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# An Analysis of Conditional Survival Rates for Ewing Sarcoma Patients

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## Abstract

Using data from the Surveillance, Epidemiology, and End Results (SEER) Program based at the National Cancer Institute in the US, conditional survival rates are reported for 1,988 Ewing Sarcoma patients diagnosed during the period 2000-2015. These patients represent the experience of 26.5% of the US population. Specifically, 5-year conditional relative survival rates are calculated for these patients for the first eight years subsequent to diagnosis of their cancer by Extent of Disease (EOD) (Localized, Regional, and Distant as coded by the SEER Program), gender, and age (<18, 18 - 34, and 35+). Findings include showing how the conditional survival rate patterns improve over time and that there are differences by gender, age, and EOD.

## Keywords

Ewing Sarcoma, Conditional Survival

## 1. Introduction

Ewing Sarcoma is a cancer primarily of children and young adults and occurs in bone and/or soft tissue. It occurs disproportionately in males (59%) versus females (41%). It occurs nine times as frequently in whites compared to blacks with Asians at an intermediate rate between the two. The incidence has been steady over the last 30 years at about 1 case per million population. The median age is 15 and more than half of the patients diagnosed are adolescents (ages 13 - 17) [1].

The purpose of this study is to examine 5-year conditional survival rate patterns for patients diagnosed during the period 2000-2015. This type of analysis provides for assessing how survival improves for eight patient cohorts defined as those identified at the beginning of the first-year post diagnosis, those alive at the beginning of the second year post diagnosis, etc., up to those alive at the be-

ginning of the eighth year post diagnosis. Analyses are provided for ages <18, 18 - 34, and 35+ with a focus on the two younger age groups.

The statistic used here is the relative survival rate. The relative survival rate assesses the excess risk of dying from cancer for a cancer patient cohort and is defined as the ratio of observed to expected survival. For younger patients, the relative survival rate is very close to the observed survival rate because expected survival will be close to 100%. Relative survival rates can be compared across age groups.

Relative survival rates are presented by categories of Extent of Disease (EOD), a variable developed and routinely coded for selected cancers by the Surveillance, Epidemiology, and End Results (SEER) Program based at the National Cancer Institute. This variable can be used to examine data for longer time periods than stage of disease which continues to evolve and as a result there is limited ability to examine trends in survival by stage over time.

The EOD as coded by SEER generally has limited value clinically as treatment for most cancers is tied to stage of disease as provided by the American Joint Committee on Cancer Staging [2]. However, for Ewing Sarcoma patients are grouped into three categories for purposes of treatment; those with localized disease with possible extension into regional tissue, those with distant metastasis, and those with recurrent disease [1]. Only the first two categories are relevant here.

Based on how Ewing Sarcoma patients are grouped for treatment purposes, EOD as routinely coded by SEER provides patient groupings that appear to be relevant to the groupings used for the treatment of Ewing Sarcoma. The EOD categories are defined as Localized: confined to the site of origin regardless of size; Regional: cancer which has passed the bounds of the site of origin but whose furthest spread was thought to be limited to neighboring organs or tissues, or to regional lymph nodes; and Distant or Remote Spread: cancer involving organs or tissues beyond those immediately draining or neighboring the site of origin [3]. The categories Localized and Regional are separated in the analysis presented here but would be treated similarly based on the classification used for treating Ewing Sarcoma.

In addition to EOD, the analysis presented uses the following age groupings (<18, 18 - 34, 35+). Choice of the age groups was based on trying to make the analysis presented as relevant as possible and also have sufficient numbers of patients to provide reasonably reliable results.

## 2. Data

The data used in this study come from the SEER Program which collects population-based data on all cancer patients diagnosed and treated in defined geographic areas of the United States. The data collected include demographics, cancer type, histology, stage, treatment, and patient follow-up including cause of death. The SEER Program is a primary source of information on cancer incidence, patient survival, and cancer mortality and currently covers roughly 48%

of the total US population, but coverage has changed over the years as geographic areas have been added and in some cases removed as the program has evolved.

Patient follow-up performed by the SEER program involves both active and passive procedures. Active procedures include examination of patient records by central registry staff for purposes of data collection and establishing a date last known alive for alive patients, and passive procedures which include mortality files being linked to a registry's database to identify patients who have died along with their cause of death. These procedures provide for high quality follow-up data and survival statistics.

The data used in this analysis come from 17 registries (geographic areas) and include 26.5% of the US population [4]. There were 1,988 patients with Ewing Sarcoma identified by the ICD-O-3 histology/behavior codes 9260/3 (a 3 indicates a malignant tumor) who were diagnosed during the time period 2000-2015 and whose data were available for analysis with EOD known for 1836. Other selection criteria included patients with known age. Exclusions included Death Certificate Only diagnoses and alive patients with zero survival time. Patients were followed through December of 2019. A limitation of SEER data is that any data analysis is confined to data included in the SEER database unless the study includes funds for a review of hospital records or obtaining patient data from some other linked source. The SEER*Stat software developed by the SEER Program was used to analyze the data [5].

Table 1 provides the distribution of patients by age and EOD. The focus of this study is on patients <35 years old, however, survival for older patients is provided for completeness. The number of patients decreases dramatically over age, however, there were nine patients diagnosed over age 80.

**Table 1.** Number of Ewing Sarcoma patients available for analysis by gender, age and Extent of Disease (EOD). The total number of patients is 1,988.

| | Males | | | |
|---|---|---|---|---|
| EOD/Age | <18 yrs (%) | 18 - 34 yrs (%) | 35+ yrs (%) | Total (%) |
| Localized | 172 (28.7) | 109 (26.1) | 51 (28.3) | 332 (27.7) |
| Regional | 219 (36.5) | 124 (29.7) | 41 (22.8) | 384 (32.1) |
| Distant | 166 (27.7) | 151 (36.1) | 71 (39.4) | 388 (32.4) |
| Unknown | 43 (7.2) | 34 (8.1) | 17 (9.4) | 94 (7.8) |
| Total | 600 (100.0) | 418 (100.0) | 180 (100.0) | 1,198 (100.0) |
| | Females | | | |
| Localized | 129 (29.8) | 62 (27.7) | 31 (23.3) | 222 (28.1) |
| Regional | 152 (35.1) | 76 (33.9) | 40 (30.1) | 268 (33.9) |
| Distant | 127 (29.3) | 70 (31.3) | 45 (33.8) | 242 (30.6) |
| Unknown | 25 (5.8) | 16 (7.1) | 17 (12.8) | 58 (7.4) |
| Total | 433 (100.0) | 224 (100.0) | 133 (100.0) | 790 (100.0) |

## 3. Results

The survival experience for patients under age 18 and ages 18 - 34 is given in Figure 1 where the conditional 5-year relative survival rates for each of eight patient cohorts are provided by post diagnosis survival time and stratified by gender, age, and EOD. For patients under 18 years old at diagnosis, there is little difference by gender in the conditional rate patterns except that females with Distant disease appear to reach a 5-year survival rate consistent with the best survival for less advanced EOD in five years. For 18 - 34-year-old Localized and Regional patients, the female rate pattern appears to be more favorable than that for males. For 18 - 34-year-old males, the conditional distant disease rates for both sexes behave in a similar fashion reaching a maximum in five to six years.

Figure 2 presents the 5-year conditional survival rates for patients 35+ years old. The pattern of the rates for this age group appear similar to that for the younger ages, however, the rates for this group have more variability than those for younger ages based on the numbers of cases (Table 1).

Table 2 provides the number of patients at risk of dying at the time of their diagnosis and for each subsequent year used to calculate conditional survival rates. Standard errors of the rates were obtained and were found to be as low as 2% but could be quite large when the number of patients was small. However, the emphasis here is on the pattern of the rates.

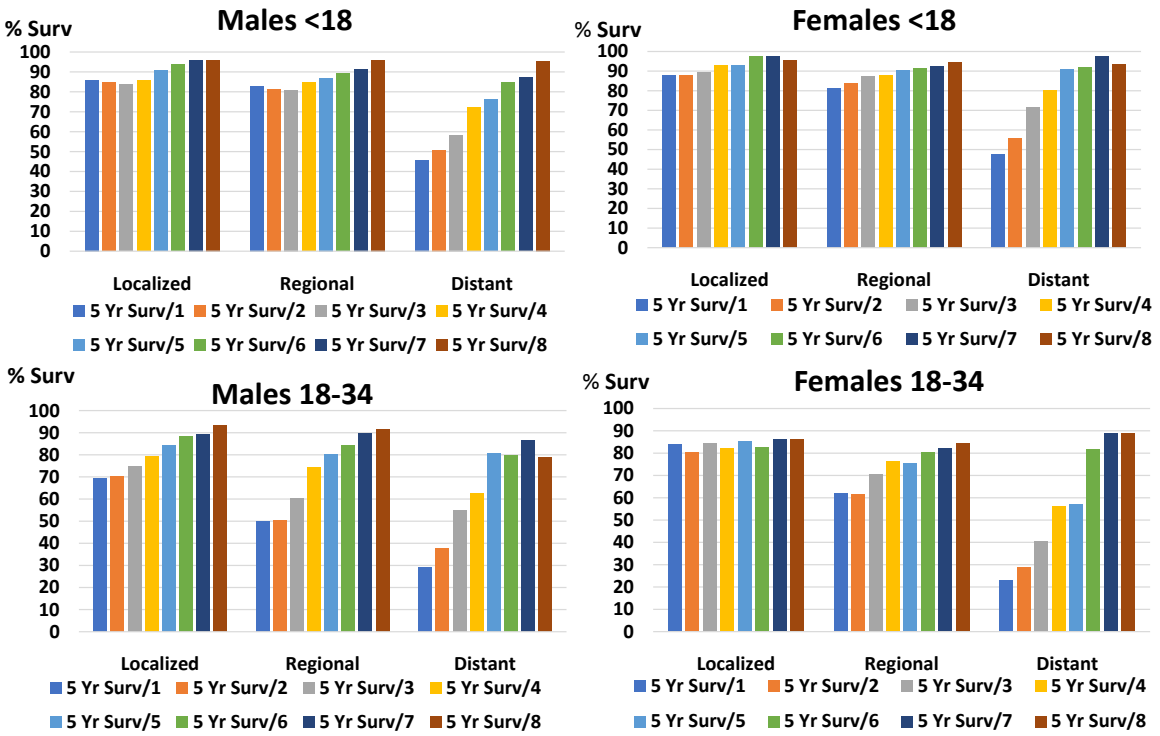



Figure 1. Five-year conditional relative survival rates for eight post diagnosis cohorts by EOD, gender, and age are given for Ewing Sarcoma patients < 35 years old.

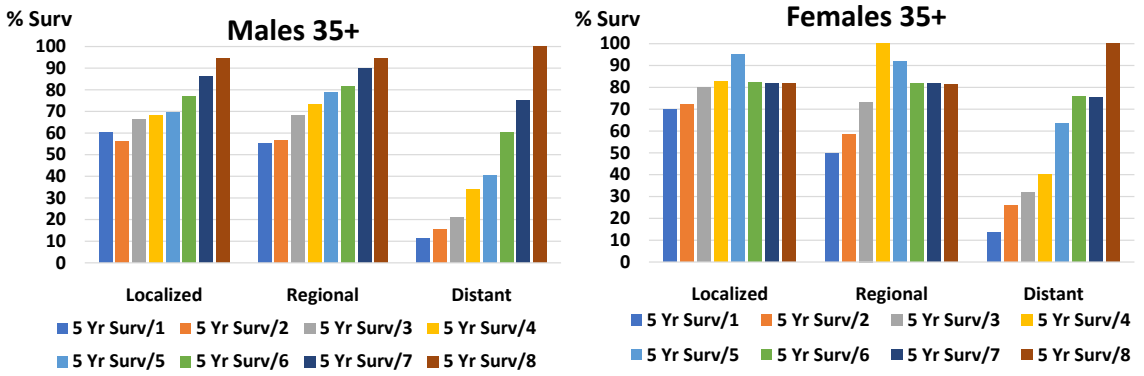



**Figure 2.** Five-year conditional relative survival rates for eight post diagnosis cohorts by extent of disease, gender, and age are given for Ewing Sarcoma patients 35+ years old.

**Table 2.** Number of Ewing Sarcoma patients at risk of dying at the beginning of each follow up year by sex, EOD, and age.

| Year/Age | Localized | | | Regional | | | Distant | | |
|---|---|---|---|---|---|---|---|---|---|
| | <18 | 18 - 34 | 35+ | <18 | 18 - 34 | 35+ | <18 | 18 - 34 | 35+ |
| **Males** | | | | | | | | | |
| 1 | 172 | 109 | 51 | 219 | 124 | 41 | 166 | 151 | 71 |
| 2 | 170 | 100 | 48 | 217 | 115 | 36 | 144 | 107 | 38 |
| 3 | 166 | 87 | 36 | 206 | 92 | 28 | 113 | 73 | 21 |
| 4 | 161 | 80 | 33 | 192 | 69 | 25 | 89 | 59 | 12 |
| 5 | 151 | 73 | 32 | 185 | 62 | 23 | 82 | 44 | 10 |
| 6 | 135 | 61 | 26 | 164 | 51 | 20 | 69 | 39 | 6 |
| 7 | 128 | 48 | 22 | 145 | 45 | 18 | 61 | 33 | 4 |
| 8 | 109 | 41 | 17 | 131 | 40 | 16 | 51 | 25 | 3 |
| **Females** | | | | | | | | | |
| 1 | 129 | 62 | 31 | 152 | 76 | 40 | 127 | 70 | 45 |
| 2 | 127 | 62 | 28 | 145 | 74 | 34 | 103 | 51 | 23 |
| 3 | 124 | 59 | 25 | 135 | 62 | 26 | 79 | 36 | 14 |
| 4 | 117 | 57 | 23 | 125 | 52 | 19 | 69 | 25 | 11 |
| 5 | 112 | 52 | 20 | 120 | 48 | 19 | 61 | 21 | 7 |
| 6 | 102 | 48 | 19 | 110 | 44 | 18 | 54 | 13 | 5 |
| 7 | 92 | 41 | 17 | 100 | 38 | 14 | 48 | 11 | 4 |
| 8 | 86 | 37 | 16 | 93 | 34 | 12 | 44 | 9 | 3 |

It was of interest to make some determination of the extent to which survival may have improved during the 19-year period of the study due to improvements in treatment. **Figure 3** presents 5-year relative survival rates for three calendar year cohorts by gender, age, and EOD. There does not appear to be an important cohort effect in survival for known categories of EOD given the variability in the rates.

The patients that were excluded from the analysis based on unknown EOD were also analyzed to see if there was anything unusual about them. The EOD was unknown for 152 patients which was 7.6% of the total. The conditional 5-year survival rates for each of the eight 5-year intervals subsequent to diagnosis by gender and age are given in Figure 4 along with a table showing the number of patients at risk of dying at the beginning of each of the eight 5-year intervals. The pattern of the rates for these patients is very similar to that for patients for whom EOD was known.

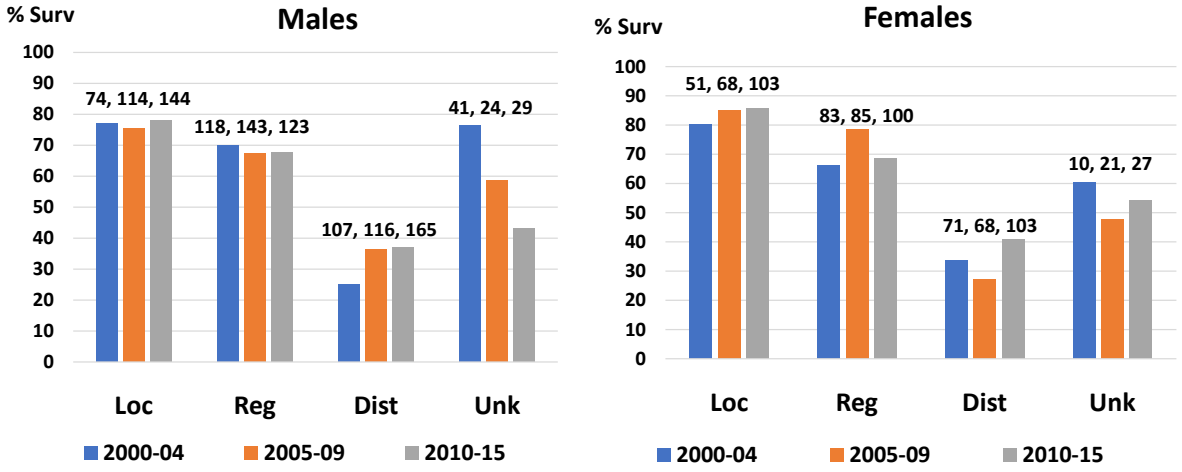
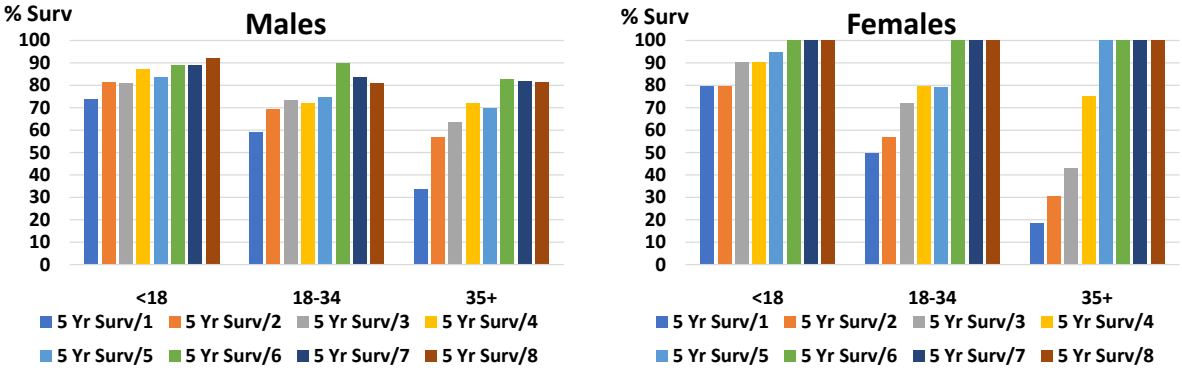



Figure 3. Five-year relative survival rates for three calendar year of diagnosis cohorts of Ewing Sarcoma patients is given by gender, and EOD along with the number of patients.




| Sex/Age | Males | | | Females | | |
|---|---|---|---|---|---|---|
| Follow-up Year | <18 | 18-34 | 35+ | <18 | 18-34 | 35+ |
| 1 | 43 | 34 | 17 | 25 | 16 | 17 |
| 2 | 38 | 29 | 10 | 25 | 14 | 10 |
| 3 | 37 | 26 | 8 | 22 | 11 | 7 |
| 4 | 32 | 25 | 7 | 21 | 10 | 4 |
| 5 | 32 | 24 | 6 | 20 | 10 | 3 |
| 6 | 28 | 20 | 5 | 18 | 7 | 3 |
| 7 | 28 | 19 | 5 | 16 | 7 | 2 |
| 8 | 27 | 18 | 5 | 15 | 6 | 2 |

Figure 4. Five-year conditional relative survival rates for eight post diagnosis cohorts with unknown EOD is given by gender, and age for Ewing Sarcoma patients. The number of patients in each cohort beginning at time of diagnosis is given in the table.

## 4. Discussion

The pattern of the survival rates presented here could be of interest to patients as it provides some basis for becoming more optimistic as patients survive subsequent to their diagnosis and treatment. However, it is recognized that a given 5-year cohort defined at a time subsequent to diagnosis will contain patients who have recurred or will recur and are alive and those who have not recurred. Those patients who have not recurred in the successive cohorts will have better survival than the rates reported here for a given cohort because of the inclusion of patients who have recurred. The pattern of the survival rates suggests that the recurrence rate decreases as survival improves in successive cohorts. Also, it is of interest to understand how long it takes for survival to approach a steady state and what the level is as that type of information provides some insight into the biological behavior of the disease and is of interest to patients.

It is possible that risk factors for a cancer can bias relative survival rates if they are also prognostic factors. In calculating relative survival rates, expected survival rates are generally based on US Life Tables. If the patient cohort is not associated with a known prognostic factor, the use of US Life Tables for obtaining expected rates is appropriate. However, if the cohort has a disproportionate number of patients with a known prognostic factor then the use of US Life Tables is not appropriate. Smoking is probably the best example as a cohort of cancer patients a large percentage of whom smoke will have excess mortality due to smoking in addition to their cancer. The only way to calculate correct relative survival rates in this case would be to base expected rates on a population that included a similar proportion of smokers. Therefore, basing expected rates on US Life Tables would not be appropriate in this case. However, this is not the case for Ewing Sarcoma as there are no known risk factors except for age, race, and gender [6] so that it is reasonable to use US Life Tables to calculate relative rates as is done here.

This type of analysis has been done before using data from the National Cancer Institute's End Results Program. Long term 5-year relative survival rates were examined for a number of cancers for patients diagnosed during 1950-59 for the purpose of determining the extent to which the relative survival rate improved over time [6]. The study demonstrated that there is value in analyzing conditional survival for the purpose of better understanding how prognosis can change for patient cohorts defined by survival time.

Not all prognostic factors for Ewing Sarcoma have been included in this analysis. Other factors include site of the tumor, whether the tumor is extraskeletal or skeletal, and tumor size or volume [7]. If any of these prognostic factors are due to the unadjusted effects of age and/or stage, then it would not be important to include them in addition to the variables included here in making statements about prognosis. Whatever the case, it is felt that the analysis presented here is of value to Ewing Sarcoma patients.

This paper is dedicated to Danielle Hankey, our granddaughter, a premed student at the University of South Carolina, and a survivor of Ewing Sarcoma.

## Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

## References

[1] Ewing Sarcoma and Undifferentiated Small Round Cell Sarcomas of Bone and Soft Tissue Treatment (PDQ®), Health Professional Version, NCI (cancer.gov). https://www.cancer.gov/publications/pdq

[2] American Joint Committee on Cancer. ACS (facs.org) SEER Stat Variables (cancer.gov). https://www.facs.org/quality-programs/cancer-programs/american-joint-committee-on-cancer/

[3] SEER Stat Variables. https://seer.cancer.gov/search?q=seer+historic+stage&x=138y=13

[4] SEER*Stat Software. https://seer.cancer.gov/data-software/documentation/seerstat/

[5] https://seer.cancer.gov/seerstat/

[6] https://www.cancer.org/cancer/ewing-tumor/causes-risks-prevention/prevention.html

[7] Hankey, B.F. and Steinhorn, S.C. (1982) Long-Term Patient Survival for Some of the More Frequently Occurring Cancers. *Cancer*, **50**, 1904-1912. https://doi.org/10.1002/1097-0142(19821101)50:9<1904::AID-CNCR2820500943>3.0.CO;2-S