Estimation of the Potentially Avoidable Excess Deaths Associated with Socioeconomic Inequalities in Cancer Survival in Germany

Lina Jansen 1,*,†, Josephine Kanbach 2,†, Isabelle Finke 1,3, Volker Arndt 4,*, Katharina Emrich 5, Bernd Holleczek 6,*, Hiltraud Kajüter 7, Joachim Kieschke 8, Werner Maier 9, Ron Pritzkuleit 10, Eunice Sirri 8, Lars Schwettmann 9,11, Cynthia Erb 12, Hermann Brenner 1,3,14 and Group for the German Cancer Survival Working ‡

1 Division of Clinical Epidemiology and Aging Research, German Cancer Research Center (DKFZ), 69120 Heidelberg, Germany; i.finke@dkfz-heidelberg.de (I.F.); h.brenner@dkfz-heidelberg.de (H.B.)
2 Faculty 11-Human and Health Science, University of Bremen, 28359 Bremen, Germany; jkanbach@uni-bremen.de
3 Medical Faculty Heidelberg, University of Heidelberg, 69120 Heidelberg, Germany
4 Epidemiological Cancer Registry Baden-Württemberg, German Cancer Research Center (DKFZ), 69120 Heidelberg, Germany; v.arndt@dkfz-heidelberg.de
5 Cancer Registry of Rhineland-Palatinate gGmbH, 55116 Mainz, Germany; emrich@krebsregister-rlp.de
6 Saarland Cancer Registry, 6619 Saarbrücken, Germany; b.holleczek@krebsregister.saarland.de
7 Landeskrebsregister Nordrhein-Westfalen gGmbH, 44801 Bochum, Germany; hiltraud.kajuter@krebsregister-nrw.de
8 Epidemiological Cancer Registry Lower Saxony, 26121 Oldenburg, Germany; kieschke@offis-care.de (J.K.); eunice.sirri@offis-care.de (E.S.)
9 Helmholtz Zentrum München-German Research Center for Environmental Health (GmbH), Institute of Health Economics and Health Care Management, 85764 Neuberger, Germany; werner.maier@helmholtz-muenchen.de (W.M.); lars.schwettmann@helmholtz-muenchen.de (L.S.)
10 Institute for Cancer Epidemiology at the University of Lübeck, Cancer Registry Schleswig-Holstein, 23538 Lübeck, Germany; Ron.Pritzkuleit@uksh.de
11 Department of Economics, Martin Luther University Halle-Wittenberg, 06099 Halle (Saale), Germany
12 Hamburg Cancer Registry, 20539 Hamburg, Germany; cynthia.erb@bwfgb.hamburg.de
13 Division of Preventive Oncology, German Cancer Research Center (DKFZ) and National Center for Tumor Diseases (NCT), 69120 Heidelberg, Germany
14 German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), 69120 Heidelberg, Germany
* Correspondence: ljansen@dkfz-heidelberg.de; Tel.: +49-6221-42-4211
† Authors contributed equally to the manuscript.
‡ Members are listed in the Acknowledgements section.

Simple Summary: In this study, we estimate the number of avoidable deaths attributable to socioeconomic inequalities in cancer survival in Germany. We used data from epidemiological cancer registries. The German Index of Multiple Deprivation (GIMD) 2010 was used to assess deprivation on a municipality level. Results show that summed over the 25 cancer sites, 4100 annual excess deaths (3.0% of all excess deaths) could have been avoided each year in Germany during the period 2013–2016 if relative survival were in all regions comparable with the least deprived regions. colorectal, oral and pharynx, prostate, and bladder cancer contributed the largest numbers of avoidable excess deaths. We also observed that cancer incidence was generally higher in more deprived areas. Our analyses demonstrate the importance of cancer prevention and of survival improvements in more deprived regions.

Abstract: Many countries have reported survival inequalities due to regional socioeconomic deprivation. To quantify the potential gain from eliminating cancer survival disadvantages associated with area-based deprivation in Germany, we calculated the number of avoidable excess deaths. We used population-based cancer registry data from 11 of 16 German federal states. Patients aged ≥15 years diagnosed with an invasive malignant tumor between 2008 and 2017 were included. Area-based socioeconomic deprivation was assessed using the quintiles of the German Index of Multiple Deprivation (GIMD) 2010 on a municipality level nationwide. Five-year age-standardized relative survival
for 25 most common cancer sites and for total cancer were calculated using period analysis. Incidence and number of avoidable excess deaths in Germany in 2013–2016 were estimated. Summed over the 25 cancer sites, 4100 annual excess deaths (3.0% of all excess deaths) could have been avoided each year in Germany during the period 2013–2016 if relative survival were in all regions comparable with the least deprived regions. Colorectal, oral and pharynx, prostate, and bladder cancer contributed the largest numbers of avoidable excess deaths. Our results provide a good basis to estimate the potential of intervention programs for reducing socioeconomic inequalities in cancer burden in Germany.

**Keywords:** cancer; survival; avoidable deaths; socioeconomic deprivation; Germany

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1. **Introduction**

Disparities in cancer survival due to area-based deprivation have been reported in many countries and for several cancer sites showing that cancer patients living in affluent regions have better survival than those living in more deprived regions [1–6]. Despite universal health insurance coverage, these disparities have also been reported for Germany [7–10]. For all cancer sites combined (“total cancer”), five-year relative survival in 2002–2006 spanned from 63.5% among patients residing in least deprived districts to 56.5% among patients residing in most deprived districts. Consequently, the relative excess risk (RER) of death was 1.20 when comparing the most deprived with all remaining districts [7].

All German studies on socioeconomic inequalities in cancer survival, as well as most studies from other countries, used relative or absolute survival and RERs or hazard ratios as outcomes. However, these estimates might not be easily interpretable by policy makers and the public. Therefore, we use instead the number of avoidable excess deaths attributed to socioeconomic inequalities in cancer survival. This is an alternative and easy to interpret estimate for the potential gain of eliminating social inequalities in cancer survival. Only a few previous studies have estimated this metric for selected countries showing, for example, that 2.5% of the excess/cancer-related deaths from 12 cancer sites studied could be prevented by eliminating regional and social class variation in survival in Nordic countries [11]. The aim of the present study is to provide an up-to-date estimate of avoidable excess deaths attributed to area-based socioeconomic inequalities in cancer survival in Germany using data from epidemiological cancer registries.

2. **Materials and Methods**

2.1. **Data Source**

The analyses were based on population-based cancer registry data from 11 out of 16 German federal states (Table 1). Of the remaining five states, Hamburg, Bremen, and Berlin were excluded a priori, as only very aggregated socioeconomic data were available. Hesse was excluded due to a high proportion of death certificate only (DCO) notified cases (>14% in 2013–2017). Data from Rhineland-Palatinate were not provided. Data were collected using a common record layout, checked for plausibility, and pooled for analysis. Patients aged ≥15 years with a diagnosis of an invasive malignant tumor (International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10): C00–C97 without C44, C77–79) in 2008–2017 and mortality follow-up until December 2017 were included. DCO cases were excluded in descriptive and survival analyses. Multiple primaries were handled according to the International Association of Cancer Registries (IACR) multiple primary rules [12]. For some registries, data were only available for fewer years of diagnosis (Table 1).
Table 1. Overview of used cancer data provided by population-based cancer registries in Germany.

| Cancer Registry       | Population (Million in 2017) | Years of Diagnosis | DCO-Cases a | Cases b |
|-----------------------|-----------------------------|--------------------|-------------|---------|
| Schleswig-Holstein    | 2.89                        | 2008–2017          | 12%         | 162,810 |
| Lower Saxony          | 7.96                        | 2008–2017          | 9%          | 456,052 |
| North Rhine-Westphalia c | 17.91                      | 2008–2017          | 11%         | 804,483 |
| Baden-Wuerttemberg    | 11.02                       | 2009–2017          | 10%         | 407,595 |
| Bavaria d             | 11.10                       | 2008–2015          | 8%          | 435,267 |
| Saarland              | 0.99                        | 2008–2017          | 6%          | 76,954  |
| Brandenburg           | 2.49                        | 2008–2015          | 8%          | 113,664 |
| Mecklenburg-Western Pomerania | 1.61                  | 2008–2015          | 6%          | 79,207  |
| Saxony                | 4.08                        | 2008–2015          | 5%          | 204,099 |
| Saxony-Anhalt         | 2.22                        | 2008–2015          | 14%         | 99,039  |
| Thuringia             | 2.15                        | 2008–2015          | 7%          | 100,801 |
| Total                 | 64.42                       | 2008–2017          | 8%          | 2,939,971 |

a Proportion of death certificate only (DCO) notified cases among invasive cancer cases (C00–C97 without C44, C77–C79) in 2013–2017; b After exclusion of DCO cases; c Restricted to administrative district Münster for years of diagnosis 2008 and 2009; d Exclusion of administrative district Schwaben due to low data quality.

Area-based socioeconomic status on a municipality level was assessed using the quintiles of the composite index of the German Index of Multiple Deprivation (GIMD) 2010 [13]. The GIMD has already been used in many epidemiological and public health studies (for example: [8,14,15]). The development of the GIMD followed the methods used in the UK to create the widely used Indices of Multiple Deprivation. [16] More information on the creation and calculation of the GIMD and its regional versions can be found elsewhere [17–20]. The index uses data of administrative statistics dating virtually all from 2010 on seven deprivation domains (income, employment, education, municipality revenue, social capital, environment, and security). The composite score, the GIMD, was derived as a weighted sum of the domains. Quintiles of the GIMD were then computed over all municipalities. These quintiles of the composite index were assigned to each patient according to the municipality of residence at the time of diagnosis. The dataset included patients from 7979 municipalities with a median population of 2242 (range 9–1,456,039, interquartile range: 825–6373) in 2017 [21].

The Ethics Committee of the medical faculty Heidelberg approved the study (approval number: S-476/2013).

2.2. Statistical Methods—Relative Survival

Period analysis was used to estimate age-standardized absolute, expected and relative survival in 2013–2017 for total cancer and for 25 most common cancer sites (representing 93.8% of all cancer conditions) by deprivation quintile [22]. Expected survival was estimated using the Ederer II method [23]. Life tables stratified by age, sex, calendar period of diagnosis, and deprivation quintile were derived from administrative population and mortality data on a municipality level [24]. For age-standardization, the age distribution of all patients diagnosed in 2013–2017 with the respective cancer site was used (five age groups: 15–44, 45–54, 55–64, 65–74, and 75+ years). The period 2013–2017 was chosen, as it allows including the most up-to-date cancer registry data as well as reducing the random variation by combining five years of diagnosis.

Differences in relative survival between deprivation quintiles were tested for statistical significance by model-based period analyses [25]. In these analyses, numbers of deaths were modeled by Poisson regression as a function of year of follow-up, age group, and socioeconomic deprivation, with the logarithm of the person-years at risk as offset.

2.3. Statistical Methods—Avoidable Excess Deaths in Study Population

Using the number of cancer patients included in the study cohort in 2013–2017 and the period survival estimates by deprivation quintile, the number of observed deaths, excess deaths, and avoidable excess deaths attributable to deprivation inequalities within five
years of diagnosis (reference: least deprived) were estimated by deprivation quintile and cancer site. The numbers of observed and expected deaths were calculated by multiplying the case number with one minus the absolute and expected survival estimate, respectively. The number of observed deaths shows how many patients died within five years of diagnosis (irrespective of the cause of death). In some contrast, the number of expected deaths indicates how many deaths would have been expected within five years when the persons would not have cancer. The number of excess deaths was derived as difference between these estimates and reflects the cancer attributable deaths within five years of diagnosis. The number of avoidable excess deaths was then derived by:

\[ \text{Number of avoidable excess deaths in quintile } Q = N_Q \times ES_Q \times (RS_{\text{least deprived}} - RS_Q) \] (1)

where \( N \) is the number of cancer cases in the deprivation quintile \( Q \), \( ES \) the expected survival in the deprivation quintile \( Q \) and \( RS \) the relative survival in the least deprived quintile (reference) and in the deprivation quintile \( Q \), respectively [26]. The number of avoidable excess deaths reflects the number of deaths attributed to cancer within five years of diagnosis that are associated with the lower relative survival in the quintile compared to least deprived quintile. These deaths are premature deaths, as deaths could not have been avoided per se but occurred earlier due to cancer. In the Supplementary Material, we show an example of how to derive the number of observed, expected, excess, and avoidable excess deaths.

We computed the number of avoidable excess deaths for each cancer site, over all cancer sites combined and as the sum over the single cancer sites. The difference between the estimation over all cancer sites and the sum over the single cancer sites is that the first estimate will not only reflect deprivation-associated survival differences but also deprivation-associated incidence differences, whereas the latter estimate reflects only deprivation-associated survival differences. Clearly, both estimates are important: Resolving socioeconomic inequalities in general in the population would affect incidence as well as survival and, thus, the estimation over all cancer sites would be most adequate. For estimating the impact of interventions targeted specifically on elimination of deprivation-associated survival differences, the sum over the single cancer sites would be more adequate. Therefore, both estimates are reported.

2.4. Statistical Methods—Avoidable Excess Deaths in Germany

To estimate the annual number of avoidable excess deaths attributed to deprivation inequalities in Germany, the number of cancer patients per deprivation quintile in Germany must be calculated. As nationwide incidence and cancer case numbers by deprivation quintile were not available, it was estimates from national incidence estimates and incidence rate ratios from the study population. Using the cancer registry datasets, the cancer incidence rates per 100,000 persons per year in 2013–2017 were estimated for each individual site and total cancer (including patients younger than 15 years and DCO cases). For each deprivation quintile, incidence rate ratios were then computed as ratios of the incidence in the quintile and in the total study population. National cancer incidence estimates for 2013–2016 (2017 was not available) were obtained for each cancer site and total cancer from the database of the Centre for Cancer Registry Data in Germany [27]. The underlying population in Germany by deprivation quintile was derived from administrative data on a municipality level [21]. National estimates and the incidence rate ratios from the study population were applied to obtain incidence estimates for each deprivation quintile of the German population using the national incidence data. The number of annual cancer cases was estimated by multiplying the incidence with the population size in each quintile. The number of avoidable excess deaths per quintile were computed as described above. In the Supplementary Material, we show an example of how to derive these estimates for Germany.

All analyses were conducted with SAS Enterprise Guide Version 7.15 (SAS Institute Inc., Cary, NC, USA).
3. Results

Table 1 shows the study population in the federal states included in the analysis. The proportion of DCO cases was comparable across the deprivation quintiles (e.g., 2013–2015: 8.6–9.3%). After exclusion of 8% of DCO cases, 2,939,971 cancer cases were included in the survival analysis (Table 2). For all cancer sites combined five-year age-standardized relative survival in 2013–2017 decreased gradually with increasing deprivation from 66.9% (standard error: 0.2) for patients living in the least deprived municipalities to 60.2% (standard error: 0.1) for patients living in the most deprived municipalities (Table 2). This difference corresponds to a significant 31% increased RERs of death in the most deprived compared to the least deprived area. A significantly lower five-year relative survival in the most compared to the least deprived regions were found for 20 of 25 most common cancer sites (Table 2). Largest absolute differences were observed for oral and pharynx (−8.6% units), ovarian (−8.3% units), and esophagus cancer (−7.0% units). RERs were largest for testicular (RER: 1.98 (95% confidence interval: 1.26–3.11)), prostate (1.62 (1.42–1.84)) and thyroid cancer (1.43 (1.10–1.87)).

Table 3 shows the numbers of observed, expected, and excess deaths within five years of diagnosis and the numbers of avoidable excess deaths compared to the least deprived quintile for patients diagnosed in 2013–2017. For all cancer sites combined, 430,398 excess deaths among 1,483,168 patients were observed. The most common cancer sites were female breast, colorectum, prostate, and lung cancer, respectively. Most excess deaths were observed for lung, colorectum, pancreas, and female breast cancer. For all cancer sites combined, 33,891 excess deaths (7.9% of all excess deaths) within five years of diagnosis could have been avoided if all regions would have the same five-year relative survival (and the same distribution of the sites of incident cancers) as the least deprived region. This estimate is much larger than the summed avoidable excess deaths across all cancer sites (N = 12,193, 3.1% of all excess deaths), as there was a higher proportion of fatal cancers in more deprived regions. Of the 25 most common cancer sites, colorectum (N = 1911, 3.8% of all excess deaths), oral and pharynx (N = 1580, 9.3%), prostate (N = 1435, 15.3%), and bladder cancer (N = 1343, 8.0%) contributed the most avoidable excess deaths. In general, there was a tendency to higher proportions of avoidable deaths for cancer sites with higher relative survival estimates (Supplementary Figure S1). The two most deprived quintiles contributed most to the avoidable excess deaths, each with a proportion of about 3.0% avoidable excess deaths among all excess deaths compared to 0.5% for the second least and 1.1% for the third least deprived quintile.

Table 4 shows the cancer incidence per 100,000 persons per year in the study population (2013–2017, left side) and in Germany (2013–2016, right side). Compared to the study population, the incidence estimates in Germany were mostly comparable or slightly higher in the German population. For female breast cancer and ovarian cancer incidence was slightly lower in the German population. In the study population, for 16 of the 25 most common cancer sites and total cancer, the incidence increased with increasing deprivation, whereas it decreased for female breast and testicular cancer. In the study population, for melanoma, soft tissue, corpus uteri, ovarian, prostate, and thyroid cancer and Hodgkin lymphoma, no consistent patterns regarding the deprivation quintiles were observed. Applying the incidence rate ratios in the study population to the overall cancer incidence in Germany, the incidence for the deprivation quintiles in Germany were derived. These estimates reflect the incidence differences across regions with different deprivation and were used to estimate the number of avoidable excess cancer deaths.
Table 2. Age-standardized five-year relative survival in 2013–2017 by cancer site and deprivation quintile in the study population.

| Cancer Site                  | ICD-10 Code | Cases (2008–17) | Age-Standardized 5-Year Relative Survival (Standard Error) | RER (95 % CI) |
|------------------------------|-------------|-----------------|----------------------------------------------------------|---------------|
|                              |             |                 | Q1 (Least Deprived) Q2 Q3 Q4 Q5 (Most Deprived) Q5–Q1 Q5 vs. Q1 |               |
| Oral and pharynx             | C00–C14    | 84,705          | 58.5 (0.9) 56.5 (0.7) 55.7 (0.6) 53.5 (0.5) 49.9 (0.7) −8.6 1.35 (1.27–1.44) |
| Esophagus                    | C15         | 40,045          | 29.2 (1.1) 27.2 (0.8) 27.0 (0.8) 24.7 (0.6) 22.2 (0.8) −7.0 1.26 (1.18–1.34) |
| Stomach                      | C16         | 96,716          | 38.1 (0.9) 38.1 (0.7) 36.7 (0.6) 35.7 (0.5) 33.2 (0.6) −4.9 1.15 (1.10–1.21) |
| Colon, rectum, and anus       | C18–C21     | 385,160         | 67.2 (0.5) 67.3 (0.4) 66.6 (0.3) 65.6 (0.3) 63.4 (0.4) −3.8 1.16 (1.12–1.20) |
| Liver                        | C22         | 44,641          | 21.0 (1.1) 18.9 (0.7) 18.1 (0.7) 18.5 (0.6) 15.9 (0.7) −5.1 1.17 (1.10–1.24) |
| Gallbladder                  | C23–C24     | 27,761          | 25.5 (1.5) 23.8 (1.1) 23.1 (1.0) 21.9 (0.8) 20.4 (0.9) −5.1 1.23 (1.14–1.34) |
| Pancreas                     | C25         | 86,438          | 12.9 (0.6) 11.9 (0.5) 12.0 (0.4) 12.4 (0.3) 11.1 (0.4) −1.8 1.13 (1.09–1.18) |
| Larynx                       | C32         | 22,829          | 69.2 (1.8) 68.4 (1.4) 66.6 (1.2) 66.3 (1.0) 63.2 (1.4) −6.0 1.31 (1.12–1.52) |
| Lung                         | C33–C34     | 308,773         | 20.8 (0.4) 21.4 (0.3) 20.7 (0.3) 20.3 (0.2) 20.0 (0.3) −0.8 1.06 (1.03–1.08) |
| Melanoma                     | C43         | 137,947         | 94.3 (0.5) 95.0 (0.4) 95.3 (0.4) 96.1 (0.3) 92.9 (0.5) −1.4 1.38 (1.15–1.65) |
| Soft tissue                  | C49         | 17,781          | 65.3 (2.0) 64.1 (1.5) 66.3 (1.4) 65.9 (1.2) 64.6 (1.7) −0.7 1.03 (0.89–1.21) |
| Breast (female)              | C50         | 454,132         | 89.2 (0.3) 89.3 (0.2) 89.1 (0.2) 88.3 (0.2) 88.3 (0.3) −0.9 1.08 (1.01–1.15) |
| Lymphoma                     | C81         | 13,691          | 86.0 (1.1) 85.6 (1.0) 85.7 (0.9) 85.3 (0.8) 84.4 (0.9) −8.3 1.28 (1.19–1.38) |
| Non-Hodgkin lymphoma         | C82–C85     | 94,469          | 79.4 (0.6) 79.7 (0.4) 79.8 (0.6) 80.4 (0.6) 81.5 (0.5) −7.7 1.14 (1.05–1.24) |
| Multiple myeloma             | C90         | 38,561          | 52.3 (1.3) 54.8 (1.1) 56.2 (1.0) 54.2 (0.8) 54.2 (0.8) −2.5 1.12 (1.02–1.22) |
| Leukemia                     | C91–C97     | 71,582          | 59.2 (1.0) 57.9 (0.8) 57.7 (0.7) 58.9 (0.6) 58.4 (0.8) −0.8 1.03 (0.96–1.11) |
| Total Cancer b               |             | 2,939,971       | 66.9 (0.2) 66.0 (0.1) 65.1 (0.1) 63.5 (0.1) 60.2 (0.1) −6.7 1.31 (1.29–1.32) |

ICD-10, 10th revision of International Statistical Classification of Diseases and Related Health Problems; Q, quintile; RER, relative excess risk; CI, confidence interval; Significant RERs are printed in bold.

Reference: Q1 (least deprived), adjusted for age at diagnosis; b C00–C97 without C44, C77–C79.
Table 3. Estimated number of deaths and excess deaths within five years of diagnosis for cancer patients diagnosed in 2013–2017 and estimated number of avoidable excess deaths caused by socioeconomic differences in the study population.

| Cancer Site                  | Cases   | Observed Deaths | Expected Deaths | Excess Deaths | Avoidable Deaths |
|------------------------------|---------|-----------------|-----------------|---------------|-----------------|
| Oral and pharynx             | 42,576  | 22,111          | 5078            | 17,033        | 1580            |
| Esophagus                    | 21,193  | 16,467          | 3250            | 13,217        | 630             |
| Stomach                      | 47,110  | 33,243          | 9695            | 23,548        | 732             |
| Colon, rectum, and anus      | 190,411 | 89,512          | 39,172          | 50,339        | 1911            |
| Liver                        | 23,200  | 19,666          | 4311            | 15,355        | 524             |
| Gallbladder                  | 13,891  | 11,353          | 2982            | 8370          | 323             |
| Pancreas                     | 45,728  | 41,064          | 8536            | 32,528        | 316             |
| Larynx                       | 11,228  | 4796            | 1589            | 3208          | 269             |
| Lung                         | 163,027 | 134,162         | 25,882          | 108,280       | 227             |
| Melanoma                     | 72,606  | 12,490          | 9405            | 3085          | −483            |
| Soft tissue                  | 9272    | 4131            | 1521            | 2610          | −6              |
| Breast (female)              | 227,311 | 44,449          | 25,829          | 21,620        | 843             |
| Cervix                       | 13,889  | 4686            | 980             | 3888          | 300             |
| Corpus uteri                 | 33,567  | 9660            | 4471            | 5190          | 38              |
| Ovary                        | 24,476  | 14,159          | 3369            | 10,790        | 519             |
| Prostate                     | 185,618 | 44,965          | 35,571          | 9394          | 1435            |
| Testis                       | 13,141  | 677             | 292             | 386           | 60              |
| Kidney                       | 44,017  | 14,454          | 7050            | 7404          | 698             |
| Bladder                      | 53,845  | 29,569          | 12,688          | 16,881        | 1343            |
| Brain                        | 19,541  | 15,422          | 2274            | 13,148        | 95              |
| Thyroid                      | 20,110  | 2229            | 1251            | 978           | −182            |
| Hodgkin lymphoma             | 7111    | 1344            | 482             | 862           | 35              |
| Non-Hodgkin lymphoma         | 49,349  | 19,648          | 8443            | 11,205        | 866             |
| Multiple myeloma             | 20,651  | 11,429          | 3817            | 7612          | −120            |
| Leukemia                     | 36,827  | 16,654          | 6678            | 11,975        | 240             |
| Total Cancer c               | 1,483,168 | 675,751       | 245,353         | 430,398       | 33,891 b        |

Deprivation quintile (Q1—least deprived, Q5—most deprived). * Number of avoidable excess deaths in the study population compared to the least deprived quintile; b The number of avoidable excess deaths is much higher than the sum of the estimates for the separate cancer sites, as the distribution of cancer sites was not comparable across deprivation quintiles; c C00–C97 without C44, C77–C79.
Table 4. Cancer incidence rates and rate ratios in the study population (2013–2017) for each deprivation quintile on a municipality level compared to the overall incidence in the study population (left side) and overall cancer incidence rate and estimated incidence rates in each deprivation quintile in Germany (2013–2016).

| Cancer Site                  | Study Population |      | Germany |      |      |      |      |      |      |      |      |      |      |
|------------------------------|------------------|------|---------|------|------|------|------|------|------|------|------|------|------|
|                              | Incidence a      | Q1   | Q2      | Q3   | Q4   | Q5   | Total | Incidence Rate Ratio b | Q1 c  | Q2 c  | Q3 c  | Q4 c  | Q5 c  |
|------------------------------|------------------|------|---------|------|------|------|------|------|------|------|------|------|------|
| Oral and pharynx             | 16.3             | 0.82 | 0.87    | 0.96 | 1.04 | 1.29 | 17.2 | 14.2 | 15.0 | 16.4 | 17.8 | 22.3 |
| Esophagus                    | 8.4              | 0.86 | 0.90    | 0.97 | 1.05 | 1.18 | 8.7  | 7.4  | 7.8  | 8.4  | 9.1  | 10.2 |
| Stomach                      | 18.8             | 0.89 | 0.90    | 0.96 | 1.01 | 1.26 | 19.2 | 17.0 | 17.2 | 18.4 | 19.5 | 24.1 |
| Colon, rectum, and anus      | 74.4             | 0.92 | 0.92    | 0.97 | 1.03 | 1.14 | 75.7 | 69.8 | 69.5 | 73.7 | 78.1 | 86.5 |
| Liver                        | 10.6             | 0.83 | 0.89    | 0.93 | 1.01 | 1.35 | 11.1 | 9.2  | 9.9  | 10.3 | 11.3 | 15.0 |
| Gallbladder                  | 6.0              | 0.85 | 0.87    | 0.95 | 0.98 | 1.39 | 6.6  | 5.6  | 5.7  | 6.3  | 6.4  | 9.2  |
| Pancreas                     | 21.0             | 0.93 | 0.87    | 0.96 | 1.03 | 1.21 | 22.0 | 20.6 | 19.2 | 21.1 | 22.8 | 26.7 |
| Larynx                      | 4.4              | 0.81 | 0.82    | 0.96 | 1.08 | 1.27 | 4.5  | 3.6  | 3.7  | 4.3  | 4.8  | 5.7  |
| Lung                         | 68.5             | 0.78 | 0.85    | 0.95 | 1.10 | 1.22 | 70.3 | 54.9 | 59.7 | 66.7 | 77.7 | 86.0 |
| Melanoma                     | 27.1             | 1.12 | 1.03    | 0.99 | 1.02 | 0.86 | 27.6 | 30.9 | 30.3 | 27.1 | 28.0 | 23.6 |
| Soft tissue                  | 3.7              | 1.02 | 0.98    | 1.01 | 0.99 | 1.02 | 3.6  | 4.0  | 3.8  | 3.9  | 4.0  |      |
| Breast (female)              | 171.4            | 1.02 | 1.00    | 1.00 | 1.01 | 0.97 | 169.4 |      |      |      |      |      |
| Cervix                       | 10.5             | 0.88 | 0.94    | 0.99 | 1.02 | 1.14 | 11.0 | 9.6  | 10.3 | 10.8 | 11.2 | 12.5 |
| Corpus uteri                 | 24.7             | 0.96 | 0.97    | 1.00 | 0.98 | 1.11 | 25.3 | 24.4 | 24.5 | 25.3 | 24.8 | 28.2 |
| Ovary                        | 19.7             | 0.99 | 1.05    | 1.05 | 0.97 | 0.93 | 18.2 | 18.1 | 19.0 | 19.1 | 17.7 | 16.9 |
| Prostate                     | 146.5            | 1.03 | 0.97    | 1.01 | 0.99 | 1.01 | 146.2 | 150.6 | 141.3 | 147.9 | 145.3 | 148.3 |
| Testis                       | 10.0             | 1.05 | 1.04    | 1.01 | 0.97 | 0.96 | 10.8 | 11.3 | 11.2 | 10.9 | 10.5 | 10.4 |
| Kidney                       | 17.7             | 0.87 | 0.90    | 0.94 | 1.01 | 1.30 | 18.6 | 16.2 | 16.7 | 17.5 | 18.8 | 24.2 |
| Bladder                      | 21.0             | 0.85 | 0.89    | 0.97 | 1.06 | 1.17 | 20.6 | 17.5 | 18.2 | 20.0 | 21.9 | 24.0 |
| Brain                        | 8.4              | 1.00 | 0.94    | 0.97 | 1.02 | 1.09 | 8.9  | 8.9  | 8.3  | 8.6  | 9.1  | 9.7  |
| Thyroid                      | 7.6              | 1.02 | 1.04    | 0.98 | 1.03 | 0.90 | 8.5  | 8.7  | 8.9  | 8.3  | 8.8  | 7.7  |
| Hodgkin lymphoma             | 2.8              | 0.98 | 0.96    | 0.97 | 1.05 | 1.02 | 3.0  | 2.9  | 2.9  | 2.9  | 3.1  | 3.1  |
| Non-Hodgkin lymphoma         | 19.5             | 0.95 | 0.95    | 0.98 | 1.03 | 1.06 | 20.1 | 19.2 | 19.1 | 19.8 | 20.7 | 21.4 |
| Multiple myeloma             | 8.7              | 0.92 | 0.93    | 0.94 | 1.07 | 1.11 | 8.4  | 7.7  | 7.8  | 7.9  | 8.9  | 9.3  |
| Leukemia                     | 16.5             | 0.97 | 0.94    | 0.98 | 1.02 | 1.08 | 17.6 | 17.0 | 16.6 | 17.2 | 18.0 | 18.9 |
| Total Cancer d               | 594.3            | 0.93 | 0.93    | 0.98 | 1.03 | 1.11 | 604.9 | 564.0 | 565.4 | 592.7 | 623.0 | 668.3 |

Q, deprivation quintile (Q1—least deprived, Q5—most deprived) a Incidence per 100,000 persons per year in the study population in 2013–2017 and in Germany in 2013–2016. b Compared to the total incidence in the study population; c Estimated from the total incidence in Germany to which the observed incidence rate ratios of the study population were applied. Due to rounding, the estimates may deviate from the German incidence; d C00–C97 without C44, C77–C79.

The annual number of cases, excess deaths and avoidable excess deaths in deprived quintiles compared to the least deprived quintile are shown in Table 5 for patients diagnosed in 2013–2016 in Germany. Per calendar year, 11,405 excess deaths (7.9% of all excess deaths) could be attributed to the inferior prognosis of cancer patients in more deprived municipalities. Again, this estimate is influenced by the different case mix across deprivation quintiles and, therefore, considerably higher than the sum over the 25 individual cancer sites (N = 4100, 3.0%). As within the study population, colorectum (N = 630, 3.9% of all colorectum excess deaths), oral and pharynx (N = 524, 9.3%), prostate (N = 456, 15.4%), and bladder cancer (N = 417, 7.9%) accounted for the largest numbers of avoidable excess deaths.
Table 5. Estimated annual number of avoidable excess deaths among cancer patients associated with area-based deprivation on a municipality level within 5 years of diagnosis for patients diagnosed in 2013–2016 in Germany.

| Cancer Site               | Cases   | Excess Deaths | Avoidable Deaths a | Proportion Excess |
|---------------------------|---------|---------------|-------------------|-----------------|
|                           |         |               | Total Q2 Q3 Q4 Q5 |                  |
| Oral and pharynx          | 14,041  | 5625          | 524               | 9.3% 0.7% 1.4% 3.6% 3.6% |
| Esophagus                 | 7082    | 4421          | 212               | 4.8% 0.4% 0.7% 2.0% 1.7% |
| Stomach                   | 15,673  | 7845          | 248               | 3.2% 0.0% 0.5% 1.2% 1.4% |
| Colon, rectum, and anus   | 61,815  | 16,362        | 630               | 3.9% −0.1% 0.4% 1.6% 1.9% |
| Liver                     | 9061    | 6002          | 206               | 3.4% 0.4% 0.8% 1.0% 1.3% |
| Gallbladder               | 5367    | 3239          | 125               | 3.9% 0.4% 0.7% 1.4% 1.4% |
| Pancreas                  | 19,797  | 12,805        | 124               | 1.0% 0.2% 0.2% 0.2% 0.4% |
| Larynx                    | 3653    | 1046          | 89                | 8.5% 0.4% 1.8% 3.0% 3.4% |
| Lung                      | 57,387  | 38,157        | 86                | 0.2% −0.1% 0.0% 0.1% 0.2% |
| Melanoma                  | 22,489  | 956           | −149              | −15.6% −2.7% −4.2% −11.8% 3.6% |
| Soft tissue               | 3184    | 896           | −3                | −0.3% 0.6% −0.7% −0.6% 0.3% |
| Breast (female)           | 70,307  | 6690          | 264               | 3.9% −0.2% 0.2% 2.7% 1.2% |
| Cervix                    | 4544    | 1273          | 99                | 7.7% 0.9% 1.5% 2.5% 2.9% |
| Corpus uteri              | 10,509  | 1628          | 15                | 0.9% −1.2% 1.0% −0.2% 1.2% |
| Ovary                     | 7552    | 3334          | 165               | 5.0% −0.1% 0.9% 2.0% 2.3% |
| Prostate                  | 58,666  | 2973          | 456               | 15.4% 1.1% 2.3% 6.9% 5.0% |
| Testis                    | 4335    | 127           | 20                | 15.5% 0.0% 0.0% 5.1% 10.4% |
| Kidney                    | 15,183  | 2556          | 241               | 9.4% 1.5% 1.2% 2.4% 4.3% |
| Bladder                   | 16,775  | 5262          | 417               | 7.9% 1.1% 1.0% 3.3% 2.6% |
| Brain                     | 7286    | 4904          | 35                | 0.7% 0.2% 0.1% 0.2% 0.3% |
| Thyroid                   | 6595    | 338           | −63               | 18.6% −4.7% −7.5% −9.4% 3.1% |
| Hodgkin lymphoma          | 2449    | 297           | 12                | 4.0% 0.5% −1.2% 2.8% 1.9% |
| Non-Hodgkin lymphoma      | 16,428  | 3733          | 200               | 7.8% 0.7% 1.2% 3.0% 2.9% |
| Multiple myeloma          | 6857    | 2531          | −36               | −1.4% −0.9% 0.1% −1.6% 0.9% |
| Leukemia                  | 14,347  | 4667          | 93                | 2.0% 0.6% 0.9% 0.2% 0.3% |
| Total Cancer c            | 493,768 | 143,471       | 11,405            | 7.9% 0.4% 1.2% 3.2% 3.2% |

Inc, Incidence, Q, deprivation quintile (Q1—least deprived, Q5—most deprived). a Number of avoidable excess deaths in Germany compared to the least deprived quintile; b The number of avoidable excess deaths is much higher than the sum of the estimates by cancer site, as the distribution of cancer sites varied across deprivation quintiles; c C00–C97 without C44, C77–C79.

4. Discussion

In this study, we provided estimates for deprivation-associated inequalities in cancer survival in Germany in 2013–2016. For all invasive cancer sites combined, our results showed a gradual decrease of five-year age-standardized relative survival with increasing deprivation. In 20 of 25 most common cancer sites we found significantly lower five-year relative survival for patients in the most deprived compared to least deprived regions. We observed largest absolute differences in relative survival for oral and pharynx, ovarian and esophagus cancer and largest excess risks for testicular, prostate, and thyroid cancer. In Germany 11,405 annual excess deaths (7.9% of all excess deaths) for total cancer within five years of diagnosis could have been avoided if all regions had the same level of five-year relative survival and the same distribution of cancer sites as the least deprived regions. Colorectal, oral and pharynx, prostate, and bladder cancer contributed the largest numbers of avoidable excess deaths.

Previous studies from Germany and other European countries also observed lower cancer survival in more deprived regions for either individual cancer sites or all cancer sites combined [1–10,28,29]. Hypothesized reasons for these socioeconomic inequalities include differences in patient or tumor characteristics and varied quality and use of and compliance with medical care [30,31]. Results from the previous German studies were overall comparable with our results. For example, for total cancer, relative survival in 2002–2006 was 7% units lower in the most compared to the least deprived district in a previous study [7], which was identical to our difference between the least and the most deprived municipalities in 2013–2017. Most previous studies on socioeconomic differences in cancer survival and all studies from Germany on this topic estimated relative or absolute survival and RERs or hazard ratios. These outcomes might be difficult to understand by the public, health policy makers, and stakeholders and, consequently, the extent of social inequalities in cancer survival may remain unclear. To clarify the meaning of the results
and to provide a better quantification of the potential gain of eliminating socioeconomic inequalities in cancer survival, alternative outcomes should be considered. Therefore, we used avoidable excess deaths to quantify the impact of deprivation on survival disparities. It indicates the number of excess deaths that could have been avoided if in all regions the patients had the same prognosis as in the most affluent regions [32]. For total cancer, it is additionally sensitive to differences in the distribution of the individual cancer sites and, thus, deprivation-associated differences in the risk of cancer.

The number of avoidable excess deaths attributed to socioeconomic inequalities in cancer survival has previously been estimated for a few European countries only. Coleman et al. analyzed cancer survival of patients diagnosed from 1986–1990 in England and Wales. They showed that summed over 41 cancer sites 12,745 of 492,902 excess deaths could have been avoided per year (2.6%) if survival in all groups were comparable to the most affluent group [4]. In a more recent study from England, the differences of avoidable deaths between the years of diagnosis from 1996–2000, 2001–2003, and 2004–2006 were examined. Although the number of avoidable excess deaths decreased by approximately 2.0% over the calendar periods, disparities in survival persisted with a sum of 7122 avoidable deaths (11.0% of excess deaths) in 2004–2006 over the 21 cancer sites [26]. This estimate was much larger than the estimated 4100 avoidable excess deaths (3.0% of all excess deaths) over the 25 cancer sites in Germany.

For Nordic countries, Dickman et al. examined the reduction in cancer deaths if regional variation of survival were eliminated. It was found that summed over 12 cancer sites 5271 excess deaths (2.5% of all excess deaths) during 2008–2012 could have been avoided [11]. The proportion of avoidable deaths varied from 1.9% in Norway to 2.9% in Finland and Sweden. In that study, it was additionally estimated that 3.0% of all excess cancer deaths in Finland could have been avoided if all patients had the same survival as patients from the highest social class. Although social class and deprivation might not be directly comparable, this estimate is similar to the German estimate. In another study from Finland, it has been shown that 4% of all cancer deaths and 3% of all deaths among colon cancer patients under 90 years of age diagnosed in 2000–2007 could have been avoided if survival were in all regions similar to the regions with highest survival estimates. Again, this estimate is comparable to the estimated 3.9% avoidable excess deaths caused by area-based deprivation for colorectal cancer in Germany [33].

The number of avoidable excess deaths does not only depend on disparities in relative survival between deprivation groups but also on disparities in cancer incidence. For total cancer and most individual cancer sites, incidence increased with increasing deprivation. However, for melanoma, female breast, prostate, and testicular cancer incidence was highest in the least deprived regions. Overall, these differences in incidence resulted in a higher incidence of cancer sites with shorter survival times in more deprived regions. Consequently, the number of annual avoidable excess deaths and the proportion of excess deaths was much higher when pooling all cancer sites (N = 11,405, 7.9%) than when summing over the 25 most common cancer sites (N = 4100, 3.0%), although they represented 93.8% of all cancers.

Previous studies also provided evidence of differences of incidence between deprivation groups [28,34–36] including a recent study from Germany [36]. Hypothesized reasons for higher incidence in lower socioeconomic groups are a higher prevalence of lifestyle risk factors such as tobacco smoking, certain occupational and environmental factors in lower socioeconomic groups as well as differences in the use of screening procedures and detection of precancerous conditions and in situ tumors. Higher breast cancer incidence in women of higher socioeconomic status might be due to later first births and lower parity [34,36]. Differences in the uptake of cancer screening and access to primary care are further explanatory factors [34,35].

Since disparities of incidence between deprivation quintiles were more prominent in our study than survival differences, efforts to reduce excess incidence of cancers with poor prognosis are as important or even more important for reducing the surplus burden
of cancer deaths in populations in more deprived municipalities than efforts to equalize cancer survival across deprivation quintiles.

In our study, colorectal cancer contributed the largest numbers of avoidable excess deaths. For this cancer site, incidence increased strongly with increasing deprivation, while 5-year relative survival decreased remarkably leading to this rather large number of avoidable excess deaths. The increased incidence might be caused by a higher prevalence of lifestyle risk factors [36] as well as lower use of screening colonoscopy. However, the inequalities in survival in Germany are less well understood and require further investigation. [8] In a previous study from Germany, they could neither be explained by differences in stage distributions nor by screening colonoscopy participation rates on district level. Nevertheless, there is evidence that screening participation might be lower in persons with a lower socioeconomic position. [37] These inequalities might increase the number of avoidable excess deaths and highlight the need for efforts to reach socioeconomically disadvantaged persons in screening programs to avoid survival inequalities.

Although our study provides the first estimates of excess deaths that could have been avoided if deprivation-associated differences in relative survival were eliminated, some limitations should be considered. As we could not include data from all German federal states, we had to estimate disparities in survival and incidence from the study population. The largest proportions of the excluded population were in the second most deprived (40%) and the middle quintile (Q3, 31%). Although the excluded population lived on average in slightly more deprived municipalities, there is no theoretical indication that the association of deprivation and incidence and survival might be different in the excluded regions. Furthermore, most of the German population was covered (78%). The largest limitation in this regard is the exclusion of the two largest cities in Germany (Berlin and Hamburg). This exclusion was necessary as the German Index of Multiple Deprivation provides only one deprivation score for the whole city. Administrative statistics covering the whole of Germany are only available on a municipality but not on neighborhood level. However, it is well known that there are major socioeconomic inequalities within cities. Therefore, using one score for such a heterogeneous population would not reflect these deprivation-associated differences but dilute the association between deprivation and survival over the whole study population. Following this reasoning, we excluded these two large cities (population approximately 3.6 (Berlin) and 1.8 (Hamburg) million, respectively) from the analyses a priori. However, they are still included in the estimation of the German incidence estimates and classified by their overall deprivation score (Berlin: Q4; Hamburg: Q3). Assuming that there will be socioeconomic inequalities in cancer survival within these cities, it can be expected that our estimated number of avoidable excess deaths for Germany might be slightly underestimated.

A further limitation is that we did not include detailed analyses of possible sex and age-specific differences across deprivation quintiles. A previous study has shown that that deprivation-associated differences in incidence might differ between men and women. [36] Providing sex- and age-specific estimates would improve the estimation of avoidable excess deaths and provide more information on the population that could be specifically targeted to avoid these excess deaths. Our study used ecological data and cannot distinguish whether the deprivation-associated differences were driven by the deprivation level of the municipality or by the individual socioeconomic status of the patient. Although the ecological approach is feasible and important, as public health interventions could be applied on the municipality level, studies including area-based as well as individual deprivation measures are additionally needed to get a better understanding of the reasons of the socioeconomic inequalities. Another limitation is the restriction to five years of follow-up. Although deaths attributed to cancer mostly occur within five years of diagnosis, we may still have missed some excess mortality in later years and, thus, might have underestimated the number of avoidable excess deaths. A strong point for our study is that we took site-specific differences of cancer incidence into account. Furthermore, the use of the GIMD 2010 on a municipality level enabled a small-scale classification of
deprivation quintiles and we used life tables stratified by deprivation quintiles to account for differences in the background mortality across deprivation quintiles.

5. Conclusions

To conclude, 11,405 excess deaths (7.9% of excess deaths) in Germany could have been avoided per calendar year in 2013–2016 if survival and cancer site distribution of the least deprived regions applied to all regions. Summing over the 25 most common cancer sites, annually 4100 excess deaths (3.0%) could have been avoided. Colorectal, oral and pharynx, prostate, and bladder cancer contributed most to the avoidable deaths. Strong differences in cancer incidence across deprivation quintiles were observed, with generally higher cancer risks in more deprived areas. Our results provide a good basis to estimate the potential of intervention programs that target reducing socioeconomic inequalities in cancer burden.

Supplementary Materials: The following are available online at https://www.mdpi.com/2072-669
4/13/2/357/s1, Figure S1: Relationship between the number of avoidable excess deaths in the study population in 2013–17 and relative survival by cancer site.

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