**Supplementary material**

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**Supplementary Table 1: HCC-specific causes of death based on SEER cause-specific death classification**

|  |  |  |  |
| --- | --- | --- | --- |
| **Sequence number** | **ICD classification** | **Any cancer** | **Site-specific codes** |
| 00 (If HCC is the only cancer) | ICD-9 | 140-239 | 530-537,556-562, 570-573, 578 |
| ICD-10 | C00-D489 | K20-K31, K51-K57, K70-K76, K92 |
| 01 (If HCC is the first of multiple cancers) | ICD-9 | 199 | 155, 159, 197.7, 211.5, 230.8, 235.2-235.5, 530-537, 556-562, 570-573, 578 |
| ICD-10 | C798, C80, C97, D489 | C22, C26, C787, D015, D134, D371-D379, K20-K31, K51-K57, K70-K76, K92 |

**Abbreviations**: AIDS, acquired immunodeficiency syndrome; HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus; ICD, International Classification of Diseases; SEER, Surveillance, Epidemiology, and End Results

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Supplementary Table 2: Trends in incidence and IBM rates of HCC, transplant rate, rate of excess deaths averted, and HCC-specific mortality rate.** | | | | | |
| **Rates** | **Trend 1** | **Trend 2** | **Trend 3** | **Trend 4** | **Overall trend** |
|  | **APC (95% CI)** | **APC (95% CI)** | **APC (95% CI)** | **APC (95% CI)** | **AAPC (95% CI)** |
| **Incidence rate** |  |  |  |  |  |
| Overall | 5.2 (4.9 to 5.5) | -0.7 (-2.7 to 1.4) |  |  | 4.0 (3.6 to 4.5) |
|  | *1987 - 2011* | *2011 - 2017* |  |  | *1987 - 2017* |
|  |  |  |  |  |  |
| Local stage | 10.2 (9.7 to 10.8) | 5.0 (2.5 to 7.5) | -0.4 (-2.3 to 1.6) |  | 7.1 (6.5 to 7.8) |
|  | *1987 - 2006* | *2006 - 2011* | *2011 - 2017* |  | *1987 - 2017* |
|  |  |  |  |  |  |
| Regional stage | 5.3 (3.7 to 7.0) | 28.6 (11.4 to 48.6) | 5.2 (4.5 to 5.9) | -10.8 (-18.8 to -2.1) | 5.6 (3.8 to 7.5) |
|  | *1987 - 1999* | *1999 - 2002* | *2002 - 2014* | *2014 - 2017* | *1987 - 2017* |
|  |  |  |  |  |  |
| Distant stage | 6.1 (4.6 to 7.7) | -10.6 (-24.3 to 5.7) | 2.4 (1.5 to 3.4) |  | 2.5 (0.7 to 4.3) |
|  | *1987 - 1999* | *1999 - 2002* | *2002 - 2017* |  | *1987 - 2017* |
|  |  |  |  |  |  |
| Unstaged | 0.7 (-0.4 to 1.8) | -12.2 (-20.9 to -2.6) | 1.9 (-0.2 to 4.1) |  | 0.7 (-2.3 to 0.9) |
|  | *1987 - 2002* | *2002 - 2006* | *2006 - 2017* |  | *1987 - 2017* |
| **IBM rate** |  |  |  |  |  |
| Overall | 17.0 (1.7 to 34.6) | 3.2 (3.0 to 3.4) | -7.1 (-12.1 to -1.7) |  | 2.9 (1.7 to 4.2) |
|  | *1991 - 1993* | *1993 - 2014* | *2014 - 2017* |  | *1991 - 2017* |
|  |  |  |  |  |  |
| Local stage | 7.8 (7.2 to 8.5) | 3.9 (2.1 to 5.7) | -2.9 (-5.8 to 0.1) |  | 4.8 (4.0 to 5.5) |
|  | *1991 - 2006* | *2006 - 2012* | *2012 - 2017* |  | *1991 - 2017* |
|  |  |  |  |  |  |
| Regional stage | 4.2 (1.0 to 7.5) | 22.4 (14.0 to 31.4) | 4.7 (3.9 to 5.5) | -9.4 (-18.0 to 0.0) | 5.3 (3.5 to 7.1) |
|  | *1991 - 1999* | *1999 - 2003* | *2003 - 2014* | *2014 - 2017* | *1991 - 2017* |
|  |  |  |  |  |  |
| Distant stage | 10.3 (5.8 to 15.1) | -10.4 (-18.6 to -1.4) | 1.9 (0.9 to 3.0) |  | 2.1 (0.2 to 4.0) |
|  | *1991 - 1998* | *1998 - 2002* | *2002 - 2017* |  | *1991 - 2017* |
|  |  |  |  |  |  |
| Unstaged | -0.5 (-1.7 to 0.8) | -14.9 (-29.2 to 2.2) | 0.9 (-0.9 to 2.8) |  | -1.7 (-3.8 to 0.5) |
|  | *1991 - 2003* | *2003 - 2006* | *2006 - 2017* |  | *1991 - 2017* |
|  |  |  |  |  |  |
| **Counterfactual IBM rate** |  |  |  |  |  |
| Local stage | 7.1 (5.0 to 9.3) | 9.5 (4.9 to 14.3) | 3.5 (1.0 to 6.1) | -3.9 (-8.0 to 0.5) | 5.3 (3.2 to 7.4) |
|  | *1991 - 2001* | *2001 - 2006* | *2006 - 2012* | *2012 - 2017* | *1991 - 2017* |
|  |  |  |  |  |  |
| **Transplant rate** |  |  |  |  |  |
|  | 13.5 (10.1 to 17.0) | 40.9 (13.0 to 75.7) | 4.5 (2.5 to 6.6) | -1.2 (-4.9 to 2.7) | 10.4 (7.6 to 13.3) |
|  | *1987 - 2000* | *2000 - 2003* | *2003 - 2011* | *2011 - 2017* | *1987 - 2017* |
|  |  |  |  |  |  |

**Abbreviations:** AAPC, average annual percent change; APC, annual percent change; CI, confidence intervals; HCC, hepatocellular carcinoma; IBM, incidence-based mortality.

Note: Trends noted in column headers reflect trends between calendar years mentioned below the APCs. For example, Trend 1 for incidence rate of local stage HCC reflects an annual 10.2% increase in incidence rate between 1987 and 2006.

**Supplementary Figure 1: Incidence and IBM rates of HCC according to stage and calendar year of cancer diagnosis.**

**Supplementary Figure 1 legend:** The figure represents the age-standardized (2000 US population) incidence and IBM rates of HCC according to calendar year or diagnosis or death, respectively. Rates are presented in separate panels by stage at cancer diagnosis: Local (panel A), regional (panel B), distant (panel C), and unstaged (panel D). Overall, incidence increased significantly for localized (AAPC, 7.1%), regional (AAPC, 5.6%), and distant stage HCC (AAPC, 2.5%). Within this overall period during which there was an increase on average, there was a sharp increase for regional stage HCC along with a corresponding decline for distant stage HCC between 2000 and 2001 (Figure S1 panels B-C, Table S2). This is likely attributable to changes in cancer staging in 2000, when the presence of multiple satellite tumor nodules in more than one liver lobe or on the parenchymal surface, previously classified as distant stage, was reclassified as regional stage.1 Incidence of unstaged HCCs did not change significantly during 1987-2017. Increasing IBM rates were specifically observed for localized stage (AAPC, 4.8%) and regional stage HCC (AAPC, 5.3%). The rising incidence and IBM rates for regional, distant, and unstaged cancers are similar to each other, demonstrating their high lethality. The IBM rates for localized HCC did not increase as sharply as the incidence rates consistent with better survival outcomes for this stage.

**Abbreviations:** IBM, incidence-based mortality



**References:**

1. Young JL Jr, Roffers SD, Ries LAG, Fritz AG, Hurlbut AA (eds). SEER Summary Staging Manual - 2000: Codes and Coding Instructions, National Cancer Institute, NIH Pub. No. 01-4969, Bethesda, MD, 2001.