LIVER (HEPATIC) CANCER

Includes invasive cancer only. Does not include carcinoma in situ or metastatic cancer.

Background

This case definition was developed by the Armed Forces Health Surveillance Division (AFHSD) for the purpose of descriptive epidemiological reports on invasive cancers among active duty Service members.[1] The case definition uses the "standard" AFHSD oncology case definition.

Clinical Description

Liver cancer, also known as hepatic cancer, refers to cancer cells that form in the tissues of the liver. The two main types of liver cancer are hepatocellular carcinoma (HCC), accounting for more than 90% of primary tumors, and bile duct cancer (cholangiocarcinoma). Most cases of HCC (85%) occur in patients with cirrhosis and more than 70% of cases are associated with chronic hepatitis B and chronic hepatitis C infection.[2] Symptoms vary by the stage of disease and the presence of cirrhosis. Early stage, non-cirrhotic related HCC is often asymptomatic, while patients with cirrhotic-related disease show symptoms of liver failure, (i.e., abdominal pain, distention, jaundice, pruritus, ascites, fever, weight loss, early satiety and a palpable mass in the upper abdomen).[3] Diagnosis relies on laboratory biomarkers, imaging studies and liver biopsy. For patients with small (< 5 cm), early-stage tumors, treatment includes surgical resection and ablation with survival rates of 70% and 35% at 5 and 10 years respectively.[4] Select patients may be candidates for liver transplantation which offers the potential of cure. Risk factors include obesity, type 2 diabetes, genetic syndromes, smoking, and exposure to toxins.

Case Definition and Incidence Rules *(March 2025 - present)*

For surveillance purposes, a case of liver cancer is defined as:

- *One hospitalization* with a case defining diagnosis of liver cancer (see ICD9 and ICD10 code lists below) in the *first* diagnostic position; or
- *One hospitalization with a procedure code* indicating radiotherapy, chemotherapy, or immunotherapy treatment (see ICD9 and ICD10 code lists below) in the *first* diagnostic position; AND a case defining diagnosis of liver cancer (see ICD9 and ICD10 code lists below) in the *second* diagnostic position; or
- *Three or more outpatient medical encounters*, occurring *within a 90-day period*, with a case defining diagnosis of liver cancer (see ICD9 and ICD10 code lists below) in the *first or second* diagnostic position.

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[1] Armed Forces Health Surveillance Center. Incident diagnoses of cancers and cancer-related deaths, active component, U.S. Armed Forces, 2005-2014. *MSMR* 2016; 23(7): 23-31.

[2] American Cancer Society. Stomach Cancer. 2024. https://www.cancer.org/cancer/types/liver-cancer.html. Accessed March 2025.

[3] MD Anderson Cancer Center. Liver Cancer. https://www.mdanderson.org/cancer-types/liver-cancer.html. Accessed March 2025.

[4] Asafo-Agyei KO, Samant H. Hepatocellular Carcinoma. [Updated 2023 Jun 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559177/. Accessed March 2025.

Case Definition and Incidence Rules *(continued)*

Incidence rules:

For individuals who meet the case definition:

- The incidence date is considered the date of the first hospitalization or outpatient medical encounter that includes a case defining diagnosis of liver cancer.
- An individual is considered an incident case *once per lifetime.*

Exclusions:

- None

Codes

The following ICD9 and ICD10 codes are included in the case definition:

Malignant neoplasm of liver and intrahepatic bile ducts	*C22 (malignant neoplasm of liver and intrahepatic bile ducts)*	*155 (malignant neoplasm of liver and intrahepatic bile ducts)*
	C22.0 (liver cell carcinoma)	155.0 (malignant neoplasm of liver, primary)
	C22.1 (intrahepatic bile duct carcinoma)	155.1 (malignant neoplasm of intrahepatic bile ducts)
	C22.2 (hepatoblastoma)	155.0 (above)
	C22.3 (angiosarcoma of liver)	
	C22.4 (other sarcomas of liver)	
	C22.7 (other specified carcinomas of liver)	
	C22.8 (malignant neoplasm of liver, primary, unspecified as to type)	
	C22.9 (malignant neoplasm of liver, not specified as primary or secondary)	151.9 (malignant neoplasm of liver, not specified as primary or secondary)

Procedures	**ICD-10-CM Codes**	**ICD-9-CM Codes**
Related treatment procedures *(Radiotherapy, chemotherapy, immunotherapy)*	Z51.0 (encounter for antineoplastic radiation therapy)	V58.0 (radiotherapy)
	Z51.1 (encounter for antineoplastic chemotherapy and immunotherapy)	V58.1 (encounter for chemotherapy and immunotherapy for neoplastic conditions)

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	- Z51.11 (encounter for antineoplastic chemotherapy)	- V58.11 (encounter for antineoplastic chemotherapy)
	- Z51.12 (encounter for antineoplastic immunotherapy)	- V58.12 (encounter for antineoplastic immunotherapy)

Development and Revisions

- This case definition was developed in March 2025 by the Defense Health Agency (DHA) Health Surveillance & Epidemiology (HSE) cancer surveillance Sub Working Group (SubWG). The case definition was developed based on reviews of the ICD10 codes, the scientific literature and previous AFHSD analyses.

- In 2024, the DHA HSE cancer surveillance SubWG evaluated and expanded the list of cancers in the AFHSD cancer report to include breast (female), bladder, brain, cervical, colorectal, kidney (renal), leukemia, liver (hepatic), lung/bronchial, non-Hodgkin lymphoma, ovarian, pancreatic, prostate, stomach (gastric) and testicular cancer.

- In a 2019 *Monthly Surveillance Medical Report (MSMR)* article, analysis of the AFHSD standard oncology case revealed the definition had a high positive predictive value (PPV) for capturing cases of common cancers, (e.g., breast, prostate, testicular), and a low-to-moderate PPV for rarer cancers, (e.g., gallbladder, intestinal, laryngeal). Analyses also revealed the case definition was less sensitive for identifying cancers of the brain and nervous system, lung and bronchus, bones and joints, and liver (PPV$\leq$ 50 percent); these cases often represented metastases rather than true incident cases. While the broad application of a single case definition may affect the sensitivity and specificity in varying ways for the individual cancers, the PPV for all the cancers included in the report are >70 percent, and most have a PPV $\geq$ 90 percent.[5]

- The standard AFHSD oncology case definition was originally developed in 2011 by the Armed Forces Health Surveillance Center (AFHSC) in collaboration with a working group of subject matter experts from the Office of the Assistant Secretary of Defense for Health Affairs (ASDHA), the United States Army Public Health Command (USAPHC) and the United States Military Cancer Institute for a report on 10 different *invasive* cancers. The case definition was developed based on reviews of the ICD9 codes, the scientific literature and previous AFHSC analyses.

Case Definition and Incidence Rule Rationale

- In the 2019 *MSMR* article, cases of liver cancer identified using the standard AFHSD oncology case definition had a total PPV of 57.1 percent [CI 28.9-82.3]: female 0.0 percent [-], male 61.5 percent [CI 31.6-86.1], among a subset of active component and retired officers.[5]

- The case finding criteria of *three or more outpatient medical encounters, within a 90-day period,* is used to identify cases that do not meet the other criteria in the definition. Exploratory analysis of Defense Medical Surveillance System (DMSS) data revealed this criterion yielded optimal specificity.[6]

    - A period of 90 days allows for the likelihood that "true" cases of liver cancer will have second and third encounters within that timeframe. The timeframe is based on the following standards of care: (1) following a biopsy of a clinically suspicious hepatic lesion, the average

[5] Webber, B, Rogers, A, Pathak, S, Robbins, A. Positive Predictive Value of an Algorithm Used for Cancer Surveillance in the U.S. Armed Forces. *MSMR* 2019; 26(12):18-23.

[6] Detailed information on these analyses is available through AFHSD; reference DMSS Requests #R230308, #R230378 and #R240009.

time to obtain a pathology report and definitive diagnosis is 1-3 weeks; (2) individuals whose biopsy results are positive for liver cancer are likely to have a follow-up visit for treatment within 4 weeks of a definitive diagnosis; and (3) individuals are likely to have follow-up visits to monitor clinical indicators of disease within the 90-day timeframe.[7]

- For outpatient encounters, the incident date is considered the first of the three encounters occurring within the 90-day period, (e.g., if an individual has four liver cancer codes on 1-Jan-12, 1-Dec-15, 8-Dec-15, and 15-Dec-15, the incident date would be 1-Dec-15; 1-Jan-12 would be considered a screening encounter and dropped).

- To maintain consistency with the standard AFHSD methodology for surveillance of invasive cancers, AFHSD uses a *once per lifetime* incidence rule. The workgroup recognizes individuals, may be considered disease free after treatment or after an extended period of time, (e.g., 5 years), with no clinical evidence of disease. Individuals who develop a second primary tumor after being disease free could, theoretically, be counted as a new incident case. However, for surveillance of cancer using administrative, (i.e., billing), data, it is difficult to identify individuals who are disease free after treatment.

Code Set Determination and Rationale

- Procedure codes (ICD10 and CPT) indicating surgical treatment of individual cancers such as hysterectomy, mastectomy, prostatectomy, and other procedures unique to certain types of cancers are not included in the code set. While procedure codes may increase the specificity of case finding criteria in select circumstances, analyses can be labor intensive and the effort does not necessarily guarantee a better case definition, (i.e., the definition may still identify false positive cases).

- *Screening for disease* codes ICD10 Z12.xx / ICD9 V76.xx (encounter for screening for malignant neoplasms) are not included in the code set. Screening codes are used for "testing for disease or disease precursors in seemingly well individuals so that early detection and treatment can be provided for those who test positive for the disease, (e.g., screening mammogram)."[8] They would not be used for follow-up medical encounters of a specific disease.

- *Personal history of malignant neoplasms* (ICD10 Z85.xx) codes are not included in the code set. While these codes may be beneficial for identifying individuals with a history of cancer, analysis of administrative data reveal these codes lack the specificity to count incident cancer cases and are inconsistently used by providers. [9] Given these findings, the AFHSD does not use personal history codes to exclude prevalent cases, (i.e., individuals with a history of cancer), nor to identify individuals who are disease free after treatment.

  Personal history codes are intended to be used by providers for individuals who have a history of cancer *and* documented evidence in the medical record that the malignancy has been "excised or eradicated and all treatment is complete." They are not used for a "self-reported" history of

[7] Liver cancer. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2023. https://www.nccn.org/guidelines/recently-published-guidelines; Accessed March 2025.

[8] ICD-10-CM Official Guidelines for Coding and Reporting. FY 2022–Updated April 1, 2022. (October 1, 2021-September 30, 2022. https://stacks.cdc.gov/view/cdc/126426. Accessed March 2025.

[9] Analysis performed by the Defense Centers of Public Health-Dayton. Encounters with at least one Z85.x code in any diagnostic position (dx1- dx20) were pulled from Comprehensive Ambulatory Professional Encounter Records (CAPER) and Standard Inpatient Data Records (SIDR) for all Tri-Service beneficiaries between October 2016 and March 2024. A total of 546,962 encounters were identified. Of these, 68,395 (13%) had at least one neoplasm diagnosis (ICD10 C00-D49). With administrative data, there is no way to determine if the neoplasm codes refer to a resolved malignancy or a new cancer diagnosis. Records with conjunction codes for follow-up (Z08), aftercare (Z51.[0.1] and screening (Z12) were queried: 420,236 (77%) had no conjunction codes in any diagnostic position suggesting providers use personal history codes independent of the purpose of the visit and potentially inconsistently.

malignancy, and they should be used in conjunction with ICD10 codes for follow-up visits (Z08- encounter for follow-up examination after completed treatment for a malignant neoplasm), aftercare visits (Z51.0 - encounter for antineoplastic radiation therapy; Z51.1- encounter for antineoplastic chemotherapy and immunotherapy), and screening visits (Z12 - encounter for screening for malignant neoplasms).[10]

Reports

The AFHSD reports on liver cancer in the following reports:

- Periodic *MSMR* articles.

Review

Mar 2025	Case definition reviewed and adopted by the AFHSD Surveillance Methods and Standards (SMS) working group.
Mar 2025	Case definition developed by the DHA HSE cancer surveillance SubWG.

Comments

- *Invasive cancer*: The complete ICD10 code set for all "malignant neoplasms of digestive organs" includes the following codes (C15-C26). The AFHSD has developed case definitions* for colorectal (C18-C20, C26.0), liver (hepatic), pancreatic, and stomach (gastric) cancer.
  - C15 Malignant neoplasm of esophagus
  - C16 Malignant neoplasm of stomach*
  - C17 Malignant neoplasm of small intestine
  - C18 Malignant neoplasm of colon*
  - C19 Malignant neoplasm of rectosigmoid junction*
  - C20 Malignant neoplasm of rectum*
  - C21 Malignant neoplasm of anus and anal canal
  - C22 Malignant neoplasm of liver and intrahepatic bile ducts*
  - C23 Malignant neoplasm of gallbladder
  - C24 Malignant neoplasm of other and unspecified parts of biliary tract
  - C25 Malignant neoplasm of pancreas*
  - C26 Malignant neoplasm of other and ill-defined digestive organs

- *In situ cancer:* The complete code set for "carcinoma in situ of other and unspecified digestive organs" includes the following codes (D01). The AFHSD uses the standard oncology case definition for surveillance of in situ cancers and is in the process of developing case definitions for select in situ cancers.

[10] Bredehoeft, Emily. Clear Up Confusion as to When Cancer Becomes "History Of." American Academy of Professional Coders (AAPC). https://www.aapc.com/blog/40016-clear-up-confusion-as-to-when-cancer-becomes-history-of/. Accessed March 2025.

D01 Carcinoma in situ of other and unspecified digestive organs

- D01.0 Carcinoma in situ of colon
- D01.1 Carcinoma in situ of rectosigmoid junction
- D01.2 Carcinoma in situ of rectum
- D01.3 Carcinoma in situ of anus and anal canal
- D01.4 Carcinoma in situ of other and unspecified parts of intestine
  - D01.40 Carcinoma in situ of unspecified part of intestine
  - D01.49 Carcinoma in situ of other parts of intestine (*includes parts of stomach*)
- D01.5 Carcinoma in situ of liver, gallbladder and bile ducts
- D01.7 Carcinoma in situ of other specified digestive organs (*includes pancreas*)
- D01.9 Carcinoma in situ of digestive organ, unspecified