Received: 16 March 2021 | Revised: 22 June 2021 | Accepted: 23 June 2021

DOI: 10.1002/ijc.33728

CANCER EPIDEMIOLOGY

IJC International Journal of Cancer

Do certified cancer centers provide more cost-effective care? A health economic analysis of colon cancer care in Germany using administrative data

Chih-Yuan Cheng[1,2] | Thomas Datzmann[3,4,5,6,7] | Diego Hernandez[1] | Jochen Schmitt[3,4,5,6,7] | Michael Schlander[1,2,8,9]

[1]Division of Health Economics, German Cancer Research Center (DKFZ), Heidelberg, Germany

[2]Mannheim Medical Faculty, University of Heidelberg, Mannheim, Germany

[3]Center for Evidence-based Healthcare (ZEGV), University Hospital and Medical Faculty Carl Gustav Carus, TU Dresden, Dresden, Germany

[4]National Center for Tumor Diseases (NCT), Dresden, Germany

[5]German Cancer Research Center (DKFZ), Heidelberg, Germany

[6]Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

[7]Helmholtz-Zentrum Dresden—Rossendorf (HZDR), Dresden, Germany

[8]Alfred Weber Institute, University of Heidelberg, Heidelberg, Germany

[9]German Cancer Consortium (DKTK), Core Center Heidelberg, Heidelberg, Germany

Correspondence
Chih-Yuan Cheng and Michael Schlander, Division of Health Economics, German Cancer Research Center (DKFZ), Im Neuenheimer Feld 280, 69120 Heidelberg, Germany.
Email: chih-yuan.cheng@dkfz-heidelberg.de (C.-Y. C.) and m.schlander@dkfz-heidelberg.de (M. S.)

Abstract

Hospital certification has become an important measure to improve cancer care quality, with the potential effect of prolonging patient survival and reducing medical spending. However, yet to be explored is the cost-effectiveness of cancer care provided in certified hospitals, considering significant additional costs incurred from certification requirements. We performed a cost-effectiveness analysis (CEA) using two colon cancer populations (N = 1909) treated in different levels of certified hospitals (CHs) vs noncertified hospitals (NCHs) from a healthcare system's perspective. We matched patient-level data of incident colon cancer cases, diagnosed between 2008 and 2013 from a large statutory health insurance in Saxony, Germany, to calculate net treatment costs by phase (initial, continuing and terminal phase). The costs were supplemented with extra costs from 31 additional services required for certification. Effectiveness measure was total survival time in life-years. Outcome of interest was incremental costs per additional life-year. The annualized net colon cancer treatment costs by phase showed a U shape with high costs in the initial (mean €26 855; 95% CI €25 058-€28 652) and the terminal phases (mean €30 096; 95% CI €26 199-€33 993). The base-case CEA results and all sensitivity analyses consistently demonstrated longer survival and lower costs for the colon cancer cohort treated in CHs vs NCHs. To conclude, we used administrative data to derive the first cost-effectiveness evidence supporting that colon cancer care delivered in the certified cancer centers in Germany improves survival outcomes and saves costs from a healthcare system's perspective. Generalization of the study results should be exercised with caution.

KEYWORDS
cancer care costs, cancer care quality, colon cancer, cost-effectiveness, hospital certification

Abbreviations: C, organ cancer centers; CC, oncological centers; CCC, Comprehensive Cancer Centers; CEA, cost-effectiveness analysis; CH, certified hospitals; CI, confidence interval; CMI, case mix index; DGAV, German Society for General and Visceral Surgery; DKG, German Cancer Society (*Deutsche Krebsgesellschaft*); DKH, German Cancer Aid (*Deutsche Krebshilfe*); DRG, diagnosis-related group; ICER, incremental cost-effectiveness ratio; IQWiG, the Institute for Quality and Efficiency in Health Care (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*); NCH, noncertified hospitals; PSA, probabilistic sensitivity analysis; RMST, restricted mean survival time; SHI, statutory health insurance.

What's new?

The implementation of quality standards aimed at ensuring high-level care for cancer patients frequently involves hospital certification or accreditation. Whether hospital certification is cost-effective, however, remains unknown. In this study, the authors examined the cost-effectiveness of certification for cancer centers in Germany by analyzing the associated costs and total survival time in life-years among colon cancer patients. Analyses revealed improved survival among colon cancer patients and reduced costs for care in certified centers compared to noncertified centers. The results support the use of cancer center certification as a means of improving patient prognosis without creating extra economic burdens to healthcare systems.

1 | INTRODUCTION

Colorectal cancer is one of the most common cancers and leading causes of death worldwide.[1] It has become fundamental to enhance the quality of colorectal cancer care by implementing quality standards—as needed for all cancer types—that are developed by professional bodies through hospital certification (as in Germany) or accreditation (as in the United States).[2-4]

In Germany, the certification for cancer care has been provided by the German Cancer Society (*Deutsche Krebsgesellschaft*, DKG) since 2003, in which a three-level pyramid model for cancer care was established (see Appendix A).[3,5] The foundation of the pyramid is laid by widespread organ cancer centers (noted as C) specializing in a specific type of cancer care. The second level consists of oncological centers (noted as CC), which are capable of handling treatments for multiple types of tumor entities. At the top of the pyramid are the Comprehensive Cancer Centers (noted as CCC), which, in addition to providing care for multiple cancer entities, are responsible for research and development of novel cancer therapies or new care standards and the coordination of the regional hospital network.[5] Centers at different levels need to meet quality criteria to be certified and recertified every 3 years.[6] Criteria include the commitment to national cancer treatment guidelines, the establishment of patient pathways, and the organization of tumor conferences.[5,7]

One way to measure the quality of cancer care is to evaluate patients' prognoses. Some studies have investigated the effectiveness of the hospital certification based on patients' survival rates and prognoses, including colon cancer, which showed improved short- and long-term survival.[4,8-11] In addition to improving clinical outcomes, DKG cancer center certification also aimed to increase "economic efficiency" by "avoiding multiple examinations, ensuring a tight organizational structure using patient routing, and common purchasing (e.g., of drugs)."[8] However, few studies to date quantified the economic benefits of cost reduction in certified cancer centers,[2] and no study was done in Germany.

Moreover, it is not clear whether the reduced spending achieved by fostering specialized cancer centers through certification could compensate for the additional costs incurred from certification requirements, where a significant part of such additional costs are currently not adequately reflected by the German reimbursement structure using a diagnosis-related group (G-DRG).[8] For example, the variable costs resulting from tasks required for the certification of a breast cancer center (a university hospital) and the following four annual audits could mount up to €237 303 (in 2007 Euros).[12] A more recent study differentiated the fixed and variable costs to estimate the additional costs for different levels of DKG-certified cancer centers in Germany and found that the estimated annual costs for an organ cancer center with 150 colon cancer patients per year totaled up to €0.2 million (in 2016 Euros).[13]

Given the current literature, cancer care provided by certified centers appears to be cost-effective from a German healthcare payer's perspective when taking into account an improved survival, potential reduced medical spending, and the fact that the additional costs related to certification are not borne by the statutory health insurance (SHI).[7,8] Nonetheless, if we take a healthcare system's perspective, will the cost-effectiveness of care from certified centers remain if the additional costs related to certification are considered? To our knowledge, this question has not been addressed in the literature, and we aim to explore it in this paper.

Based on a colon cancer cohort from a previous study[4] using a large administrative healthcare dataset from a German SHI company, we estimated the costs of colon cancer care and overall survival in certified hospitals (CHs) and noncertified hospitals (NCHs), respectively, and supplemented it with estimations of additional costs stemming from certification requirements for CHs.[13] Finally, we investigated the cost-effectiveness of colon cancer care provided by CHs from a healthcare system's perspective.

2 | METHODS

We performed a cost-effective analysis (CEA) of colon cancer care provided by CHs based on two colon cancer patient cohorts treated in CHs vs NCHs, from a healthcare system's perspective. The costs consisted of two parts: net colon cancer treatment costs reimbursed

by the SHI for both CHs and NCHs, as well as the nonreimbursed additional costs arising from certification requirements for CHs. Effectiveness was measured by the total survival time among colon cancer patients treated in CHs and NCHs, respectively. The outcome of interest was the incremental cost per additional life-year. We assumed the cohorts started treatments at the same time and lived past the median survival time in the respective group. The base-case costs and effectiveness (total life-years) were discounted with a 3% annual rate,[14] and all costs were inflated using the Health Consumer Price Index for Germany[15] to 2019 Euro. The analyses were performed using R software, version 3.6.0.

2.1 | Data source

To analyze the reimbursable treatment costs and the survival data for colon cancer patients, we used an administrative database of a large SHI company (AOK PLUS) covering approximately 2 million people (~50% of the general population) in the federal state of Saxony, Germany. It contained pseudonymized inpatient, outpatient, and individual information at the patient-level in the years 2005-2014. Further details regarding the database are described elsewhere.[4] We followed the data protection and security procedures precisely as laid out in the Data Use and Transfer Agreement with AOK PLUS. Further details about data protection are provided in the Data Availability Statement section. For the nonreimbursed additional costs, we drew from a study by Hölterhoff et al,[13] contracted by German Cancer Aid (*Deutsche Krebshilfe*, DKH) and German Cancer Society (DKG). It included estimated additional costs arising from various services or tasks demanded to meet cancer center certification criteria.[13]

2.2 | Costs—Net colon cancer treatment costs

2.2.1 | Phase of cancer care

We followed previously described methods[16-20] to estimate the costs of cancer care by phases—the initial, continuing and terminal phase. The initial phase comprises the first 12 months postdiagnosis, whereas the terminal phase consists of the last 12 months before death. The continuing phase is the remaining period in between the initial and terminal phases. A "U-shaped" distribution of the costs is expected,[16,19,20] namely high costs are to be observed in the initial and terminal phases while low costs are expected in the continuing phase. Assuming not every patient survived more than 24 months to be included in all three phases, patients' follow-up periods were allocated sequentially first to the terminal, then to the initial, and lastly to the continuing phase.[16,17,20]

2.2.2 | Patient identification

In a previous study,[4] we identified 6186 patients with incident colon cancers. The included patients met the following criteria: (a) continuously

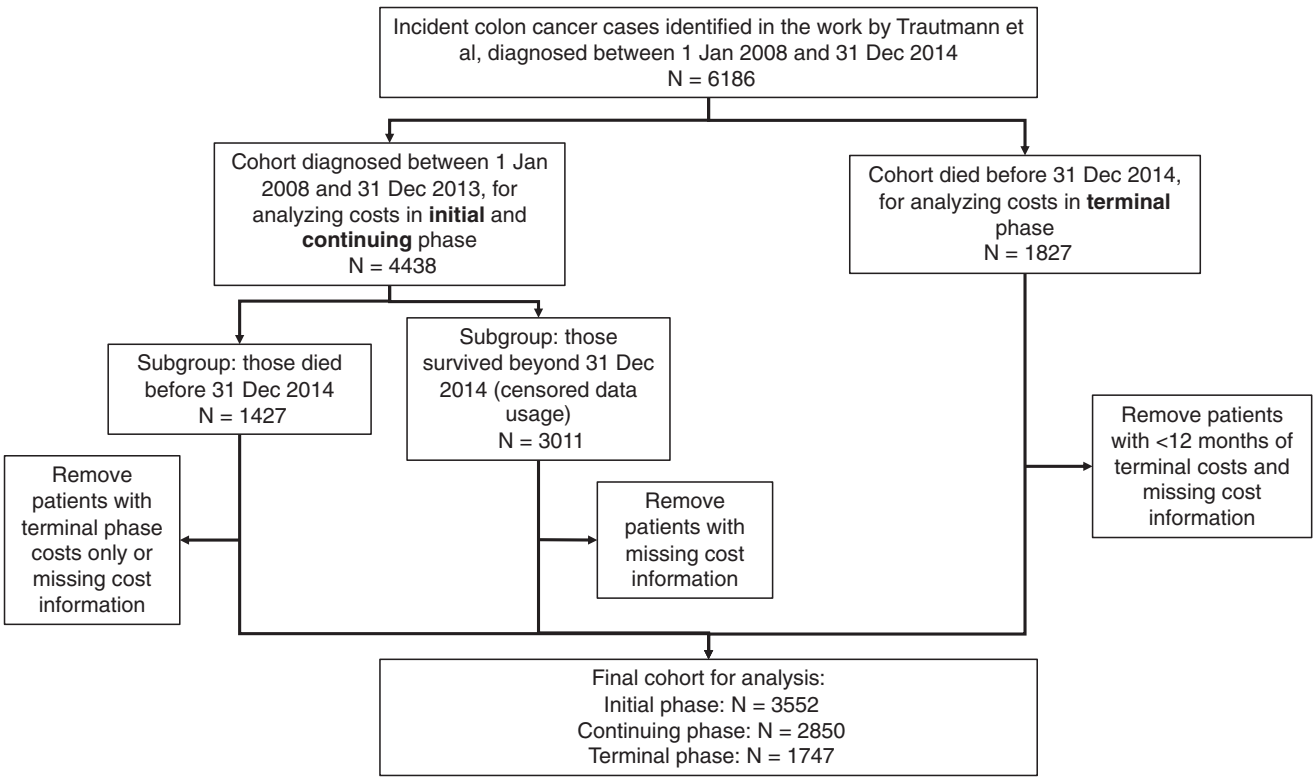

FIGURE 1 Patient selection flowchart

insured by AOK PLUS throughout the study period or until death; (b) with an inpatient diagnosis of malignant neoplasm at the colon/rectosigmoid junction (ICD-10-GM C18/C19) and at least one hospitalized surgical treatment between January 1, 2008 and December 31, 2014; (c) no inpatient diagnosis (C18/C19) within 3 years prior to the diagnosis; (d) no outpatient visits with diagnosis C18/C19 prior to 1 year before the diagnosis. The diagnosis date was defined as the first hospital admission due to the diagnosis C18/C19.

In the present study, we introduced further criteria to select the study population. Given that some patients survived beyond the observational period (December 31, 2014), making it impossible to assign the terminal phase, we kept only the patients who died before December 31, 2014 to analyze the terminal phase costs (N = 1827).

For the analysis of the initial and continuing phases, to ensure at least 12-month follow-up, we included only the patients diagnosed between January 1, 2008 and December 31, 2013 (N = 4438). Among this cohort, some also survived beyond the observational period. Therefore, we censored the use of cost information for this subgroup of survivors until December 31, 2013 (N = 3011). This guaranteed the remaining costs for the survivors could be properly allocated to the initial and continuing phases. See Figure 1 for the patient selection flowchart.

2.2.3 | Control group selection

We performed two separate 1:10 propensity score matching with a standard caliper width of 0.05[21] for cases in (a) the initial and continuing phase and (b) the terminal phase, respectively. General matching criteria included birth year (grouped by 10-year interval), sex, and four selected comorbidities (see Appendix B for further details). The year and quarter of death and hospital admission within 1 year before death were additionally used to match terminal phase controls. Controls for cases in initial and continuing phases were matched by year from 2008 to 2013 and combined afterwards. For each year, only controls with at least one hospital admission (of any cause) were included. For each of the matched controls in the initial and continuing phase cohort, we assigned a pseudodiagnosis date which corresponded to the diagnosis date of a patient.[16]

2.2.4 | Cost calculation

We summed all the inpatient and outpatient (including consultation, procedures and medications) costs as well as the entire follow-up months for each subject by the allocated phase. We then calculated the mean monthly costs by phase for the patient and control groups, respectively. To prevent skewness from extreme outliers (especially in the control group), we winsorized the extreme cost estimates for each phase in both patient and control groups to the top and bottom 5% values within the cohort before calculating the means.[19] The average monthly net colon cancer treatment costs for each phase were the difference of the mean monthly phased costs between the patient and control groups, and they were then annualized. All net treatment costs were calculated with 95% confidence intervals (CI).

TABLE 1 Description of the parameters used in the formula

Parameter	Description
Total life-years	
LY_{CH}	Total life-years within the CH cohort
LY_{NCH}	Total life-years within the NCH cohort
$Surv_{CH12}$	Restricted mean survival time for the patients treated in CMI 1 and 2 CHs, that is, C-level hospitals
$Surv_{CH34}$	Restricted mean survival time for the patients treated in CMI 3 and 4 CHs, that is, CCCs and CCs
$Surv_{NCH12}$	Restricted mean survival time for the patients treated in CMI 1 and 2 NCHs
$Surv_{NCH34}$	Restricted mean survival time for the patients treated in CMI 3 and 4 NCHs
N_{CMI12}	Number of patients treated within CMI 1 and 2 hospitals
N_{CMI34}	Number of patients treated within CMI 3 and 4 hospitals
Total costs	
$Cost_{CH}$	Total costs within the CH cohort
$Cost_{NCH}$	Total costs within the NCH cohort
$Cost_{CH-T}$	Total colon cancer net treatment costs within the CH cohort
$Cost_{NCH-T}$	Total colon cancer net treatment costs within the NCH cohort
$Cost_{CH12}$	Average colon cancer net treatment costs for patients treated in CMI 1 and 2 CHs, that is, C-level hospitals
$Cost_{CH34}$	Average colon cancer net treatment costs for patients treated in CMI 3 and 4 CHs, that is, CCCs and CCs
$Cost_{NCH12}$	Average colon cancer net treatment costs for patients treated in CMI 1 and 2 NCHs
$Cost_{NCH34}$	Average colon cancer net treatment costs for patients treated in CMI 1 and 2 NCHs
$Cost_{Add}$	Total additional costs resulted from additional services required by certification
$Cost_{Add-F}$	Total annual additional costs which are fixed costs for each level of hospitals (CCC, CC or C)
$Cost_{Add-V}$	Average annual additional variable costs per colon cancer patient for each level of hospitals (CCC, CC or C)
N_{center}	Number of different levels of hospitals (CCC, CC or C)
$N_{patient}$	Number of patients treated in each level of hospitals (CCC, CC or C)

TABLE 2 Characteristics of the study population[a]

	Patients (N = 4438)			Patients in CHs (N = 1218)			Patients in NCHs (N = 3220)			Controls (N = 44 378)		
	Init (N = 3552)	Cont (N = 2850)	Term (N = 1747)	Init (N = 970)	Cont (N = 795)	Term (N = 416)	Init (N = 2582)	Cont (N = 2055)	Term (N = 1331)	Init (N = 21 853)	Cont (N = 20 035)	Term (N = 18 036)
Age[b] (median, IQR)	74 (67-80)	73 (66-79)	79 (72-85)	74 (67–80)	73 (66-80)	80 (72-85)	74 (67-80)	73 (66-79)	79 (72-84)	74 (67-80)	74 (67-80)	82 (74-88)
Female (N, %)	1695 (48%)	1338 (47%)	852 (49%)	469 (48%)	370 (47%)	203 (49%)	1226 (47%)	968 (47%)	649 (49%)	10 491 (48%)	9619 (48%)	9155 (51%)
Cancer severity (N, %)												
Low	2289 (64%)	1956 (69%)	791 (45%)	662 (68%)	578 (73%)	213 (51%)	1627 (63%)	1378 (67%)	578 (43%)			
Moderate	740 (21%)	613 (22%)	259 (15%)	180 (19%)	146 (18%)	51 (12%)	560 (22%)	467 (23%)	208 (16%)			
Advanced	523 (15%)	281 (10%)	697 (40%)	128 (13%)	71 (9%)	152 (37%)	395 (15%)	210 (10%)	545 (41%)			
Comorbidity (N, %)												
No comorbidity	380 (11%)	334 (12%)	88 (5%)	114 (12%)	100 (13%)	27 (6%)	266 (10%)	234 (11%)	61 (5%)	1434 (7%)	1378 (7%)	0 (0%)
1–2 comorbidities	1775 (50%)	1443 (50%)	751 (43%)	493 (51%)	413 (52%)	163 (39%)	1282 (50%)	1030 (50%)	588 (44%)	10 124 (46%)	9489 (47%)	8894 (49%)
3–4 comorbidities	1397 (39%)	1073 (38%)	366 (52%)	363 (37%)	282 (35%)	226 (54%)	1034 (40%)	791 (38%)	682 (51%)	10 295 (47%)	9168 (46%)	9142 (51%)
CMI of the hospitals where patients were treated (N, %)												
CMI 1/2	1864 (51%)	1494 (51%)	880 (46%)	490 (51%)	408 (51%)	192 (46%)	1374 (54%)	1086 (54%)	688 (53%)			
CMI 3/4	1647 (49%)	1322 (49%)	844 (54%)	480 (49%)	387 (49%)	224 (54%)	1167 (46%)	935 (46%)	620 (47%)			

Abbreviations: CH, certified hospital; CMI, case-mix index; Cont, continuing phase; IQR: interquartile range; Init, initial phase; NCH, noncertified hospital; Term, terminal phase.

[a]Percentages might not sum up to 100% due to rounding.

[b]Age of diagnosis for initial and continuing phase, and age of death for terminal phase.

TABLE 3 Results of the phased annualized net colon cancer treatment cost analysis and survival analysis (costs in 2019 Euro)

Overall patient group	Patients in CHs[a]			Patients in NCHs		
	Overall	CMI 1/2	CMI 3/4	Overall	CMI 1/2	CMI 3/4
Annualized net treatment costs (mean, 95% CI)[b]						
Initial	€ 26 855 (25 058-28 652)	€ 24 880 (22 008-27 753)	€ 24 564 (20 455-28 673)	€ 25 203 (21 185-29 221)	€ 27 596 (25 373-29 820)	€ 26 135 (23 816-28 455)	€ 29 146 (25 078-33 215)
Continuing	€ 1211 (745-1678)	€ 477 (−237 to 1191)	€ 480 (−608 to 1568)	€ 473 (−442 to 1390)	€ 1496 (911-2081)	€ 1174 (398-1949)	€ 1751 (856-2646)
Terminal	€ 30 096 (26 199-33 993)	€ 26 849 (20 399-33 300)	€ 27 364 (18 677-36 051)	€ 26 405 (16 999-35 812)	€ 31 108 (26 408-35 809)	€ 24 113 (18 637-29 591)	€ 38 417 (30 488-46 341)
Survival time (years)[b]							
RMST (95% CI)	5.0 (4.9, 5.1)	5.2 (5.0, 5.3)	5.3 (5.0, 5.5)	5.0 (4.8, 5.3)	4.9 (4.8, 5.0)	4.9 (4.8, 5.0)	4.9 (4.7, 5.0)
Median (95% CI)	5.9 (5.7, 6.2)	6.5 (6.0, NA)[c]	6.9 (6.1, NA)[c]	6.0 (5.3, NA)[c]	5.8 (5.5, 6.1)	6.0 (5.7, 6.3)	5.5 (5.0, 6.1)

Abbreviations: CH, certified hospital; CI, confidence interval; CMI, case-mix index; NCH, noncertified hospital; RMST, restricted mean survival time.

[a]In CHs, CMI 1/2 is proxy for Cs, and CMI 3/4 is proxy for CCCs and CCs.

[b]Both costs and survival time reported here are undiscounted.

[c]The upper 95% confidence CIs of median survival in the CHs group could not be calculated as the upper CI was longer than our follow-up time.

To work out colon cancer care costs for patients treated in CHs compared to NCHs, we focused on the certification for colon cancer centers from DKG.[5] Out of the 54 hospitals in Saxony, 11 of them were DKG-certified during the study time (see Appendix A).[4] Patients were deemed to receive treatments in a CH if the hospital was already or had become certified during the study period. Among the DKG-certified hospitals, we used case mix index (CMI) as a proxy to approximate the level of hospitals (C, CC or CCC), where CMI 1 and 2 hospitals approximate C-level hospitals while CMI 3 and 4 hospitals represent CCs and CCCs.[22] For more description of CMI, see Appendix B.

2.3 | Costs—Additional costs of DKG-certified hospitals

We utilized data from the study by Hölterhoff et al[13] to inform the additional costs resulting from the additional services required to obtain a DKG cancer center certification, which are currently not financed through reimbursement from German SHI. Through surveying 11 DKG-certified CCCs, 8 CCs, and 5 Cs throughout Germany, the study collected annual costs arising from 31 services and categorized them into fixed and variable costs for each level of cancer centers. The fixed costs were estimated per center while variable costs per cancer patient by cancer type. The details of the 31 services and the estimated costs are shown in Appendix C.

2.4 | Effectiveness—Survival time

Trautmann et al performed a robust survival analysis in our previous work.[4] Due to censored survival data, we followed their approach and used Kaplan-Meier method to estimate the survival time. Both restricted mean survival time (RMST) and median survival time for patients treated in CHs and NCHs since the admission of their first treatment were reported. Further subgroup analysis by CMI was also performed. Given that RMST has been shown to demonstrate the intervention effects more intuitively,[23,24] it was used for calculating the total survival time in the CEA.

2.5 | Cost-effectiveness analysis

We designed two scenarios for the CEA.

2.5.1 | Base-case scenario

In the base-case scenario, we assumed two hypothetical cohorts treated in CHs and NCHs to calculate the outcome of interest, the incremental costs per additional life-year. We used the average annual number of colon cancer patients in each level of the surveyed CHs in Hölterhoff et al's report (269 in CCCs, 224 in CCs, and 124 in Cs)[13]

TABLE 4 Results of cost-effectiveness analysis—base case and sensitivity analyses (costs in 2019 Euro)

	CH (N = 1909)[a]			NCH (N = 1909)[a]		
	Total net treatment costs	Total additional service costs	Total survival life-years	Total net treatment costs	Total survival life-years	ICER (€/LY)[b]
Base case[c]	€ 87 309 566	€ 13 771 841	8414	€ 107 769 175	8048	Dominant (−€ 18 284)
SA1: No CMI as proxy[c]	€ 87 268 674	€ 13 771 841	8445	€ 104 134 097	8063	Dominant (−€ 8113)
SA2: 0% discount rate[d]	€ 101 605 033	€ 14 184 996	9792	€ 124 435 183	9294	Dominant (−€ 17 353)
SA3: 5% discount rate[e]	€ 79 107 754	€ 13 509 520	7624	€ 98 144 230	7329	Dominant (−€ 18 768)
Adjusted case[c]	€ 87 309 566	€ 6 245 976	8414	€ 107 769 175	8048	Dominant (−€ 38 858)
SA1: No CMI as proxy[c]	€ 87 268 674	€ 6 245 976	8445	€ 104 134 097	8063	Dominant (−€ 27 850)
SA2: 0% discount rate[d]	€ 101 605 033	€ 6 433 356	9792	€ 124 435 183	9294	Dominant (−€ 32 912)
SA3: 5% discount rate[e]	€ 79 107 754	€ 6 127 005	7624	€ 98 144 230	7329	Dominant (−€ 43 838)

Abbreviations: CH, certified hospital; CI, confidence interval; ICER, incremental cost-effectiveness ratio; LY, life-year; NCH, noncertified hospital; SA1-3, Sensitivity Analyses 1-3.

[a]In the hypothetical CH cohort, 269 treated in one CCC, 896 in four CCs and 744 in 6 Cs; in the NCH cohort, 1165 treated in CMI 3/4 hospitals and 744 in CMI 1/2 hospitals.

[b]Dominant means longer survival/more life-years and lower costs.

[c]Both costs and life-years were discounted at 3% annual rate in the base case, adjusted case and SA1.

[d]Both costs and life-years were not discounted in SA2.

[e]Both costs and life-years were discounted at 5% annual rate in SA3.

and the 11 DKG-certified hospitals in Saxony (1 CCC, 4 CCs, and 6 Cs)[4,25] to establish the hypothetical CH population, which summed up to 1909 hypothetical patients (see Appendix A). The same number of patients in each hospital level (using CMI as a proxy) was also used for the NCH population. The following formula describes the base-case analysis, and the description of the notations used in the formula are in Table 1.

2.5.2 | Total life-years

$$LY_{CH} = Surv_{CH12} \times N_{CMI12} + Surv_{CH34} \times N_{CMI34}$$

$$LY_{NCH} = Surv_{NCH12} \times N_{CMI12} + Surv_{NCH34} \times N_{CMI34}$$

Total life-years in both CH and NCH cohorts were calculated using the RMST in each subgroup by CMI and the number of patients within each subgroup.

2.5.3 | Total costs

$$\begin{aligned} Cost_{CH} &= Cost_{CH-T} + Cost_{Add} \\ &= (Cost_{CH12} \times N_{CMI12} + Cost_{CH34} \times N_{CMI34}) \\ &\quad + (Cost_{Add-F} \times N_{center} + Cost_{Add-V} \times N_{patient}) \end{aligned}$$

$$Cost_{NCH} = Cost_{NCH-T} = Cost_{NCH12} \times N_{CMI12} + Cost_{NCH34} \times N_{CMI34}$$

Total costs within the CH cohort comprised the net treatment costs of colon cancer and the additional costs deriving from additional services. In contrast, total costs in the NCH cohort only consisted of the net treatment costs. Given patients usually received the additional services during the first year of disease, we only considered 1 year of the additional costs.

2.5.4 | Incremental cost-effectiveness ratio

$$\text{ICER} = \frac{Cost_{CH} - Cost_{NCH}}{LY_{CH} - LY_{NCH}}$$

The outcome of interest was the incremental costs per additional life-year for colon cancer treatment in the CH cohort comparing with the NCH cohort.

2.5.5 | Adjusted-case scenario

In the adjusted-case scenario, the two hypothetical populations and all parameters remained the same as the base case, except the additional costs. To our understanding, not all of the 31 additional services

required for certification directly benefit patients' treatment outcomes. Therefore, in the adjusted case, we excluded nine fixed-cost services and two variable-cost services, which appear not to directly impact the patients' treatment outcome (for details about excluded services see Appendix C).

2.6 | Sensitivity analyses

To examine the impact of the input data on the outcome, we designed the following one-way sensitivity analyses for both above mentioned scenarios: (a) Given the uncertainty using CMI as a proxy for the level of hospitals, we performed the economic analysis only with the overall average costs by CHs and NCHs, not further by the subgroup divided by CMI (Sensitivity Analysis 1, SA1); (b) We altered the discount rate with 0% and 5% for both costs and total life-years, as recommended by the Institute for Quality and Efficiency in Health Care (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*, IQWiG)[14] (SA2 and SA3). We also performed a probabilistic sensitivity analysis (PSA) by randomly sampling 5000 values between the upper and lower bounds of the net treatment costs and survival's 95% CIs from a uniform distribution to examine the robustness of CEA results.

3 | RESULTS

3.1 | Net colon treatment costs

There were 21 853, 20 035 and 18 036 matched controls for initial, continuing and terminal phases, respectively. The characteristics of the patient and control populations (including age, sex, cancer severity, number of comorbidities, and CMI of the hospitals where the patients were treated) are presented in Table 2. Given that the outcome of interest was to compare between the patients treated in CHs and NCHs, we also described the patient characteristics between the CH and NCH cohorts in Table 2.

Overall, the mean annualized net treatment costs were the highest in the terminal phase (€30 096; 95% CI €26 199-€33 993), followed by the initial phase (€26 855; 95% CI €25 058-€28 652) and continuing phase (€1211; 95% CI €745-€1678) (Table 3).

Subgroup analyses by hospital certification status and further by CMI are presented in Table 3. In general, the mean net treatment costs were higher in the NCH group than in the CH group, with the greatest difference in the terminal phase (€26 849; 95% CI €20 399-€33 300 in CHs vs €31 108; 95% CI €26 408-€35 809 in NCHs). We observed a similar trend when further breakdown by CMI, with one major exception that the mean net treatment costs in terminal phase in CMI 1/2 CHs were higher than in NCHs (€27 364; 95% CI €18 677-€36 051 in CHs vs €24 113; 95% CI €18 637-€29 591 in NCHs). We also presented additional subgroup analyses by cancer severity and the number of comorbidities, in Appendix D.

3.2 | Survival time

RMST was longer in the CH cohort compared to the NCH cohort: 5.2 years (95% CI 5-5.3 years) in CHs vs 4.9 years in NCHs (95% CI 4.8-5 years). The same pattern of RMST in further subgroup analyses by CMI was observed (Table 3). Kaplan-Meier curves are presented in Appendix E.

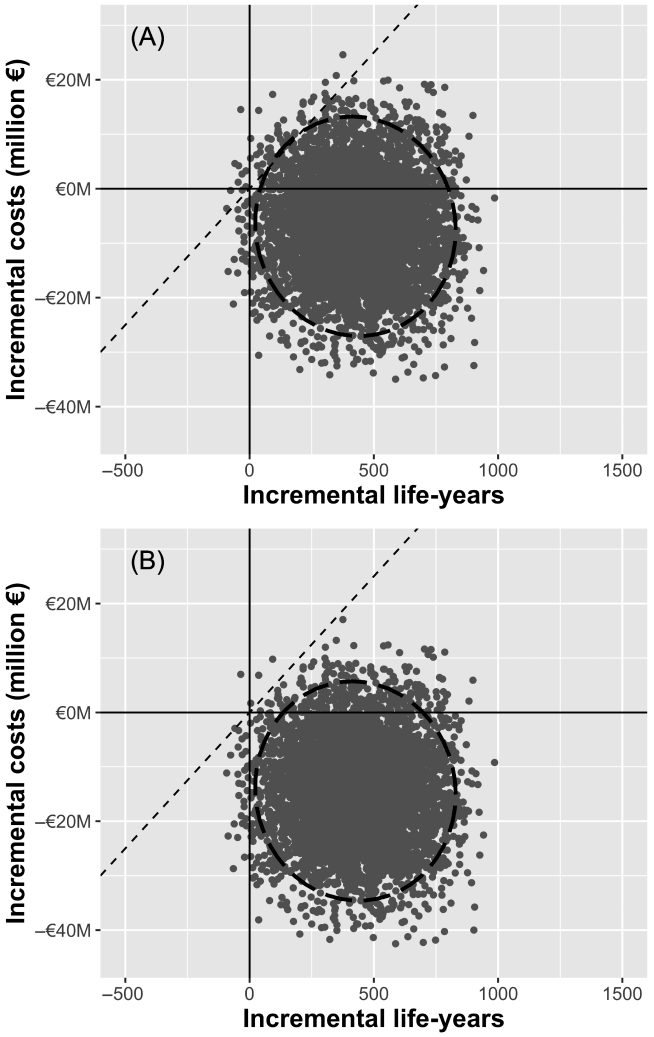

FIGURE 2 Scatter plots of the PSA results: (A) Base-case scenario; (B) Adjusted-case scenario. The PSA was done by randomly drawing 5,000 values within 95% CI of net treatment costs and survival. The extra costs from additional services were not altered and were added to each of the random net treatment costs to calculate the total treatment costs, and hence incremental costs between the groups treated in certified and non-certified hospitals. Dotted line: willingness-to-pay at €50 000/LYG; Dashed circle: 95% confidence ellipse

3.3 | Cost-effectiveness

The base-case CEA utilized the mean annualized net treatment costs from the subgroup analyses by certification status and CMI, the additional costs resulted from the 31 services identified by Hölterhoff et al,[13] and an annual discount rate of 3% on costs and total life-years.[26] The base-case results of colon cancer care in CHs dominated that in NCHs (more life-years and lower costs, with a negative ICER of −€18 284 per additional life-year). The adjusted-case analysis used the same settings as the base case, except that 11 of the 31 services identified by Hölterhoff et al[13] were excluded on the ground that they do not directly impact patients' treatment outcomes. Again, the results in CHs dominated that in NCHs (−€38 858 per additional life-year).

3.4 | Sensitivity analyses

The results of one-way sensitivity analyses are in Table 4. For both scenarios, not using CMI as proxy (SA1) drove the ICERs closer to zero but remained cost-saving (−€8113 and −€27 850 per additional life-year for the base- and adjusted-case, respectively). Using different annual discount rates (SA2 and SA3) had minimal impact on the results for both scenarios. See Appendix F for tornado graphs. PSA results (Figure 2) showed 98.7% and 99.9% of probability for the base- and adjusted-case, respectively, that the ICERs from the CH cohort remain dominant over the NCH cohort if €50 000 per life-year is used as the willingness-to-pay threshold.

4 | DISCUSSION

To our knowledge, this is the first CEA from a healthcare system's perspective to examine the cost-effectiveness of colon cancer care provided in certified cancer centers, where we measured the clinical effectiveness by using patients' survival after receiving cancer care. The results were very encouraging: the two scenarios and all their sensitivity analyses showed better survival and cost-saving results.

Our mean net colon cancer treatment costs by phase showed a "U-shaped" pattern, which is consistent with the cancer treatment cost estimations in the literature.[16,19,20,27-30] Among the literature, one study used comparable methods to analyze another German SHI dataset to estimate the mean net colorectal cancer treatment costs. Their cost estimates for the initial, continuing and terminal phases were €33 280, €2944 and €66 176 (inflated to 2019 Euro),[19] which were higher than our results. However, the former study did not match for comorbidity in their control group. In contrast, we matched for comorbidity in our study, and it consequently resulted in higher treatment costs in the control group,[31] which, in turn, narrowed the cost difference between patient and control groups and led to lower net treatment costs.

The base-case CEA result demonstrated a favorable outcome. Despite €13.7 million of additional costs due to additional services demanded for certification in the CH cohort, the colon cancer care in CHs vs NCHs was shown to be cost-saving, in which two hypothetical cohorts of 1909 colon cancer patients treated in CHs and NCHs in Saxony were analyzed. This was likely due to better survival outcomes and lower treatment costs attributed to more efficient care in CHs, as shown in the literature.[2,4,8-11] The favorable CEA results were insensitive to the alteration of discount rates (SA2 and SA3) and remained robust in the PSA.

There were two major sources of uncertainty in this CEA, which we addressed in the adjusted-case scenario and a sensitivity analysis (SA1). The first one was rooted in the 31 additional services identified by Hölterhoff et al.[13] Although those 31 services were required to obtain the DKG-certification and ultimately improve the cancer care quality, it does not mean all services directly benefit patients' treatment outcomes. For example, the two services composed of the most significant part of the fixed costs were center coordination and clinical study management. However, they entailed predominantly administrative costs, which had little to do with patient treatment. Along with this rationale, the base-case scenario should be regarded as a conservative estimation, where all 31 additional services were considered, hence higher total additional costs. On the other hand, the adjusted-case scenario was designed to capture a picture closer to reality, where only the additional services that directly influence patients' treatment outcomes were included. The results of the adjusted-case analysis and all sensitivity analyses of this scenario were cost-saving, all with lower costs compared to the base-case scenario and its sensitivity analyses.

The second significant uncertainty stemmed from using CMI as a proxy for the level of hospitals in the CH cohort, which was examined in SA1 for both scenarios. Since the hospitals were masked in the AOK PLUS dataset due to data protection reasons, the only parameter which correlates with hospital levels was CMI. A higher CMI is shown to associate with teaching hospitals and level-1 hospitals,[22] which are relatively comparable with CCCs (usually university hospitals) and CCs. Therefore, we assigned the top two quartiles of CMI, namely CMI 3 and 4, to approximate CCCs and CCs. To address the potentially arbitrary approximation, we performed net treatment cost and survival analyses without using CMI as a proxy for hospital levels in SA1. The results of SA1 for both base-case and adjusted case scenarios remained cost-saving.

There were two further constraints in the evaluation of additional services that we could not formulate to test in the CEA. In reality, NCHs can also provide some of the 31 additional services, but we lacked the data of the extent of NCHs' service provision and the quantification of those costs. Furthermore, those additional services resulting in fixed costs are primarily overhead costs or capital investment, which will be shared by all the patients treated in that CH, not just among colon cancer patients. Therefore, the fixed costs divided to each colon cancer patient should be lower in reality. Nonetheless, the two constraints both narrow the gap of additional service costs between CHs and NCHs, which would lead to more favorable CEA outcomes. Thus, the two constraints further signal that our base-case CEA result is a conservative estimation.

4.1 | Study limitations

A few study limitations were recognized. Firstly, the study results were based on the costs estimated using an SHI dataset and the number of CHs at different levels from one of the 16 states in Germany. Hence, caution should be exercised if the results were to be generalized to the whole of Germany or other countries. For instance, access to CHs due to potentially uneven geographical distribution of CHs in certain regions might alter the demographic picture of the patients treated in CHs, which might impact the net treatment costs estimation for both patients treated in CHs and NCHs. Moreover, if there are more CCCs in other regions, the fixed additional costs in the CH cohort will increase, which might lead to a less favorable ICER.

Secondly, the additional cost data from the study by Hölterhoff et al came from 24 surveyed DKG certified hospitals,[13] which accounted for only 2% of the overall DKG certified centers (see Appendix A)[5]; also, the sample of Cs in the report was small and underrepresented the reality. Therefore, we cannot be certain if the additional cost data are representative of DKG certified centers within all of Germany.

Thirdly, RMST was chosen to represent the effectiveness, but it is likely to underestimate the real mean survival time due to the censored nature of survival data. However, given that the final output of interest on the effectiveness side was the difference of total life-years between the patient cohorts treated in CHs and NCHs, the use of RMST should not lead to a significant bias in the results. We also tested using median survival as the effectiveness measure to reassure the cost-effectiveness results, and the conclusion remained unchanged (see Appendix G for cost-effectiveness results using median survival).

Fourthly, there are some common limitations related to the use of administrative data. One potential concern is upcoding or "DRG creep,"[32,33] in which patients appear sicker in the claims data, and the hospitals could benefit from higher reimbursement. We did not know if such a phenomenon exists in the AOK PLUS dataset, which would potentially bias the cost estimation. Another concern lies in the lack of clinical details[34] (eg, cancer staging) and probable underreporting of comorbidities[32] in the administrative data, which might affect the cost estimates in our subgroup analyses for costs (see Appendix D).

Lastly, we only considered DKG-certification in this study. However, Trautmann et al[4] also demonstrated survival benefits for patients treated in hospitals certified for coloproctology and minimally invasive surgery by the German Society for General and Visceral Surgery (DGAV). Future studies should investigate if DGAV-certification requirements also incur additional costs and its cost-effectiveness.

5 | CONCLUSION

We analyzed administrative data to derive the first cost-effectiveness evidence to support that colon cancer care provided by the German Cancer Society (DKG)-certified cancer centers can improve survival outcomes and save costs from a healthcare system's perspective. Future research should draw on broader national data, if available, to perform both the cost analysis and CEA on hospital certification for cancer care nationwide in Germany. Similar studies should also be done for different healthcare systems in other countries, as the results cannot be directly applied given significant variations among international healthcare systems.

ACKNOWLEDGMENTS

We are grateful for the collaboration with the Saxonian Statutory Health Insurance Company AOK PLUS and data support from Martin Seifert. We also thank Karla Hernandez-Villafuerte, Habibollah Arefian, Jasper Ubels, Anett Molnar, and Muchandifunga Muchadeyi for their useful comments, as well as Rachel Eckford for her proofreading of the manuscript. The views in this article are the authors' and not necessarily those of German Cancer Research Center (DKFZ). Chih-Yuan Cheng was supported by a 3-year studentship from the Helmholtz International Graduate School for Cancer Research. The funder had no active role in any stage of the research. Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST

Unrelated to this study, JS received institutional funding for IITs from Sanofi, Novartis, ALK, and Pfizer, and acted as a consultant from Novartis, Lilly, Sanofi, and ALK. All authors declare no conflict of interest.

ETHICS STATEMENT

Given the nature of secondary data analysis, the need for an ethics approval was waived. The study was performed in accordance with the Declaration of Helsinki and follows the principles of Good Practice in Secondary Data Analysis.[35]

DATA AVAILABILITY STATEMENT

The study is supported by AOK PLUS, with whom the Center for Evidence-based Healthcare has a Data Use and Transfer Agreement. Personal data of the beneficiaries were pseudonymized through AOK PLUS before data sharing. Personal identifiers were masked or deleted (exact names were pseudonymized prior to receiving the data; no social security numbers were provided). Quasi-identifiers were generalized (year of birth only, deletion of the last digit of the zip code, etc.). The processing and analysis of sensitive data took place exclusively on the specially protected servers at Dresden University Hospital. Results of data analyses were shared in aggregate form only. Anonymized data that are minimally required to replicate the outcomes of the study will be made available upon reasonable request to the corresponding author, and following approval by AOK PLUS.

ORCID

Chih-Yuan Cheng https://orcid.org/0000-0001-6220-0524

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Cheng C-Y, Datzmann T, Hernandez D, Schmitt J, Schlander M. Do certified cancer centers provide more cost-effective care? A health economic analysis of colon cancer care in Germany using administrative data. *Int. J. Cancer*. 2021;1-11. https://doi.org/10.1002/ijc.33728