it is impossible to judge the accuracy of the death certificate for persons who have developed more than one independent cancer in their lifetime. Therefore, persons with multiple primaries were eliminated. For patients with only a clinical diagnosis of cancer (not confirmed microscopically), the diagnosis itself may be inaccurate as to the actual primary site or possibly even the fact of cancer. The inclusion of these patients would introduce a bias in the results.

It is interesting and disappointing to observe that the detection rate (detection rate is defined as the proportion of hospital diagnoses with cancer of a certain site in which the cause of death reflects the same hospital diagnosis) of primary liver cancer quoted in this earlier paper was 50 percent, whereas in this new study, more than 15 years later, and based on SEER data, the equivalent figure is still about the same, or 53 percent.

For many years, in the United States, the mortality

'The emphasis on morphology may help the physician to avoid using the term "cancer of liver" on death certificates and to make clear whether the liver cancer is primary or secondary.'

Table 2. Underlying cause of death for patients diagnosed with intrahepatic bile duct cancer of liver, 1973-80, with ICD-9 codes¹

Underlying cause of death	Number	Percent
Primary liver cancer (155.0)	14	9.0
Intrahepatic bile duct cancer (155.1)	38	24.4
Liver cancer, NOS (197.8, 155.2) ²	20	12.8
Liver cancer, secondary (197.7)	3	1.9
Gallbladder (156.0)	3	1.9
Extrahepatic bile duct cancer (156.1)	41	26.2
Biliary tract cancer (156.9)	6	3.9
Cancer of pancreas (157)	7	4.5
Other specific cancers (140-208)	4	2.6
Unknown cancer (195-199)	11	7.0
Cirrhosis of liver (571)	3	1.9
Other noncancers	6	3.9
Total (ICD code)	156	100.0

¹Reference 5.
²197.8 in ICD-8 (reference 4), 155.2 in ICD-9 (reference 5).

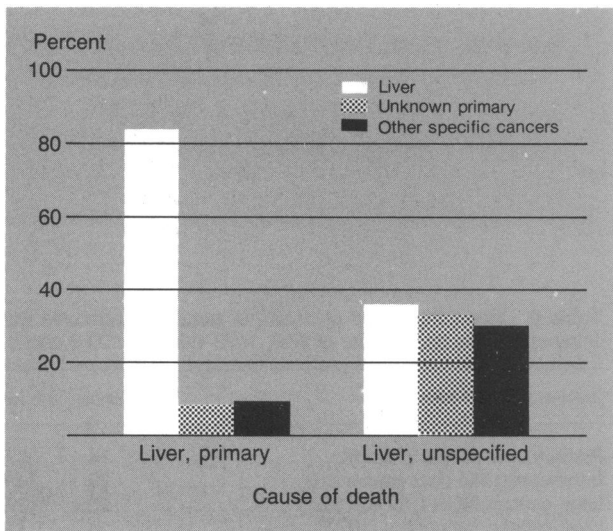
Table 3. Numbers of hospital diagnoses for cases with an underlying cause of death of liver cancer¹, by categories

Diagnosis	Primary liver, 155.0	Intra-hepatic bile duct, 155.1	Liver, Nos ² 197.8, ICD-8 155.2, ICD-9	Total liver, 155 and 197.8
Liver	2,470	154	1,185	3,809
Intrahepatic bile duct	20	99	31	150
Gallbladder	15	47	94	156
Extrahepatic bile duct	24	153	70	247
Unspecified biliary	11	24	24	59
Pancreas	45	13	122	180
Colon and rectum	18	5	149	172
Lung	32	0	87	119
Other specific cancers	98	11	403	512
Unknown primary	244	31	1,055	1,330
Total	2,977	537	3,220	6,734

¹Coding is ICD-9 (reference 3), except where noted.
²NOS is not otherwise specified.

from cancer of the liver, NOS (197.8 for ICD-8 and 155.2 in ICD-9), has been greater than from primary liver cancer, with ratios of liver, NOS, to primary liver cancer running from 1.36 in 1973 to 1.10 in 1982. In

Figure 5. Hospital diagnoses for deaths attributed to liver cancer: primary versus liver, NOS, United States, 1973–80



recent years, through 1986, the ratios have been about 1.00. This may indicate that physicians are becoming more specific about whether liver was the primary site of cancer.

In addition, 26 percent of the patients diagnosed with intrahepatic bile duct cancer of liver (155.1) died of extrahepatic bile duct of liver (156.1), which includes bile duct or passage, NOS. Based on hospital diagnoses, nearly 40 percent of the deaths labeled liver cancer were actually secondary (metastatic to the liver from some other primary site).

The applicability of these results to mortality analyses, however, has not been discussed in detail. Based on all SEER cancer incidence cases diagnosed in the years 1973–86, there were 1,252 deaths in the years 1985–86 with a UCD of 155.–. Mortality data from NCHS for 1985–86 show 1,249 deaths among SEER populations for the same cause of death, 155.–. These numbers can differ because residency can change between diagnosis and death, there may have been more than one diagnosis of cancer, the diagnosis might have been earlier than 1973, or rarely, the hospital record showed that a person never had cancer when the corresponding death certificate has a UCD of liver cancer. Since the numbers are very close, it would appear that the incidence file could be used to calculate the underreporting of primary liver cancer mortality by using only 155.0, and the overreporting of liver cancer mortality could be calculated by using 155.– from the mortality file.

Of the 1,252 deaths with a UCD of 155.–, only 794 had a hospital diagnosis that also stated primary liver (155.0) or intrahepatic bile duct cancer (155.1). In

addition, there were 162 persons diagnosed with liver cancer whose death certificates reflected some other cancer as the UCD. Therefore, the number of liver cancer deaths (corrected by information from the hospital diagnosis) was 956 (794 plus 162), and liver cancer mortality would be overreported by 31 percent [(1,252 minus 956 divided by 956)] if ICD-9 category 155.–, which includes primary liver, intrahepatic bile duct, and liver, NOS, is used.

Since many of these hospital diagnoses were not confirmed microscopically, one may not want to assume that the hospital diagnosis is correct. If the unconfirmed diagnoses and multiple primaries are eliminated, there were 848 deaths, or 68 percent of the original deaths. Even with reducing the deaths to this number, the estimate for the overreporting is of the same magnitude, 27 percent.

Based on similar calculations, the 654 deaths with a UCD of 155.0, primary liver cancer, would be underreported by 26 percent if all diagnoses and deaths were used and by 23 percent if limited to confirmed diagnoses in patients with only one primary.

A reasonable conclusion is, therefore, that the use of 155.0 alone would yield an underreporting of primary liver cancer mortality by approximately 23 to 26 percent, and the use of 155.– would yield an overreporting of the mortality by nearly the same amount, 27 to 31 percent. Along the same lines, a combination of 155.0 and 155.2 could be used to calculate liver cancer. For example, excluding intrahepatic bile duct, the results are similar to those with 155.–, with an overreporting of 18 to 24 percent.

In order to limit the scope of this study, other factors such as age, race, sex, and geographic area were not included. Further analysis of additional cancer sites is currently under way. However, further studies on the accuracy of death certificates will not solve the problems of differences in the reporting of liver cancer statistics. When dealing with these statistics, it is important to remember the changes in liver cancer categories presented in this paper. The problem arises when one country or researcher uses 155.0 and another uses the category 155.–, which includes not only primary (155.0) and intrahepatic bile duct (155.1), but also liver, NOS (155.2). If everyone does not use the same rubrics, data are not comparable.

What can be done about the confusion? On the advice of the International Agency for Research on Cancer working party for revising the neoplasm chapter, the World Health Organization has completely revised the category for liver in the forthcoming ICD-10 (10), basing the classification on histological type. The revision will go into effect in 1993, and the classification for liver cancer is

C22 *Malignant neoplasm of liver and intrahepatic bile ducts*
Excludes: biliary tract, unspecified (C24.9)
secondary malignant neoplasms of liver (C78.7)

C22.0 Liver cell
Hepatocellular carcinoma
Hepatoma

C22.1 Intrahepatic bile duct
Cholangiocarcinoma

C22.2 Hepatoblastoma

C22.3 Angiosarcoma of liver
Kupffer cell sarcoma

C22.4 Other sarcomas of the Liver

C22.7 Other specific types

C22.9 Liver, unspecified

This will permit identification of other specific histologic types of primary liver cancer, some of which are presently coded to liver, NOS, in ICD-9. The emphasis on morphology may encourage the physician to avoid using the term "cancer of liver" on death certificates and to make clear whether the liver cancer is primary or secondary. At present, slightly more than half of the death certificates in the United States specifying liver cancer mention histology. No data are available from other countries. In ICD-10 the rules will be changed to again allow cancer of secondary sites to be specified as the UCD when no primary site is known. Therefore, if all the physician knows is "metastatic cancer to liver," it will be coded as such.

Certifying physicians should clearly specify the histological type of liver cancer on the death certificate. The certifier should also state whether the liver or the intrahepatic bile duct of the liver is the primary site or whether the liver is a metastatic site from some other primary site, which should be specified, or from an unknown site. Coders cannot second guess what the physician meant when he or she signed the certificate. It should be pointed out to physicians signing death certificates that they should be more specific when specifying bile duct cancer on a death certificate, since cancer of bile duct, NOS, is classified as extrahepatic bile duct.

A new death certificate (11) has been introduced in the United States and is gradually being adopted by the States. It allows for one physician to certify the fact of death, and at a slightly later date, the physician usually

responsible for the care of the patient may certify the medical causes of death. Querying of physicians about the certification will be encouraged. This may mean that the certificate will reflect more accurately the entire disease process leading to death.

Liver cancer is one of the top 10 causes of cancer deaths in the United States. In some countries it ranks even higher. For example, in Japan, primary liver cancer is the third leading cause of cancer death. Liver cancer is an important disease, and we must be able to monitor mortality as well as incidence with equivalent rubrics in all parts of the world.

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