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# Lung cancer survival in Germany: A population-based analysis of 132,612 lung cancer patients

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ABSTRACT

*Objectives:* Lung cancer is the most common cancer-related death worldwide. In Germany it accounts for 25% of cancer deaths in men, and 14% in women. The aim of this study is to provide an overview of 5-year relative survival by sex, age, histology, and tumour stage in Germany representing a population of 26.7 million people.

*Materials and methods:* The study is based on a pooled German dataset including data from 12 population-based cancer registries covering around one third of the German population. A total of 132,612 patients diagnosed with lung cancer from 2002 to 2010 were included in the analysis. Survival estimates for the time period 2007–2010 were calculated using period analysis. Differences in survival between sexes were tested for statistical significance by model-based period analysis (poisson regression model). The relative excess risk (RER) of death (women vs. men) was extracted from the model with the $p$ value for the difference in RER.

*Results:* The overall age adjusted 5-year relative survival was 15.5% (standard error (SE) 0.2) for men and 20.3% (SE 0.3) in women. Survival differed markedly according to age (men: <60 years 18.5% vs. 80+ years 8.4% and women 23.7% vs. 10.6%, respectively), histology (largest difference between histological groups: men 25.7 and women 44.4% points) and stage (men: UICC Ia 62.9%, vs. UICC IV 4.6% and women 75.2% vs. 7.0%, respectively).

Our study showed survival advantages for women compared to men, most notably in younger aged patients (RER 0.83, $p < 0.0001$), patients with adenocarcinoma (RER 0.80, $p < 0.0001$), and patients with lower stage cancer (RER 0.62, $p < 0.0001$).

*Conclusions:* This study presents up-to-date survival estimates for lung cancer in Germany. Compared to other European countries survival was relatively high. Women showed higher survival than men independent of age, histology and stage. The reasons for the survival differences require further clarification.



## 1. Introduction

In Germany as well as in other European industrialised countries, lung cancer is among the three leading forms of cancer both in terms of incidence and mortality. Since the end of the 1990s age-standardised incidence and mortality rates are showing an opposing trend between men and women: Incidence and mortality have decreased steadily for men by around 20% but have increased

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in women by approximately 30% [1,2]. This development is caused by the changing behaviour with respect to smoking. Nonetheless, currently there are still two-times more men than women diagnosed with lung cancer in Germany [3].

The prognosis for lung tumours is unfavourable and improvements in survival in recent decades have been minimal. Between the mid-1970s and the beginning of the millennium, 5-year relative survival from lung cancer in the USA increased only modestly from 13% to 16% [4]. For Europe, the EUROCARE-5 study (European Registry Based Study on Survival and Care of Cancer Patients) estimated a mean age-standardised 5-year lung cancer survival of 13% for patients diagnosed in 2000–2007. Relative survival varied nearly twofold between European countries, with the lowest survival being observed in Bulgaria (6.2%), UK with Wales (8.6%) and Scotland (8.7%), and the highest survival in Germany (15.6%) and Austria (16.7%) [5]. Differences in health care systems as well as in the distribution of diagnostic and treatment practices in the whole population are possible explanations for geographical differences in survival [6]. Further explanations are differences in the used data base especially regarding the quality of cancer registration which includes completeness of data and ascertainment of vital status [7].

In this study, using population-based cancer registry data, we analysed lung cancer survival in Germany with respect to sex, age, stage at diagnosis and histology. The aim of this investigation is the identification of factors which affect the relatively high survival rates for lung cancer in Germany.

## 2. Materials and methods

### 2.1. Study population

The study is based on a pooled national dataset including data from cancer registries in 12 out of 16 federal states in Germany, covering a population of 26.7 million people. Only regions with sufficient data quality were included in the analysis data set. Data quality was assessed by proportion of death certificate only notified and autopsy only (DCO) cases over all malignant cancers. Cancer registries were included if the overall proportion of DCO cases was below 13% in 2002–2010, or decreased steadily over time and was overall below 14%. A cut-off at 13% was chosen, as the same cut-off was used in the European Cancer Registry based study on survival and care of cancer patients (EUROCARE-5 study) [5]. If these criteria were not fulfilled for the whole region covered by a cancer registry, only those administrative districts that fulfilled these criteria were included.

The analysis included patients with primary invasive lung cancer (ICD-10: C33-34) diagnosed in 2002–2010 who were at least 15 years old at the time of diagnosis. Patients were followed up with respect to vital status until December 31, 2010. Cases notified by DCO were excluded.

Topography and histology of tumours were coded according to ICD-O-3 [8]. The histology codes were grouped into the following six categories: adenocarcinoma, squamous cell carcinoma, large cell carcinoma, small cell carcinoma, other specified tumours and other unspecified tumours [9]. Tumour stages were coded in accordance with the tumour–node–metastasis (TNM) classification of malignant tumour [10].

For the analyses, patients were categorized by sex, age at diagnosis (15–59, 60–69, 70–79 and 80+ years), tumour histology and stage at diagnosis.

### 2.2. Statistical methods

Five-year relative survival estimates for the time period 2007–2010 were calculated using period analysis, providing more up-to-date survival estimates than traditional cohort based analysis. The period analysis included only survival experience during the period from 2007 to 2010 [11].

Relative survival was derived as a ratio of the observed survival of the included patients divided by the expected survival of the underlying population. Expected survival was computed according to the Ederer II method [12] using national life tables stratified by age, sex, and calendar year obtained from the German Federal Statistical Office. We calculated 5-year relative survival stratified by sex, age group, stage and histological type. Age-standardised survival was estimated using weights defined by the International Cancer Survival Standard [13].

Model-based period analysis was used to investigate differences in survival between men and women and to perform statistical significance testing [14]. Poisson regression models were fit to the number of excess deaths, using year of follow-up and sex as explanatory variables (of categorical type) and included the logarithm of the person-years at risk as offset. The relative excess risk (RER) of death for women compared to men was extracted from the model together with the corresponding $p$ value for the difference in RER between the sexes. Analyses were repeated with additional adjustment for age, histology group, and stage at diagnosis.

All analyses were performed with the SAS software (version 9.2), using special macros for period analysis [15] and their adaptation for model-based analysis [14]. Statistical significance was tested two-sided using a significance level of 0.05.

## 3. Results

After exclusion of DCO cases (13.5%) a total of 132,612 lung cancer cases were included in the analysis (Table 1). The percentage of DCO cases varied between registries, ranging from 8.0% in Saarland to 16.4% in Lower Saxony. The proportion of cancers with microscopic confirmation was 93.3%. Nearly three-quarters of lung cancer tumours (72%) were diagnosed in men.

The basic characteristics of the patients included in the analyses according to sex, histological group, age, period of diagnosis, and stage are presented in Table 2. Among men, the most common histological category was squamous cell carcinoma (32.0%), with a substantially higher proportion in men than in women (17.1%). Adenocarcinoma was the second most common histological group (27.3%). Among women, the most common histological groups are adenocarcinoma (37.6%), other unspecified tumours (17.5%), and squamous cell carcinoma (17.1%). Large cell carcinoma was the least frequent histological group in both sexes (3.1%). In both sexes, lung cancer patients in the oldest age group (80+ years) had the highest proportion of unspecified tumours (men 32.8%, women 39.2%) whereas patients in the youngest age group (15–69 years) had the highest proportion of adenocarcinoma (men 31.7%, women 43.7%). In both sexes, the number of lung cancer patients rose steadily from 39,207 cases in 2002–2004 to 48,326 cases in 2008–2010.

Staging of cancer at the time of diagnosis is the most important predictor of survival, and treatment options are based on stage. In our study, information on stage of tumours at diagnosis was often missing (44%). Because lung cancer is asymptomatic in early stages, only 14% of cases with stage information were classified in stage I. There was no difference in the proportion of tumours with earlier stages (Ia,b) between men and women. In both sexes, small cell carcinoma patients had the highest proportion of stage IV tumours (men: 72.4%; women: 69.1% of those with stage information).

The overall age adjusted 5-year relative survival for the time period 2007–2010 was 16.9%, with substantial variation between men (15.5%) and women (20.3%; Table 3). Survival varied by age, with increasing age being associated with reduced relative survival.

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