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Cure models, survival probabilities, and solid organ transplantation for patients with colorectal cancer

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Abstract

A previous cancer diagnosis can preclude patients from consideration for solid organ transplantation. Statistical models may improve candidate selection. We fitted statistical cure models and estimated five-year cancer-specific survival (5yCSS) for colorectal cancer patients in the United States using registry data. The median cure probability at cancer diagnosis for patients in the general population was 0.67. Among 956 colorectal cancer patients who underwent solid organ transplantation, the median time since diagnosis was 6.3 years and the median 5yCSS at transplantation was 0.96. Patients with a 5yCSS below 0.90 had increased posttransplant cancer-specific mortality (hazard ratio 3.31, 95% confidence interval 1.52–7.21). Compared with recently

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Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

published guidelines, our models suggested shorter wait times for some groups of colorectal cancer patients (e.g., stage IIA cancers) and longer wait times for others (stages IIB, IIIB, IIIC, IV). In conclusion, colorectal cancer patients undergoing solid organ transplantation had excellent prognoses, reflecting selection incorporating existing guidelines and clinical judgement. Nonetheless, 5yCSS probabilities estimated from cure models offer additional prognostic information for patients considered for transplantation and identify situations where current guidelines might be revised. We developed a web-based tool for clinicians to calculate 5yCSS probabilities for use in transplant evaluation for individual colorectal cancer patients (<https://dceg.cancer.gov/tools/risk-assessment/calculator-of-colorectal-cancer-survival-probability>).

Background

Solid organ transplantation can enable long-term survival for patients with end-stage organ disease. To prevent rejection, recipients must take immunosuppressive medications that increase the risk of cancer (1, 2) and may also promote the recurrence of cancer among individuals with a prior cancer diagnosis (3, 4).

The decision regarding whether a patient can be placed on the transplant waitlist takes account of comorbid medical conditions that would make transplantation at high risk for failure or of limited benefit (5, 6). Most organ transplants are not performed as treatment for cancer, but a prior cancer diagnosis is a common comorbidity among transplant candidates and recipients. Moreover, a prior cancer diagnosis is associated with increased posttransplant mortality related, in part, to cancer recurrence (7, 8). Because many cancers recur in the first few years after diagnosis, guidelines for evaluating transplant candidates with a history of cancer typically recommend a waiting period that depends on the type of cancer and stage at diagnosis (9–13). A “5-year cancer survival rate of near 80%” is used as a benchmark for proceeding to transplantation in recent guidelines (13).

For patients with a history of cancer, the selection process is intended to identify those individuals for transplantation who have an acceptably low risk of cancer recurrence and death from their cancer (i.e., cancer-specific mortality). This approach corresponds to identifying patients who have a high likelihood of being cured of their cancer, which can be modeled statistically as a cure probability (14–16). For a population of cancer patients, the cure probability is defined as the proportion of people who will not die from their cancer no matter how long they are followed.

Using data from the Transplant Cancer Match (TCM) Study, we recently demonstrated that estimated cure probabilities provide a useful metric to assess prognosis in cancer patients undergoing organ transplantation (17). Our study evaluated 5425 cancer patients with 17 different types of malignancy who underwent solid organ transplantation in the United States (US). These cancer patients’ cure probabilities were typically very high at the time of transplantation, reflecting a good cancer prognosis due to careful selection. Importantly, however, we found that those patients whose cure probability was in the lowest third (i.e., tertile) had increased cancer-specific mortality following transplantation (adjusted hazard ratio [HR] 2.08, 95% confidence interval [95%CI] 1.48–2.93, vs. the highest tertile).

Our prior study is an important proof-of-principle of the potential utility of cure models for candidate selection for transplantation. However, it had several limitations. First, because we included 17 different cancer types, the statistical models were not tailored to any single cancer, complicating their application to individual patients. Second, we did not attempt to validate the models or recommend a clinically useful threshold for decision-making. Third, we did not provide a tool for clinicians to estimate an individual patient's prognosis.

Colorectal cancer is a common malignancy among people considered for organ transplantation. In the present study, we developed and validated statistical cure models tailored to colorectal cancer and applied them to US patients undergoing solid organ transplantation during 1991–2019. Based on these models, we provide estimates that a colorectal cancer patient will not die from their cancer in the next five years, calculated both at the time of their cancer diagnosis and updated to accommodate the passage of time since their cancer diagnosis. We illustrate how these probabilities can inform guidelines for transplant candidate selection. In addition, we developed a web-based tool based on these models that clinicians can use to calculate probabilities for individual patients at any time at or after their cancer diagnosis to assist in transplant evaluations.

Methods

Colorectal cancer patients

Details regarding data sources and patient selection are provided in the Supplemental Methods. We identified colorectal cancer patients from the US general population using data from 17 cancer registries in the Surveillance, Epidemiology, and End Results program (SEER, (<https://seer.cancer.gov/>)). We included adults (ages 20–79 years) who were diagnosed with colorectal cancer as a first primary malignancy, restricted to diagnosis years 2004–2015 to allow assessment of American Joint Committee on Cancer staging, version 6 (AJCC6).

We separately identified colorectal cancer patients who received a solid organ transplant after their cancer diagnosis. These patients were selected from the TCM Study (1) (<https://transplantmatch.cancer.gov/>), a linkage of the Scientific Registry of Transplant Recipients (the US national solid organ transplant registry) with 32 cancer registries. The inclusion criteria were the same as for SEER cases, but the range of diagnosis years was broader (1976–2017) to capture more cases, so AJCC6 stage was allowed to be missing. For transplanted patients, we therefore relied primarily on SEER historic stage (which categorizes stage as localized, regional, or distant and is available across calendar periods). Although we did not exclude patients who received a liver transplant for isolated liver metastases, none of the transplants in the study had this indication.

Deaths due to colorectal cancer were identified using information on the underlying cause of death that the cancer registries obtained from death certificates, using the SEER cause of death recode variable for SEER patients and International Classification of Diseases codes (version 9: 153–154; version 10: C18–C20) for transplanted patients. The TCM Study was not considered human subjects research by the National Cancer Institute and was approved, as required, by participating registries.

Statistical analyses

We compared characteristics between the general and transplant populations of colorectal cancer patients using chi-square and Wilcoxon rank sum tests. We used statistical cure models to describe the cancer-specific mortality of patients, treating non-cancer deaths as censoring events. Cure models assume that there are two groups of cancer patients: 1) those who will eventually die from their cancer, and 2) those who will not (the “cured” group) (14–16). By modeling both the probability that a patient belongs to the cured group and the survival function for the non-cured group, cure models allow estimation of various statistics of interest, including the probability that a patient will not die from their cancer over a given time period, e.g. the next 5 years (i.e., 5-year cancer-specific survival [5yCSS]), starting at any timepoint at or after their diagnosis. These 5yCSS probabilities were conditioned on survival to the indicated timepoint, so they correspond to the 5-year cancer-free survival probabilities for patients who have survived to that timepoint.

Details of the cure models are provided in the supplemental material. These models were fitted to the SEER colorectal cancer patient population, separately in strata defined by subsite (proximal colon, distal colon, or rectum), sex, and stage (SEER historic or AJCC6 stage). Each stratum-specific model included age and initial cancer treatment (surgery, radiation, chemotherapy, coded as yes vs. no/unknown). We evaluated potential bias and accuracy of the models using leave-one-registry-out cross-validation with the SEER data (see supplemental materials).

We applied the models developed using SEER data to estimate the cure probabilities for the transplanted colorectal cancer patients at cancer diagnosis. We also used the models to estimate 5yCSS at cancer diagnosis and transplantation among transplanted patients. We then used Cox proportional hazards regression to assess the association between the estimated 5yCSS at transplantation and cancer-specific mortality after transplantation. These survival models assessed the 5yCSS probabilities as a linear trend across quartiles as well as using a threshold probability. We assessed a threshold of 0.80 based on recent guidelines (13). However, as there were few transplanted patients with 5yCSS < 0.80 and because recipients with 5yCSS < 0.90 had worse posttransplant cancer-specific mortality than those with 5yCSS ≥ 0.90, we also considered a threshold of 0.90.

Based on the SEER data, we report the distribution of cure probabilities for colorectal cancer patients in the general population at diagnosis and 5yCSS at yearly intervals 0–5 years after diagnosis. We compared these 5yCSS probabilities to the wait times recommended in recent transplantation guidelines (13). The guidelines refer to wait times after the completion of cancer treatment; we calculated the 5yCSS probabilities corresponding to those wait times assuming that cancer treatment would be completed 6 months after diagnosis. We then compared the wait time based on a threshold 5yCSS of 0.80 or 0.90 to that recommended in the guidelines.

Results

Colorectal cancer patients in the US general population

We evaluated data for 230,465 colorectal cancer patients in the US general population, including 89,691 individuals with proximal colon cancer, 69,247 with distal colon cancer, and 71,527 with rectal cancer (Table 1). Fifty-five percent of patients were male, and the median age at diagnosis was 60–64 years.

The cure probabilities at the time of cancer diagnosis showed a bimodal distribution (Figure 1A) and results using the two staging systems were highly correlated (Spearman R 0.90, Figure 1B). Based on models incorporating SEER historic stage, the median cure probability was 0.67 among all colorectal cancer patients, 0.70 among colon cancer patients, and 0.61 among rectal cancer patients. Cure probabilities at the time of diagnosis decreased with advancing SEER historic stage (median 0.88 for localized stage, 0.65 for regional stage, 0.08 for distant stage). Based on the cure models, Table 2 shows median 5yCSS estimates for colon and rectal cancer patients at diagnosis and 1–5 years after diagnosis.

Over a median follow-up of 5.6 years, 74,190 individuals (32.2%) died from colorectal cancer and 41,428 (18.0%) from other causes. As shown in Figure 2, the cure probability at cancer diagnosis was strongly predictive of cancer-specific mortality, and with increasing time since cancer diagnosis, the cumulative proportion of patients who died due to their cancer approached the asymptote predicted by the cure models, i.e. the cure probability.

As described in the supplemental materials, the cure probabilities from the cross-validation showed a similar distribution and were highly correlated with the cure probabilities from our main analysis. The cross-validated cure probabilities also were predictive of subsequent death from colorectal cancer (receiver operator characteristic curve area 0.822 for SEER historic stage, 0.842 for AJCC6 stage).

Colorectal cancer patients who received a solid organ transplant

Table 1 also shows the characteristics of 956 colorectal cancer patients in the US who received a solid organ transplant after their cancer diagnosis. Compared to colorectal cancer patients in the general population, the transplanted patients were more likely to be male (66.9%, $p<0.001$) and were younger (median age 54.5 years at diagnosis, $p<0.001$). Almost two-thirds of transplanted cancer patients (64.9%) were diagnosed with a localized SEER historic stage cancer, and only 2.0% with a distant stage cancer, which differed significantly from patients in the general population ($p<0.001$). By design, the range of calendar years of cancer diagnosis was wider for transplanted patients than colorectal cancer patients in the general population, with an earlier median year of diagnosis (2002 vs. 2009, $p<0.001$; Table 1). As a result, only 288 transplanted patients (30.1%) had a recorded AJCC6 stage.

Among transplanted patients, the 5yCSS probabilities at the time of transplantation exhibited a unimodal distribution with a median of 0.96 based on SEER historic stage. The distribution of 5yCSS probabilities was similar for the SEER and AJCC6 stage models (median probabilities were 0.96 and 0.97, respectively, based on 288 patients, Figure

1C), and the results using the two staging systems were strongly correlated ($R=0.89$, Supplemental Figure 1).

The transplanted patients had been diagnosed with colorectal cancer a median of 6.3 years before their transplant (interquartile range 3.5–10.1, range 0.2–27.2 years). Among transplanted patients, the median 5yCSS probability estimated at the time of their cancer diagnosis was 0.95 based on SEER historic stage (Supplemental Figure 2). The median 5yCSS probabilities were thus similar at the time of transplantation and at cancer diagnosis, but a small number of patients had large increases (Figure 1D).

During a median of 12.0 years of follow-up after transplantation, 28 transplanted patients (2.9%) died from colorectal cancer and 362 (37.9%) from other causes (see Supplemental Table 1 for the distribution of causes of death). Among transplanted patients, there was a significant trend of decreasing cancer-specific mortality with increasing 5yCSS at transplantation (HR 0.62, 95%CI 0.42–0.90, per quartile; $p=0.01$). Using 0.90 as a cutoff, transplanted patients with 5yCSS probability at transplantation below this value had a significantly higher cancer-specific mortality than those at/above this threshold (8.5% vs. 2.1% died from colorectal cancer; HR 3.31, 95%CI 1.52–7.21; $p=0.003$). In comparison, only 29 transplant recipients had 5yCSS probabilities at transplantation below 0.80, and only two died from colorectal cancer in this group; the association between 5yCSS below 0.80 and cancer-specific mortality was not significant (HR 1.75, 95%CI 0.41–7.43; $p=0.45$).

Using a 5yCSS of 0.90 to determine an acceptable risk with transplantation, 572 (59.8%) transplanted patients had 5yCSS at/above this threshold at cancer diagnosis, 838 (87.7%) had 5yCSS at/above this threshold at transplantation, and 266 (27.8%) crossed the threshold between cancer diagnosis and transplantation. Compared with transplanted patients whose 5yCSS was below 0.90, those with higher survival probabilities were less likely to be male (65.5% vs. 77.1%, $p=0.016$) and were older at transplantation (median age 54.2 vs. 50.6 years, $p<0.001$) (Supplemental Table 2A). Patients with 5yCSS at/above 0.90 at transplantation, compared with those with 5yCSS below 0.90, also had less advanced cancer stage at diagnosis ($p<0.001$), were more likely to receive a kidney transplant ($p=0.032$), and had longer times from cancer diagnosis to transplantation (median 6.8 vs. 4.1 years, $p<0.001$) (Supplemental Table 2A). Similar results were seen using a threshold 5yCSS of 0.80 (Supplemental Table 2B).

Comparison of survival probabilities and wait time guidelines

Among patients in the general population, 5yCSS probabilities generally increased with longer time since colorectal cancer diagnosis among those patients still alive (Table 2). This increase over time was minimal for patients diagnosed with localized cancer and more pronounced for those with regional or distant stage cancers, although 5yCSS probabilities for distant stage cancer patients remained low even 5 years after diagnosis (Table 2). For instance, for AJCC6 stage I colon cancer, the median 5yCSS probability was 0.97 at diagnosis and 0.98 at 5 years after diagnosis. In contrast, the median 5yCSS probabilities at diagnosis and 5 years after diagnosis were 0.18 and 0.61 for AJCC6 stage IV colon cancer.

As illustrated in Table 3 and reviewed in the Discussion section below, there are discrepancies between the median 5yCSS probabilities for colorectal cancer patients in the US general population and recent recommendations for transplantation wait times (13). Additionally, there is wide variation in the 5yCSS probabilities among colorectal cancer patients at each timepoint after diagnosis (Figure 3). Furthermore, the 5yCSS probabilities at some timepoints span a range around the threshold probability of 0.80 or 0.90, e.g., for stage IIB colon cancer (Figure 3A), stage IV colon cancer (Figure 3B), and stage IIB rectal cancer (Figure 3C). The distributions of 5yCSS probabilities for each cancer subsite and stage are presented in Supplemental Figure 3.

Discussion

In the present study, we developed and validated statistical cure models for patients with colorectal cancer. The distribution of cure probabilities for colorectal cancer patients in the US general population was distinctly bimodal, corresponding to their differing prognoses based on demographic and clinical factors. The cancer-specific survival probabilities generated from these models were predictive of subsequent mortality from cancer, both among cancer patients in the general population and among patients transplanted during 1991–2019.

Cure models are an attractive framework for assessing prognosis of cancer patients (14–16) and have intuitive appeal in the setting of evaluating of organ transplantation candidates (17). If a patient can be considered likely to be cured of their cancer (i.e., that the cancer will not lead to death), then it seems reasonable to discount the prior cancer history when evaluating the candidate for transplantation. In this study, we used the cure models to derive 5yCSS probabilities, with the idea that these would be readily interpretable by clinicians. Offering transplantation to a patient with a high risk of cancer recurrence (i.e., low 5yCSS) might be considered inappropriate, both from the perspective of the patient and with respect to responsible stewardship of the scarce supply of donor organs.

Several characteristics of the colorectal cancer patients who received an organ transplant after their cancer diagnosis reflect careful selection by transplant providers (Table 1). They were younger than patients in the general population and, notably, almost all had been diagnosed with localized or regional stage cancer. Over a median period of 6.3 years between cancer diagnosis and transplantation, the 5yCSS probabilities increased modestly for most patients, but some patients had large increases during this interval (Figure 1D). As a result, at the time of transplantation, the median estimated 5yCSS was 0.96, and 87.7% of transplanted patients had 5yCSS probabilities of at least 0.90. The long average time interval between cancer diagnosis and transplantation partly reflects caution among providers, as the interval was longer for patients with regionally advanced or metastatic cancer (Supplemental Table 3). Another reason for the long time intervals is that some patients were diagnosed with cancer before developing end-stage organ disease.

Due to careful selection by clinicians, very few recipients in our study died from their cancer after transplantation. Nonetheless, cancer-specific mortality was more than three-fold higher among recipients whose 5yCSS was less than 0.90 at the time of transplant (HR

3.31, 95%CI 1.52–7.21). If our results based on transplants during 1991–2019 can be extrapolated to the present and future, they suggest that a threshold 5yCSS of 0.90 could be appropriate to consider in offering a transplant to an individual with a history of colorectal cancer. The characteristics of the minority of transplanted patients with an estimated 5yCSS below 0.90 reflect a combination of adverse clinical characteristics (e.g., advanced cancer stage, short time from diagnosis to transplantation) as well as countervailing influences on clinicians' decisions to proceed with transplantation even in the presence of a relatively poor cancer prognosis (e.g., young patient age, transplantation of an organ other than kidney) (Supplemental Table 2A).

Because of their utility in predicting cancer-specific mortality, these models can inform interpretation and possibly lead to revision of guidelines regarding which patients should be considered eligible for transplantation (Table 3). For some situations, our results suggest that wait times might be shortened. For example, Al-Adra et al. recommend a waiting time of 2 years after completion of cancer treatment for patients with AJCC6 stage IIA colon cancer (13). In contrast, our results indicate that transplantation may be safe much earlier, because such patients (like those with stage I colon cancer) already have a median 5yCSS above 0.90 at the time of cancer diagnosis.

Nonetheless, while our results suggest that decreases in wait times for some patients may be justified, it is important to remain cautious. Mortality is high among cancer patients (including those with colorectal cancer) who are already immunosuppressed at the time of their cancer diagnosis (18–20), suggesting that intact immunity is especially important in controlling cancer at the time of initial cancer diagnosis and treatment. Thus, if transplantation were offered too soon after a cancer diagnosis, immunosuppression could potentially promote cancer progression or cause relapse even among patients with very good prognoses.

In other scenarios, the wait times may need to be longer than currently recommended. In particular, Al-Adra et al. recommend that patients with stage IIB, IIIB, and IIIC colorectal cancer should be considered eligible for transplantation at 3–5 years after completion of cancer treatment (13). As shown in Table 3, this range of wait times may be reasonable if 0.80 is the threshold 5yCSS for offering a transplant but may be insufficient if the threshold is 0.90. Finally, the median 5yCSS for patients with stage IV colorectal cancer remains quite low 5 years after diagnosis (Table 3), emphasizing that offering transplantation to such individuals (with the possible exception of liver transplantation for patients with isolated liver metastases) (13, 21, 22) should be undertaken with the understanding that there is a high risk of relapse.

Although the median 5yCSS estimated for patients at specified times since cancer diagnosis (Table 2) is informative, there is substantial variability among patients based on their demographic and treatment characteristics (Figure 3, Supplemental Figure 3). We therefore developed a web-based tool (description with link: <https://dceg.cancer.gov/tools/risk-assessment/calculator-of-colorectal-cancer-survival-probability>; direct link: <https://appshare.cancer.gov/crcprobability>) that allows providers to calculate 5yCSS individualized for a specific patient at the time of evaluation for listing or transplantation. This

individualized estimate could be especially useful in the transplant setting when the range of 5yCSS probabilities in the general population data crosses 0.80 or 0.90 (Figure 3). The tool also provides the estimated 5yCSS at different timepoints after cancer diagnosis, allowing clinicians to determine the potential benefit of waiting longer before offering a transplant.

Importantly, we did not have data to fit cure models specifically for cancer patients with end-stage organ disease, although their 5yCSS probabilities might differ from those predicted by our models. Our models also do not include information on molecular tumor characteristics, details of cancer treatment (which might differ between transplanted patients and others in the general population), or updated information available to clinicians about the status of the patient's cancer at the time of evaluation. Thus, the individual patient probabilities provided by our web-based tool should be viewed as a rough guide for the provider's own estimate of the patient's 5yCSS probability. The individualized 5yCSS estimate would have to be lowered if the clinician needed to account for additional adverse patient characteristics or, obviously, clinical or laboratory evidence for cancer recurrence. Correspondingly, the provider could increase the estimated 5yCSS if there was no evidence for disease after a thorough assessment.

We note several study limitations. First, the cure models were developed using US data, so they may not generalize to other countries. Second, many transplanted patients developed cancer before 2004, so AJCC6 stage was frequently missing in this group. Nonetheless, SEER historic stage was available for many more patients, and we showed that probabilities using SEER historic and AJCC6 stages were highly correlated. Furthermore, SEER historic stage is a simple classification scheme that could still be utilized for calculating 5yCSS probabilities even after AJCC staging is updated. Third, imaging and cancer staging procedures are continually improving. This effect, over time, generally "upstages" cancers, when, for example, an increased sensitivity of imaging reclassifies patients from non-metastatic to metastatic disease. Finally, cancer care is continually improving, and a survival probability estimated for a patient in the past is likely lower than for a similar patient treated now and in the future; thus, our 5yCSS estimates likely represent conservative (i.e., worst-case) scenarios for current and future patients. Future iterations of our models will be needed to reflect changes in diagnosis and treatment.

This study has multiple strengths, including that the cancer patients were systematically identified from large population-based databases and were representative of US cancer patients and transplant recipients. We used cross-validation to internally validate our cure models. Also, our estimated 5yCSS probabilities at diagnosis are similar to 5-year relative survival estimates provided by the American Cancer Society (see Table 2 vs. relative survival of 91%, 72%, and 13%, respectively, for localized, regional, and distant stage colon cancer) (<https://www.cancer.org/cancer/types/colon-rectal-cancer/detection-diagnosis-staging/survival-rates.html>). Finally, in Table 3 we provide suggested wait times based on 5yCSS thresholds of 0.80 (as proposed by al-Adra et al. (13)) or 0.90. Nonetheless, our webtool allows for more flexible transplant provider decision-making for an individual patient and varying risk threshold.

We focused on colorectal cancer because it is a common malignancy among both transplant candidates and the general population. This or similar approaches could be used in the future for other cancers provided that sufficient data from cancer registries or other large representative sources are available. A challenge for some cancers is that important prognostic information (e.g., Breslow depth for melanoma) may be difficult to obtain. Another difficulty for some cancers is the need to incorporate updated clinical information after cancer diagnosis on routinely obtained measures of residual disease (i.e., the prognosis of transplanted patients will be much better than for patients in the general population if screening during transplant evaluation has ruled out residual cancer).

In conclusion, we believe that cure models are a useful framework for developing wait time guidelines and evaluating individual cancer patients for organ transplantation. The complex decision to offer transplantation may be improved by incorporating cancer prognostic information throughout the evaluation process.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

5yCSS	5-year cancer-specific survival
95%CI	95% confidence interval
AJCC6	American Joint Committee on Cancer staging, version 6
HR	hazard ratio
SEER	Surveillance, Epidemiology, and End Results
TCM	Transplant Cancer Match
US	United States

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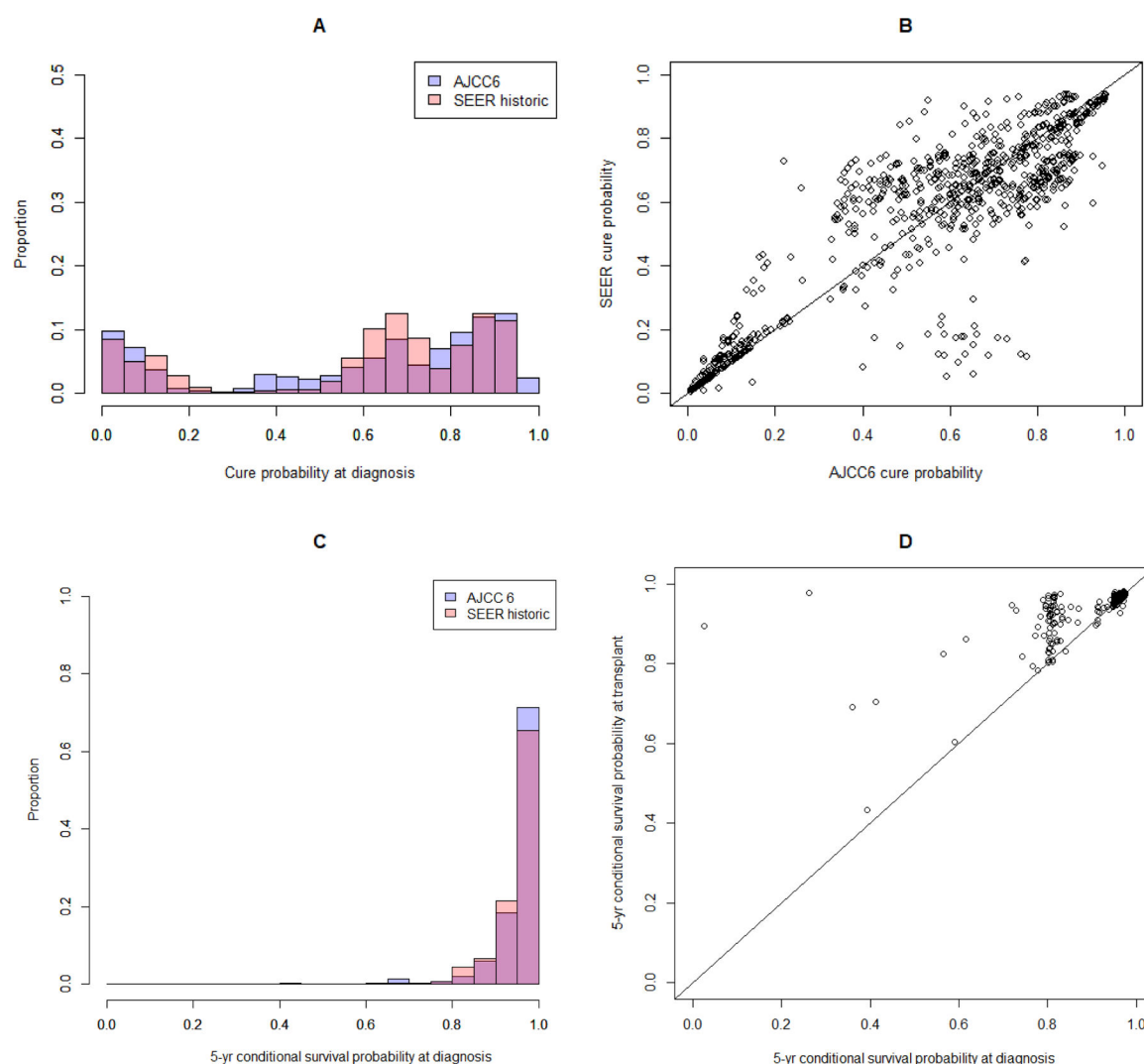


Figure 1.

Panel A. Cure probabilities at cancer diagnosis for colorectal cancer patients in the United States general population (SEER, N=230,465). Results are shown as overlapping histograms using SEER historic stage and AJCC6 stage cure models (red and blue bars, respectively, with the overlap shown as purple).

B. Scatterplot comparing cure probabilities at cancer diagnosis using SEER historic stage and AJCC6 stage cure probabilities, for colorectal cancer patients in the United States general population (SEER). Results for a random 1% sample are shown.

C. Five-year cancer-specific survival estimated at transplantation for patients who received a solid organ transplant after diagnosis. Results are shown for N=288 patients with a known AJCC6 stage as overlapping histograms using SEER historic stage and AJCC6 stage cure models (red and blue bars, respectively, with the overlap shown as purple).

D. Scatterplot comparing five-year cancer-specific survival estimated at cancer diagnosis and transplantation for N=956 transplanted patients. Probabilities were calculated using SEER historic stage.

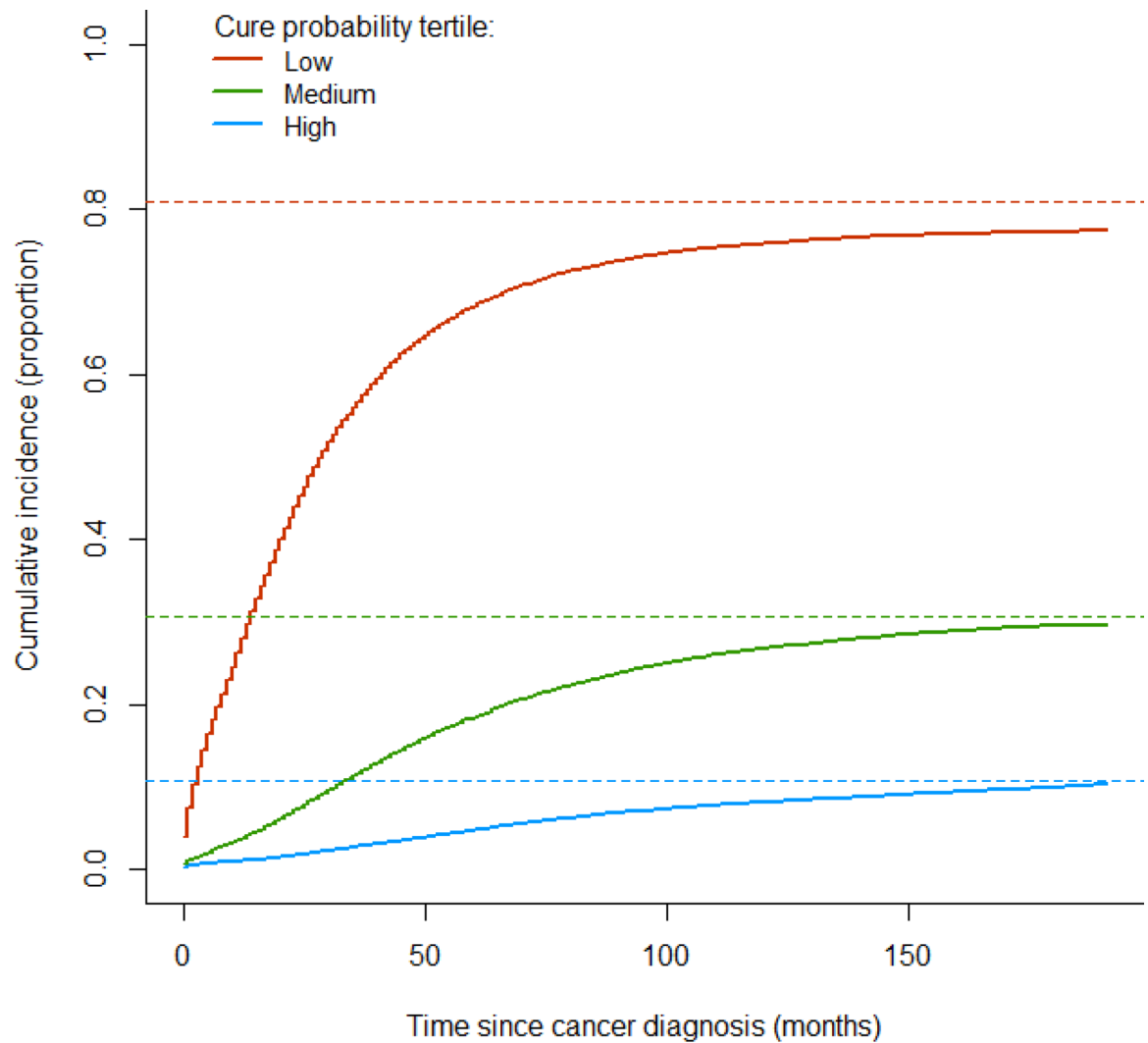


Figure 2.

Kaplan-Meier curves illustrating the cumulative incidence of cancer-specific mortality among colorectal cancer patients in the United States general population (SEER, N=230,465). Patients are divided into tertiles based on cure probabilities calculated at diagnosis using AJCC6 stage. The horizontal lines correspond to 1 minus the mean cure probability in each group, i.e., the proportion of patients predicted to eventually die from their cancer.

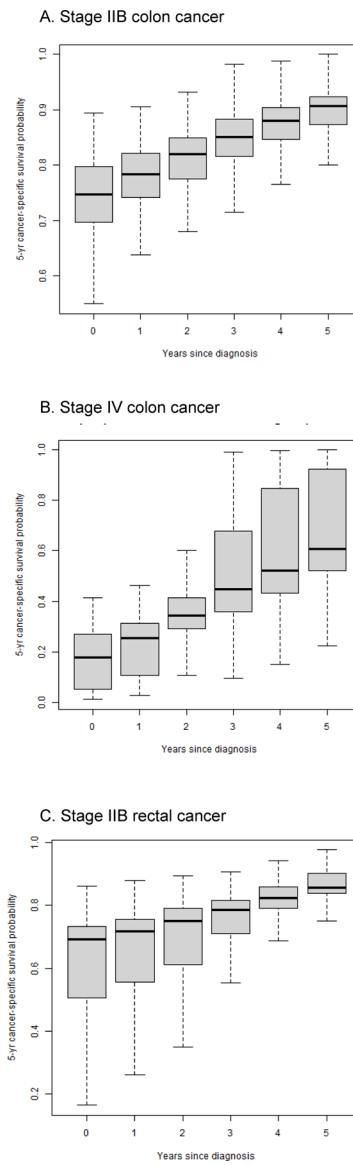


Figure 3.

Five-year cancer-specific survival probabilities as a function of time since cancer diagnosis among colorectal cancer patients in the United States general population (SEER). The distribution of results at each timepoint is shown as a boxplot, for patients with AJCC6 stage IIB colon cancers (panel A), AJCC6 stage IV colon cancer (panel B), and AJCC6 stage IIB rectal cancer (panel C). For timepoints after diagnosis, the probabilities reflect the probability of cancer-specific survival for the next five years, conditioned on surviving to that timepoint.

Table 1.

Characteristics of colorectal cancer patients in the US general population and those who received a solid organ transplant

	US general population patients, N (%)	Transplanted patients, N (%)
Total	230,465 (100)	956 (100)
Subsite		
Proximal colon	89,691 (38.9)	367 (38.4)
Distal colon	69,247 (30.0)	365 (38.2)
Rectum	71,527 (31.0)	224 (23.4)
Male sex	127,669 (55.4)	640 (66.9)
Age at diagnosis, years		
20–49	33,937 (14.7)	265 (27.7)
50–59	59,634 (25.9)	434 (45.4)
60–69	71,143 (30.9)	241 (25.2)
70–79	65,751 (28.5)	16 (1.7)
Calendar year of diagnosis		
1976–2000	0 (0)	394 (41.2)
2001–2005	38,660 (16.8)	265 (27.7)
2006–2010	96,039 (41.7)	209 (21.9)
2011–2017	95,766 (41.6)	88 (9.2)
SEER historic stage		
Localized	88,810 (38.5)	620 (64.9)
Regional	88,308 (38.3)	317 (33.2)
Distant	53,347 (23.1)	19 (2.0)
AJCC6 stage *		
I	56,844 (24.7)	166 (57.6)
IIA	48,985 (21.3)	62 (21.5)
IIB	8,699 (3.8)	5 (1.7)
IIIA	8,347 (3.6)	11 (3.8)
IIIB	35,632 (15.5)	30 (10.4)
IIIC	21,712 (9.4)	10 (3.5)
IV	50,246 (21.8)	4 (1.4)
Surgery		
Yes	204,513 (88.7)	870 (91.0)
No/unknown	25,952 (11.3)	86 (9.0)
Radiation		
Yes	38,838 (16.9)	77 (8.1)
No/unknown	191,627 (83.1)	879 (91.9)
Chemotherapy		
Yes	109,891 (47.7)	198 (20.7)
No/unknown	120,574 (52.3)	758 (79.3)
Transplanted organ		

	US general population patients, N (%)	Transplanted patients, N (%)
Kidney	--	569 (59.5)
Liver	--	249 (26.0)
Heart or lung	--	113 (11.8)
Other/multiple	--	25 (2.7)
Transplant year		
1991–2005	--	247 (25.8)
2006–2010	--	269 (28.1)
2011–2019	--	440 (46.0)

Abbreviations: AJCC6 American Joint Committee on Cancer (version 6); SEER Surveillance, Epidemiology, and End Results

* Due to missing data, AJCC6 stage results are available for only 288 transplanted patients.

Table 2.

Median five-year cancer-specific survival probabilities among US colorectal cancer patients, as a function of cancer subsite, stage at diagnosis, and time since cancer diagnosis *

Cancer subsite and stage		Years since cancer diagnosis					
		0	1	2	3	4	5
Colon cancer							
SEER historic stage	Overall	0.80	0.82	0.84	0.88	0.90	0.93
	Localized	0.95	0.95	0.95	0.96	0.96	0.97
	Regional	0.78	0.80	0.82	0.86	0.89	0.91
	Distant	0.21	0.31	0.41	0.50	0.58	0.66
AJCC6 stage	Overall	0.84	0.84	0.86	0.88	0.90	0.93
	I	0.97	0.98	0.97	0.98	0.98	0.98
	IIA	0.91	0.91	0.92	0.93	0.94	0.95
	IIB	0.75	0.78	0.82	0.85	0.88	0.91
	IIIA	0.92	0.92	0.93	0.94	0.95	0.96
	IIIB	0.78	0.79	0.81	0.84	0.87	0.90
	IIIC	0.61	0.64	0.69	0.75	0.81	0.85
	IV	0.18	0.25	0.34	0.45	0.52	0.61
Rectal cancer							
SEER historic stage	Overall	0.80	0.80	0.80	0.82	0.85	0.88
	Localized	0.92	0.92	0.92	0.93	0.94	0.94
	Regional	0.79	0.78	0.79	0.81	0.84	0.86
	Distant	0.11	0.14	0.26	0.39	0.49	0.58
AJCC6 stage	Overall	0.82	0.81	0.81	0.83	0.86	0.88
	I	0.94	0.94	0.94	0.94	0.95	0.95
	IIA	0.87	0.86	0.87	0.88	0.88	0.90
	IIB	0.69	0.72	0.75	0.79	0.82	0.86
	IIIA	0.89	0.89	0.90	0.91	0.92	0.93
	IIIB	0.79	0.78	0.78	0.80	0.83	0.86
	IIIC	0.67	0.66	0.67	0.71	0.75	0.79
	IV	0.11	0.14	0.25	0.39	0.48	0.58

* Five-year cancer-specific survival probabilities were estimated for SEER cancer patients using cure models. The probabilities at each timepoint are calculated for those patients remaining alive at the specified timepoint, so they reflect the probability of not dying from cancer in the next five years conditional on surviving to that timepoint. The presented estimates are slightly different for overall colorectal cancer, overall colon cancer, and overall rectal cancer depending on which staging system is used in the cure models.

Table 3.
Comparison of recommended wait times with five-year cancer-specific survival probabilities

Cancer subsite and AJCC6 stage	Recommended wait time, measured since completion of treatment ¹	Equivalent recommended wait time, measured since cancer diagnosis ¹	Median 5yCSS at this recommended wait time ²	Earliest wait time, measured since cancer diagnosis, when 5yCSS is at least 0.80	Earliest wait time, measured since cancer diagnosis, when 5yCSS is at least 0.90
Colon cancer					
I	1 year	1.5 years	0.97–0.98	0 years	0 years
IIA	2 years	2.5 years	0.92–0.93	0 years	0 years
IIB	3–5 years	3.5–5.5 years	0.85–0.91	2 years	5 years
IIIA	3–5 years	3.5–5.5 years	0.94–0.96	0 years	0 years
IIIB	3–5 years	3.5–5.5 years	0.84–0.90	2 years	5 years
IIIC	3–5 years	3.5–5.5 years	0.75–0.85	4 years	> 5 years
IV	5 years	5.5 years	0.61	> 5 years	> 5 years
Rectal cancer					
I	1–2 years	1.5–2.5 years	0.94	0 years	0 years
IIA	3–5 years	3.5–5.5 years	0.88–0.90	0 years	5 years
IIB	3–5 years	3.5–5.5 years	0.79–86	4 years	> 5 years
IIIA	3–5 years	3.5–5.5 years	0.91–0.93	0 years	2 years
IIIB	3–5 years	3.5–5.5 years	0.80–0.86	3 years	> 5 years
IIIC	3–5 years	3.5–5.5 years	0.71–0.79	> 5 years	> 5 years
IV	5 years	5.5 years	0.58	> 5 years	> 5 years

Abbreviations: 5yCSS 5-year cancer-specific survival

¹Recommended wait times are from Al-Adra et al. (13), which measures wait time from the completion of cancer treatment. The equivalent wait time measured from cancer diagnosis is calculated by assuming that cancer treatment is completed at 6 months after diagnosis.

²Five-year cancer-specific survival probabilities are taken from the estimates in Table 2, for the years bracketing the recommended waiting time in Al-Adra et al. (13). For recommended wait times of 5 years after the end of cancer treatment (i.e., 5.5 years after cancer diagnosis), the median probability at 5 years after cancer diagnosis is presented.