



# Transatlantic differences in Survival for Lip Cancer: Europe vs. United States

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## Abstract

### Educational Objective:

To compare relative survival for lip cancer between Europe and the United States, as well as regions within Europe.

**Objectives:** To determine the relative survival (RS) rates for lip cancer across geographic regions of Europe, and to compare those with rates for the United States (U.S.).

**Study Design:** Retrospective database analysis.

**Methods:** The EUROcare and the Surveillance, Epidemiology, and End Results (SEER) databases were queried for cases of lip cancer (excluding skin of the lip) reported between 2000 and 2007. Frequency and RS rates were obtained. Subgroup analysis was performed by age group and gender. For Europe, subgroup analysis was also performed by country and by geographic region.

**Results:** A total of 23,747 cases of lip cancer were identified, 18,676 in Europe and 5,071 in the U.S. There were no differences in RS between the U.S. (1-year: 98.3%, 5-year: 90.6%) and Europe overall (1-year: 97.1%, 5-year: 87.5%). When comparing regions, RS for Eastern Europe (1-year: 94.9%, 5-year: 84.4%) was lower than the US and all other European regions except for Central Europe ( $p < 0.05$ ). There were no differences in survival between the remaining geographic regions, and between European regions and the U.S. RS for the U.S. (1&5-year) did not vary between age groups. In Europe, the  $\geq 75$  years old group (84.2%) had lower 5-year RS than both the 15-44 (94.7%) and 45-54 year old (92.5%) age groups ( $p < 0.05$ ). Survival did not vary across genders.

### Conclusions:

There are no differences in survival for lip cancer between the U.S. and Europe overall. However, survival in Eastern Europe is worse than in the U.S. and other parts of Europe. Further investigation is necessary to explain these differences.

- In total, 23,747 cases of LC diagnosed between 2000 and 2007 were identified. There were 18,676 cases identified in Europe, and 5,071 in the U.S. **Table 1** lists the demographic distributions of LC in Europe and the United States.
- One through five year RS for the U.S. and Europe is illustrated in **Figure 1**.
- One and five year RS by geographic region is illustrated in **Figure 2**.

**Table 1: Percentage of the population covered for each European region**

Region	Percentage
Europe Overall	50%
Eastern Europe (Bulgaria, Czech Republic, Estonia, Latvia, Lithuania, Poland, Slovakia)	50%
Central Europe (Austria, Belgium, France, Germany, Switzerland, The Netherlands)	35%
Northern Europe (Denmark, Finland, Iceland, Norway, Sweden)	100%
Southern Europe (Croatia, Italy, Malta, Portugal, Slovenia, Spain)	36%
United Kingdom & Ireland (England, Wales, Scotland, Northern Ireland, Republic of Ireland)	100%

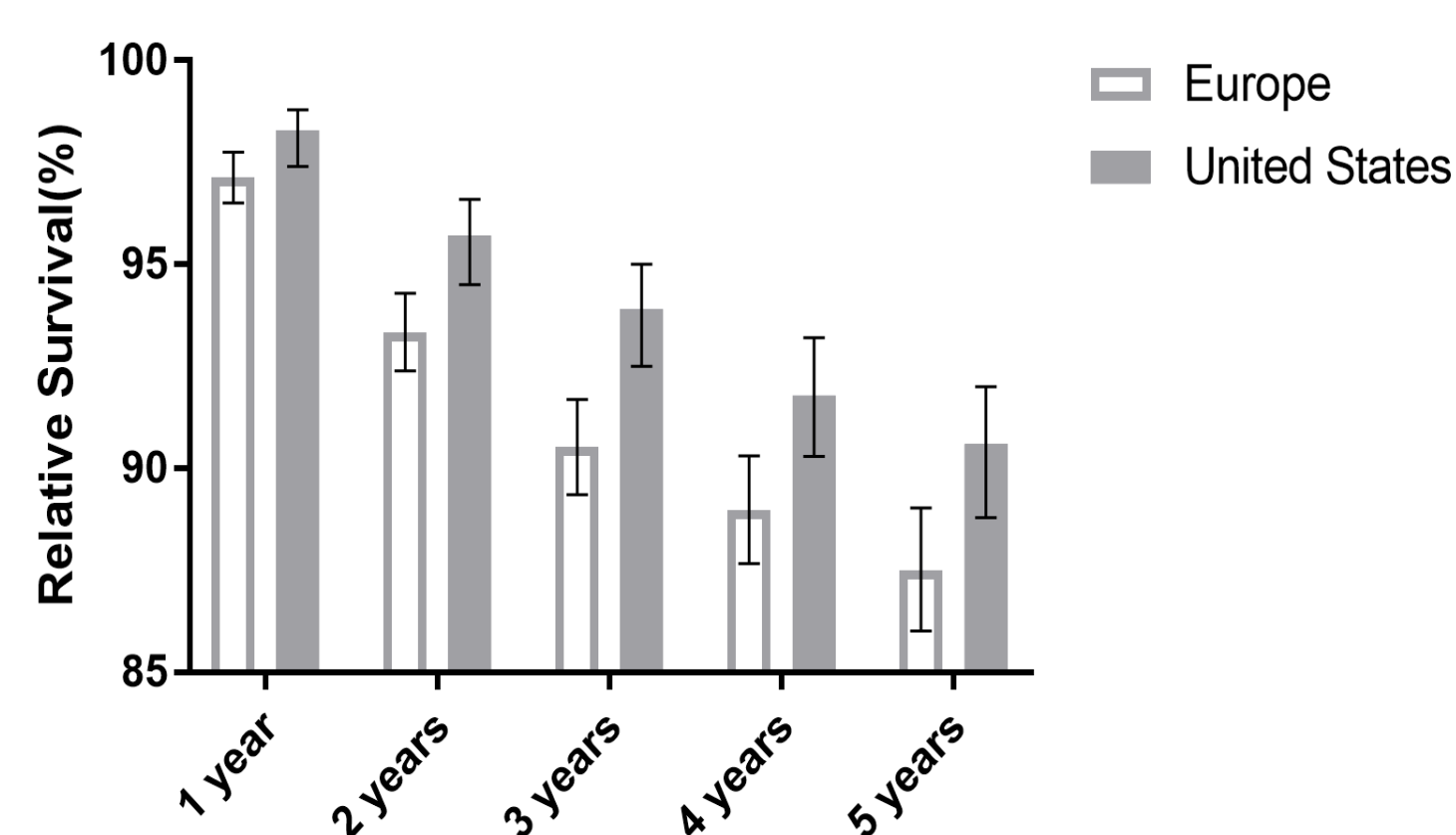
## Results

**Table 2. Demographics of Lip Cancer**

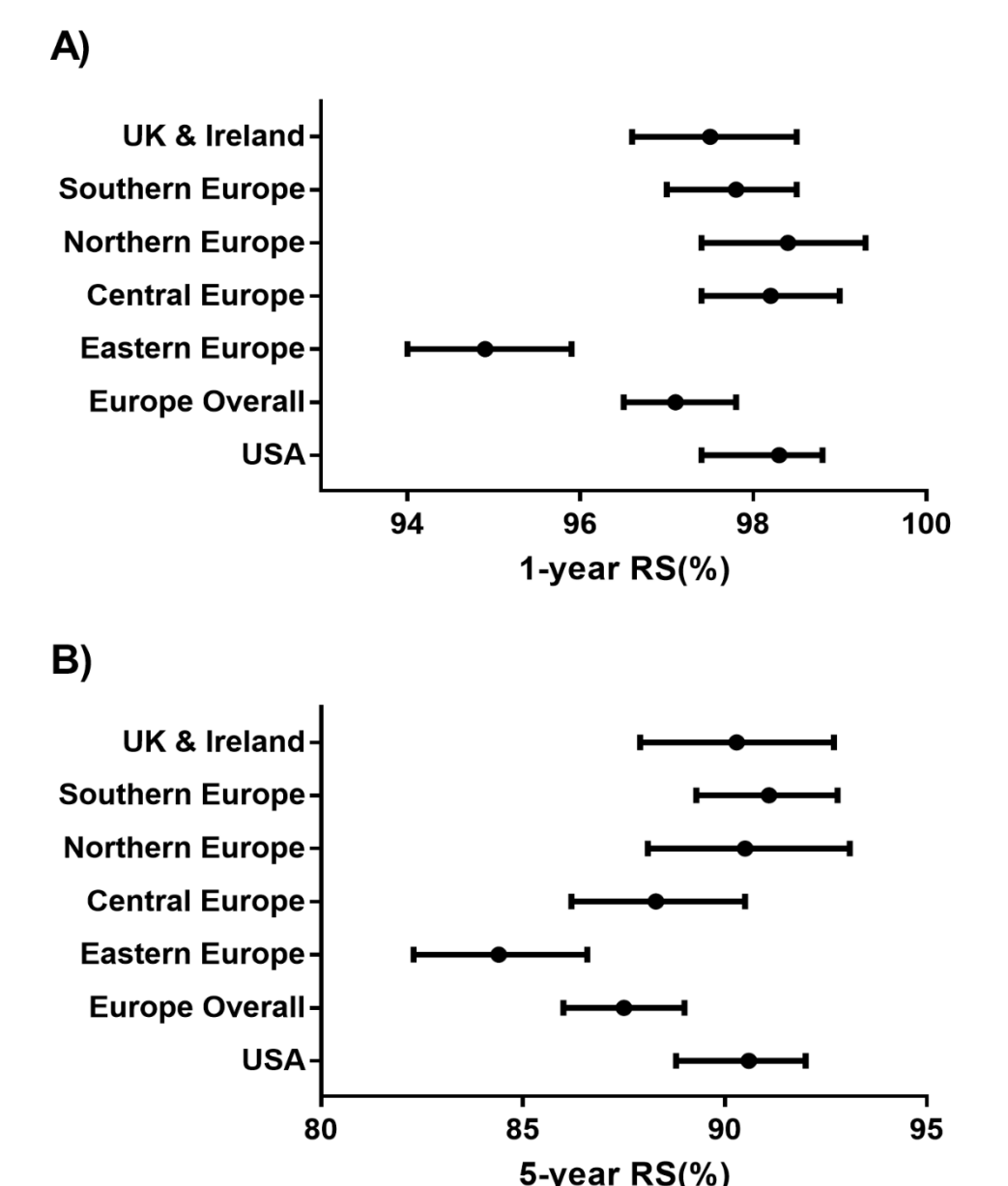
	Europe Overall		C. Europe		U.K. & Ireland		S. Europe		E. Europe		N. Europe		United States	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Total	18,676		3,462		2,875		4,805		4,395		3,139		5,071	
Age groups														
15-44 years	609	3.3%	121	3.5%	162	5.6%	168	3.5%	88	2.0%	70	2.2%	454	9.0%
45-54 years	1,451	7.8%	279	8.1%	243	8.5%	383	8.0%	358	8.1%	188	6.0%	659	13.0%
55-64 years	3,282	17.6%	621	17.9%	513	17.8%	825	17.2%	835	19.0%	488	15.5%	939	18.5%
65-74 years	5,956	31.9%	1,142	33.0%	753	26.2%	1,614	33.6%	1,579	35.9%	868	27.7%	1,177	23.2%
75+ years	7,378	39.5%	1,299	37.5%	1,204	41.9%	1,815	37.8%	1,535	34.9%	1,525	48.6%	1,842	36.3%
Gender														
Male	13,437	71.9%	2,447	70.7%	1,980	68.9%	3,710	77.2%	3,246	73.9%	2,054	65.4%	3,790	74.7%
Female	5,239	28.1%	1,015	29.3%	895	31.1%	1,095	22.8%	1,149	26.1%	1,085	34.6%	1,281	25.3%

## Introduction

- The lips are a unique anatomical site affected by a large spectrum of pathologies. They are composed of a variety of tissue types, including skin and mucosa, which are commonly involved in systemic disease. Near-constant exposure to numerous irritants, including microtrauma and environmental exposures, make them particularly susceptible to disease. They are the most common site of oral cavity malignancy, comprising 25-30% of cases.<sup>1,2</sup> The overwhelming majority of malignancies in the lip are carcinomas<sup>3</sup>, and squamous cell carcinoma (SCC) of the mucosa is the most common lip cancer (LC) histology.<sup>4</sup>
- Compared to other head and neck malignancies, LC has a more favorable prognosis; 5-year survival rates between 80% and 95% have been reported.<sup>1-3</sup> With these variations of incidence and risk factors, differences in LC between geographic regions warrant further study.



**Figure 1.** 1 through 5 year relative survival (RS) for the U.S. and Europe



**Figure 2.** relative survival (RS) by region A) 1-year B) 5-year

## Methods and Materials

- The EUROpean Cancer REgistry (EUROcare) and the Surveillance, Epidemiology, and End Results (SEER) databases were queried for cases of HNC reported between 2000 and 2007.
- SEER covers approximately 28% of the U.S. population, and EUROcare covers approximately 50%. **Table 1** outlines the percent coverage for each region in EUROcare.
- International Classification of Disease for Oncology 3 (ICD-O-3) topographical codes C00.0-C00.9 (External upper lip; External lower lip; External lip, NOS; Mucosa of upper lip; Mucosa of lower lip; Mucosa of lip, NOS; Commissure of lip; Overlapping lesion of lip; Lip, NOS) were used to select lip cancers. Notably, "skin of lip" was not one of the ICD-O-3 codes selected.
- Patients with hematologic malignancies were excluded using ICD-O-3 morphologic codes 9590-9989.
- Patients <15 years of age were excluded. All Death Certificate Only (DCO) cases were also excluded.
- Cases were stratified by age, gender, anatomic site, and extent of disease. The EUROcare results were further stratified by country and geographic region.
- RS was calculated by dividing overall survival (actuarial method) by expected cumulative survival. Expected cumulative survival was calculated using the Ederer II method. All survival analyses were performed using SEER\*Stat.

## Discussion

- LC survival is similarly excellent in the US and most European countries and regions. This is consistent with numerous other studies finding excellent LC survival rates in European and US populations, ranging from 80 to 97% at five years.
- The few countries with significantly poorer survival were Eastern European. Poorer survival in Eastern Europe compared to the US and other European regions has been observed for other head and neck cancers<sup>5</sup> as well as other neoplasms.<sup>6</sup> This has been attributed to factors such as lower GDP in Eastern Europe<sup>6</sup>, poorer quality of healthcare<sup>7</sup>, and differences in lifestyle<sup>8</sup>. Eastern European populations are ethnically distinct from the populations of other European regions, suggesting that genetics may contribute to the survival disparity as well. More research is needed to determine what environmental factors are responsible for this disparity, and whether genetic factors are involved.

## Conclusions

- There are no differences in survival for lip cancer between the U.S. and Europe overall. However, survival in Eastern Europe is worse than in the U.S. and other parts of Europe. Further investigation is necessary to explain these differences.

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