Manuscript Title: Rectal Cancer Survival in the United States by Race and Stage (2001-2009): Findings from the CONCORD-2 study

Running Title: Rectal cancer survival by race and stage

Djenaba A. Joseph, MD, MPH[1]; Chris J. Johnson, MPH[2]; Arica White, PhD[1]; Manxia Wu[1]; Michel P. Coleman, FFPH[3]
Affiliations:

[1]Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA

[2]Cancer Data Registry of Idaho, Idaho Hospital Association, Boise, ID

[3]Cancer Survival Group, Non-Communicable Disease Epidemiology Unit, London School of Hygiene and Tropical Medicine, London, UK

Corresponding Author: Djenaba A. Joseph, MD, MPH, Centers for Disease Control and Prevention, Division of Cancer Control and Prevention, 4770 Buford Hwy, MS F76, Atlanta, GA 30341; phone: (770)488-3157; fax: (770)488-4639; email: dajoseph@cdc.gov

Funding: This research was supported through an interagency agreement between the National Cancer Institute and Centers for Disease Control and Prevention (CDC). This Supplement edition of *Cancer* has been sponsored by the (CDC), an Agency of the Department of Health and Human Services. The ideas expressed in the articles are those of the authors and do not necessarily reflect the official position of the Centers for Disease Control and Prevention.

Conflict of Interest Disclosures: None

Author Contributions: D. A. Joseph conceptualized the article, interpreted the data, drafted the article and coordinated the writing team. C. J. Johnson, A. White and M. Wu contributed to the data interpretation, drafting, critical review and revision of the article. M. P. Coleman conceptualized the article, acquired the data, coordinated the analysis and contributed to revision of the article. All authors approved the final draft of the article.

Precis: There was little improvement in overall net survival for rectal cancer, with wide variation between states and persistent, but narrowing disparities between blacks and whites.

Keywords: rectal cancer, colorectal cancer, population-based survival, trends

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Cancer Institute.

Abstract

Background: In the first CONCORD study, overall 5-year survival for rectal cancers diagnosed between 1990 and 1994 was below 60%, with large racial disparities in most participating states. We have updated these findings to 2009 by examining population-based survival by stage at diagnosis, race, and calendar period.

Methods: We used data from the CONCORD-2 study to compare survival among people (age 15-99 years) diagnosed in 37 states covering up to 80% of the U.S. population. Survival was adjusted for background mortality (net survival) using state- and race-specific life tables and age-standardized using the International Cancer Survival Standard weights. Survival up to five years is presented by race (all, black and white) for 2001-2003 and 2004-2009 to account for changes in collecting SEER Summary Stage 2000.

Results: There was a small increase in 1-, 3- and 5-year net survival between the two time periods (84.6%, 70.7% and 63.2% respectively in 2001-2003; 85.1%, 71.5%, and 64.1% respectively in 2004-2009). Blacks had lower 1-, 3-, and 5-year survival than whites in both periods; the absolute difference in survival between blacks and whites declined only for 5-year survival. Blacks had lower 5-year survival than whites for each stage at diagnosis in both time periods.

Conclusions: There was little improvement in net survival for rectal cancer, with persistent, but narrowing disparities between blacks and whites. Additional investigation is needed to identify and implement effective interventions to ensure consistent and equitable use of high-quality screening, diagnosis, and treatment to improve survival for rectal cancer.

Introduction

Worldwide, colorectal cancer is the third most common cancer in men and the second most common cancer in women.[1] More than half of cases occur in more developed countries. Although incidence is lower in less developed regions of the world, mortality is higher, with the highest mortality in Central and Eastern Europe.[1] In the United States, of cancers that affect both men and women, colorectal cancer is the second most common cancer and the third most common cause of cancer death.[2]

Rectal cancer comprises approximately one-third of incident colorectal cancers in the United States[2] Although commonly combined with colon cancer for reporting purposes due to anatomic location and shared screening methods, rectal cancer differs substantially from colon cancer, particularly in terms of clinical management. The incidence of rectal cancer declined 2.2% per year from 2003 through 2012, with greater declines among men compared to women and among whites compared to blacks. For all sub-populations, declines in incidence have been smaller than those seen for colon cancer.[3] Mortality for rectal cancer has also declined, again to a lesser extent than for colon cancer. Similar patterns of disparities are seen with rectal cancer, with men having higher incidence and mortality than women, and blacks having higher incidence and mortality than other racial/ethnic groups.[3]

Population-based cancer survival provides an indicator of the overall effectiveness of the health care system to deliver screening, early diagnosis, and evidenced-based treatment services to all people in the population being served.[4] Survival differences between populations may be attributable to disparities in access to early diagnosis and optimal treatment.[5] The first CONCORD study analyzed survival data from 31 countries for patients diagnosed with cancer during 1990-1994 and followed up to 1999. In the United States five-year relative survival for rectal cancer was 57.0% for men and 59.9% for women, with consistently lower survival among blacks compared to whites for the 22 metropolitan and state cancer registries included in the study.[6] The CONCORD-2 study analyzed survival data from 67 countries for patients diagnosed with cancer during 1995-2009 and followed up to December 31, 2009 or later.[5] The 5-year net survival for rectal cancer was highest

(more than 70%) in Cyprus, Iceland, and Qatar, and high (60% - 69%) in North America, South Korea, Oceania, and nine European countries, with the United States having the ninth highest survival overall. The 5-year net survival increased over the study period for most countries, and in the U.S. it increased from 60% in 1995-1995 to 64% in 2005-2009. This study uses data from CONCORD-2 to provide the first detailed assessment of rectal cancer survival in the U.S. by stage at diagnosis and by race during two time periods, 2001-2003 and 2004-2009 as a means to assess the effectiveness of screening, diagnostic, and treatment services for rectal cancer in the U.S.

Material and Methods

Data Source

We used data from 37 state-wide cancer registries that participated in the CONCORD-2 study,[5] covering approximately 80% of the U.S. population, and consented to inclusion of their data in the more detailed analyses reported here. We analysed individual tumour records for people (age 15-99 years) who were diagnosed with cancer of the rectum, anus and anal canal (ICD-O-3[7] C20.9, C21.1-C21.2, C21.8) during 2001-2009 and followed up to December 31, 2009. Cancers of the anus and anal canal were included for consistency with previous analyses of rectal cancer survival.[5] We included the first primary, invasive cancers of the rectum, anus and anal canal, regardless of whether the cancer was the patient's first, second or higher-order cancer. If a patient was diagnosed with two or more primary, invasive cancers of the rectum, anus, or anal canal during 2001-2009, only the first cancer was considered in the survival analyses.

Patients were grouped by year of diagnosis into two calendar periods (2001-2003 and 2004-2009) to reflect changes in the methods used by U.S. registries to collect SEER Summary Stage (SS) 2000 at diagnosis.

During 2001–2003, most registries coded SS2000 directly from the medical records.[8] During 2004–2009, all registries derived SS2000 using the Collaborative Staging System.[9]

Survival analyses

We analysed survival by state, race (all, black, white), SS2000 (local, regional, distant, unknown) and calendar period of diagnosis. We estimated net survival up to 5 years after diagnosis and 95% confidence intervals (CI) using the Pohar Perme estimator.[10] We analysed survival by state, race, stage at diagnosis and calendar period of diagnosis. Net survival can be interpreted as the probability of survival up to a given time since diagnosis, after controlling for other causes of death (background mortality). To control for wide differences in background mortality among participating registries, we constructed life tables of all-cause mortality in the general population of each state from the number of deaths and the population, by single year of age, sex, calendar year and, where possible, by race (black, white), using a flexible Poisson model.[11] These life tables have been published.[12]

We estimated net survival using the cohort approach for patients diagnosed in 2001-2003, since all patients had been followed up for at least five years by December 31, 2009. We used the complete approach to estimate net survival for patients diagnosed from 2004-2009, because five years of follow-up data were not available for all patients. Net survival was estimated for five age-groups (15-44, 45-54, 55-64, 65-74, 75-99 years). We obtained age-standardized survival estimates using the International Cancer Survival Standard (ICSS) weights.[13] If two or more of the five age-specific estimates could not be obtained, we present only the pooled, unstandardized survival estimate for all ages combined. Unstandardized estimates are italicized in Tables 2 and 3. Changes in, geographic variations, and differences in age-standardized survival by race are presented graphically in bar-charts and funnel plots.[14] Funnel plots of net survival for 2001-2003 and 2004-2009 provide insight into the variability of cancer survival in the United States by race and state and show how much a particular survival estimate deviates from the pooled estimate of U.S. registries (horizontal line) given the

precision (within 95% and 99.8% control limit) of each estimate. More details on data and methods are provided in the accompanying article by Allemani et al.[1,15]

Results

Of the 241,578 cases of rectal cancer included in the analyses, 84.8% occurred in whites and 10% among blacks (data not shown). Of the 24,505 cases among blacks, 91.7% occurred in 16 states (AL, CA, FL, GA, LA, MD, MI, MS, NJ, NY, NC, OH, PA, SC, TN and TX); 10 states were in the geographic region of the South.

Stage Distribution (Table 1)

For all reported cases combined, there was an increase in the proportion of cases diagnosed at localized and distant stage between 2001-2003 and 2004-2009 (from 44.3% to 45.9% and from 13.2% to 14.4% respectively), and a decrease in the proportion diagnosed at regional stage (from 31.0% to 29.8%). Among blacks, the proportion diagnosed at localized stage increased (from 42.5% to 46.1%); at regional stage decreased (from 27.8% to 26.0%); and at distant stage increased (14.8% to 16.1%) between the two time periods. Among whites, the proportion diagnosed at localized and distant stage increased (from 44.5% to 45.7% and from 13.1% to 14.3% respectively), and at regional stage remained essentially unchanged (from 31.5% to 30.5%).

Between the two time periods, the absolute difference between whites and blacks in the proportion diagnosed at localized stage was eliminated (from 2.0% higher among whites to slightly higher for blacks); increased slightly for regional stage (from 3.7% to 4.5%); and remained unchanged for distant stage (from 1.7% to 1.8%).

Net Survival (Table 2)

There was a very small increase in 1-, 3- or 5-year net survival from 84.6%, 70.7% and 63.1% respectively in 2001-2003 to 85.1%, 71.5%, and 64.0% respectively in 2004-2009. Among whites, there was very little change

in survival between the two time periods. Among blacks, there were increases in 1-, 3-, and 5-year survival from 80.3%, 63.4% and 54.8% respectively during 2001-2003 to 81.6%, 64.5% and 57.5% respectively during 2004-2009. Blacks had lower 1-, 3-, and 5-year survival than whites in both time periods; the absolute difference in net survival between blacks and whites declined only for 5-year survival from 8.8% in 2001-2003 to 6.7% in 2004-2009.

Net survival by stage at diagnosis (Table 3)

In both time periods, 5-year net survival was highest for localized stage, followed by regional, then distant stage. There was no change in 5-year net survival between 2001-2003 and 2004-2009 for patients diagnosed at localized stage, but increased slightly for those diagnosed at a regional stage(from 61.2% to 63.3%) and at distant stage (from 11.1% to 14.2%).

Among whites, 5-year survival increased for distant stage (from 11.3% in 2001-2003 to 14.4% in 2004-2009) and for regional stage (from 61.9% to 63.8%), but was essentially unchanged for localized stage. Among blacks, 5-year survival increased for regional and distant stages (absolute increases of 4.9% and 2.3% respectively from 2001-2003 to 2004-2009) and remained essentially unchanged for localized stage. Blacks had lower 5-year survival than whites at each stage at diagnosis in both time periods. Between the two time periods, the absolute difference in 5-year survival between blacks and whites decreased for localized stage (from 7.2% to 5.0%) and regional stage (from 10.2% to 7.2%), but was essentially unchanged for distant stage.

Net survival by state (Figure 1)

In the 37 participating states, 5-year net survival ranged from 57.2% to 70.1% for patients diagnosed during 2001-2003 and from 54.6% to 69.1% for those diagnosed during 2004-2009 (Appendix). The largest increase in 5-year survival between the two time periods was 7.5% and the largest decrease was -5.7% (Figure 1).

Net survival by state and by race (Figure 2)

Figure 2 provides a visual picture of the variation in 5-year net survival by race and by state for each time period. The plots show how much a particular survival estimate deviates from the pooled U.S. value (the "target", represented by the horizontal line), given the precision of each estimate.[14] It was not possible to produce age-standardized net survival estimates for blacks in every state, when a sufficiently robust life table for blacks could not be created, but in 2001-2003, 5-year net survival for blacks (20 states) was generally lower than for whites (37 states). For several states, the survival estimates for blacks were below the control limits, suggesting lower survival than would be expected by chance, even after the lower precision of those survival estimates had been taken into account. By 2004-2009, there was a general shift upwards in survival among both blacks and whites, but 5-year age-standardized net survival was still generally lower for blacks than for whites.

Discussion

This study presents the first comprehensive assessment of rectal cancer survival over two time periods by race, stage at diagnosis, and by state, covering 80% of the U.S. population. Compared to patients diagnosed during 1990-1994, examined in the first CONCORD study, 5-year rectal cancer survival has improved, and the absolute difference in 5-year survival between blacks and whites has declined.[6] Between 2001-2003 and 2004-2009, the stage distribution for rectal cancer changed slightly with small increases in the proportion diagnosed at localized and distant stage, and decreases in the proportion diagnosed at regional stage; the proportion with unknown stage also declined. There was a modest improvement in overall 5-year rectal cancer survival from the earlier to later time period due to changes in the stage distribution and some improvement in survival for patients diagnosed at regional or distant stage. Compared to whites, blacks had a lower 5-year survival overall and for each stage at diagnosis in both time periods. The absolute difference in survival between blacks and whites decreased, largely due to increases in 5-year survival among blacks, particularly for patients diagnosed at regional or distant stage. There was considerable variation in 5-year survival by state, both overall and by each

stage at diagnosis. The largest gains in survival were seen for distant stage, with the highest 5-year survival increasing from 16.8% to 24.5% between the two time periods.

As described by White, et al elsewhere in this supplement, the distribution of colon cancer cases between blacks and whites was similar to the distribution described in this paper.[16] Unlike colon cancer, there was no distinct migration towards earlier stage at diagnosis seen for rectal cancer, although the proportion of cases diagnosed at localized and regional stages was higher for rectal cancer in both time periods. The 5-year stage specific net survival was higher for colon cancer for both localized and regional stages and equivalent for distant stage. Overall 1-, 3-, and 5-year net survival was similar for both cancers. As with colon cancer, blacks had lower overall and stage specific survival than whites. At least one previous study has noted a higher proportion of patients diagnosed at localized and regional stages for rectal cancer than for colon cancer, but did not note differing stage-specific survival, likely due to different methodology used for case definition and survival estimation.[17,18] The lower survival for localized and regional stage may reflect the different treatment strategies for these stages and biologic response of rectal cancer to these treatment strategies relative to colon cancer..[19]

The absence of an overall migration towards earlier stage at diagnosis despite a steady increase in the use of colorectal cancer screening tests over the past 15 years[20] may be due to several factors: stage migration that occurred prior to the study period as rectal cancers may have been more easily detected with fecal occult blood testing and flexible sigmoidoscopy which have been in use longer than colonoscopy; better detection of proximal cancers with the widespread use of colonoscopy as suggested by the relative increase in proximal cancers compared to distal;[17,21-23] the younger age distribution of rectal cancer cases and the increasing proportion diagnosed under the age of 50 prior to eligibility for screening;[17, 21, 22] and the relative proportion of cases that were prevented compared to those detected early. The increased proportion of blacks diagnosed at localized stage and decreased proportion diagnosed at regional stage may reflect the delayed uptake of screening in this population relative to whites. The increased proportion of blacks and whites diagnosed at

distant stage may reflect better classification of unknowns, possibly through improvements in diagnostic imaging studies, or continued low screening use among some portions of the population, since screening uptake varies by educational attainment, insurance status, income and other factors.[24]

There was very little improvement in 1-, 3-, or 5-year net survival overall or for whites, while blacks had greater improvements in all three, with the largest improvement in 5-year survival. Survival is dependent on several factors including stage at diagnosis, tumor grade, access to treatment, the quality and appropriateness of the treatment provided, and patient factors such as co-morbidities that mitigate the effectiveness of or ability to tolerate treatment.[18,23-25] Numerous studies have examined colon and rectal cancer disparities in survival or mortality and have found that blacks more often presented with advanced stage disease, were younger, were more likely to have lower socio-economic status (SES), were less likely to receive surgery, and more likely to have more co-morbidities.[17,26,27] After adjustment for SES, stage of diagnosis, treatment, co-morbidities and other factors, these studies found that the difference in survival between blacks and whites was reduced significantly or eliminated, suggesting that these factors confound or mediate the relationship between race and survival. The improvement in net survival for blacks suggests that some progress may have been made in ensuring that blacks have access to and receive equitable treatment.

Overall 1-, 3-, and 5-year net survival also varied considerably by state. Variation in survival between states may reflect variations in stage at diagnosis, which in turn partially reflect differences in colorectal cancer screening prevalence; variations in access to care, particularly in states with large rural areas; and variations in the proportion of the state's population that is uninsured, of low SES, or racial/ethnic minority.[28] Some studies have found an association between rural residence and an increased risk of death following diagnosis with colorectal cancer.[29,30] A subsequent study found that the increased risk of death was explained by decreased odds of receiving treatment in rural areas and by census tract SES.[31] An assessment of guideline-concordant chemotherapy, adequate lymph node assessment, and receipt of radiation therapy for rectal cancer found lower rates of these intervention in Appalachia when compared to New York Medicaid and Medicare patients.[32,33] The

study also found that patients treated in non-Commission on Cancer designated hospitals and hospitals with lower surgical volumes were less likely to receive complete lymph node evaluation.[32] The extent that these findings are replicated in multiple states may partially explain the geographic variation in net survival. Alternatively, the variations in survival between states may reflect variation in the quality and completeness of survival data between states rather than reflecting true survival differences.

Our study found no change in 5-year net survival during 2001-2009 for patients diagnosed with rectal cancer at a localized stage, but improvements in 5-year survival for regional and distant stages, with the largest increase for distant stage. This likely reflects advancements in chemotherapy regimens for distant disease that became available in the early 2000s.[23] An analysis of Medicare patients found that increased use of screening and improved chemotherapy regimens over time resulted in earlier stage of diagnosis and increased survival, although the majority of the improvement in survival was attributable to improvements in treatment with substantial improvements in relative survival for advanced disease.[23] In this study, 5-year survival increased for both blacks and whites diagnosed at distant stage, but only blacks saw gains in survival when diagnosed at a regional stage. Despite these improvements, blacks continued to have lower stage-specific 5-year survival compared to whites which suggests either differential dissemination of and/or less access to effective treatment. The large variation in stage-specific 5-year survival among states, particularly for regional and distant stage also suggests that some areas of the country do not have access to or have unequal distribution of high quality rectal cancer treatment.

Strengths and Limitations

The CONCORD 2 study is the largest comparative study of population-based cancer survival in the United States, and includes high quality data covering 80% of the U.S. population. Standardized collection, reporting and analysis of the data ensures a high degree of comparable data. A strength of this study is the high proportion of cases that were microscopically confirmed. For patients diagnosed with rectal cancer during the 15-year period 1995-2009 of the CONCORD-2 study, microscopic verification was available for 98.7% of patients

among all U.S. registries combined and was above 97% among participating states.[5] As reported here, microscopic verification was similar among blacks and whites, and among men and women diagnosed during 2001-2009 suggesting that most patients were clinically investigated. The low percentage of cases for which the diagnosis was based on clinical rather than pathological evidence is not likely to be the result of selective case ascertainment among participating cancer registries, since all the registries were certified by NAACCR as having met data quality and completeness standards.[34] The high proportion of microscopically verified cases may explain why rectal cancer survival rates are typically higher than in European countries as clinically diagnosed cases tend to be older, have more advanced disease and shorter survival.[5]

This study has several limitations. First, the definition of rectal cancer included cancers of the anus and anal canal and excluded cancers of the recto-sigmoid junction for consistency with previous international studies of rectal cancer survival. Rectal and anal cancers are distinct cancers affecting different populations, have different etiologies, and different treatments.[35] To the extent that the net survival of anal cancer differed substantially from rectal cancer, the estimated net survival proportions presented here may be over- or under-estimates of the true net survival for rectal cancer. Second, data on race/ethnicity were limited to blacks and whites, due to insufficient data for other racial/ethnic groups by state. Third, data quality and completeness varied by state; therefore, true differences in survival between states may be difficult to detect. Fourth, follow-up procedures in the United States differ according to federal funding source.[36] All SEER registries are required to conduct follow-up of all registered cases to ascertain vital status. NPCR registries are only funded to ascertain deaths through linkages with state vital records and the National Death Index. As a result, NPCR registries may slightly overestimate survival time and miss some deaths reported through hospital cancer registries and physician offices as death ascertainment is conducted primarily through data linkages.[37] These limitations may account for the somewhat higher survival estimates for several large NPCR registries as evidenced in the funnel plots. Fifth, the manner in which SEER Summary Stage 2000 data were collected and reported changed for all registries in 2004 as described in the methods section of this paper. The impact of this change was most evident

in NPCR funded registries where the percentage of cases with unknown stage decreased somewhat when stage was derived rather than manually coded.

Implications for clinical practice

To fully realize the full benefit of colorectal cancer screening in terms of incidence and mortality reduction, increased efforts are needed not only to ensure increased uptake of colorectal cancer screening tests, but also to ensure that people receive complete follow-up for abnormal screening tests, timely, high-quality, and complete treatment for diagnosed cancers, and adequate post-treatment surveillance. The wide differences in net survival between blacks and whites, and by state, reflect both the uneven use of effective treatment and the distribution of factors that affect recommendation of and uptake of treatment (SES, health literacy, health care access, insurance coverage, physician recommendation, and patient factors such as health beliefs, culture, and co-morbidities). Additional investigation may be needed to assess adherence to standards of treatment for rectal cancer and to develop effective interventions to improve recommendation of and adherence to high-quality treatment.

Implications for cancer control

A national effort has been started to increase colorectal cancer screening rates to 80% by 2018. Achieving this goal would require that 24.4 million adults aged 50-75 years be screened.[38] The anticipated impact of achieving this goal is a 17% reduction in incidence and a 22% reduction in mortality by 2020.[39] The Centers for Disease Control and Prevention (CDC) has funded states, universities, tribes and tribal organizations, and territories to implement programs such as the Colorectal Cancer Control Program (CRCCP) and the National Comprehensive Cancer Control Program (NCCCP).[37] The CRCCP funds grantees to partner with healthcare systems implement evidence-based interventions to increase colorectal cancer screening rates, with a focus on populations known to have lower colorectal cancer screening rates. The NCCCP funds grantees to support comprehensive cancer control efforts by building coalitions and developing and implementing plans to address the cancer burden.

Many of these efforts have focused on efforts to increase the uptake of screening and on cancer survivorship. Additional public health efforts are needed to ensure that people get complete follow-up of an abnormal screening test, prompt access to high quality treatment, and that they complete recommended treatment. Partnerships between public health and health care delivery systems, particularly within the NCCCP and state cancer coalitions could be a valuable mechanism to explore facilitators and barriers to appropriate treatment recommendation and adherence among providers and patients and to explore and implement evidence-based interventions to improve these measures.

Conclusions

There was little improvement in overall net survival for rectal cancer, with wide variation between states and with persistent disparities between blacks and whites for all stages at presentation. Additional investigation is needed to identify and implement effective interventions to ensure consistent and equitable use of high-quality screening, diagnosis, and treatment to improve rectal cancer survival for all population groups in all states.

References

1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on June 30, 2016.
2. U.S. Cancer Statistics Working Group. United States Cancer Statistics: 1999–2012 Incidence and Mortality Web-based Report. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2015. Available at: www.cdc.gov/uscs.
3. Howlader N, Noone AM, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER web site, April 2016.
4. Weir H. et al. Population-Based Cancer Survival (2001–2009) in the United States: Findings from the CONCORD-2 Study. Cancer. 2017.
5. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet. 2015; 385: 977–1010.
6. Coleman MP, Quaresma M, Berrino F, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). Lancet Oncol. 2008;9:730-56.
7. Fritz AG, Percy C, Jack A, Shanmugaratnam K, Sobin LH, Parkin DM, Whelan SL, eds. International Classification of Diseases for Oncology (ICD-O). 3rd ed. Geneva: World Health Organization; 2000.
8. Young JL, Roffers SD, Ries LAG, Fritz AG, Hurlbut AA. SEER Summary Staging Manual - 2000: Codes and Coding Instructions. NIH Pub. No. 01-4969. Bethesda, MD: National Cancer Institute; 2001.
9. Surveillance Epidemiology and End Results program. Collaborative Stage. Bethesda, MD: National Cancer Institute, 2004. http://seer.cancer.gov/tools/collabstaging/ (accessed 1 April 2016).
10. Pohar Perme M, Stare J, Estève J. On estimation in relative survival. Biometrics. 2012; 68: 113-20.
11. Rachet B, Maringe C, Woods LM, Ellis L, Spika D, Allemani C. Multivariable flexible modelling for estimating complete, smoothed life tables for sub-national populations. BMC Public Health. 2015; 15.
12. Spika D, Rachet B, Bannon F, et al. Life tables for the CONCORD-2 study. London: CONCORD Central Analytic Team, 2015. http://csg.lshtm.ac.uk/tools-analysis/life-tables/ (accessed 1 April 2016).
13. Corazziari I, Quinn MJ, Capocaccia R. Standard cancer patient population for age standardising survival ratios. Eur J Cancer. 2004; 40: 2307-16.
14. Quaresma M, Coleman MP, Rachet B. Funnel plots for population-based cancer survival: principles, methods and applications. Stat Med. 2014; 33: 1070-80.
15. Allemani C, Harewood R, Johnson C, et al. Population-based cancer survival in the US: data, quality control and statistical methods. Cancer. 2017.
16. White A, et al. Colon Cancer Survival in the United States by Race and Stage (2001-2009): Findings from the CONCORD-2 study. Cancer. 2017
17. Siegel R, DeSantis C, Jemal A. Colorectal cancer statistics, 2014. CA Cancer J Clin. 2014;64:104-117.
18. Le H, Ziogas A, Lipkin SM, Zell JA. Effects of socioeconomic status and treatment disparities in colorectal cancer survival. Cancer Epidemiol Biomarkers Prev. 2008;17:1950-62.
19. Tamas K, Walenkamp AME, de Vries EGE, et al. Rectal and colon cancer: not just a different anatomic site. Cancer Treat Rev. 2015;41:671-79.
20. CDC. Cancer Screening – United States, 2010. MMWR 2012;60:41-45.

21. Austin H, Henley SJ, King J, Richardson LC, Eheman C. Changes in colorectal cancer incidence rates in young and older adults in the United States: what does it tell us about screening. Cancer Causes Control. 2014;25:191-201.
22. Bailey CE, Hu CY, You YN, Bednarski BK, Rodriguez-Bigas MA, Skibber JM, et al. Increasing disparities in age-related colon and rectal cancer in the United States, 1975-2010. JAMA Surg. 2015;150:17-22.
23. Tong L, Ahn C, Symanski E, Lai D, Du XL. Relative impact of earlier diagnosis and improved treatment on survival for colorectal cancer: a U.S. database study among elderly patients. Cancer Epidemiol. 2014;38:733-40.
24. CDC. Vital Signs: colorectal cancer screening test use - United States, 2012. MMWR. 2013;62:1-8.
25. Lansdorp-Vogelaar I, Kuntz KM, Knudsen AB, van Ballegooijen M, Zauber AG, Jemal A. Contributions of screening and survival differences to racial disparities in colorectal cancer rates. Cancer Epidemiol Biomarkers Prev. 2012;21:728-36.
26. Wallace K, Hill EG, Lewin DN, Williamson G, Oppenheimer S, Ford ME, et al. Racial disparities in advanced stage colorectal cancer survival. Cancer Causes Control. 2013;24:463-71.
27. White AL, Vernon SW, Franzini L, Du XL. Racial disparities in colorectal cancer survival: to what extent are racial disparities explained by differences in treatment, tumor or hospital characteristics? Cancer. 2010;116:4622-31.
28. Jemal A, Siegel RL, Ma J, Islami F, DeSantis C, Sauer AG, et al. Inequalities in premature death from colorectal cancer by state. J Clin Oncol. 2015;33:829-35.
29. Singh GK, Williams SD, Siahpushh M, Mulhollen A. Socioeconomic, rural-urban, and racial inequalities in U.S. cancer mortality: part I – all cancers and lung cancer and part II – colorectal, prostate, breast, and cervical cancers. J Cancer Epidemiol. 2011;2011:107497.
30. Hines RB, Markossian TW. Differences in late-stage diagnosis, treatment, and colorectal cancer-related death between rural and urban African-Americans and whites in Georgia. J Rural Health. 2012;28:296-305.
31. Hines R, Markossian T, Johnson A, Dong F, Bayakly R. Geographic residency status and census tract socioeconomic status as determinants of colorectal cancer outcomes. Am J Public Health. 2014;104:63-71.
32. Fleming ST, Mackley HB, Camacho F, Seiber EE, Gusani NJ, Matthews SA, et al. Clinical, sociodemographic and service provider determinants of guideline concordant colorectal cancer care for Appalachian residents. J Rural Health. 2014;30:27-39.
33. Sinclair AH, Schymura MJ, Boscoe FP, et al. Measuring colorectal cancer care quality for the publicly insured in New York state. Cancer Medicine. 2012;1:363-71.
34. North American Association of Central Cancer. Certification criteria. Available at Registries.http://www.naaccr.org/Certification/Criteria.aspx). Accessed June 30, 2016.
35. Joseph DA, Miller JW, Wu X, Chen VW, Morris CR, Goodman MT, et al. Understanding the burden of human papillomavirus-associated anal cancers in the U.S. Cancer. 2008;113(10 suppl):2892-900.
36. White MC, Babcock F, Hayes NS, et al. The Evolution of Cancer Registry Data and Public Health Cancer Control Programs in the United States. Cancer. 2017
37. Johnson CJ, Weir HK, Fink AK, et al. The impact of National Death Index linkages on population-based cancer survival rates in the United States. *Cancer Epidemiol* 2013; 37: 20-8.
38. Fedewa SA, Ma J, Sauer AG, et al. How many individuals will need to be screened to increase colorectal cancer screening prevalence to 80% by 2018? Cancer. 2015;121:4258-65.

39. Meester RGS, Doubeni CA, Zauber AG, et al. Public health impact of achieving 80% colorectal cancer screening rates in the United States by 2018. Cancer. 2015;121:2281-5.

Table 1. Rectal cancer: number of cases for people (age 15-99 years) diagnosed 2001-2009 and distribution (%) by SEER Summary Stage 2000 (SS2000) at diagnosis, by race and calendar period of diagnosis.

		2001-2003			2004-2009		
SS2000		**All races**	**White**	**Black**	**All races**	**White**	**Black**
No. of patients		77,557	66,915	7,178	164,021	137,898	17,327
Localized	(%)	44.3	44.5	42.5	45.9	45.7	46.1
Regional	(%)	31.0	31.5	27.8	29.8	30.5	26.0
Distant	(%)	13.2	13.1	14.8	14.4	14.3	16.1
Unknown	(%)	11.4	11.0	14.9	9.9	9.5	11.7

Table 2. Rectal cancer: age-standardized net survival (%) at 1-, 3- and 5-years for people (age 15-99 years) diagnosed 2001-2009, by race and calendar period of diagnosis.

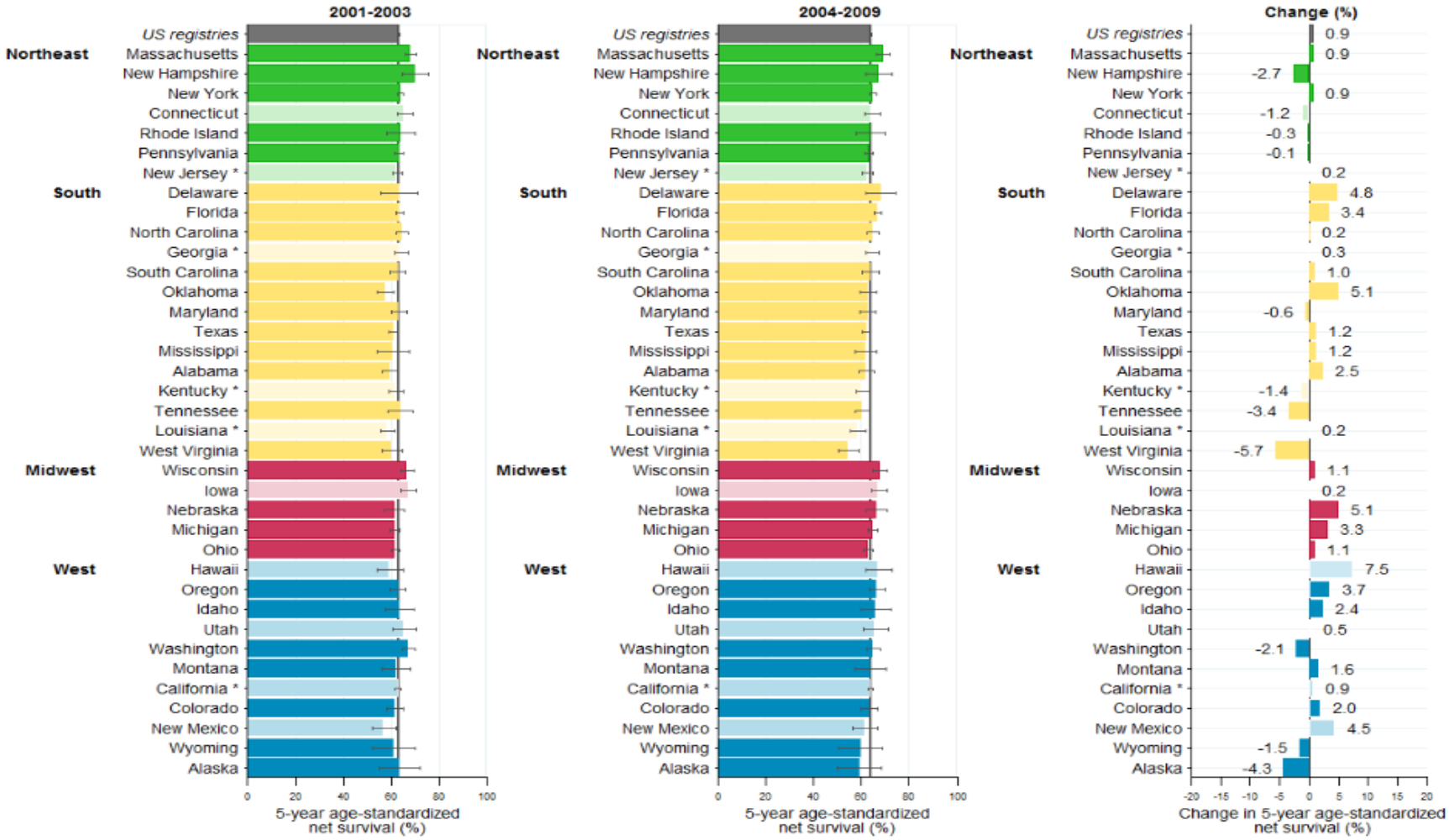
	2001-2003												2004-2009											
	All races				**White**				**Black**				**All races**				**White**				**Black**			
Years	**NS (%)**	**95% CI**			**NS (%)**	**95% CI**			**NS (%)**	**95% CI**			**NS (%)**	**95% CI**			**NS (%)**	**95% CI**			**NS (%)**	**95% CI**		
1	**84.6**	84.3	-	84.9	**84.9**	84.6	-	85.1	**80.3**	79.2	-	81.4	**85.1**	84.9	-	85.3	**85.3**	85.0	-	85.5	**81.6**	80.8	-	82.3
3	**70.7**	70.3	-	71.0	**71.2**	70.8	-	71.6	**63.4**	62.0	-	64.8	**71.5**	71.1	-	71.8	**71.8**	71.5	-	72.1	**64.5**	63.4	-	65.6
5	**63.1**	62.7	-	63.6	**63.6**	63.2	-	64.1	**54.8**	53.3	-	56.3	**64.0**	63.6	-	64.4	**64.2**	63.7	-	64.7	**57.5**	56.0	-	59.0

Table 3. Rectum cancer: 5-year age-standardized net survival (%) (15-99 years) diagnosed 2001-2009, by SEER Summary Stage (SS2000) at diagnosis, race and calendar period of diagnosis.

	2001-2003												2004-2009											
	All races				White				Black				All races				White				Black			
SS2000	**NS (%)**				**NS (%)**				**NS (%)**				**NS (%)**				**NS (%)**				**NS (%)**			
All stages	**63.1**	62.7	-	63.6	**63.6**	63.2	-	64.1	**54.8**	53.3	-	56.3	**64.0**	63.6	-	64.4	**64.2**	63.7	-	64.7	**57.5**	56.0	-	59.0
Localized	**83.0**	82.4	-	83.6	**83.3**	82.7	-	84.0	**76.1**	73.6	-	78.6	**82.2**	81.6	-	82.9	**82.2**	81.5	-	82.9	**77.2**	74.6	-	79.7
Regional	**61.2**	60.5	-	62.0	**61.9**	61.0	-	62.7	**51.7**	48.9	-	54.6	**63.3**	62.5	-	64.1	**63.8**	62.9	-	64.7	**56.6**	53.7	-	59.6
Distant	**11.1**	10.4	-	11.8	**11.3**	10.6	-	12.0	**8.7**	6.7	-	10.6	**14.2**	13.4	-	15.0	**14.4**	13.6	-	15.3	**11.0**	9.0	-	13.1
Unknown	**53.5**	52.2	-	54.7	**53.3**	52.0	-	54.6	**48.2**	44.7	-	51.7	**54.1**	52.9	-	55.3	**53.3**	51.9	-	54.6	**50.9**	47.4	-	54.4

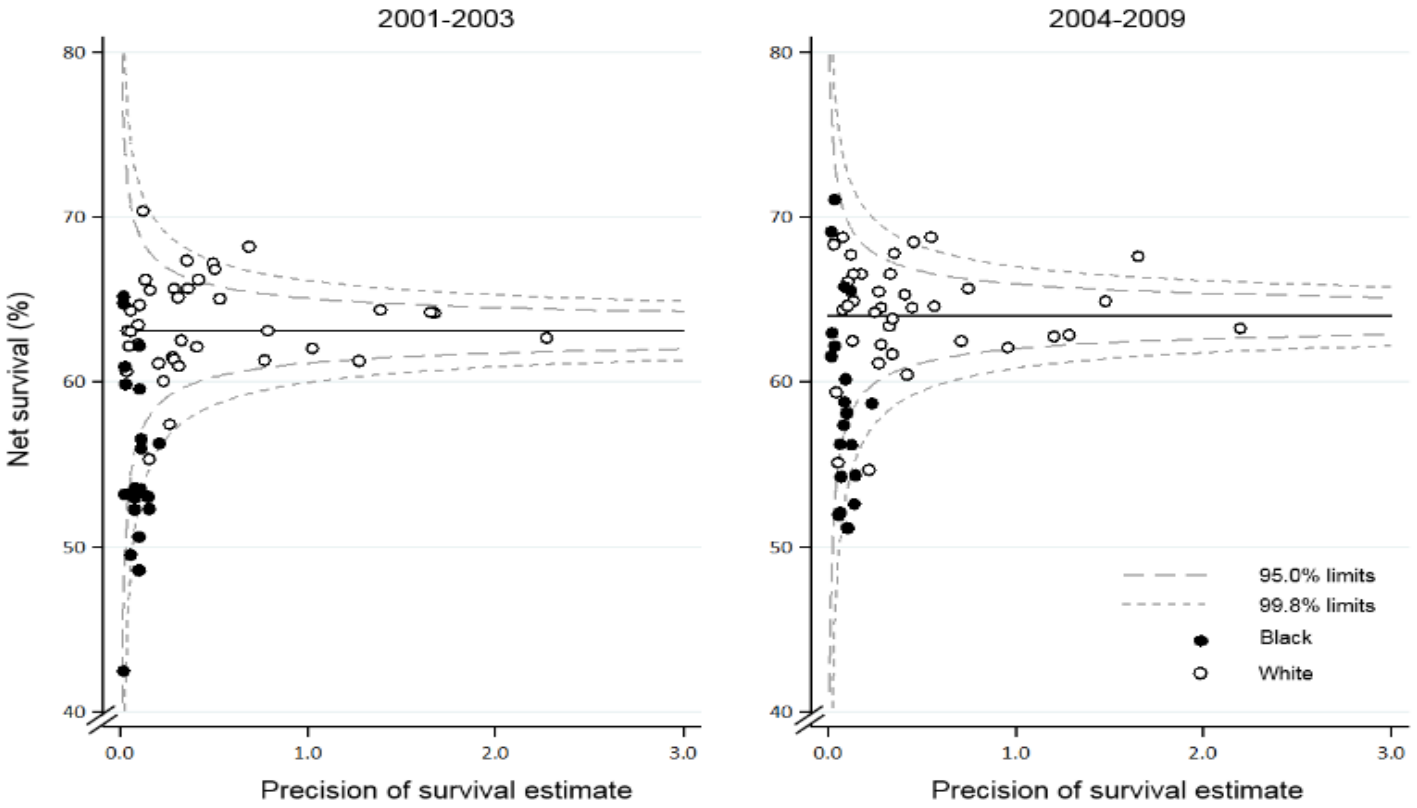
Figures

Figure 1. Rectal cancer: 5-year age-standardized net survival (%) for adults (15-99 years) diagnosed during 2001-2003 and 2004-2009, and absolute change (%): states grouped by U.S. Census Region.



Note: Data from 37 statewide cancer registries (covering 80.6% of the population) are ranked within U.S. Census Region by the survival estimate for 2004-2009. Dark colors denote states affiliated with the National Program of Cancer Registries (NPCR); pale colors denote states affiliated with the Surveillance, Epidemiology and End Results (SEER) Program; ? denotes states affiliated with both federal surveillance programs. Change (%) not plotted if a survival estimate was not available for one calendar period or one or more estimates was not age-standardized.

Figure 2. Rectal cancer: 5-year age-standardized net survival (%) for adults (15-99 years), by state, race and calendar period of diagnosis.



Note: the pooled (US) survival estimate for each calendar period is shown by the horizontal (solid) line with corresponding 95.0% and 99.8% control limits (dotted lines).