**Table S1.** Clinical and demographic characteristics of the study population

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | | Without an SPM [ n (%)]  N=8,3598 | With an SPM [ n (%)]  N=1,3571 |
| Gender | Male | 40,375 (48.3) | 7,190 (53.0) |
|  | Female | 43,223 (51.7) | 6,381 (47.0) |
| Age | <60 | 20,792 (24.9) | 3,291 (24.3) |
|  | 60-70 | 30,873 (36.9) | 5,753 (42.4) |
|  | >70 | 31,933 (38.2) | 4,527 (33.4) |
| Race | Black | 8,613 (10.3) | 1,421 (10.5) |
|  | White | 68,488 (81.9) | 11,158 (82.2) |
|  | Other | 6,497 (7.8) | 992 (7.3) |
| Marital status | Divorced | 10,458 (12.5) | 1,578 (11.6) |
|  | Married | 48,156 (57.6) | 8,537 (62.9) |
|  | Separated | 941 (1.1) | 113 (0.8) |
|  | Single | 10,573 (12.6) | 1,354 (10.0) |
|  | Widowed | 13,470 (16.1) | 1,989 (14.7) |
| Grade | Grade Ⅰ | 11,748 (14.1) | 1,834 (13.5) |
|  | Grade Ⅱ | 31,347 (37.5) | 5,132 (37.8) |
|  | Grade Ⅲ | 35,988 (43.0) | 5,550 (40.9) |
|  | Grade IV | 4,515 (5.4) | 1,055 (7.8) |
| Tumor size(mm) | 0-20 | 18,303 (21.9) | 4,584 (33.8) |
|  | 20-50 | 44,763 (53.5) | 6,619 (48.8) |
|  | 50-100 | 18,525 (22.2) | 2,184 (16.1) |
|  | >100 | 2,007 (2.4) | 184 (1.4) |
| TNM stage | I | 37,905 (45.3) | 7,055 (52.0) |
|  | II | 7,945 (9.5) | 1,163 (8.6) |
|  | III | 19,843 (23.7) | 3,161 (23.3) |
|  | IV | 15,042 (18.0) | 1,617 (11.9) |
|  | Occult/ UNK Stage | 2,863 (3.4) | 575 (4.2) |
| Summary stage | Localized | 33,526 (40.1) | 6,527 (48.1) |
|  | Regional | 32,186 (38.5) | 4,948 (36.5) |
|  | Distant | 17,886 (21.4) | 2,096 (15.4) |
| Surgery history | Yes | 32,049 (38.3) | 3,434 (25.3) |
|  | No | 51,549 (61.7) | 10,137 (74.7) |

Notes: Age: indicates age of diagnosis; Other, American Indian/AK Native, Asian/Pacific Islander; TNM, Tumor-Node-Metastasis, TNM stage was derived AJCC 6th Edition (2004-2015).

**Table S2.** Effects of demographic and clinical factors on the development of SPM

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Variables |  | N (%)  N=97,169 | HR | 95% CI | *P* |
| Gender | Male | 47,565(48.95) | 1.00 |  |  |
|  | Female | 49,604(51.05) | 0.83 | 0.80-0.86 | <0.001\* |
| Age | <60 | 24,083(24.78) | 1.00 |  |  |
|  | 60-70 | 36,626(37.69) | 1.17 | 1.12-1.22 | <0.001\* |
|  | >70 | 36,460(37.52) | 0.96 | 0.91-1.01 | 0.124 |
| Marital status | Divorced | 12,036(12.39) | 1.00 |  |  |
|  | Married | 56,693(58.34) | 1.12 | 1.06-1.18 | <0.001\* |
|  | Separated | 1,054(1.08) | 0.84 | 0.69-1.00 | 0.061 |
|  | Single | 11,927(12.27) | 0.91 | 0.84-0.97 | 0.013\* |
|  | Widowed | 15,459(15.91) | 1.06 | 0.99-1.13 | 0.091 |
| Race | White | 79,646(81.97) | 1.00 |  |  |
|  | Black | 10,034(10.33) | 0.86 | 0.81-0.90 | <0.001\* |
|  | Other | 7,489(7.71) | 0.89 | 0.82-0.96 | <0.001\* |
| Surgery | No | 35,483(36.52) | 1.00 |  |  |
|  | Yes | 61,686(63.48) | 1.55 | 1.47-1.63 | <0.001\* |
| Grade | Grade Ⅰ | 13,582(13.98) | 1.00 |  |  |
|  | Grade Ⅱ | 36,479(37.54) | 1.06 | 1.00-1.11 | 0.052 |
|  | Grade Ⅲ | 41,538(42.75) | 1.08 | 1.01-1.14 | 0.013\* |
|  | Grade IV | 5,570(5.73) | 1.62 | 1.49-1.74 | <0.001\* |
| Summary stage | Localized | 40,053(41.22) | 1.00 |  |  |
|  | Regional | 37,134(38.22) | 0.89 | 0.84-0.94 | <0.001\* |
|  | Distant | 19,982(20.56) | 0.96 | 0.87-1.06 | 0.462 |
| TNM stage | I | 44,960(46.27) | 1.00 |  |  |
|  | II | 23,004(23.67) | 0.90 | 0.83-0.97 | 0.010\* |
|  | III | 16,659(17.14) | 1.11 | 1.04-1.18 | <0.001\* |
|  | IV | 9,108(9.37) | 0.83 | 0.74-0.92 | <0.001\* |
|  | Occult/ UNK Stage | 3,438(3.54) | 1.33 | 1.22-1.45 | <0.001\* |
|  | 20-50 | 51,382(52.88) | 0.63 | 0.60-0.65 | <0.001\* |
|  | 50-100 | 20,709(21.31) | 0.54 | 0.51-0.57 | <0.001\* |
|  | >100 | 2,191(2.25) | 0.42 | 0.36-0.49 | <0.001\* |

Notes: SPM, second primary malignancy CI, confidence interval; Age, age when the patients were diagnosed with lung cancer; Other, American Indian/AK Native, Asian/Pacific Islander; TNM, Tumor-Node-Metastasis, TNM stage was derived AJCC 6th Edition (2004-2015). \* indicate significant (<0.05) *P*-values.

**Table S3.** Effect of demographic and clinical factors on the OS of patients with SPM

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variables | N (%)  (n=13,571) | Median survival time (95% CI) (months) | Univariate analysis | | |  | Multivariate analysis | | |
| HR | 95% CI | *P* |  | HR | 95% CI | *P* |
| Gender |  |  |  |  |  |  |  |  |  |
| Male | 6,381(47.02) | 111.00(108.12-113.88) | 1.00 |  |  |  | 1.00 |  |  |
| Female | 7,190(52.98) | 98.00(95.66-100.34) | 1.16 | 1.12-1.21 | <0.001\* |  | 1.24 | 1.19-1.30 | <0.001\* |
| Age |  |  |  |  |  |  |  |  |  |
| <60 | 3,291(24.25) | 143.00(137.61-148.39) | 1.00 |  |  |  | 1.00 |  |  |
| 60-70 | 5,753(42.39) | 109.00(106.31-111.69) | 1.54 | 1.46-1.63 | <0.001\* |  | 1.58 | 1.50-1.67 | <0.001\* |
| >70 | 4,527(33.36) | 79.00(76.83-81.18) | 2.53 | 2.39-2.67 | <0.001\* |  | 2.52 | 2.38-2.67 | <0.001\* |
| Marital status |  |  |  |  |  |  |  |  |  |
| Divorced | 1,578(11.63) | 100.00(95.51-104.49) | 1.00 |  |  |  | 1.00 |  |  |
| Married | 8,537(62.91) | 111.00(108.57-113.43) | 0.86 | 0.81-0.91 | <0.001\* |  | 0.81 | 0.76-0.86 | <0.001\* |
| Separated | 113(0.83) | 95.00(82.52-107.48) | 1.24 | 1.00-1.54 | 0.054 |  | 1.23 | 0.99-1.53 | 0.066 |
| Single | 1,354(9.98) | 104.00(97.3-110.7) | 0.92 | 0.84-1.00 | 0.046\* |  | 0.96 | 0.88-1.04 | 0.308 |
| Widowed | 1,989(14.66) | 84.00(79.96-88.04) | 1.28 | 1.19-1.38 | <0.001\* |  | 1.04 | 0.96-1.12 | 0.323 |
| Race |  |  |  |  |  |  |  |  |  |
| Black | 1,421(10.47) | 99.00(93.61-104.39) | 1.00 |  |  |  | 1.00 |  |  |
| White | 11,158(82.22) | 104.00(102.02-105.98) | 0.94 | 0.86-1.01 | 0.080 |  | 0.95 | 0.89-1.01 | 0.117 |
| Other | 992(7.31) | 111.00(105.01-116.99) | 0.87 | 0.79-0.97 | 0.004\* |  | 0.86 | 0.78-0.95 | 0.002\* |
| Year of diagnosis |  |  |  |  |  |  |  |  |  |
| 1992-2000 | 6,057(44.63) | 114.00(111.07-116.93) | 1.00 |  |  |  | 1.00 |  |  |
| 2001-2009 | 5,695(41.96) | 100.00(97.72-102.28) | 1.23 | 1.18-1.29 | <0.001\* |  | 1.16 | 1.11-1.21 | <0.001\* |
| 2010-2016 | 1,819(13.4) | 73.00(69.76-76.24) | 2.10 | 1.93-2.28 | <0.001\* |  | 1.73 | 1.59-1.89 | <0.001\* |
| Grade |  |  |  |  |  |  |  |  |  |
| Grade Ⅰ | 1,834(13.51) | 113.00(107.43-118.57) | 1.00 |  |  |  | 1.00 |  |  |
| Grade Ⅱ | 5,132(37.82) | 105.00(102.11-107.9) | 1.11 | 1.04-1.18 | 0.003\* |  | 1.12 | 1.04-1.19 | 0.001\* |
| Grade Ⅲ | 5,550(40.9) | 100.00(97.25-102.75) | 1.17 | 1.10-1.25 | <0.001\* |  | 1.18 | 1.11-1.26 | <0.001\* |
| Grade IV | 1,055(7.77) | 99.00(93.04-104.96) | 1.20 | 1.1-1.31 | <0.001\* |  | 1.16 | 1.06-1.27 | 0.001\* |
| Summary stage |  |  |  |  |  |  |  |  |  |
| Localized | 6,527(48.1) | 110.00(107.29-112.72) | 1.00 |  |  |  | 1.00 |  |  |
| Regional | 4,948(36.46) | 101.00(98.09-103.91) | 1.10 | 1.06-1.15 | <0.001\* |  | 1.08 | 1.03-1.13 | 0.001\* |
| Distant | 2,096(15.44) | 91.00(86.49-95.51) | 1.26 | 1.19-1.33 | <0.001\* |  | 1.13 | 1.07-1.20 | <0.001\* |
| Surgery |  |  |  |  |  |  |  |  |  |
| No | 3,434(25.3) | 73.00(70.44-75.56) | 1.00 |  |  |  | 1.00 |  |  |
| Yes | 10,137(74.7) | 115.00(112.82-117.18) | 0.55 | 0.53-0.58 | <0.001\* |  | 0.59 | 0.56-0.62 | <0.001\* |
| Tumor size(mm) |  |  |  |  |  |  |  |  |  |
| 0-20 | 4,584(33.78) | 106.00(102.76-109.24) | 1.00 |  |  |  | 1.00 |  |  |
| 20-50 | 6,619(48.77) | 103.00(100.48-105.52) | 1.02 | 0.98-1.07 | 0.288 |  | 1.02 | 0.97-1.06 | 0.462 |
| 50-100 | 2,184(16.09) | 102.00(97.82-106.18) | 1.04 | 0.98-1.10 | 0.214 |  | 1.01 | 0.95-1.07 | 0.845 |
| >100 | 184(1.36) | 100.00(79.53-120.47) | 1.08 | 0.91-1.28 | 0.403 |  | 1.07 | 0.90-1.28 | 0.428 |
| TNM stage |  |  |  |  |  |  |  |  |  |
| I | 7,055(51.99) | 107.00(104.44-109.56) | 1.00 |  |  |  | 1.00 |  |  |
| II | 1,163(8.57) | 102.00(96.81-107.19) | 1.02 | 0.95-1.10 | 0.589 |  | 1.01 | 0.94-1.09 | 0.765 |
| III | 3,161(23.29) | 100.00(96.11-103.89) | 1.09 | 1.04-1.14 | 0.001 |  | 1.00 | 0.96-1.06 | 0.872 |
| IV | 1,617(11.92) | 97.00(91.67-102.33) | 1.11 | 1.04-1.18 | 0.001 |  | 1.03 | 0.96-1.09 | 0.450 |
| Occult/ UNK Stage | 575(4.24) | 106.00(99.38-112.62) | 1.03 | 0.94-1.14 | 0.518 |  | 0.94 | 0.85-1.04 | 0.214 |

Notes: OS, overall survival; SPM, second primary malignancy; CI, confidence interval; Age, age when the patients were diagnosed with lung cancer; Other, American Indian/AK Native, Asian/Pacific Islander; TNM, Tumor-Node-Metastasis, TNM stage was derived AJCC 6th Edition (2004-2015). \* indicate significant (<0.05) *P*-values..