Assessment of the Potential of Concentrating Cancer Care in Hospitals With Certification Through Survival Analysis

Potenzialabschätzung für die Konzentration der Versorgung von Krebspatient:innen in Kliniken mit DKG-Zertifizierung mittels Überlebenszeitanalyse

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Key words
cancer, certification, survival analysis

Schlüsselwörter
Krebs, Zertifizierung, Überlebenszeitanalyse

Bibliography
Gesundheitswesen 2023; 85 (Suppl. 3): S197–S204
DOI 10.1055/a-2132-6797
ISSN 0949-7013

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

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Deutsche Version und Zusätzliches Material unter: https://doi.org/10.1055/a-2132-6797

ABSTRACT

Background Certification programs seek to improve the quality of complex interdisciplinary models of care such as cancer treatment through structuring the process of care in accordance with evidence-based guidelines. In Germany, the German Cancer Society (Deutsche Krebsgesellschaft, DKG) provides a certification programme for cancer care that covers more than one thousand centers. In a recent retrospective cohort study, it has been shown on a large, nationwide data set based on data from a statutory health insurance and selected clinical cancer registries, that there is a benefit in survival for cancer patients who have received initial treatment in hospitals certified by the DKG. Here, we deduce two absolute measures from the relative benefit in survival with the aim to quantify this benefit if all patients had been treated in a certified center.

Methods The WiZen study analysed survival of adult patients insured by the AOK with a cancer diagnosis between 2009 and 2017 in certified hospitals vs. non-certified hospitals. Besides Kaplan-Meier-estimators, Cox regression with shared frailty was used for 11 types of cancer in total, adjusting for patient-specific information such as demographic characteristics and comorbidities as well as hospital characteristics and temporal trend. Based on this regression, we predict adjusted survival curves that directly address the certification effect. From the adjusted survivals, we calculated years of life lost (YLL) and number needed to treat (NNT), along with a difference in deaths 5 years after diagnosis.

Results Based on our estimate for the 537,396 patients that were treated in a non-certified hospital included in the WiZen study, corresponding to 68,7 % of the study population, we find a potential of 33,243 YLL per year in Germany based on the size of the German population as of 2017. The potential to avoid death cases 5 years from diagnosis totals 4,729 per year in Germany.

Conclusion While Cox regression is an important tool to evaluate the benefit that arises from variables with a potential impact on survival such as certification, its direct results are not well suited to quantify this benefit for decision makers in health care. The estimated years of life lost and the number of deaths that could have been avoided 5 years from diagnosis avoid mis-interpretation of the hazard ratios commonly used in survival analysis and should help to inform key stakeholders in health care without specialist background knowledge in statistics. Our measures, directly adressing the effect of certification, can furthermore be used as a starting point for health-economic calculations. Steering the care of cancer patients primarily to certified hospitals would have a high potential to improve outcomes.

ZUSAMMENFASSUNG

Hintergrund Zertifizierungsprogramme zielen darauf ab, die Qualität komplexer interdisziplinärer Versorgungsmodelle wie der Krebsbehandlung zu verbessern, indem der Versorgungsprozess nach evidenzbasierten Leitlinien strukturiert wird. In Deutschland bietet die Deutsche Krebsgesellschaft (DKG) ein Zertifizierungsprogramm für die Krebsversorgung an, das mehr als tausend Zentren umfasst. In einer kürzlich durchgeführten retrospektiven Kohortenstudie wurde anhand eines großen, bundesweiten Datensatzes, der auf Daten einer gesetzlichen Krankenversicherung und ausgewählter klinischer Krebsregister basiert, gezeigt, dass es einen Überlebensvorteil für Krebspatienten gibt, die in von der DKG zertifizierten Krankenhäusern erstbehandelt wurden. Hier leiten wir aus dem relativen Überlebensvorteil zwei absolute Maße ab. Dies geschieht mit dem Ziel, das Potential dieses Vorteils zu quantifizieren für die Annahme, dass alle Patienten in einem zertifizierten Zentrum behandelt worden wären.

Methoden In der WiZen-Studie wurde das Überleben von erwachsenen AOK-Versicherten mit einer Krebsdiagnose zwischen 2009 und 2017 in zertifizierten Krankenhäusern im Vergleich zu nicht zertifizierten Krankenhäusern analysiert. Neben Kaplan-Meier-Schätzern wurde für insgesamt 11 Krebsarten eine Cox-Regression mit sog. „shared frailty“ verwendet, die für patientenspezifische Informationen wie demografische Merkmale und Komorbiditäten sowie Krankenhausmerkmale und den zeitlichen Verlauf adjustiert wurde. Auf der Grundlage dieser Regression berechnen wir adjustierte Überlebenskurven, die den Zertifizierungseffekt direkt berücksichtigen. Anhand dieser adjustierten Überlebenskurven werden die verlorenen Lebensjahre (Life Years lost, YLL) berechnet. Ebenfalls berechnet wird die Number needed to treat (NNT) für Überleben 5 Jahre nach Diagnosestellung und die daraus resultierende Anzahl vermeidbarer Todesfälle.

Ergebnisse Basierend auf unserer Schätzung für die 537.396 Patienten, die in der WiZen-Studie in einem nicht zertifizierten Krankenhaus behandelt wurden, was 68,7 % der Studienpopulation entspricht, finden wir ein Potenzial von 33.243 YLL pro Jahr in Deutschland, berechnet auf Grundlage der deutschen Bevölkerung im Jahr 2017. Das Potenzial zur Vermeidung von Todesfällen 5 Jahre nach der Diagnose beträgt in Deutschland 4.729 Fälle pro Jahr.

Schlussfolgerung Die Cox-Regression ist zwar ein wichtiges Instrument zur Bewertung des Nutzens, der sich aus Adjustierung mit Variablen mit potenziellem Einfluss auf das Überleben ergibt, wie z. B. der Zertifizierung, aber ihre direkten Ergebnisse sind nicht gut geeignet, um diesen Nutzen für Entscheidungsträger im Gesundheitswesen zu quantifizieren. Die geschätzten verlorenen Lebensjahre und die Anzahl der Todesfälle 5 Jahre nach Diagnose, die hätten vermieden werden können, beugen einer Fehlinterpretation der in der Überlebensanalyse üblicherweise verwendeten Hazard Ratios vor und können dazu beitragen, eine Ergebnisdarstellung für wichtige Akteure im Gesundheitswesen ohne spezielles Hintergrundwissen in Statistik zu erreichen. Die hier vorgestellten Maße, die sich direkt auf die Auswirkungen der Zertifizierung beziehen, können darüber hinaus als Ausgangspunkt für gesundheitsökonomische Berechnungen verwendet werden. Die Steuerung von Krebspatient:innen in zertifizierte Krankenhäuser hätte ein hohes Potenzial, das Überleben bei Krebs zu verbessern.

Introduction

According to the National Cancer Plan, all cancer patients should receive treatment in accordance with evidence-based treatment guidelines [1]. With this aim, the German Cancer Society (Deutsche Krebsgesellschaft, DKG) has, as of 2003, established a certification programme that focuses on structuring the entire process of care in an evidence-based, guideline-adherent manner and is currently the largest in Europe [2, 3]. In order to obtain a DKG certificate, hospitals need to meet a specified set of professional and quality requirements based on S3-guidelines [2]. These requirements cover the entire process of oncological care. Structural requirements include e. g. multidisciplinary communication, psychooncological support, as well as connection to the outpatient sector, social care, and rehabilitation. Certified hospitals need to file annual reports via entity specific surveys and indicator sheets covering key figures, part of which are quality indicators as defined in S3-guidelines to retain the certificate. Requirements, surveys and indicator sheets are publicly available via the DKG website.

Hospitals that do not hold a certificate may meet the same structural requirements for cancer therapy, but are not obliged to do so. It is hence reasonable to assume that the measures required to meet certification criteria ultimately improve outcomes. The aim of the “WiZen”- study whose results serve as a basis for this article was to provide reliable evidence about the effectiveness of certification: The “WiZen Study” (Wirksamkeit der Versorgung in onkologischen Zentren/Effectiveness of care in oncological centres), funded by the Innovation Fund of the Joint Federal Committee (Gemeinsamer Bundesausschuss, G-BA, Funding number: 01VSF17020), provides a large and comprehensive analysis of survival in hospitals certified by the DKG vs. non-certified hospitals on the basis of nationwide AOK data and data from several clinical cancer registries. The study finds that - irrespective of the entity - treatment in a certified hospital increases the chances of survival of patients with incident cancer [4–6], consolidating previous evidence on beneficial effects of certification both nationally [7–10] and internationally [11–15]. The statutory health insurance AOK was covering, as of 2017, a total population of around 22 million adults. The study contains cohorts of patients with incident cancer for 11 entities in total ranging from 10,596 patients (cervical carcinoma) to 172,901 patients (lung carcinoma) in the years 2009–2017. Survival analysis was conducted for eleven entities separately, including Kaplan-Meier-estimates and Cox regression with shared frailty. These entities were colon and rectal cancer, lung cancer, pancreatic cancer, breast cancer, ovarian, endometrial and cervical cancer, prostate cancer, head and neck cancers and brain tumors, defined via ICD-10 codes, see Supporting ▶ **Table 1**. For each entitity, a set of covariates was considered that consisted of patients' demographic information (age, sex), disease-related information (distant metastasis, secondary malignoma, comorbidities) and hospital-level information (hospital status – teaching, university hospital, and ownership, as well as number of beds) and the calendar year of treatment to take into account effects of medical progress. The relative survival advantages were between 3 and 26 percent for the 11 entities and cohorts studied (▶ **Fig. 1**).

Across entities, less than half of patients with incident cancer were treated in certified hospitals during the study period (2009–2017) and the proportion of patients treated in certified hospitals was 31.3 % during the observation period. The proportion of patients who have been not been treated in a certified hospital ranges from 36.5 (breast cancers) to 92.5 per cent (brain cancers), ▶ **Fig. 2**.

Given that, as a result of the WiZen study, the certification effect showed a benefit in survival across entities, the question arises what this benefit would have encompassed had all patients been treated in a certified center. While survival analysis constitutes a powerful tool to evaluate effect of treatments for diseases such as cancer its direct results are not well suited to quantify this benefit:

Cox regression addresses the effect of multiple variables upon the survival time, and is hence suited to quantify the effect of certification. However, results of a Cox regression are typically presented in terms of Hazard ratios, i. e. the relative impact a given variable has on the (time-dependent) hazard with respect to a given reference level, e. g. presence vs. absence of a covariate. The hazard ratio constitutes a relative measure whereas in many settings the impact on a given population in terms of absolute numbers is required. This is particularly true for patients, who can interpret an absolute risk or chance such as the number needed to treat (NNT) much better than a relative risk or hazard ratio. For health policy makers, quantification of the total absolute effect as characterized by Years Life Lost (YLL) is of high importance [16]. In addition, the interpretation of a hazard ratio requires a specialized background in survival analysis and calls for careful communication [17]. The hazard ratio is thus critisized for not being particularly suited to illustrate study findings to, e. g. decision makers and other stakeholders in health care and concepts to avoid using it altogether are emerging [18–21].

In this article, we compute two absolute measures from adjusted survival curves that incorporate the results from Cox regression, but do not rely on solely reporting the hazard ratios. The first measure is the number needed to treat (NNT), which allows to quantify the difference in deaths after a given point in time after diagnosis between two groups. The second measure is years of life lost (YLL), which is commonly used in the communication of statistical assessment for burden of disease for e. g. cancer and diabetes by. e. g. the Robert-Koch-Institute (RKI) and the National Cancer Institute (NCI) [22–24]. We deduct both measures from survival curves as predicted by adjusted Cox regression, allowing us to focus on the cerfication effect only.

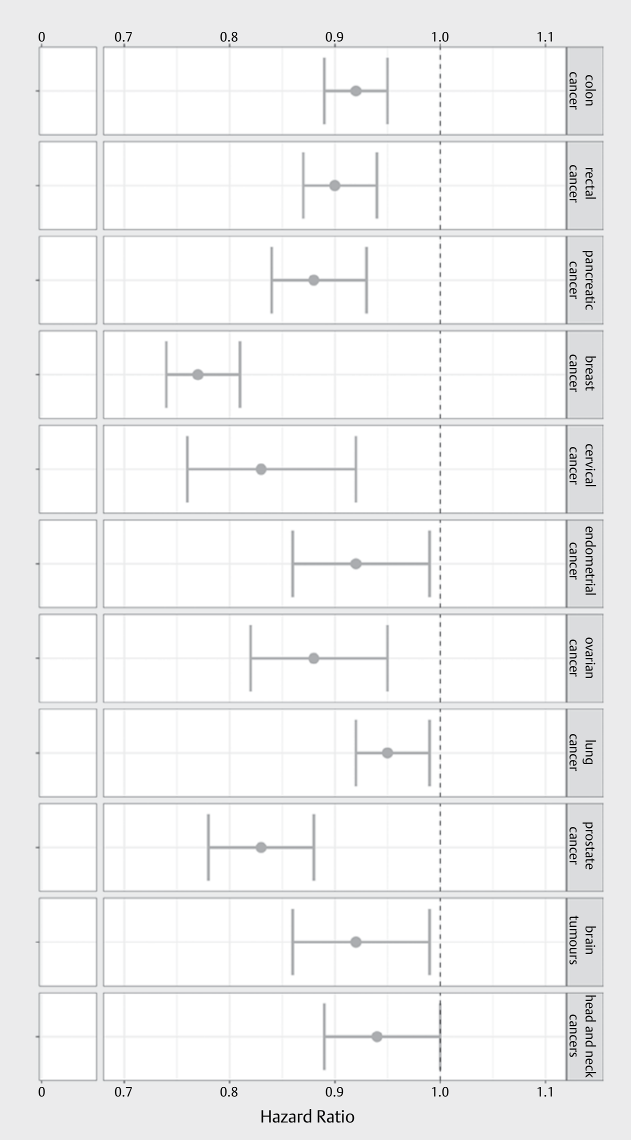
Our approach allows for combination of results from multivariate statistical analysis with a framework that we feel is suited for communication of the effectiveness of a health-care intervention with non-statisticians.

Methods

We use Cox regression with shared frailty [25, 26] for each entity separately for a given set of covariates detailed in [4] and summa-

▶ **Table 1** Analysis of Life Years Lost per year for the tumour entities investigated.

Entity	n (non-certified)	proportion (%) (non-certified)	Difference in area between survival functions	Difference for non- certified population (YLL)	Potentially lost life years YLL/yr in Germany (year of reference, 2017)
Colon cancer	68,826	62.7	0.21	14,495	5,114
Rectal cancer	29,370	57.1	0.24	7,042	2,484
Pancreatic cancer	39,892	88.0	0.17	6,649	2,346
Breast cancer	52,451	36.5	0.29	15,465	5,456
Cervical cancer	16,031	77.1	0.32	5,078	1,791
Endometrial cancer	7,769	73.3	0.38	2,984	1,053
Ovarian cancer	24,222	80.5	0.13	3,116	1,099
Lung cancer	139,115	80.0	0.05	7,152	2,523
Prostate cancer	57,112	70.0	0.25	14,305	5,047
Brain tumors	58,032	92.5	0.19	11,304	3,988
Head and neck cancers	44,576	84.5	0.15	6,642	2,343
total	537,396	-		-	**33,243**



▶ **Fig. 1** Adjusted hazard ratios (95 % confidence intervals) of overall survival for treatment in DKG-certified vs. non-certified hospitals for the eleven entifies considered.

rized in Table S2. The resulting hazard ratios for each covariate indicate the extent to which the prognosis changes relatively with respect to a reference level of each variable. A hazard ratio > 1 indicates a poorer prognosis for the assoated variable compared to the reference level, and a hazard ratio < 1 indicates a beneficial effect. The Cox regression assumes that on a baseline which is determined in the regression, the adjusted hazard behaves proportionally to the baseline hazard with respect to the hazard ratio of a specific covariate ("proportional hazards assumption"). The probability of survival (or death) is then calculated as a prediction of a survivor function, based on an exponential transformation of the adjusted hazard function . This prediction of a survivor curve, is based on the entire model result, i. e. the hazard (ratios) of all covariates as well as the baseline hazard. The prediction must be made on a model population. The model population used here is defined by the mean value over all covariates of the actual population, i. e. mean value of age group, mean value of sex m/f, mean value of oncological second disease, etc. Stratifying variables are excluded from mean calculation. The prediction based on the model results on the model population yields an adjusted survival curve. This survival function in analogy to a Kaplan-Meier-curve starts with value one at time zero and decreases over time in a non-linear fashion. Since we are interested in a survival probability in certified/non-certified centres, the survival function is computed upon stratification by certified/non-certified hospitals.

Hence, two predictions using all estimators from the model on the mean model populations are performed, for an "all certified" and an "all non-certified" case. The covariates, with the exception of certification, are therefore identical for both strata. Fig. 3 shows a schematic representation of these two predictions. From these predictions, we compute two measures, i) the number of life years lost and ii) the number needed to treat (NNT) for one additional patient to survive at least five years after diagnosis. As the survival function is time-dependent, all considerations that result in absolute measures must be supplemented with a time reference.

Life Years Lost (YLL)

The years of life lost due to initial treatment in a certified center compared to a non-certified hospital correspond to the area separated by the two survival curves. It is therefore the difference between the areas under the respective survival curves. As the time of follow-up is restricted, we introduce a cutoff to the area, which corresponds to censoring for all values that exceed cutoff. Our total observation time is nine years; we set the cutoff to eight years to account for uncertainty in the prediction towards the end of the observation time, hence estimating a lower bound of the area. This area is now rescaled with the population in the non-certified setting, pop_{ncert} , resulting in an estimate of Years of life lost (YLL) due to the fact the hospitals were non-certified:

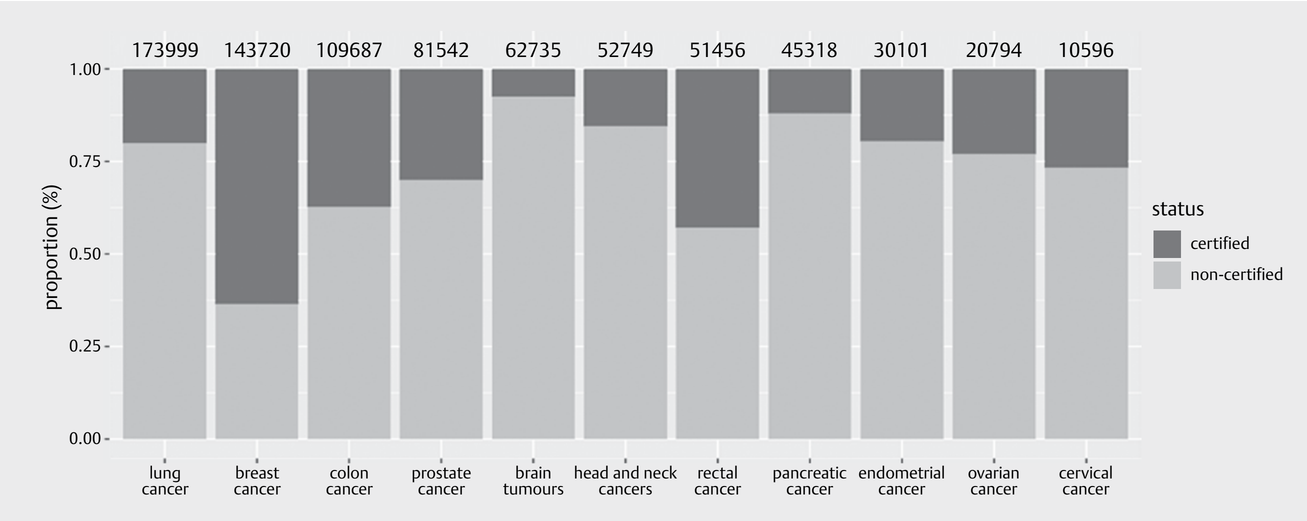
$$YLL = area * pop_{ncert}$$

Note that in our variant for life years lost, we do not explicitely take into account a person's age at onset of disease as is common in epidemiology for computation of years of life lost due to mortality. Here, the age at the onset of diagnosis is incorporated as covariate into the prediction of the survival curve and through the median population.

NNT and avoidable deaths within 5 years of diagnosis

The number needed to treat (NNT) related to the certification effect, is given by the inverse difference in the two survival functions for a given time t_{surv}. We set this survival time to t_{surv}. = 5 years, as the 5-year survival is an important outcome and a broadly used epidemiological measure for the burden of disease in oncology. This time period is also relevant for patients because after this time the incidence of recurrences is significantly reduced in most cases and follow-up care is usually also terminated.

$$NNT = \frac{1}{s(t_{surv})_{cert} - s(t_{surv})_{ncert}}$$



▶ **Fig 2** Proportion of patients that have/have not received treatment in a DKG-certified hospital per entity, along with the number of patients in each entity.

where s(t) is the simulated survival at time *t* for stratum *X*. Rescaling with the population in the non-certified setting results in an estimate of the number of deaths that could have been avoided within 5 years from diagnosis:

$$N_{avoidable\ deaths} = pop_{ncert}/NNT$$

Results

Adjusted survival functions were computed based on Cox regression with shared frailty for each entity separately for a given set of covariates. This set was identical for each entity with the exception of comorbidities that are entity-specific as defined by clinical experts, see Supporting Table S2. Within the WiZen study, we fitted Cox regression models upon gradually increasing the sets of covariates and found that the cerfication effect does not depend substantially on the choice of model [4]. The concordance (Harrels' C) for these models is increasing with model complexity. The increase is substantial upon adding disease-related information to the core set (certification, age, sex), and marginal upon addition of hospital-related covariates and year of diagnosis. It becomes maximal and ranges from 0.67 to 0.82 for the model including the full set of covariates across entities, Supporting Table S3. We thus compute adjusted survivals for each entity from the model with the best concordance, i. e. the one including all covariates, with hazard ratios ranging from 0.77 to 0.92 across entities, Supporting Table S4.

Life Years Lost (YLL)

The estimation of the potential of care through treatment of patients with incident cancer into certified hospitals is based on the difference of the area under the adjusted survival function of the treatment in certified hospitals and the treatment in non-certified hospitals simulated from the Cox regression (see Fig. 3). Due to the limited observation period of the WiZen study of 9 years, the period up to 8 years after diagnosis was considered as the cutoff limit. The results are therefore conservative and include only the years of life lost within this period.

Taking into account the proportion of the national population insured by AOK, which was $AOK_{coverage\ 2017}$ = 31.5 % (people insured by the AOK as of July 2017: 25.990.759, German population 2017: 82.522.000, [27]), we estimate for "Life Years Lost/yr in Germany" based on the WiZen project results for the overall population in Germany from:

$$\frac{YLL_{Germany}}{yr} = area * \frac{pop_{ncert}}{observation\ period\ 9yrs * AOK_{coverage\ 2017}}$$

The following ▶ **Table 1** shows the Life Years Lost for the 11 entities examined. The number of people affected for each entity determines the benefit in survival on a population level. The total number of patients treated in a non-certified hospital ranges from 7,769 for endometrial to 139,115 patients for lung cancer. The size of the population hence adds an essential contribution to the total YLL. The size of the area between survival functions serves as a guideline to the extent of the certification effect for each entity: if the area increases the benefit in overall survival increases as well. Hence, the YLL becomes maximal for entities that have a larger benefit, but also many people affected, as is the case for e. g. breast, colon and prostate cancer in contrast to lung cancer (small effect) or endometrial cancer (less people affected).

In total, there is a potential of around 33,200 life years saved per year in Germany.

NNT and avoidable deaths within 5 years of diagnosis

In a next step, the number needed to treat is computed based on the WiZen results. Using the population of patients treated in certified and non-certified centres, we then use the NNT which indicates the potential to avoid one death within 5 years of diagnosis to assess the potential for the total of avoided deaths within 5 years after diagnosis.

▶ **Table 2** Analysis of potentially avoidable deaths within 5 years after diagnosis per year for the tumour entities investigated.

Entity	n (non- certified)	proportion (%) (non- certified)	crude 5-yr survival rate, non-certified	difference certified/non-certified from adjusted 5-yr-survival rate *	number needed to Treat (NNT) *	deaths 5 yrs post-diagnosis that could have been avoided/yr (Germany) *
Colon cancer	68,826	62.7	0.467	0.031	32	754
Rectal cancer	29,370	57.1	0.433	0.036	28	372
Pancreatic cancer	39,892	88.0	0.065	0.014	70	202
Breast cancer	52,451	36.5	0.719	0.046	22	859
Cervical cancer	16,031	77.1	0.357	0.046	22	258
Endometrial cancer	7,769	73.3	0.533	0.057	18	156
Ovarian cancer	24,222	80.5	0.650	0.020	51	168
Lung cancer	139,115	80.0	0.169	0.006	179	274
Prostate cancer	57,112	70.0	0.712	0.039	26	789
Brain tumors	58,032	92.5	0.480	0.027	37	555
Head and neck cancers	44,576	84.5	0.453	0.022	46	341
total	537,396	-	-	-	-	**4,729**

* from adjusted survival curve.

The calculation of avoidable deaths results from the difference of the survival curves after 5 years (Fig. 3), in analogy to the procedure for Life Years Lost related to the federal population 2017 as:

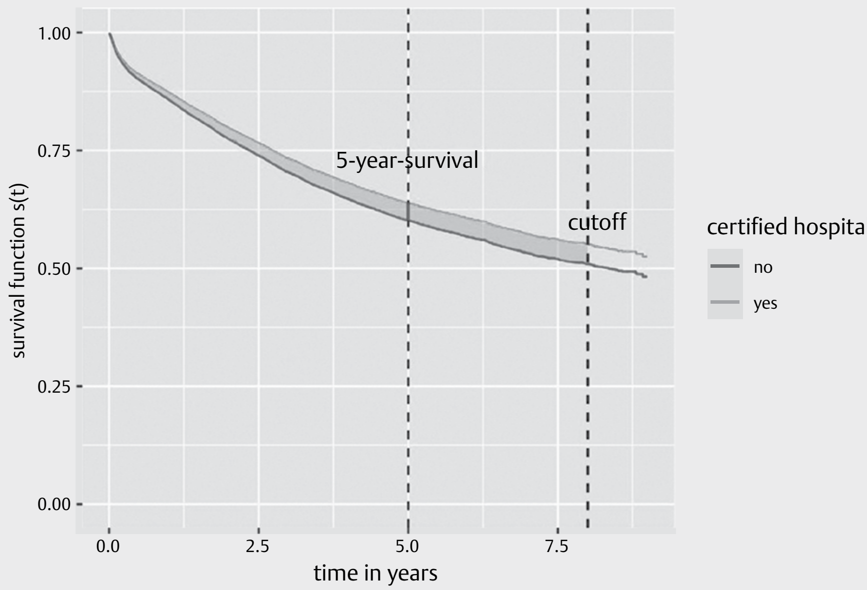
$$\frac{N_{avoidable\ deaths\ Germany}}{yr} = \frac{pop_{ncert}}{NNT * observation\ period\ 9yrs * AOK_{coverage\ 2017}}$$

The results are shown in ▶ **Table 2** for each entity individually. For cancers with very low chance of (crude) survival after five years, such as pancreatic cancer and lung cancer, the difference in the survival function is small as well, reflecting the lesser (overall) chance of preventing death with fighting the most deadly cancers. In analogy to YLL, the number of avoidable deaths scales with the size of the population for each entity, and, as a consequence, a large number of people who have not been treated in a certified setting provides a larger potential for avoidable deaths 5 years post-diagosis, which we find for colon, breast, and prostate cancer. In total, approx. 4,700 deaths per year could have been avoided 5 years post diagnosis if all patients had been treated in a certified cancer.

Discussion

We illustrated how to derive Life years lost and the Number needed to treat from adjusted survival functions that were computed based on the results of the WiZen study. We have derived these measures from the cohort used in the WiZen study which includes AOK-insured patients that were diagnosed with one out of eleven types on cancers within the years 2009–2017. Based on the 537 396 patients or 68,7 % of the study population in the cohort who have not received treatment in a certified hospital, we estimated a total of 33 243 YLL per year for the entire German population as of 2017. The corresponding potential to avoid death cases for as long as five years within diagnosis sums up to 4 729 per year in Germany. Both YLL and NNT depend on the entity specific survival that was estimated based on the Cox regressions, as well as the size of the population under consideration. The difference in survival curves (both in area and for the 5 year limit) tends to be smaller for cancers with overall low survival prospects, such as pancreatic cancer. Beyond this observation, we currently do not have any additional information about the range of differences, which may arise from many factors both on the cohort and on the intervention level. As the size of the population under consideration varies significantly, the greatest contribution to the total deaths that could be avoided arise from cancers that have either high incidence such as e. g. breast and colon cancer or a very low proportion of certified centers such as brain tumours. To date, we are not aware of any literature about YLL and the assesment of avoidable deaths in the context of certification, beyond the national [7–10] and international [11–15] evidence about the benefits of structuring the process of cancer care, be it via certification or accredition.

Our findings have a set of limitations: As in any communication of statistical results, it needs to be pointed out that the estimates presented here are based on various assumptions and do, to some extent, depend on the method [28]. The rescaling from the original population that covers patients insured by the AOK,which is roughly one third of the German population, to the entire size of the population serves as a rough estimate to estimate the total YLL and the number of deaths within 5 yrs from diagnosis that could have been avoided. The validity of this extrapolation is based on the assumption that the cohort on which the survivals were predicted adequately represents the epidemiology of the disease in Germany, which we feel is a valid assumption given the large size of the cohort. Another limitation and one of the most unfortunate shortcomings of health insurance data is that these contain very litte information on important cancer-related measures such as staging and grading. The quality of the data, and hence, the model prediction could be improved by e. g. linking SHI data with data from cancer registries as evaluated in [29].



▶ **Fig 3** Schematic representation of the calculation of Life Years Lost, corresponding to the area between two adjusted survival curves in the period up to 8 years ("cutoff"). Also shown is the difference in survival after 5 years, as used in the calculation of avoidable deaths.

The strength of this assesment lies in that our estimates avoid the reporting, and thus potential for misinterpretation, of the hazard ratio and can be used to inform political decision makers about the extent of the benefit in survival found in the WiZen study. As our estimates provide absolute results such as the amount of deaths within five years of diagnosis, they can be used in health-economic analyses that deal with e. g. certification and cost-effectiveness [30].

CONCLUSION

For each individual entity, steering into certified centres would have a relevant effect on preventable deaths within 5 years of diagnosis. The Number Needed To Treat, i. e. the number of additional patients to be treated in a certified centre in order to avoid a death 5 years post-diagosis, also depends on the general prognosis of the entities. For example, the Number Needed To Treat is higher for cancers with a generally poor prognosis, such as lung cancer or pancreatic cancer.

Through illustrating the potential in survival benefit from certification in the past decade, our analysis provides a starting point for a broader discussion of political implications that would either foster certification and/or install a coordinated effort to steer patients into certified hospitals.

Ethics declaration

The WiZen study was approved by the ethics committee of the TU Dresden (approval number: EK95022019, IRB 00001473, OHRP IORG0001076). Data processing and analyses was conducted in line with the Declaration of Helsinki and the General Data Protection Regulation of the European Union.

Contributor's Statement

None

Fundings

Innovationsfonds — 01VSF17020

Conflict of Interest

VB, JS, and OS work at a university hospital with certified cancer centers. In addition, they received funding from the Innovation Committee of the Federal Joint Committee during the conduct of the study. Unrelated to this study, JS reports institutional grants for investigator-initiated research from the German GBA, the BMG, BMBF, EU, Federal State of Saxony, Novartis, Sanofi, ALK, and Pfizer. He also participated in advisory board meetings as a paid consultant for Sanofi, Lilly, and ALK. Unrelated to this study, OS worked as a paid consultant for Novartis. He is also a member of the certification commission "Skin Cancer Centers" of the German Cancer Society and a member of the expert panel in the project "Development of Criteria for the Evaluation of Certificates and Quality Seals in Accordance with Section 137a (3) Sentence 2 Number 7 SGB V" for the Institute for Quality Assurance and Transparency in Health Care (IQTIG). The other authors declare that they have no conflict of interest.

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