

RISK OF RECURRENCE IN CERTAIN EARLIER-STAGE CANCERS:

Non–Small Cell Lung Cancer (NSCLC), Head and Neck Squamous Cell Carcinoma (HNSCC), Melanoma, and Renal Cell Carcinoma (RCC)



As a surgeon, you play a critical role beyond the resection of the primary tumor.¹ The risk of recurrence after resection is a concern, even in earlier-stage cancers.^{2–6} Below is some helpful information to keep in mind as you assess your patients' risk of recurrence in collaboration with your medical oncologist colleagues.^{1,7}



- Recurrence due to metastatic spread is a multistep process that can take months or years before it becomes detectable.²



- Dissemination of cancer cells from primary to distant sites can occur even before diagnosis of the primary tumor.^{2,8}
- The risk of recurrence may vary based on tumor type.^{2,8}



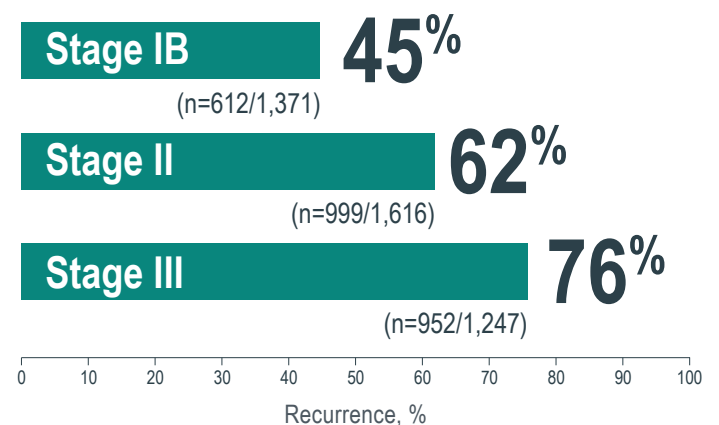
Rate of recurrence or death, after resection, with or without adjuvant chemotherapy, within 5 years by stage of NSCLC.³

Lung Adjuvant Cisplatin Evaluation (LACE): A pooled analysis by the LACE Collaborative Group.³

Study Details: The LACE study was a retrospective, pooled analysis by the LACE Collaborative Group that included 4,584 patients with completely resected NSCLC across 5 randomized trials from 1994 to 2001. Of these patients, 2,281 received adjuvant cisplatin-based chemotherapy. The primary end point was overall survival (OS) and a secondary end point was disease-free survival (DFS). The interactions between patient subgroups or treatment types and chemotherapy effect on OS were analyzed using hazard ratios and log-rank tests stratified by trial.³

Inclusion and Exclusion Criteria: Trials eligible for inclusion were those that randomly assigned more than 300 patients with completely resected NSCLC to receive postoperative cisplatin-based chemotherapy vs no chemotherapy or cisplatin-based chemotherapy plus postoperative radiotherapy (administered sequentially) vs postoperative radiotherapy alone.³

Rate of Recurrence or Death Within 5 Years by Stage³



Additional recurrence data in NSCLC from a separate study are included on the next page.



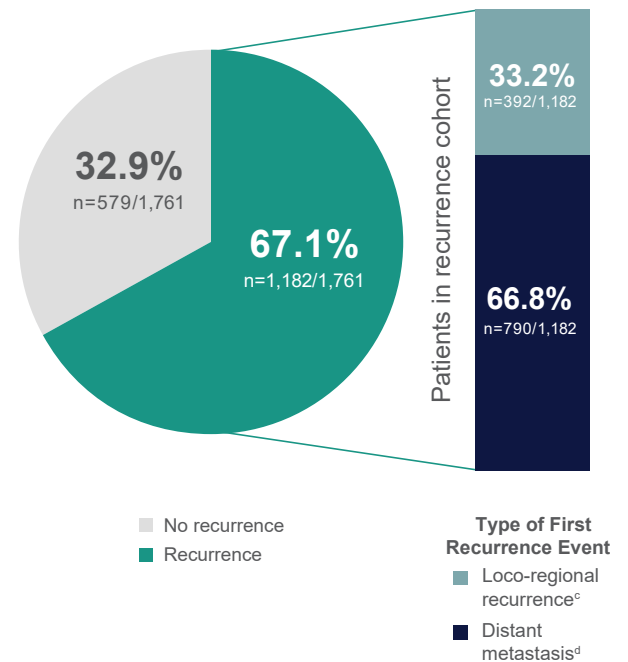
NSCLC after resection: Rate and type of first recurrence.⁹

Data from a retrospective observational study of patients with stage IB (tumor size ≥ 4 cm)–IIIA NSCLC, after resection, with or without adjuvant chemotherapy.^{9,a}

Study Details: Data collected from the SEER-Medicare database for the years 2007–2019 were used to identify patients with newly diagnosed stage IB (tumor size ≥ 4 cm)–IIIA NSCLC (per AJCC 7th edition) who received primary surgery (lobectomy, bilobectomy, or pneumonectomy) within 6 months of initial NSCLC diagnosis, with or without adjuvant chemotherapy, and did not receive neoadjuvant chemotherapy or neoadjuvant/adjuvant radiation therapy. A total of 1,761 patients with earlier-stage NSCLC who received primary surgery met the eligibility criteria and were included in the study, including 1,182 (67.1%) patients identified with disease recurrence anytime during follow-up (median follow-up time from initial surgery to death: 55.0 months).⁹

Limitations: The SEER-Medicare database only includes Medicare patients aged ≥ 65 ; therefore, the results from this study may not reflect outcomes among a younger patient population with NSCLC. Patients who did not receive treatment in the event of recurrence or did not have codes associated with metastasis in their claims were also missed. The data used in this study were obtained from 2007 to 2019, which was before the approval of any targeted or immunotherapies for NSCLC in the United States. Coding inaccuracies may have led to misclassification bias and misidentification of patients with NSCLC recurrence. Some clinical information, such as complete resection status, is not available in the data. Therefore, a 90-day treatment-free interval was used to indicate the end of primary treatment and served as a proxy for the disease-free state.⁹

Rate and Type of Recurrence After Resection^{9,b}

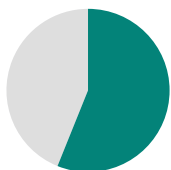


Recurrence rate in patients with locoregionally advanced head and neck squamous cell carcinoma (LA HNSCC) from a retrospective observational study.⁵

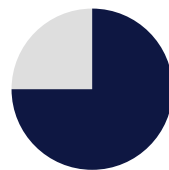
Data from the SEER-Medicare database

Study Details: A retrospective, observational study to assess real-world clinical outcomes for patients with primary LA HNSCC. The study utilized the SEER-Medicare database to identify patients with newly diagnosed primary LA HNSCC of the oropharynx, larynx, hypopharynx, or oral cavity (between 2007 and 2019).^e Additional eligibility criteria included age ≥ 66 years at diagnosis, and primary treatment for LA HNSCC within 4 months after initial diagnosis. Of the 2,180 patients included in the analysis, 626 patients (28.7%) received primary surgery and were included in the resected cohort (median follow-up: 20.8 months), while 1,554 patients (71.3%) formed the unresected cohort (median follow-up: 22.6 months).⁵

Resected cohort (n=626)



56.1%
5-year cumulative incidence rate of recurrence⁵



75%
of the recurrences experienced by patients in the resected cohort occurred within the first year following primary treatment initiation.⁵

56.3% of patients in the resected cohort received radiation therapy (RT), or RT with systemic therapy post-surgery and 26.8% of patients underwent primary surgery alone.⁵

Limitations: The findings may have limited generalizability due to the exclusive inclusion of Medicare beneficiaries aged 66 years or older. HNSCC recurrence was identified using an algorithm that relied on various procedure codes, diagnosis codes, drug codes, and clinical opinions; therefore, coding inaccuracies may lead to misclassification bias and the misidentification of patients with HNSCC recurrence. Additionally, some important prognostic factors, including HPV status, ECOG performance status, alcohol use, and smoking history, were not available in the data. The results may be confounded by these variables.⁵

AJCC = American Joint Committee on Cancer; ECOG = Eastern Cooperative Oncology Group; HPV = human papillomavirus; NSCLC = non-small cell lung cancer; SEER = Surveillance, Epidemiology, and End Results.

^aPer AJCC 7th edition. ^bOutcome of primary surgery (complete vs partial resection) is not available in the data. ^cLoco-regional recurrence was defined as a new diagnosis of loco-regional disease, and/or additional surgery, curative radiation therapy, and chemoradiation following a 90-day treatment-free interval after the initial surgery. ^dDistant metastasis was defined as a diagnosis of metastatic disease, and/or additional palliative radiation therapy, and systemic therapy for advanced NSCLC following a 90-day treatment-free interval after the initial surgery. ^ePrimary LA HNSCC at initial diagnosis was defined as: 1) Oropharynx (diagnosed 2007–2017), larynx, hypopharynx, and oral cavity cancer at TNM stages of T1N1M0, T2N1M0, any T with N2/N3 and M0, and T3/T4 with any N and M0 at diagnosis; 2) Oropharynx cancer (diagnosed 2018–2019) with SEER stages III–IV and M0 at diagnosis. Staging was determined by AJCC 6th/7th/8th editions.⁵





The risk of recurrence after complete resection in stage IIB and IIC melanoma: A retrospective analysis.⁴

Study Design for Real-World Retrospective Chart Review: This study was a retrospective chart review of real-world data from 567 adult patients who were followed for a median of 38.8 months after complete resection of stage IIB or IIC cutaneous melanoma between 2008 and 2017. Patients in this study had at least 2 visits after diagnosis recorded within the US Oncology Network, a community-based network of over 480 cancer centers in 25 states. Eighty (14.1%) patients in the study received adjuvant treatment for stage IIB or IIC melanoma; of those who received adjuvant treatment, 77 (96.3%) received IFN-alpha. Recurrence in this study was defined as physician-documented recurrence or progression.⁴

37%

(n=140/375)

RECURRENCE RATE
in patients with completely resected
Stage IIB melanoma

43%

(n=83/192)

RECURRENCE RATE
in patients with completely resected
Stage IIC melanoma



50%

(n=70/140)

of those patients with completely resected **stage IIB melanoma** whose disease recurred after resection experienced **distant metastasis as their first recurrence.**



58%

(n=48/83)

of those patients with completely resected **stage IIC melanoma** whose disease recurred after resection experienced **distant metastasis as their first recurrence.**

The risk of recurrence after complete resection in stage III melanoma: A retrospective analysis.^{10,11}

Study Design for Multicountry Retrospective Chart Review: This study was a retrospective chart review of 251 adult patients who had undergone complete resection from 2011–2016 for stage III cutaneous melanoma followed by a minimum of 2 years of watch-and-wait. Patients included in this study were from North America, South America, and Europe.¹⁰

44%

(n=40/91)

RECURRENCE RATE
in patients with completely resected
Stage IIIA melanoma¹¹

44.5%

(n=49/110)

RECURRENCE RATE
in patients with completely resected
Stage IIIB melanoma¹¹

74%

(n=37/50)

RECURRENCE RATE
in patients with completely resected
Stage IIIC melanoma¹¹



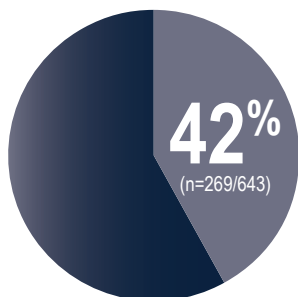
53%

(n=125/251)

Of those patients with completely resected **stage IIIA, IIIB, or IIIC melanoma** whose disease recurred after resection experienced **unresectable or distant metastatic disease as their first recurrence.**^{10,11}



For certain patients with renal cell carcinoma (RCC) after nephrectomy, an observational analysis of 643 patients using SEER-MEDICARE DATA from 2007 to 2016 revealed⁶:

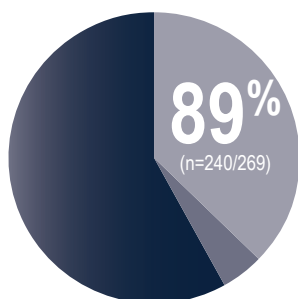


of certain patients with RCC post nephrectomy EXPERIENCED RECURRENCE⁶

ANALYSIS POPULATION^{6,12}

- T2, Grade 4, N0, M0
- T3, N0, M0
- T4, N0, M0
- T any stage, N+, M0
- Median follow-up duration of analysis was 23 months.
- 95% of patients analyzed had T3 tumors.

Of those patients who experienced recurrence,



HAD METASTATIC DISEASE⁶

ANALYSIS LIMITATIONS⁶

- Recurrence was inferred from the database codes rather than directly determined based on clinical data.
- The analyzed SEER-Medicare data represent patients ≥65 years. Hence, the results from this analysis may not reflect outcomes among the younger patient population.
- Impacts of recurrence may be confounded by unmeasured characteristics. Caution must be used when considering causal inference from this analysis.

In an analysis of the same SEER-Medicare data from 2007 to 2016 for a subset of patients with RCC post nephrectomy, all patients with T3N0 tumors were at risk of recurrence⁶

5-Year Post Nephrectomy Recurrence Rates^{6,12}

45%
of T3N0 patients in this observational analysis

EXPERIENCED RECURRENCE

37% T3 Grades 1–2
(N=297)

50% T3 Grade 3
(N=250)

72% T3 Grade 4
(N=64)

Note: Patients were followed from the date of initial nephrectomy until the earliest of recurrence or censoring at 1) death, 2) end of Medicare Part A, B, or D eligibility, and 3) end of data availability on December 31, 2016.¹²

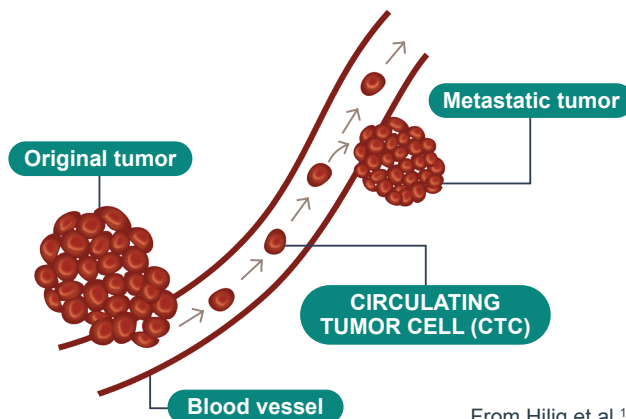
ANALYSIS POPULATION⁶

- T2, Grade 4, N0, M0
- T3, any grade, N0, M0

Analysis limitations (above) continued to apply throughout the analysis.

Micrometastases May Contribute to Metastatic Recurrence

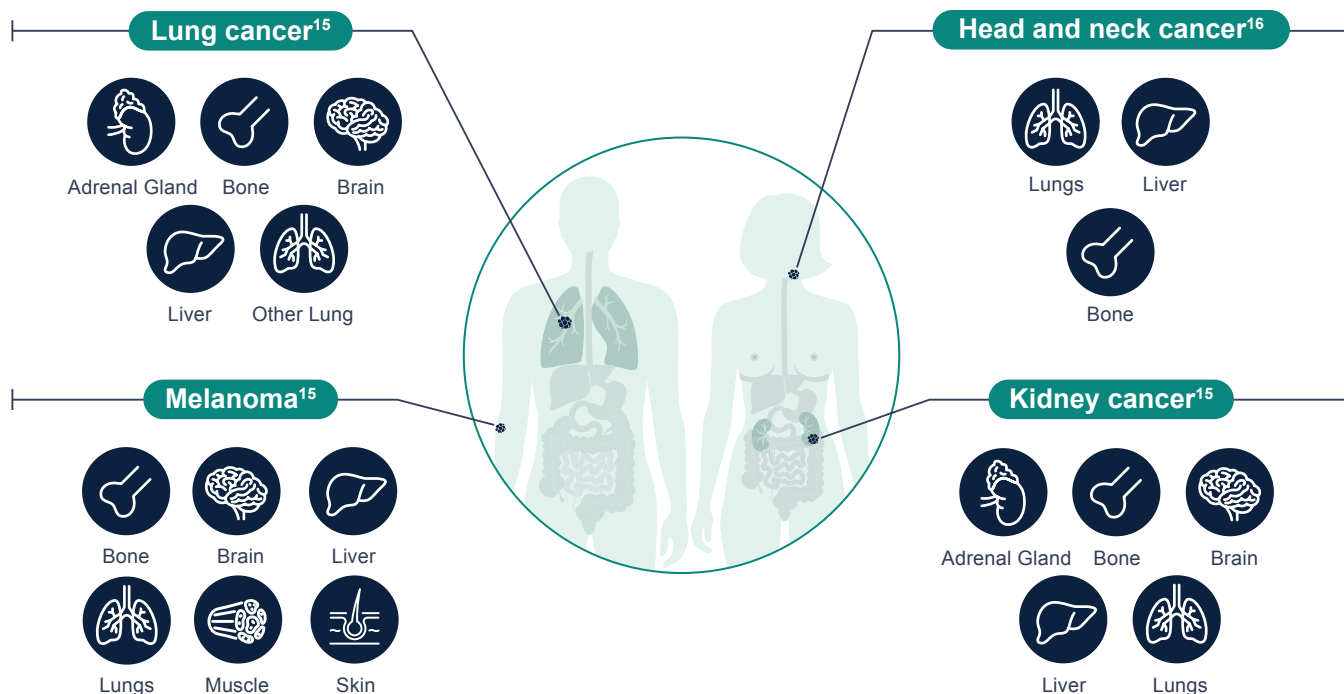
Micrometastases are small numbers of cancer cells that spread from the primary tumor to distant sites in the body. They may be undetectable on a screening or diagnostic test.¹⁴



From Hilig et al.¹⁴

Main Sites of Metastasis for Certain Tumor Types^a

Cancer can spread to almost any part of the body, although different types of cancer are more likely to spread to certain organs than others.¹⁵



Collaborate with your multidisciplinary treatment team, including medical oncologist colleagues, to assess your patients' risk of recurrence.^{1,7}

^aNot including the lymph nodes.¹⁵

References

1. Berardi R et al. *Cancer Manag Res*. 2020;12:9363–9374.
2. Sauer S et al. *Front Oncol*. 2021;11:659963.
3. Pignon JP et al. *J Clin Oncol*. 2008;26(21):3552–3559.
4. Samlowski W et al. *Future Oncol*. 2022;18(33):3755–3767.
5. Zheng D et al. *Front Oncol*. 2025;15:1606990.
6. Sundaram M et al. *J Manag Care Spec Pharm*. 2022;28(10):1149–1160.
7. Selby P et al. *Am Soc Clin Oncol Educ Book*. 2019;39:332–340.
8. Klein CA. *Nat Rev Cancer*. 2020;20(11):681–694.
9. West H et al. *Clin Lung Cancer*. 2023;24(3):260–268.
10. Mohr P et al. *Melanoma Manag*. 2019;6(4):MMT33.
11. Mohr P et al. *Melanoma Manag*. [supplemental material]. 2019. doi:10.2217/mmt-2019-0015
12. Sundaram M et al. *J Manag Care Spec Pharm*. [supplementary materials]. 2022. doi:10.18553/jmcp.2022.22133
13. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Kidney Cancer V1.2026. National Comprehensive Cancer Network. Accessed July 28, 2025. www.nccn.org
14. Hillig T et al. *APMIS*. 2014;122(6):545–551.
15. Metastatic cancer: when cancer spreads. National Cancer Institute. Updated January 17, 2025. Accessed October 9, 2025. <https://www.cancer.gov/types/metastatic-cancer>
16. Metastatic squamous neck cancer with occult primary treatment (PDQ®)-health professional version. National Cancer Institute. Updated May 14, 2025. Accessed December 9, 2025. <https://www.cancer.gov/types/head-and-neck/hp/adult/metastatic-squamous-neck-treatment-pdq>