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Cricket Gullickson December 28, 2020

Colorectal cancer survival in sub-Saharan Africa by age, stage at diagnosis, and Human Development Index: A population-based registry study

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Abstract

Colorectal cancer survival in sub-Saharan Africa by age, stage at diagnosis, and Human Development Index: A population-based registry study

By Cricket Gullickson

Background: Although colorectal cancer is the fifth most commonly diagnosed cancer in Africa and its burden is rising, there are limited population-level survival data for planning and assessing the effectiveness of local colorectal cancer control programs in the region. Herein, we provide the first estimates of population-based survival data for many countries in sub-Saharan Africa.

Methods: 1,707 persons diagnosed with colorectal cancer from 2005-2015 were randomly selected from 13 population-based cancer registries operating in 11 countries (Benin, Cote d'Ivoire, Ethiopia, Kenya, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Uganda, and Zimbabwe) in sub-Saharan Africa. Vital status was ascertained from medical charts or through next of kin. 1-, 3-, and 5-years overall survival rates for all registries combined and for each registry were calculated using the Kaplan Meier estimator. Multivariable analysis was used to examine the associations of 5-year overall survival with age at diagnosis, stage, and country-level Human Development Index (HDI). All analyses were performed using Stata, and all statistical tests were two-sided and considered significant when $P < 0.05$.

Results: Overall survival across all registries combined was 72.0% (95% CI 69.5-74.4%) at 1 year, 50.4% (95% CI 47.6-53.2%) at 3 years, and 43.5% (95% CI 40.6-46.3%) at 5 years. Factors associated with poorer survival included living within a country with lower HDI, late stage at diagnosis, and younger or older age at diagnosis (<50 or ≥ 70 years). For HDI, for example, the risk of death was 1.6 (95% CI 1.2-2.1) times higher for individuals residing in medium HDI countries and 2.7 (95% CI 2.2-3.4) times higher for individuals residing in low HDI countries compared to those residing in high HDI countries.

Conclusions: Survival for colorectal cancer remains considerably low in sub-Saharan African countries. Strengthening health systems to ensure access to prevention, early diagnosis, and appropriate treatment will likely be critical in improving outcomes in colorectal cancer in the region.

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Introduction

Colorectal cancer is the fifth most common invasive malignancy in Africa.[1] While the disease is more common in the north of the continent,[1] there is evidence that incidence of colorectal cancer in sub-Saharan Africa is rising as many areas within the region experience rapid socioeconomic development, urbanization, and associated lifestyle changes, as well as increasing life expectancy.[2, 3]

Several previous studies reported that colorectal cancer survival in sub-Saharan Africa is poor,[4-9] likely attributable to late diagnosis due to inadequate access to screening services, and limited treatment options. Most of these studies, however, used hospital-based cancer registries rather than population-based registries, and their findings have limited generalizability to the population at large for guiding and assessing the effectiveness of local colorectal cancer programs. Population-based cancer registries are now increasingly available in sub-Saharan Africa due to the collaboration between the International Agency for Research on Cancer (IARC) and the African Cancer Registry Network (AFCRN)— which serves as a regional hub for cancer registration on the continent[13]— for estimating population-based survival data in several parts of sub-Saharan Africa.

The goal of the current study was to estimate the observed and relative population-based colorectal cancer survival in sub-Saharan Africa, and to investigate the associations of age, stage at diagnosis, and human development index with relative survival 1, 3 and 5 years after diagnosis using data from 13 population-based cancer registries operating across 11 countries of the AFCRN.

Methods

Study Population

Data pertaining to newly diagnosed colorectal cancer patients were obtained from the AFCRN, in collaboration with 13 individual member registries in Cotonou (Benin), Abidjan (Cote d'Ivoire), Addis Ababa (Ethiopia), Eldoret (Kenya), Nairobi (Kenya), Mauritius, Maputo (Mozambique), Namibia, Eastern Cape (South Africa), Seychelles, Kampala (Uganda), Bulawayo (Zimbabwe), and Harare (Zimbabwe). Of those, Mauritius, Namibia, and Seychelles have national coverage and Eastern Cape covers a rural area, while the remaining registries represent primarily large urban populations. The analysis dataset included a random sample of 1,707 incident colorectal cancer cases (ICD-10: C18, 19, 20) randomly selected from each registry with diagnosis dates between 2005 and 2015. The number of cases sampled per registry varied based on feasibility of obtaining follow-up information. All patients were 20 years or older at the time of diagnosis. Survival time was calculated as the interval between the date of colorectal cancer diagnosis and the date of last contact, death, or end of study (December 31, 2017), depending on which occurred first.

Variables of Interest

Vital Status

Among all registries that provided data for analysis, only Mauritius relied exclusively on linkages with national death records. In all other registries, clinical records were reviewed for vital status information and the date of last contact. If vital status could not be ascertained through record review, the registry staff attempted to contact patients or their relatives through telephone calls or home visits. If vital status could not be determined through these means, participants were censored at the date of the last known contact.

Stage at diagnosis

Information on stage at diagnosis was collected at the time of registration using the tumor, node and metastasis (TNM) stage groupings of the Eighth Edition of the American Joint Committee on Cancer (AJCC) classification.[14] If TNM data were not available, the summary stage information was used. Stages I and II were grouped as "early stage" category, while Stages III and IV were grouped as "late stage". Records without this information were categorized as "missing stage". Stage information was not available for Mauritius.

Country-level Human Development Index

A country's HDI is determined by the average life expectancy at birth, years of education, and per capita income.[15] Each registry was assigned to a category of low, medium, or high HDI according to the classification used in the United Nations Development Program's 2015 Human Development Report.[15]

Data Analyses

The total number of colorectal cancer cases, proportion of excluded cases, and percentage of histologically verified cancers were calculated for each registry. Cases were excluded if they had: 1) an unknown date of diagnosis, 2) zero follow-up or no follow-up information, 3) diagnoses of anal or appendiceal cancer, or 4) histological tumor types that were atypical for primary colorectal cancer (i.e., Kaposi sarcoma, neuroendocrine, carcinoid, squamous cell, lymphoma, etc.).

The analysis dataset included 1,707 patients randomly selected from colorectal cancer cases reported to the 13 participating population-based registries across 11 countries. A total of 259 individuals (15.2%) were excluded from the analyses for the following reasons: 181 individuals (10.6%) had no follow-up or had inconsistent follow-up dates; 4 individuals had

unknown diagnosis dates or diagnosis dates that fell outside the study period (0.2%); 7 individuals (0.4%) were under the age of 20; 14 individuals (0.8%) had a diagnosis of anal cancer; 8 individuals (0.5%) had a diagnosis of appendiceal cancer; and 45 individuals (2.6%) had colorectal tumors with atypical histology (25 squamous cell carcinomas, 3 carcinoid tumors, 3 rhabdoid carcinomas, 3 basaloid carcinomas, 3 papillary carcinomas, 2 neuroendocrine tumors, 1 Kaposi sarcoma, 1 leiomyosarcoma, 1 lymphoma, 1 giant cell tumor, 1 myxoid liposarcoma, and 1 small cell carcinoma).

Observed survival

The semi-compete approach to survival analysis is commonly used when estimating survival using data from cancer registries.[16] This approach includes only patients who have a defined minimum potential follow-up time at the closing date, rather than including all patients diagnosed prior to the closing date.[16] Using this approach, observed survival probabilities were calculated at 1, 3, and 5 years of follow-up. Kaplan-Meier survival curves were constructed both overall, and by HDI, age group and stage at diagnosis. All comparisons of Kaplan-Meier survival curves were accompanied by log-rank tests. The proportion of participants lost to follow-up was also calculated at 1, 3, and 5 years.

Relative and expected survival

Ederer II relative survival estimates were also calculated at 1, 3, and 5 years of follow-up using the "strs" command in Stata.[17] Expected survival probabilities were calculated for each registry by creating age-specific life tables for the general population in each country during the study period. Mortality rates by year, sex, country, and five-year age-group were obtained from the World Health Organization Mortality database.[17] These abridged tables were expanded using a Poisson regression model to create a complete lifetable by one-year age group.

Excess hazards model

To model excess mortality, flexible Poisson regression models with restricted cubic splines were created using the "rcsgen" command in Stata.[18] Monthly intervals were used, with the assumption that baseline hazards were constant within each interval. The effects of country-level HDI, sex, stage, and age at diagnosis on excess mortality were assessed in both univariate and multivariate models. All models were further evaluated for two-way interactions between HDI and each of the covariates. The results of models were expressed as adjusted hazard ratios (HR) and the corresponding 95% confidence intervals (CI).

Results

Among the 1,448 individuals included in the final survival analysis dataset, 717 died during the study period. Overall, 85.9% of patients had histologically verified colorectal cancer, although that proportion ranged from 45.9% in Kampala, Uganda, to 98.2% in Seychelles (Table 1). A majority of cases were adenocarcinomas (89.9%), followed by unspecified carcinomas (4.8%), unspecified malignant neoplasms (3.6%), and other specified carcinomas (e.g., signet ring cell carcinoma, or adenosquamous carcinoma) (1.6%).

The average age at diagnosis was 58.1 years overall, ranging from 48.8 years in Maputo, Mozambique, to 62.2 years in Mauritius (Table 2). The median duration of follow-up was 1.7 years, ranging from 0.3 years in Maputo, Mozambique, and Kampala, Uganda, to 4.8 years in Mauritius. Stage information was available for 25.1% of patients. Of those with known stage, only 33.0% of patients were diagnosed with Stage I or II disease, and Seychelles accounted for 41.1% of those diagnosed at an early stage.

Loss to follow-up

Loss to follow-up was highest in the first year after diagnosis, with Eldoret having the highest loss to follow-up at 40.5% and Mauritius and Seychelles having the lowest at 0%. When assessed in a Cox model, loss to follow-up at one year was not associated with age or known stage in any registry. Follow-up extended to five years in nine of the 13 registries. Among registries that followed cases for up to 5 years, the percentage with complete follow-up and known vital status ranged from 1.0% in Kampala to 45.4% in Mauritius.

Overall survival

The overall observed survival in this cohort was 72.0% (95% CI 69.5-74.4%) at 1 year, 50.4% (95% CI 47.6-53.2%) at 3 years, and 43.5% (95% CI 40.6-46.3%) at 5 years (Figure 1A).

Figure S1 shows overall observed Kaplan-Meier survival curves by registry, with the lowest 5-year observed survival in Kampala at 4.5% (95% CI 0.4-17.2%) and the highest in Mauritius at 60.3% (95% CI 55.6-64.7%).

Relative survival for all registries combined was 75.6% (95% CI 73.1-78.0) at 1 year, 57.2% (95% CI 54.1-60.3) at 3 years, and 54.0% (95% CI 50.5-57.5) at 5 years. By HDI, survival was lowest in low HDI countries. By registry, relative survival at one year after diagnosis ranged from 52.5% (95% CI 36.9-66.2) in Bulawayo, Zimbabwe, to 87.2% (95% CI 83.3-90.4) in Mauritius. Similarly, the relative survival at five years after diagnosis ranged from 5.6% (95% CI 0.5-21.4) in Kampala, Uganda, to 75.7% (95% CI 69.8-81.2) in Mauritius (Figure 2).

Survival by age, stage, and country-level HDI

Individuals diagnosed between the age of 50 and 69 years had a higher overall survival probability than those in the younger or older age groups (Figure 1B, log rank test p-value = 0.007). The overall 5-year survival among patients in the 50- to 69-year age group was 47.4% (95% CI 43.1-51.5%), compared to 38.8% (95% CI 33.2-44.3%) in those under 50 and 40.9% (95% CI 35.7-46.1%) in those age 70 and older.

Early-stage disease was also associated with better survival relative to late-stage colorectal cancer (Figure 1C, log-rank test p-value <0.001) with 5-year survival estimates of 52.1% (95% CI 42.0-61.2%) and 29.2% (95% CI 22.9-35.9%), respectively.

As HDI increased so did colorectal cancer survival (Figure 1D, log-rank test p-value <0.001). Individuals from high HDI areas had a 5-year overall survival of 57.0% (95% CI 52.8-61.0%) compared to 46.4% (95% CI 38.8-53.8%) in those from medium HDI registries and 25.2% (95% 21.0-29.6%) in those from low HDI registries. There were differences in relative

survival by country-level HDI, even within the same stage category (Figure 3). 5-year relative survival for individuals with Stage I -II colorectal cancer was 73.9% (95% CI 55.2-89.3) in high HDI registries, compared to 51.0% (95% CI 29.7-71.2) in low HDI registries. Similarly, individuals diagnosed with Stage III-IV colorectal cancer in registries with high country-specific HDI had higher relative survival (31.8% [95% CI 17.4-48.3]) than those from registries with low country-specific HDI (17.9% [95% CI 8.5-30.6]).

Excess hazards model

In the multivariable Poisson regression models, there was statistically significant interaction between county-level HDI and stage at diagnosis. For this reason, the results of the multivariable models are presented both overall (adjusted for stage) and separately for each stage category (Table 3).

In the overall multivariable model, using individuals from countries with high HDI as reference, mortality was 1.6 times higher (95% CI 1.2-2.1) for patients from countries with medium HDI and 2.7 times higher (95% CI 2.2-3.4) for patients from countries with low HDI. Compared to persons diagnosed with colorectal cancer under the age of 50, the HR (95% CI) estimates for those 50-59 and over 69 years of age were 0.8 (0.6-1.0) and 0.9 (0.7-1.1), respectively. There was no evidence that colorectal cancer mortality differed in male and female patients (HR: 1.0; 95% CI: 0.9-1.2).

In the stage-specific models, the results for HDI differed across strata. Among persons diagnosed with early-stage colorectal cancer and among those whose disease remained unstaged, the associations between HDI and mortality were generally similar to those observed in the overall multivariable analyses. By contrast, in the model limited to patients with late-stage cancer, those from medium HDI countries experienced lower mortality (HR: 0.4; 95% CI: 0.2-

0.7) and those from low HDI countries had similar mortality (HR: 1.1; 95% CI: 0.7-1.7) compared to patients who were reported to registries in high HDI countries. The point estimates of the association between age and colorectal mortality did not differ appreciably by stage; however, the 95% CIs around those estimates were wider than those in the overall model. None of the stage-specific associations between sex and mortality demonstrated significant departures from the null.

Discussion

This study comparing colorectal cancer survival across 13 population-based cancer registries in 11 African countries found that survival substantially varies across registries, with rates considerably lower in the low HDI registries. The overall 5-year relative survival of 54% in this cohort of colorectal cancer patients diagnosed between 2005 and 2015 was generally similar to that reported in Western Europe in the 1980s and 1990s. For example, the 5-year relative survival was 56% for those diagnosed with colorectal cancer between 1988-1999 in France,[19] and 56% for males and 60% for females diagnosed between 1993-1997 in Norway.[20] By contrast, the 5-year relative survival for individuals diagnosed with colon cancer and rectal cancer between 2010-2014 in the Netherlands was 62% and 65%, respectively.[21] Of note, three-quarters of patients who remained within our cohort at five years of follow-up were from countries with high HDI, which indicates that the actual five-year survival across the region may be lower.

Although information on colorectal cancer survival using data from population-based cancer registries in sub-Saharan Africa is limited, our estimates may be compared to those found previously in other studies using more local data. For example, patients diagnosed with colorectal between the years of 1993-1997 in the Kampala Cancer Registry were found to have a 5-year absolute survival of 7%,[10] and those diagnosed with colorectal cancer between the years of 1993-1997 in Harare were found to have a 5-year relative survival of 17%.[22] By comparison, during our study period (2009-2013), the 5-year absolute and relative survival estimates in the Kampala and Harare registries were 5% and 39%, respectively. Thus, while colorectal cancer survival in Harare is clearly higher now than it was in the mid-1990s, it does not appear to have improved in Kampala during the decade between the two study periods.

Stage at diagnosis is an established predictor of colorectal cancer mortality.[5, 23, 24] In this cohort we confirmed previous findings from sub-Saharan Africa indicating that later stage at diagnosis was associated with poorer survival.[25] The association remained even after adjusting for age, sex, and country-level HDI. While staging information was limited in this cohort, 66% of those with known stage were diagnosed at a late stage. Other studies on colorectal cancer in sub-Saharan Africa have observed a similarly high proportion of individuals presenting at a late stage. For example, in a study conducted across five hospitals in Nigeria between 2013 and 2017, 89% of colorectal cancer patients presented at Stages III or IV.[26] The high proportion of patients presenting with advanced stage colorectal cancer is likely attributable to multiple factors, including a lack of widespread screening programs, limited access to adequate care, scarcity of and appropriately trained professionals, and cancer-related stigma, which may affect care utilization in some communities.[25, 27, 28 29]

HDI is a composite measure of a country's average life expectancy, years of education, and per capita income.[15] Lower country-level HDI in this study was associated with poorer survival after adjustment for other covariates in the overall and two of the three stage-specific (early stage, and missing stage) multivariate models. The five-year relative colorectal cancer survival in our sub-cohort of patients from low HDI countries was 31%; lower than the corresponding estimates seen in Europe in the 1970s, where overall 5-year relative survival estimates for those diagnosed between 1978-1980 were 40% and 38% for colon and rectal cancer, respectively.[30] Even when diagnosed at an early stage, individuals with colorectal cancer who lived in low HDI countries were more than two times more likely to die than those who lived in high HDI countries, suggesting that factors associated with HDI play an important role in colorectal cancer survival in sub-Saharan Africa independent of stage at diagnosis. The

association between lower economic development in a country and poorer cancer outcomes likely reflects the strength and accessibility of the country's health system and its ability to provide timely and appropriate diagnoses and treatments, as well as the level of health awareness in the population.[31] In countries that had multiple registries, observed and relative survival estimates were higher in capital cities than in more rural areas, consistent with findings from other studies.[31] This likely reflects the fact that oncological and surgical centers are concentrated in capital cities and urban centers.[25, 31]

A somewhat unexpected finding was the absence of an association when comparing mortality in low and high HDI countries and the inverse association when comparing low and medium HDI countries in the model restricted to cases with advanced colorectal cancer. The discrepancy between this result and the results from other models that showed all associations between HDI and mortality in the hypothesized direction was likely due to the lack of geographic diversity in the underlying data, and possibly confounding by rural-urban status. It is worth noting that in the late-stage disease specific model, all 47 patients diagnosed and treated in a high HDI country were from the countrywide registry in the Seychelles, an island nation with just over 50% of the population living in urban areas and only about 28% of the population residing in its largest city.[32] By contrast, 54% of the 68 late-stage colorectal cancer patients from countries with medium HDI lived in Nairobi, a large city that has relatively well-developed health care infrastructure. Similarly, of the 124 individuals diagnosed at a late stage from countries with low HDI, all came from the large urban areas of Cotonou (n=7), Abidjan (n=10), Addis Ababa (n=12), Maputo (n=1), Bulawayo (n=19), Kampala (n=7), and Harare (n=69).

We also observed survival differences by age group. Patients diagnosed between the ages of 50 and 69 years had better survival than those in the younger and the older age groups.

Previous work has shown that colorectal cancer prognosis tends to be poorer in patients over 75 years of age, likely due to increased comorbidities and operative mortality and less aggressive treatment.[33] Colorectal cancer survival also tends to be lower in those diagnosed under the age of 40, perhaps due to more aggressive tumor types and delays in diagnosis.[34]

This study has several methodological limitations. Random sampling was used to collect data from 13 population-based cancer registries across 11 countries, but the sample sizes for several registries were small due to limited resources, and restricted ability to ascertain vital status, especially as the time from diagnosis increased. Another notable problem with the available data is the incomplete stage information, which was available for only 25% of the total cohort. In addition, no data were collected on other known determinants of colorectal cancer prognosis, such as treatment and tumor biology, all of which may need to be considered in the future analyses.[35, 36]

These limitations notwithstanding, the present study offers a more robust understanding of colorectal cancer survival in sub-Saharan Africa. In addition to providing survival estimates, this work also identifies important factors influencing colorectal cancer survival in the region. Strengthening healthcare systems to increase screening capacity and improve access to oncological care will be important as colorectal cancer incidence in sub-Saharan Africa continues to further increase.

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Tables and Figures

Table 1. Numbers of colorectal cancer diagnoses, included and excluded cases, and data quality indicators by cancer registry

Country	HDI 2015	Registry	Period of diagnosis	Number of randomly sampled cases for survival study	Histologically verified n (% of cases included)	Included in analyses *n* (%)
Benin	Low	Cotonou	2013-2014	20	15 (79.0)	19 (95.0)
Cote d'Ivoire	Low	Abidjan	2011-2013	112	55 (65.5)	84 (75.0)
Ethiopia	Low	Addis Ababa	2012	139	95 (74.8)	127 (91.4)
Kenya	Medium	Eldoret	2009-2013	73	32 (86.5)	37 (50.7)
Kenya	Medium	Nairobi	2009-2013	150	115 (83.9)	137 (91.3)
Mauritius	High	Mauritius	2005-2009	460	442 (97.8)	452 (98.3)
Mozambique	Low	Maputo	2014-2015	25	19 (82.6)	23 (92.0)
Namibia	Medium	Namibia	2012-2015	80	53 (96.4)	55 (68.8)
Seychelles	High	Seychelles	2008-2013	121	106 (98.2)	108 (89.3)
South Africa	Medium	Eastern Cape	2008-2013	69	24 (60.0)	40 (58.0)
Uganda	Low	Kampala	2009-2013	149	45 (45.9)	98 (65.8)
Zimbabwe	Low	Bulawayo	2012-2013	60	43 (79.6)	54 (90.0)
Zimbabwe	Low	Harare	2009-2013	249	199 (93.0)	214 (85.9)

Abbreviations: HDI, Human Development Index (United Nations Development Program Human Development Report 2015)

Table 2. Patient characteristics: mean age at diagnosis, median years of follow-up, losses to follow up, and observed (all-cause) survival

Country, Registry	Cases, N	Mean diagnosis age, years	Year 1			Years 2 and 3			Years 4 and 5		Median follow-up, years (min-max)
			Deaths, N (%)	LTFU, N (%)	1-year OS*,%	Deaths, N (%)	LTFU, N (%)	3-year OS*, %	Deaths, N (%)	5-year OS*, %	
Benin, Cotonou	19	54.3	3 (15.8)	4 (21.1)	82.1	3 (15.8)	2 (10.5)	59.2	3 (15.8)	21.2**	2.9 (0-3.7)
Cote d'Ivoire, Abidjan	84	52.5	16 (19.0)	33 (39.3)	73.8	15 (17.9)	1 (1.2)	42.1	4 (4.8)	32.5	0.4 (0-5.7)
Ethiopia, Addis Ababa	127	50.9	40 (31.5)	14 (11.0)	65.4	32 (25.2)	15 (11.8)	35.8	8 (6.3)	21.7**	1.2 (0-5.0)
Kenya, Eldoret	37	53.1	11(29.7)	15 (40.5)	56.1	3 (8.1)	3 (8.1)	39.7	1 (2.7)	19.9	0.5 (0-6.5)
Kenya, Nairobi	137	55.2	23 (20.4)	36 (26.3)	79.6	18 (13.1)	16 (11.7)	59.1	3 (2.2)	54.1	1.1 (0-8.3)
Mauritius	452	62.2	73 (16.2)	0 (0.0)	83.9	82 (18.1)	0 (0.0)	65.7	23 (5.1)	60.3	4.8 (0-9.0)
Mozambique, Maputo	23	48.8	6 (26.1)	8 (34.8)	67.6	0 (0)	9 (39.1)	67.6**	-	-	0.3 (0-2.0)
Namibia	55	55.3	11 (20.0)	9 (16.4)	77.9	10 (18.2)	3 (5.5)	54.9	3 (5.5)	47.1	1.8 (0-6.0)
Seychelles	108	65.0	34 (31.5)	0 (0.0)	68.5	18 (16.7)	0 (0.0)	51.9	9 (8.3)	43.4	3.3 (0-8.8)
South Africa, Eastern Cape	40	52.4	13 (32.5)	7 (17.5)	64.4	7 (17.5)	4 (10.0)	37.6	1 (2.5)	33.4	0.9 (0-6.2)
Uganda, Kampala	98	51.5	34 (34.7)	35 (35.7)	51.0	17 (17.3)	6 (6.1)	16.1	3 (3.1)	4.5	0.3 (0-8.0)
Zimbabwe, Bulawayo	54	60.0	23 (42.6)	15 (27.8)	45.8	5 (9.3)	7 (13.0)	29.7	1 (1.9)	22.2**	0.5 (0-4.4)
Zimbabwe, Harare	214	61.1	81 (37.9)	5 (2.3)	60.9	50 (23.4)	0 (0.0)	37.4	13 (6.1)	30.0	1.6 (0-8.4)

Abbreviation: LTFU, lost to follow-up; OS= observed survival

* Calculated using Kaplan-Meier method

**Represents that the last patient was censored before the end of the period. In Cotonou, Benin, the last patient was censored at 3.72 years. In Addis Ababa, Ethiopia, the last patient was censored at 4.99 years. In Maputo, Mozambique, the last patient was censored at 2.04 years. In Bulawayo, Zimbabwe, the last patient was censored at 4.42 years

Table 3. Multivariable Poisson regression models* of colorectal cancer mortality in relation to country-level HDI, age at diagnosis, sex, and disease stage

Variable	Overall model adjusted for stage				Early stage model				Late stage model				Unknown stage model			
	N cases	HR	95% CI	p-value	N cases	HR	95% CI	p-value	N cases	HR	95% CI	p-value	N cases	HR	95% CI	p-value
Country-level HDI																
High HDI	560	1 (Ref)			51	1 (Ref)			47	1 (Ref)			462	1 (Ref)		
Medium HDI	269	1.6	1.2-2.1	0.002	27	1.6	0.6-4.3	0.311	68	0.4	0.2-0.7	0.003	174	2.1	1.5-3.0	<0.001
Low HDI	619	2.7	2.2-3.4	<0.001	46	2.6	1.1-6.0	0.024	125	1.1	0.7-1.7	0.785	448	3.1	2.4-4.0	<0.001
Age at diagnosis																
<50 years	391	1 (Ref)			37	1 (Ref)			68	1 (Ref)			286	1 (Ref)		
50-69 years	677	0.8	0.6-1.0	0.016	56	0.8	0.4-1.6	0.498	107	0.8	0.5-1.2	0.196	514	0.8	0.6-1.0	0.042
≥70 years	380	0.9	0.7-1.1	0.350	31	0.7	0.2-2.4	0.601	65	1.1	0.7-1.8	0.750	284	0.8	0.6-1.1	0.272
Sex																
Male	731	1 (Ref)			70	1 (Ref)			114	1 (Ref)			547	1 (Ref)		
Female	717	1.0	0.9-1.2	0.702	54	0.5	0.3-1.1	0.095	126	1.2	0.8-1.8	0.305	537	1.1	0.9-1.3	0.504
Stage at diagnosis																
Early	124	1 (Ref)														
Late	240	1.8	1.2-2.7	0.005												
Unknown	1,084	1.5	1.0-2.2	0.035												

Abbreviations: HDI, human development index; N cases, number of cases; HR, hazard ratio, CI, confidence interval; Ref, reference

* Each model examines the association between country-level HDI, and colorectal cancer mortality; overall model adjusts for age at diagnosis, stage at diagnosis, and sex; stage-specific models adjust only for age at diagnosis, and sex.

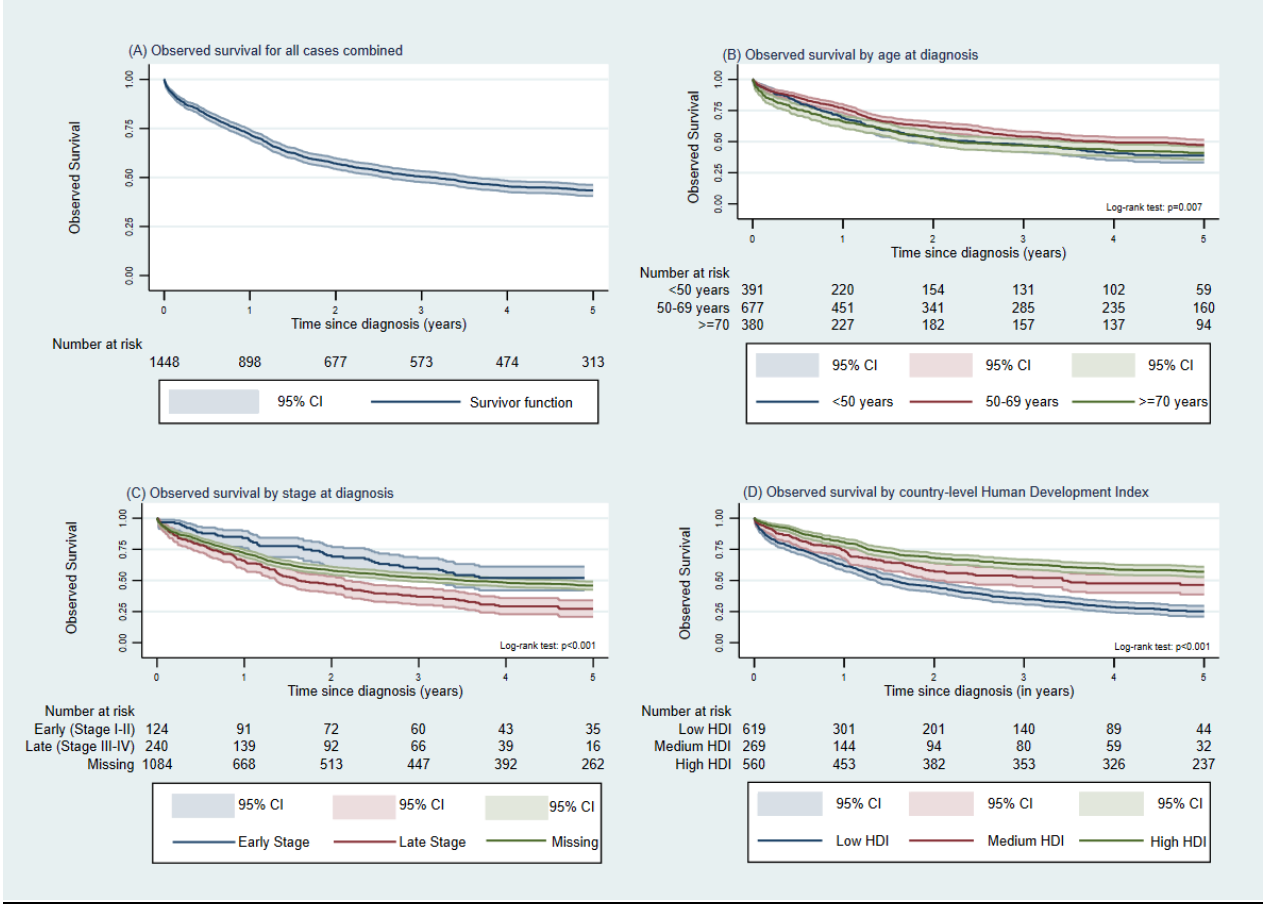

Figure 1: Kaplan-Meier survival curves among colorectal cancer patients: 13 registries

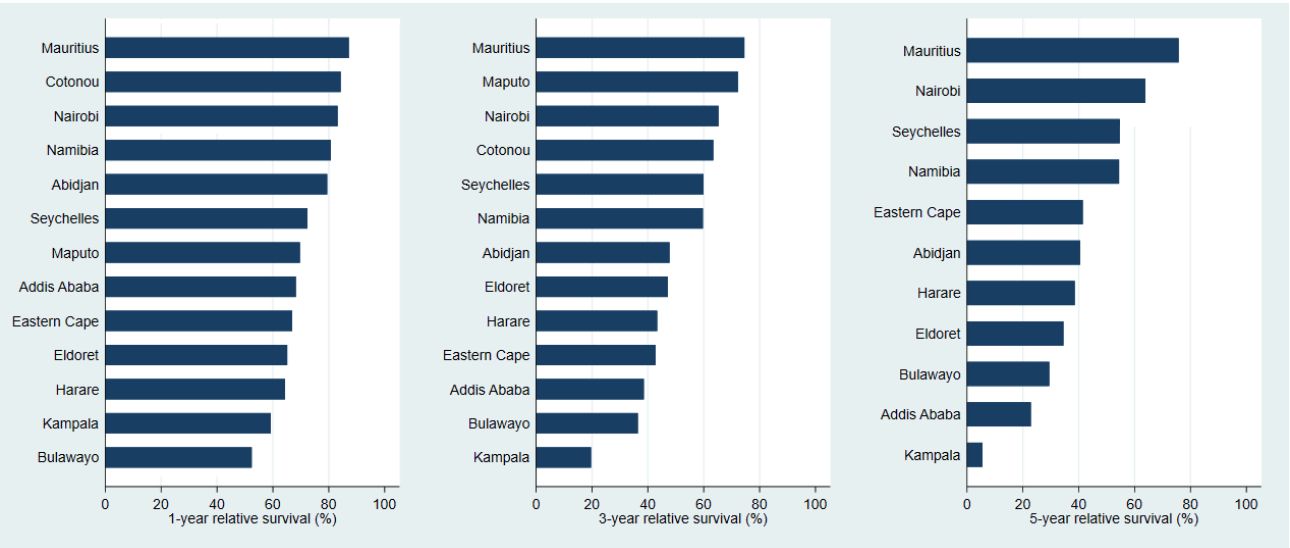

Figure 2: Relative survival from colorectal cancer at 1, 3, and 5 years after diagnosis, by registry

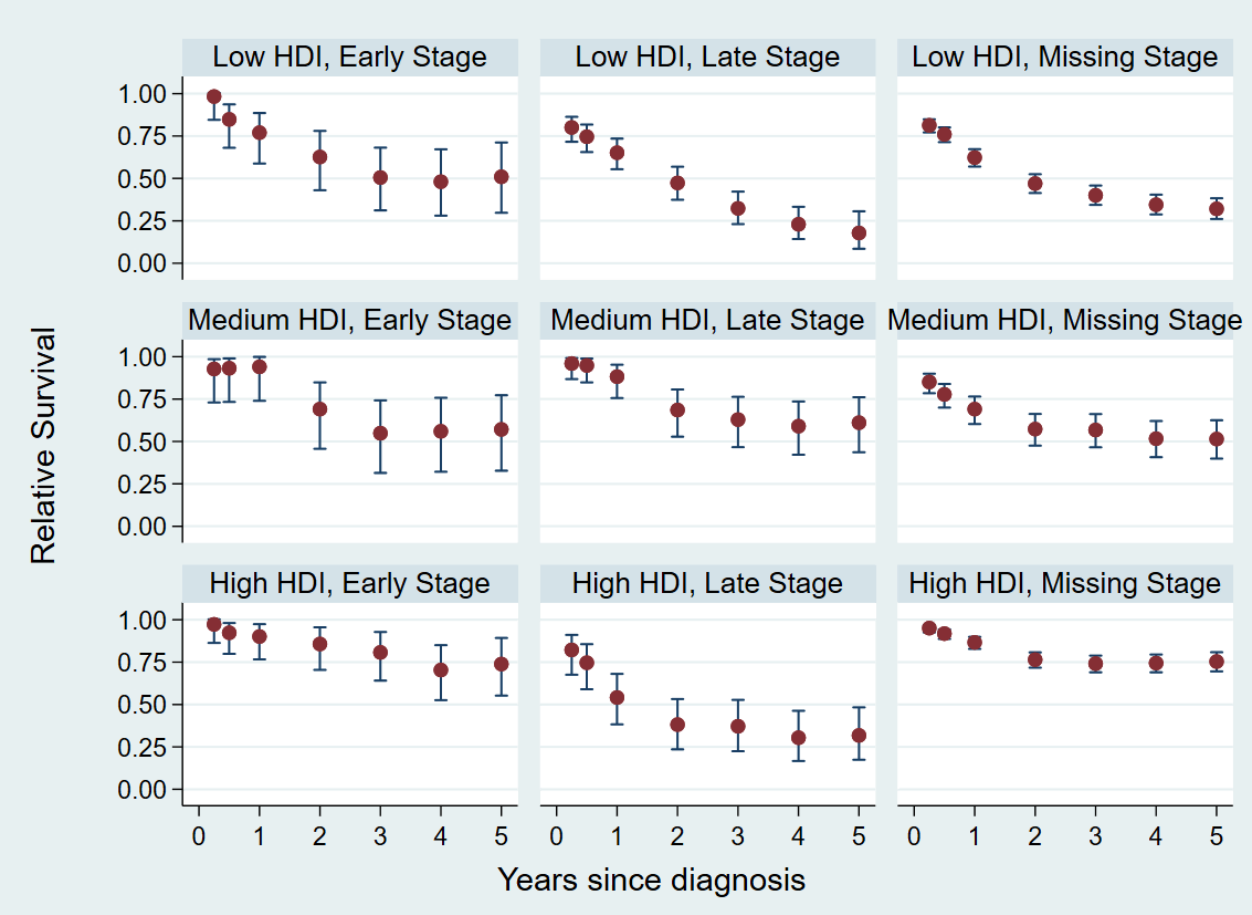

Figure 3: Relative survival by country HDI and stage at diagnosis

Supplemental Figures

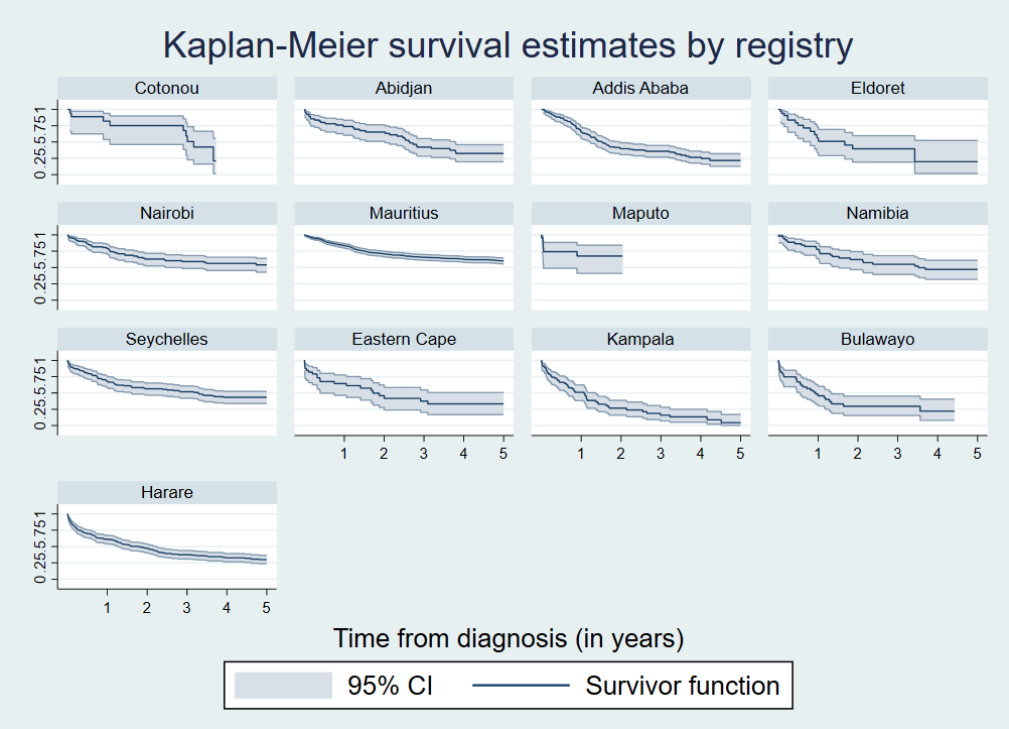

Figure S1: Overall Kaplan-Meier survival by registry

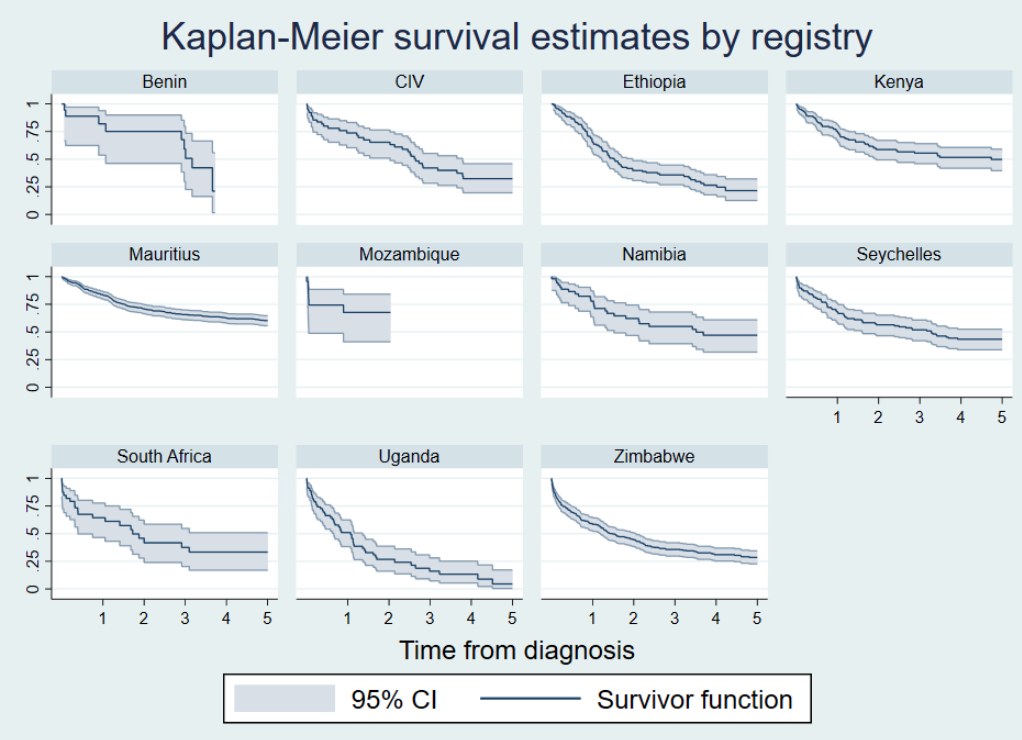

Figure S2: Overall Kaplan-Meier survival by country