Cancer detection to treatment: Health disparities and factors that contribute to them

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Abstract

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Despite advances in strategies for cancer prevention and early detection, marked disparities in incidence and mortality in several forms of cancer have persisted and grown. Disparities have been observed across the census tract environment, and recently, during the coronavirus disease 2019 (COVID-19) global pandemic. Such factors, the census tract environment and the COVID-19 pandemic, may create and/or exacerbate existing disparities via impacts on patterns of routine screening and delays in cancer treatment that are not equitably experienced across population subgroups. The **objective** of the proposed study is to examine research gaps in the cancer prevention continuum and health disparities related to screening and time-to-treatment, specifically for colorectal and cervical cancers. To address this objective, we will leverage data in large population-based cohorts with survey, electronic health records, and administrative data across multiple sites in the US. In **Aim 1**, we will quantify the associations between area-level colorectal and cervical cancer screening prevalence and the census tract environment. In **Aim 2**, we will characterize the impacts of the COVID-19 pandemic on the utilization of tests and

procedures used for cancer screening and diagnosis by **a)** comparing the utilization of these tests and procedures before (2019-2020) and during (2020-2021) the COVID-19 pandemic and **b)** examining whether sociodemographic characteristics and policies related to the COVID-19 pandemic were associated with cancer screening during the pandemic. In **Aim 3**, we will characterize the relationship with race and ethnicity and socioeconomic factors on diagnosis-to-treatment interval in patients diagnosed with cancer, and its survival effects according to these factors. Findings will inform the allocation of resources and infrastructure changes to both reduce disparities in the future and those widened by events like the COVID-19 pandemic, particularly for disparities not equitably experienced across population subgroups.

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Table of Contents

List of Tables & Figures

Aim 1. Socioeconomic status, urban vs. rural status, and likelihood of completing colorectal and cervical cancer screening

Aim 2. COVID-19 effects on colorectal and cervical cancer screening in the Kaiser Permanente Research Bank

Aim 1

Socioeconomic status, urban vs. rural status, and likelihood of completing colorectal and cervical cancer screening

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ABSTRACT

Background/Aims

There is striking variation in colorectal cancer (CRC) and cervical cancer incidence globally, as well as across the United States (US). However, there has been limited research in the US on how specific differences in features of the neighborhood environment, such as, transportation, land use, housing and/or urbanicity, may influence screening uptake and thus impact CRC and cervical cancer outcomes.

Methods

The Population-based Research to Optimize the Screening Process (PROSPR) consortium uses electronic medical records and administrative databases to collect information on demographics, healthcare utilization, health insurance, orders, test results, and pathology results. For each patient's residential census tracts, we determined neighborhood socioeconomic status (nSES) using Yost scores (which incorporate information on poverty, education, home value, income, employment, mortgage, and rent) and urbanicity using Rural-Urban Commuting Area (RUCA) codes (which incorporate information on population density, urbanization, and daily commuting). Incident cancer screening was defined using diagnostic tests or procedures. Logistic regression using generalized estimating equations was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the associations of census tract-level nSES and urbanicity with incidence of CRC or cervical cancer screening, adjusting for birth year, race and ethnicity, sex, cohort entry year, and indication of pregnancy

Results

There were n=2,747,362 and n=403,319 participants in the CRC and cervical cancer cohorts included in this analysis, respectively. Yost score was similarly associated with lower cervical

cancer screening (lowest quintile vs. highest quintile, OR: 0.67, 95% CI: 0.64, 0.70) and CRC screening (lowest quintile vs. highest quintile, OR: 0.69, 95% CI: 0.67, 0.70). RUCA was not associated with CRC or cervical cancer screening.

Conclusion

Our results suggest that there may be an association of census tract-level nSES with CRC and cervical cancer screening. It may suggest that policy makers and health systems should target interventions to areas of low SES.

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer among both men and women in the United States (US), with over 152,000 estimated new CRC cases in 2024.[1] Over the past 30 years, CRC incidence rates have declined among those aged 50 years and older, which may be largely due to adherence to screening and surveillance guidelines.[2] Similar to CRC, cervical cancer can be detected in a precancerous state via routine screening modalities. Due to such screening, cervical cancer incidence has declined for decades in the US; however, it continues to be the second leading cause of cancer deaths in the US among women aged 20 to 39.[3]

Despite advances in strategies for cancer prevention, early detection, and treatment, there continue to be marked socioeconomic disparities in incidence and mortality for several forms of cancer – including colorectal and cervical cancers. These disparities can be attributed, in part, to differences in the prevalence of individual-level modifiable risk factors (e.g., smoking and obesity)[4,5] or healthcare-related factors (e.g., access to timely and effective screening).[6] However, disparities in cancer incidence and mortality may also be exacerbated by area-level factors, socioeconomic status, and other environmental factors. For example, differences in screening have been observed in rural vs. urban areas;[7-10] remote rural patients have been shown to have as low as 45% up-to-date CRC screening prevalence compared to 54% among urban patients.[7] Barriers that may contribute to these health disparities include less access to financial resources and transportation, schedule availability, and lack of a medical home or primary care provider.[11,12]

While numerous studies have evaluated the relationships between individual-level socioeconomic status and receipt of different forms of cancer screening, literature examining the relationship of area-level socioeconomic status with cancer screening is more limited.[13,14] The

Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) is a unique community- and healthcare system-based cohort across the US aimed to understand the cancer screening process (recruitment, screening, diagnosis, referral for treatment). In this large cohort, we examined whether area-level urbanicity and socioeconomic status were associated with cervical and colorectal cancer screening.

METHODS

Study Population and Design

We conducted a study within the PROSPR cohort, a multi-site and multi-cancer consortium funded by the National Cancer Institute. Specifically, our study utilizes information from two data resources within PROSPR: the Multilevel Optimization of the Cervical Cancer Screening Process in Diverse Settings & Populations (METRICS) and the Optimizing Colorectal Cancer Screening PREcision and Outcomes in CommunIty-baSEd Populations (PRECISE). Study sites for these PROSPR populations include: Kaiser Permanente Washington (cervical and CRC), Kaiser Permanente Northern California (CRC), Kaiser Permanente Southern California (CRC), Parkland Health & Hospital System (cervical and CRC), and Partners HealthCare/Mass General Brigham (cervical). PROSPR uses electronic health records and administrative databases to collect data on demographics, healthcare utilization, health insurance, orders, test results, and pathology results from patients in multiple healthcare systems. Study protocols and human subjects considerations were reviewed and approved by the institutional review boards at the University of Washington and the Fred Hutchinson Cancer Center.

We identified 1,060,110 adults in METRICS. Among these individuals, we limited our investigation to individuals with no prior cervical cancer, individuals with relevant complete vital

organs (cervix), who identify as female, and with no prior HIV diagnosis. We additionally restricted analyses to adults who were age-eligible (21-65 years) for cervical cancer screening during 2019 and who were enrolled in one of the participating METRICS health systems sometime during 2019 with 1 or more years of prior healthcare system data regardless of screening status. We excluded adults who did not have a known or geocoded residence, those missing both exposure variables (see below), or missing census tract designation.

For CRC screening, we identified 7,658,553 adults in PRECISE. Among these individuals, we limited our study participants to individuals with no prior diagnosis of CRC, individuals with relevant complete vital organs (no indication of proctectomy or colectomy), and individuals without a prior colorectal cancer genetic syndrome diagnosis (Lynch, inflammatory bowel disease (IBD), or familial adenomatous polyposis (FAP)). We additionally restricted our sample to adults who were age-eligible (50-75 years) for colorectal cancer screening during 2019. As with our analyses within METRICS, we ensured that participants were enrolled in one of the participating PRECISE health systems sometime in 2019 with 1 or more years of prior healthcare system data, and excluded adults who did not have known or geocoded residence or were missing both exposure variables. The analytic samples are summarized in **Figure 1**.

Exposure

The exposures of interest were urbanicity and area-level socioeconomic status, ascertained at the census tract level. Neighborhood-level data was based on individuals' residences geocoded to the census tract-level upon cohort entry.[15] Census tract boundaries and Metropolitan Statistical Area definitions were used from 2010. For measures at the census tract environment, data from 2008-2012 were used. The Census Bureau defined urbanicity as the urban-rural classification of geographic areas, where urban areas represent densely developed territory,

and encompass residential, commercial, and other non-residential urban land uses. Rural-Urban Commuting Area (RUCA) codes classify census tracts using population density, urbanization, and daily commuting. RUCA categories consisted of urban or metropolitan (population of 50,000 or more), micropolitan or large town (10,000-49,999), small rural town (2,000-9,999), and isolated small rural town (under 2,500).[16] For the analysis, RUCA was categorized into urban (urban or metropolitan) and rural (micropolitan or large town, small rural town, isolated small rural town) due to a smaller sample size and power in rural areas. Area-level socioeconomic status was defined using Yost scores, where are created using information on poverty, education, home value, income, employment, mortgage, and rent from the Census Bureau.[17] Yost scores range from 0-100, with higher Yost scores indicating higher socioeconomic status.[17] Yost scores provided were pre-categorized into quintiles based on national values.

Outcomes

Cancer screening adherence was defined using up-to-date screening, which measures the proportion of the target population who are up-to-date on screening at a particular point in time.[18] A participant was considered up-to-date on cervical cancer screening as of December 31st, 2019 if they had received a Pap test during a 3-year span or a co-test (HPV and pap test) during a 5-year span culminating at the end of 2019. Likewise, a participant was considered up-to-date on colorectal cancer screening as of December 31st, 2019 if they received a fecal immunochemical test (FIT) or guaiac-based fecal occult blood test (gFOBT) during a 1-year span or a colonoscopy during a 10-year span through the end of 2019. Outcome status was classified as binary (up-to-date vs. not up-to-date).

Statistical Analysis

We used descriptive statistics to evaluate patient demographics. Continuous variables were described with mean and standard deviation while categorical variables were described with frequencies and percentages.

To assess the associations between urbanicity and area-level socioeconomic status and up-to-date screening adherence, we employed logistic regression models using generalized estimating equations (GEE) to account for census tract and site clusters and robust standard errors to calculate adjusted odds ratios (aORs) and 95% confidence intervals (CIs). We adjusted for covariates selected *a priori*, including birth year, race and ethnicity (Hispanic, Non-Hispanic American Indian or Alaska Native, Non-Hispanic Asian and Native Hawaiian or Pacific Islander, Non-Hispanic Black, Non-Hispanic White, multiple, other), sex (male, female), cohort entry year, and any indication of pregnancy (yes, no) (METRICS only). In sensitivity analyses, we limited the study population to individuals who were geocoded to their census tract based on complete and valid addresses (99%), and evaluated associations stratified by race and ethnicity. In addition, we performed sensitivity analyses in METRICS with follow-up time of 3 and 5 years and in PRECISE with follow-up time of 5 and 10 years that coincide with cancer-specific screening guidelines. To account for potential correlation between race and ethnicity and Yost score, we also performed an adjusted analysis without adjusting for race and ethnicity. We also performed sensitivity analyses stratifying for insurance status and healthcare system. Results for Parkland were not provided due to sample size and convergence issues that tended to be a majority urban and lower Yost score.

All statistical analyses were two-sided and a p-value of <0.05 was considered statistically significant. All analyses were conducted using SAS (Version 9.4, SAS Institute, Inc., Cary, NC, USA).

RESULTS

Our final study population for METRICS was 403,319 adults, with the majority of participants aged 30-59 years (30-39 years: 26.3%, 40-49 years: 21.8%, 50-59 years: 20.3%) and/or living in urban census tracts (99.7%) (**Table 1**). With respect to race and ethnicity, 43.6% of participants identified as Non-Hispanic White and 31.0% identified as Hispanic. Over half (55.7%) of participants reported having commercial insurance, and 62.5% were considered up-to-date with cervical screening.

Our final study population for PRECISE was 2,747,362 adults, with the majority of participants between the ages of 50-69 years (50-59 years: 45.9%, 60-69% years: 38.7%). Similar to in PRECISE, 45.8% of participants identified as Non-Hispanic White and 24.6% identified as Hispanic, over half (59.1%) of participants reported having commercial insurance, and almost all participants (98.7%) lived in urban census tracts; 69.3% of PRECISE participants were considered up-to-date with colorectal cancer screening.

Compared to those residing in areas classified in the highest Yost quintile (highest socioeconomic status), those in the lowest Yost quintile were 0.67 (95% CI: 0.64, 0.70) and 0.69 (95% CI: 0.67, 0.70) times as likely to be up-to-date on cervical cancer screening and colorectal cancer screening, respectively (**Table 2**). Those residing in areas classified in the second to fourth quintiles of Yost score were also significantly less likely to be up-to date with cervical and colorectal cancer screening, with odds ratios ranging from 0.79 to 0.93. These associations were very similar across evaluated cancer sites. There were no statistically significant associations between urbanicity and up-to-date screening (**Table 2**). When stratifying by race and ethnicity, results were similar for Yost scores. However, there were significant associations

when looking at urbanicity. Among Non-Hispanic White participants, those living in rural areas (consisting of micropolitan or large town, small rural town, and isolated small rural town) were more likely to be up-to-date with cervical cancer screening than were those residing in urban areas (aOR: 1.20, 95% CI: 1.06, 1.36). Among American Indian or Alaska Native participants, those living in rural areas were less likely to be up-to-date with cervical cancer screening (aOR: 0.22, 95% CI: 0.05, 0.91). However, while these results were statistically significant, they are based on small numbers in rural areas (**Table 3**).

Similar results were observed when only examining individuals with census tracts based on complete and valid addresses (**Supplemental Table 1**). After excluding participants due to follow-up time, results were similar (**Supplemental Table 2**). While stratifying by healthcare system, we found that the associations between cancer screening are similar. However, we also found that in Kaiser Permanente Southern California, individuals in more rural areas were less likely to be up-to-date with CRC screening (isolated small town vs. urban, aOR: 0.87, 95% CI: 0.76, 0.99 (**Supplemental Table 3**). Other sensitivity provided similar results.

DISCUSSION

In this community-based and healthcare system-based study conducted in the PROSPR's METRICS (cervical cancer) and PRECISE (colorectal cancer) populations, we observed associations of area-level socioeconomic status with being up-to-date for cervical and colorectal cancer screening. Lower area-level socioeconomic status was associated with lower rates of up-to-date cervical and colorectal cancer screening. However, no association was found between urbanicity and up-to-date cervical and colorectal cancer screening. These findings are consistent with other research on area-level socioeconomic status and cervical[19,20] and colorectal cancer screening.[19,21]

Prior studies have shown that individual-level socioeconomic measures, such as household income, education, and employment, may be associated with cancer screening.[22,23] Economic influences beyond the individual-level may also plausibly have a role in cancer screening patterns; however, prior studies have been inconsistent in their findings. A study using the Behavioral Risk Factor Surveillance System (BRFSS) found that county poverty proportion, as measured by the percentage of the population living below the federal poverty line, was not associated with Pap smears.[19] Another BRFSS study found similar results when assessing cervical cancer screening and area-level percentage living in poverty and percentage with low education.[24] However, these studies in BRFSS used self-report for cancer screening information and relied on a population with telephones, affecting generalizability. Another study found that area-level poverty, measured by percent of households living in poverty, was associated with increased risk of not having a cervical cancer screening in the past two years.[20] Our findings were similar when using Yost score, an aggregate measure of area-level socioeconomic status for cervical cancer screening at the census tract level. With respect to colorectal cancer, prior investigation using BRFSS data found that the prevalence of never having had a colonoscopy, sigmoidoscopy, and FIT increases with increasing proportion of poverty.[19] Another study using the Population Health Assessment in Cancer Center Catchment Areas found that area-level socioeconomic status deprivation, as measured by various measures including neighborhood stability and Yost score, was associated with lower screening adherence.[21] Our study found similar results for area-level socioeconomic status and CRC screening.

Our study also found that there was no association between urbanicity and being up-to-date with cervical and colorectal cancer screening. When stratifying by race and ethnicity, there were associations of urbanicity with screening among certain racial and ethnic subgroups; however, these stratified findings should not be over-interpreted due to the small numbers in rural areas.

Our results differ from other studies that have suggested rurality is associated with reduced odds of being up-to-date with cervical[25] and colorectal cancer screening.[26,27] However, these differences in findings may be due to our smaller population in rural areas.

Possible mechanisms for the effects of area-level socioeconomic status on screening patterns may relate to inadequate health insurance coverage, lack of regular health care providers, and differences in educational attainment. Persons with Medicaid coverage and private fee-for-service coverage were more likely to receive screening tests than those who had no coverage.[28] Additionally, lacking a usual source of care may decrease screening as well, which may occur in areas with fewer resources and lower area-level socioeconomic status.[29] Neighborhood socioeconomic status may indicate areas of lower educational resources, which perhaps could reflect lower education, which has been shown to be associated with lower screening rates.[29] Area-level contexts and associated neighborhood environments can influence the cancer continuum.[30] Lower socioeconomic status areas may have inadequate access to health care resources, and poorer community engagement and distrust with the health care system. Studies have indicated that area deprivation, a composite area-based indicator spanning poverty, education level, housing, and employment, has also been found to alter cancer screening rates for in-person tests and procedures.[31] These areas may also have a lack of transportation resources, which may further hinder individuals from getting screened. There also may be competing factors when it comes to health prioritizations; for example, one study found associations between cancer screening nonadherence and food insecurity, renting a home, and overcrowding.[32]

Some limitations should be considered in interpreting our results. Our study utilized administrative boundaries (census tracts) as part of our geospatial analyses. However, these boundaries may not be adequate proxies for measurements related to neighborhood

socioeconomic status or urbanicity, as well as not accurately representing the individual-level residential environment.[33] However, census tracts are small-area geographies developed by the US Census Bureau that have been widely used in previous epidemiologic research and have been predictive of cancer incidence and mortality.[13,34] Our study may not have had sufficient numbers of participants located in rural areas to detect effects if they were present, particularly for analyses stratified by race and ethnicity. Our analyses also aggregated screening tests for different cancer sites as events for each census tract to assess up-to-date screening. However, when performing analyses for separate screening modalities for cervical (Pap test and co-test) and colorectal (colonoscopy and FIT) cancer, results were similar when examining Yost scores. We observed that co-tests and FIT screening was more likely used in rural areas while Pap and colonoscopies were less likely used in rural areas. Although we examined two established measures of urbanicity and area-level socioeconomic status, there may be additional census tract data that may impact cancer screening adherence. Our study population was also based on healthcare systems, which may affect the generalizability of our results. Lastly, while we adjusted for available relevant covariates, there may be residual confounding due to lack of information that were not available in our datasets such as transportation access. However, strengths of our study include being one of the largest community- and healthcare system-based studies on urbanicity and area-level socioeconomic status and cervical and colorectal screening to date, spanning across five different geographic regions across the US from five heterogenous health care delivery systems. Our study was also racially and ethnically diverse, providing enhanced statistical power to detect associations.

In conclusion, our results suggest that lower area-level socioeconomic status, but not urban vs. rural status, is associated with lower screening adherence for cervical and colorectal cancer. Based on these results, we suggest that community outreach programs focus on low-SES areas to increase proportion of up-to-date screening.

REFERENCES

1. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA: a cancer journal for clinicians*. Jan-Feb 2024;74(1):12-49. doi:10.3322/caac.21820

2. Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. *CA: a cancer journal for clinicians*. May 2020;70(3):145-164. doi:10.3322/caac.21601

3. Islami F, Fedewa SA, Jemal A. Trends in cervical cancer incidence rates by age, race/ethnicity, histological subtype, and stage at diagnosis in the United States. *Preventive medicine*. Jun 2019;123:316-323. doi:10.1016/j.ypmed.2019.04.010

4. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA: a cancer journal for clinicians*. 2021;71(1):7-33. doi:https://doi.org/10.3322/caac.21654

5. Stein CJ, Colditz GA. Modifiable risk factors for cancer. *British journal of cancer*. 2004/01/01 2004;90(2):299-303. doi:10.1038/sj.bjc.6601509

6. Freeman HP, Chu KC. Determinants of cancer disparities: barriers to cancer screening, diagnosis, and treatment. *Surg Oncol Clin N Am*. Oct 2005;14(4):655-69, v. doi:10.1016/j.soc.2005.06.002

7. Cole AM, Jackson JE, Doescher M. Urban-rural disparities in colorectal cancer screening: cross-sectional analysis of 1998-2005 data from the Centers for Disease Control's Behavioral Risk Factor Surveillance Study. *Cancer Med*. Dec 2012;1(3):350-6. doi:10.1002/cam4.40

8. Meilleur A, Subramanian SV, Plascak JJ, Fisher JL, Paskett ED, Lamont EB. Rural residence and cancer outcomes in the United States: issues and challenges. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. Oct 2013;22(10):1657-67. doi:10.1158/1055-9965.Epi-13-0404

9. Chandak A, Nayar P, Lin G. Rural-Urban Disparities in Access to Breast Cancer Screening: A Spatial Clustering Analysis. *J Rural Health*. Mar 2019;35(2):229-235. doi:10.1111/jrh.12308

10. Alyabsi M, Meza J, Islam KMM, Soliman A, Watanabe-Galloway S. Colorectal Cancer Screening Uptake: Differences Between Rural and Urban Privately-Insured Population. *Front Public Health*. 2020;8:532950. doi:10.3389/fpubh.2020.532950

11. Phelan JC, Link BG, Diez-Roux A, Kawachi I, Levin B. "Fundamental causes" of social inequalities in mortality: a test of the theory. *J Health Soc Behav*. Sep 2004;45(3):265-85. doi:10.1177/002214650404500303

12. Doubeni CA, Corley DA, Zauber AG. Colorectal Cancer Health Disparities and the Role of US Law and Health Policy. *Gastroenterology*. May 2016;150(5):1052-1055. doi:10.1053/j.gastro.2016.03.012

13. Wray AJD, Minaker LM. Is cancer prevention influenced by the built environment? A multidisciplinary scoping review. *Cancer*. Oct 1 2019;125(19):3299-3311. doi:10.1002/cncr.32376

14. Gomez SL, Shariff-Marco S, DeRouen M, et al. The impact of neighborhood social and built environment factors across the cancer continuum: Current research, methodological considerations, and future directions. *Cancer*. Jul 15 2015;121(14):2314-30. doi:10.1002/cncr.29345

15. Beaber EF, Kamineni A, Burnett-Hartman AN, et al. Evaluating and Improving Cancer Screening Process Quality in a Multilevel Context: The PROSPR II Consortium Design and Research Agenda. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. Aug 2 2022;31(8):1521-1531. doi:10.1158/1055-9965.Epi-22-0100

16. Rural-Urban Commuting Area Codes. Updated September 25, 2023. 2024. https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes/

17. Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer causes & control : CCC*. Oct 2001;12(8):703-11. doi:10.1023/a:1011240019516

18. Chubak J, Hubbard R. Defining and measuring adherence to cancer screening. *J Med Screen*. 2016;23(4):179-185. doi:10.1177/0969141316630766

19. Schootman M, Jeffe DB, Baker EA, Walker MS. Effect of area poverty rate on cancer screening across US communities. *J Epidemiol Community Health*. Mar 2006;60(3):202-7. doi:10.1136/jech.2005.041020

20. Datta GD, Colditz GA, Kawachi I, Subramanian SV, Palmer JR, Rosenberg L. Individual-, neighborhood-, and state-level socioeconomic predictors of cervical carcinoma screening among U.S. black women: a multilevel analysis. *Cancer*. Feb 1 2006;106(3):664-9. doi:10.1002/cncr.21660

21. Mayhand KN, Handorf EA, Ortiz AG, et al. Effect of Neighborhood and Individual-Level Socioeconomic Factors on Colorectal Cancer Screening Adherence. *Int J Environ Res Public Health*. 2021;18(9)doi:10.3390/ijerph18094398

22. Ioannou GN, Chapko MK, Dominitz JA. Predictors of colorectal cancer screening participation in the United States. *Am J Gastroenterol*. Sep 2003;98(9):2082-91. doi:10.1111/j.1572-0241.2003.07574.x

23. Broberg G, Wang J, Östberg AL, et al. Socio-economic and demographic determinants affecting participation in the Swedish cervical screening program: A population-based case-control study. *PloS one*. 2018;13(1):e0190171. doi:10.1371/journal.pone.0190171

24. Coughlin SS, King J, Richards TB, Ekwueme DU. Cervical cancer screening among women in metropolitan areas of the United States by individual-level and area-based measures of socioeconomic status, 2000 to 2002. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. Nov 2006;15(11):2154-9. doi:10.1158/1055-9965.Epi-05-0914

25. Locklar LRB, Do DP. Rural-urban differences in HPV testing for cervical cancer screening. *J Rural Health*. Sep 10 2021;doi:10.1111/jrh.12615

26. Hughes AG, Watanabe-Galloway S, Schnell P, Soliman AS. Rural-Urban Differences in Colorectal Cancer Screening Barriers in Nebraska. *J Community Health*. Dec 2015;40(6):1065-74. doi:10.1007/s10900-015-0032-2

27. Shete S, Deng Y, Shannon J, et al. Differences in Breast and Colorectal Cancer Screening Adherence Among Women Residing in Urban and Rural Communities in the United States. *JAMA Netw Open*. Oct 1 2021;4(10):e2128000. doi:10.1001/jamanetworkopen.2021.28000

28. Potosky AL, Breen N, Graubard BI, Parsons PE. The association between health care coverage and the use of cancer screening tests. Results from the 1992 National Health Interview Survey. *Med Care*. Mar 1998;36(3):257-70. doi:10.1097/00005650-199803000-00004

29. Breen N, Wagener DK, Brown ML, Davis WW, Ballard-Barbash R. Progress in cancer screening over a decade: results of cancer screening from the 1987, 1992, and 1998 National Health Interview Surveys. *Journal of the National Cancer Institute*. Nov 21 2001;93(22):1704-13. doi:10.1093/jnci/93.22.1704

30. Gomez SL, Glaser SL, McClure LA, et al. The California Neighborhoods Data System: a new resource for examining the impact of neighborhood characteristics on cancer incidence and outcomes in populations. *Cancer causes & control : CCC*. Apr 2011;22(4):631-47. doi:10.1007/s10552-011-9736-5

31. Kurani SS, McCoy RG, Lampman MA, et al. Association of Neighborhood Measures of Social Determinants of Health With Breast, Cervical, and Colorectal Cancer Screening Rates in the US Midwest. *JAMA Network Open*. 2020;3(3):e200618-e200618. doi:10.1001/jamanetworkopen.2020.0618

32. Kasper G, Momen M, Sorice KA, et al. Effect of neighborhood and individual-level socioeconomic factors on breast cancer screening adherence in a multi-ethnic study. *BMC Public Health*. Jan 2 2024;24(1):63. doi:10.1186/s12889-023-17252-9

33. Rainham D, McDowell I, Krewski D, Sawada M. Conceptualizing the healthscape: contributions of time geography, location technologies and spatial ecology to place and health research. *Social science & medicine (1982)*. Mar 2010;70(5):668-76. doi:10.1016/j.socscimed.2009.10.035

34. Kolak M, Bhatt J, Park YH, Padrón NA, Molefe A. Quantification of Neighborhood-Level Social Determinants of Health in the Continental United States. *JAMA Netw Open*. Jan 3 2020;3(1):e1919928. doi:10.1001/jamanetworkopen.2019.19928

Table 1. Population characteristics among screening eligible participants in 2019

Characteristic	**METRICS (cervical) N=403,319 n (%)**	**PRECISE (colorectal) N=2,747,362 n (%)**
Age (years)		
25-29	79,456 (19.7)	
30-39	106,134 (26.3)	
40-49	87,982 (21.8)	
50-59	81,697 (20.3)	1,261,518 (45.9)
60-69	48,060 (11.9)	1,061,959 (38.7)
70-79		423,885 (15.4)
Sex		
Male		1,427,932 (52.0)
Female	403,319 (100.0)	1,319,364 (48.0)
Race and ethnicity		
Non-Hispanic White	175, 916 (43.6)	1,258,575 (45.8)
Non-Hispanic Black	48,209 (12.0)	227,305 (8.3)
Hispanic	124,826 (31.0)	677,025 (24.6)
Asian and Native Hawaiian or Pacific Islander	31,209 (7.7)	412,530 (15.0)
American Indian or Alaska Native	927 (0.2)	7,883 (0.3)
Multiple	7,050 (1.8)	23,739 (0.9)
Other	3,157 (0.8)	1,499 (0.1)
Insurance		
Medicare (alone)	6,432 (1.6)	345,924 (12.6)
Medicaid (including dual Medicare/Medicaid)	77,097 (19.1)	104,209 (3.8)
Commercial insurance	224,600 (55.7)	1,623,109 (59.1)
Uninsured	45,098 (11.2)	41,380 (1.5)
Multiple	3,903 (1.0)	501,265 (18.3)
Proportion of households at or below Federal Poverty Limit	16.5 ± 12.3	12.5 ± 9.5
Proportion with 4-year college degree or higher	20.1 ± 12.0	20.5 ± 10.5

Percentages may not add up to 100 due to rounding and missing values.

Table 2. Associations between neighborhood socioeconomic status and up-to-date cancer screening for cervical and colorectal cancer among screening eligible participants

	Cervical			
Exposure	**Up-to-Date n (%)**	**N**	**Adjusted* OR (95% CI)**	**p-trend**
Rural-Urban Commuting Area***				
Urban	251,242 (62.5)	402,134	1.00 (ref)	
Rural	726 (61.3)	1,185	1.08 (0.97, 1.21)	
Yost Quintiles				<0.001
Q1	55,008 (59.9)	91,893	0.67 (0.64, 0.70)	
Q2	35,781 (62.0)	57,716	0.82 (0.77, 0.86)	
Q3	33,346 (62.9)	53,026	0.91 (0.87, 0.95)	
Q4	49,494 (62.5)	79,169	0.93 (0.90, 0.97)	
Q5	74,417 (62.5)	115,357	1.00 (ref)	
	Colorectal			
Exposure	**Up-to-Date n (%)**	**N**	**Adjusted** OR (95% CI)**	**p-trend**
Rural-Urban Commuting Area***	1,880,871 (69.4)	2,711,826	1.00 (ref)	
Urban	24,251 (68.2)	35,536	0.99 (0.95, 1.03)	
Rural				<0.001
Yost Quintiles	158,008 (62.2)	253,912	0.69 (0.67, 0.70)	
Q1	232,918 (66.3)	351,464	0.79 (0.78, 0.80)	
Q2	313,110 (68.0)	460,348	0.84 (0.83, 0.85)	
Q3	485,617 (70.2)	691,952	0.90 (0.89, 0.91)	
Q4	707,544 (72.4)	977,355	1.00 (ref)	
Q5	1,880,871 (69.4)	2,711,826	1.00 (ref)	

*Adjusted for birth year, race and ethnicity, pregnancy, cohort entry year

**Adjusted for birth year, sex, race and ethnicity, cohort entry year

*** Urban or metropolitan (50,000 or more); Rural consists of micropolitan or large town (10,000-49,999), small rural town (10,000-49,999) and isolated small rural town (under 2,500)

Abbreviations: OR – odds ratio, CI – confidence interval, Q – quintile

Table 3. Adjusted associations between neighborhood socioeconomic status and up-to-date cancer screening for cervical and colorectal cancer among screening eligible participants stratified by race and ethnicity

	Cervical*					
Exposure	**Non-Hispanic White n=175,916**	**Black n=48,209**	**Hispanic n=124,826**	**API n=31,209**	**AIAN n=927**	**Multiple n=7,050**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Rural urban commuting area						
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Rural**	1.20 (1.06, 1.36)	2.64 (0.59, 11.86)	0.96 (0.58, 1.60)	0.81 (0.47, 1.40)	0.22 (0.05, 0.91)	0.84 (0.53, 1.33)
Yost Quintiles						
Q1	0.59 (0.54, 0.65)	0.64 (0.56, 0.74)	0.73 (0.68, 0.78)	0.63 (0.51, 0.77)	0.71 (0.41, 1.22)	0.94 (0.71, 1.23)
Q2	0.88 (0.82, 0.95)	0.76 (0.64, 0.89)	0.85 (0.77, 0.93)	0.88 (0.78, 0.99)	0.78 (0.50, 1.23)	1.06 (0.90, 1.26)
Q3	0.97 (0.92, 1.03)	0.92 (0.78, 1.08)	0.92 (0.83, 1.01)	0.88 (0.80, 0.98)	1.26 (0.84, 1.91)	0.91 (0.78, 1.06)
Q4	0.98 (0.93, 1.02)	0.88 (0.74, 1.05)	0.90 (0.82, 0.99)	0.96 (0.89, 1.05)	0.96 (0.64, 1.44)	0.94 (0.82, 1.07)
Q5	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
	Colorectal**					
Exposure	**White n=1,258,575**	**Black n=227,305**	**Hispanic n=677,025**	**API n=412,530**	**AIAN n=7,883**	**Multiple n=23,739**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Rural urban commuting area***						
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Micropolitan	0.94 (0.89, 1.00)	0.98 (0.81, 1.19)	1.01 (0.94, 1.09)	0.94 (0.81, 1.09)	0.97 (0.59, 1.57)	1.00 (0.61, 1.63)
Small rural town	0.99 (0.89, 1.09)	1.03 (0.53, 2.02)	0.93 (0.82, 1.05)	0.91 (0.77, 1.07)	0.88 (0.41, 1.87)	0.48 (0.15, 1.54)
Isolated small rural town	1.05 (0.97, 1.13)	1.20 (0.90, 1.62)	1.02 (0.89, 1.17)	1.05 (0.78, 1.43)	1.04 (0.47, 2.26)	0.72 (0.31, 1.68)
Rural urban commuting area						
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Rural****	0.98 (0.94, 1.03)	1.04 (0.86, 1.25)	1.00 (0.94, 1.06)	0.95 (0.85, 1.07)	0.97 (0.67, 1.39)	0.81 (0.54, 1.22)
Yost Quintiles						
Q1	0.67 (0.65, 0.69)	0.64 (0.60, 0.67)	0.76 (0.74, 0.78)	0.82 (0.79, 0.86)	0.76 (0.62, 0.92)	0.76 (0.67, 0.86)
Q2	0.76 (0.75, 0.78)	0.82 (0.78, 0.86)	0.86 (0.84, 0.88)	0.86 (0.83, 0.89)	0.74 (0.63, 0.87)	0.87 (0.79, 0.96)
Q3	0.82 (0.80, 0.83)	0.86 (0.83, 0.90)	0.90 (0.88, 0.92)	0.87 (0.85, 0.90)	0.86 (0.75, 0.99)	0.89 (0.81, 0.97)
Q4	0.88 (0.87, 0.90)	0.91 (0.87, 0.95)	0.94 (0.92, 0.96)	0.96 (0.94, 0.99)	0.88 (0.78, 1.00)	0.90 (0.83, 0.97)

Q5	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)

*Adjusted for birth year, pregnancy, cohort entry year

**Adjusted for birth year, sex, cohort entry year

***Urban or metropolitan (50,000 or more), micropolitan or large town (10,000-49,999), small rural town (2,000-9,999), isolated small rural town (under 2,500)

****Rural consists of micropolitan or large town, small rural town, and isolated small rural town

Abbreviations: OR – odds ratio, CI – confidence interval, Q – quintile, API – Asian, Pacific Islander or Native Hawaiian, AIAN – American Indian or Alaska Native

Supplemental Table 1. Associations between neighborhood socioeconomic status and up-to-date cancer screening for cervical and colorectal cancer among screening eligible participants with census tracts based on complete and valid addresses

	Cervical n=399,761		Colorectal n=2,715,002	
Exposure	**Unadjusted**	**Adjusted***	**Unadjusted**	**Adjusted****
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Rural-Urban Commuting Area***				
Urban			1.00 (ref)	1.00 (ref)
Micropolitan			0.92 (0.86, 0.99)	0.97 (0.92, 1.02)
Small rural town			0.96 (0.80, 1.14)	0.98 (0.88, 1.09)
Isolated small rural town			1.03 (0.94, 1.13)	1.06 (0.99, 1.14)
Rural-Urban Commuting Area				
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Rural****	0.95 (0.85, 1.05)	1.08 (0.97, 1.20)	0.95 (0.90, 1.01)	0.99 (0.95, 1.04)
Yost Quintiles				
Q1	0.82 (0.78, 0.86)	0.67 (0.64, 0.70)	0.63 (0.61, 0.64)	0.69 (0.67, 0.70)
Q2	0.90 (0.84, 0.95)	0.82 (0.77, 0.86)	0.75 (0.73, 0.76)	0.79 (0.78, 0.80)
Q3	0.93 (0.89, 0.98)	0.91 (0.87, 0.95)	0.81 (0.80, 0.82)	0.84 (0.82, 0.85)
Q4	0.92 (0.87, 0.96)	0.93 (0.89, 0.97)	0.90 (0.88, 0.91)	0.90 (0.89, 0.91)
Q5	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)

*Adjusted for birth year, race and ethnicity, pregnancy, cohort entry year

**Adjusted for birth year, sex, race and ethnicity, cohort entry year

***Urban or metropolitan (50,000 or more), micropolitan or large town (10,000-49,999), small rural town (2,000-9,999), isolated small rural town (under 2,500)

****Rural consists of micropolitan or large town, small rural town, and isolated small rural town

Abbreviations: OR – odds ratio, CI – confidence interval, Q – quintile

Supplemental Table 2. Adjusted associations between neighborhood socioeconomic status and up-to-date cancer screening for cervical and colorectal cancer among screening eligible participants with 3 and 5 years of follow-up

	Cervical*		Colorectal	
Exposure	**3 Years n=310,679**	**5 Years n=236,809**	**5 Years** n=2,219,276**	**10 Years*** n=1,577,103**
	OR (95% CI)	**OR (95% CI)**		
Rural urban commuting area****				
Urban			1.00 (ref)	1.00 (ref)
Micropolitan			0.95 (0.90, 1.01)	0.93 (0.88, 0.99)
Small rural town			0.90 (0.81, 1.01)	0.86 (0.79, 0.94)
Isolated small rural town			1.04 (0.97, 1.12)	1.03 (0.93, 1.13)
Rural urban commuting area				
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Rural*****	1.28 (1.10, 1.50)	1.32 (1.07, 1.63)	0.97 (0.92, 1.01)	0.94 (0.90, 0.98)
Yost Quintiles				
Q1	0.61 (0.57, 0.64)	0.61 (0.58, 0.65)	0.66 (0.65, 0.68)	0.67 (0.65, 0.68)
Q2	0.76 (0.71, 0.82)	0.77 (0.72, 0.84)	0.76 (0.75, 0.78)	0.75 (0.74, 0.76)
Q3	0.89 (0.83, 0.94)	0.90 (0.85, 0.96)	0.81 (0.80, 0.82)	0.80 (0.78, 0.81)
Q4	0.94 (0.89, 0.98)	0.96 (0.92, 1.01)	0.88 (0.87, 0.90)	0.87 (0.86, 0.88)
Q5	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)

*Adjusted for birth year, race and ethnicity, pregnancy, cohort year

**Adjusted for birth year, sex, race and ethnicity, cohort year

***Adjusted for birth year, sex, race and ethnicity

****Urban or metropolitan (50,000 or more), micropolitan or large town (10,000-49,999), small rural town (2,000-9,999), isolated small rural town (under 2,500)

*****Rural consists of micropolitan or large town, small rural town, and isolated small rural town

Abbreviations: OR – odds ratio, CI – confidence interval, Q – quintile

Supplemental Table 3. Adjusted associations between neighborhood socioeconomic status and up-to-date cancer screening for cervical and colorectal cancer among screening eligible participants stratified by healthcare system

	Cervical*		
Exposure	**KPWA n=110,066**	**PH-UTSW n=139,267**	**MGB n=153,986**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**
Rural urban commuting area			
Urban	1.00 (ref)		1.00 (ref)
Rural**	1.00 (0.87, 1.15)		0.89 (0.64, 1.24)
Yost Quintiles			
Q1	0.91 (0.83, 1.01)		1.04 (0.98, 1.10)
Q2	0.91 (0.86, 0.97)		0.99 (0.94, 1.05)
Q3	0.92 (0.88, 0.97)		0.99 (0.95, 1.04)
Q4	0.95 (0.91, 0.99)		0.94 (0.90, 0.99)
Q5	1.00 (ref)		1.00 (ref)

	Colorectal**			
Exposure	**KPWA n=122,537**	**UTSW n=68,528**	**KPNC n=1,266,124**	**KPSC n=1,290,273**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Rural urban commuting area***				
Urban	1.00 (ref)		1.00 (ref)	1.00 (ref)
Micropolitan	0.96 (0.84, 1.09)		0.97 (0.91, 1.03)	0.87 (0.78, 0.96)
Small rural town	0.91 (0.75, 1.09)		0.95 (0.88, 1.03)	0.66 (0.56, 0.78)
Isolated small rural town	0.82 (0.51, 1.21)		1.04 (0.97, 1.12)	0.87 (0.76, 0.99)
Rural urban commuting area				
Urban	1.00 (ref)		1.00 (ref)	1.00 (ref)
Rural****	0.93 (0.82, 1.04)		0.98 (0.94, 1.02)	0.84 (0.78, 0.92)
Yost Quintiles				
Q1	0.85 (0.79, 0.91)		0.72 (0.71, 0.74)	0.78 (0.77, 0.80)
Q2	0.81 (0.77, 0.85)		0.77 (0.76, 0.79)	0.83 (0.82, 0.85)
Q3	0.88 (0.85, 0.92)		0.82 (0.80, 0.83)	0.87 (0.85, 0.88)
Q4	0.93 (0.90, 0.97)		0.89 (0.88, 0.90)	0.92 (0.91, 0.93)
Q5	1.00 (ref)		1.00 (ref)	1.00 (ref)

*Adjusted for birth year, pregnancy, race and ethnicity, cohort entry year

Supplemental Table 4. Adjusted associations between neighborhood socioeconomic status and up-to-date cancer screening for cervical and colorectal cancer among screening eligible participants stratified by insurance status

	Cervical*				
Exposure	**Medicare (alone) n=6,432**	**Medicaid (including dual Medicare/Medicaid) n=77,097**	**Commercial Insurance n=224,600**	**Uninsured n=45,098**	**Multiple n=3,903**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Rural urban commuting area					
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)		1.00 (ref)
Rural**	0.95 (0.50, 1.80)	0.99 (0.61, 1.63)	1.03 (0.91, 1.17)		1.69 (0.83, 3.45)
Yost Quintiles					
Q1	0.72 (0.60, 0.86)	1.15 (1.07, 1.22)	0.82 (0.76, 0.88)	1.06 (0.91, 1.22)	1.01 (0.77, 1.35)
Q2	0.82 (0.67, 1.01)	1.13 (1.05, 1.21)	0.97 (0.93, 1.01)	1.05 (0.90, 1.22)	0.96 (0.75, 1.24)
Q3	0.93 (0.77, 1.13)	1.06 (0.99, 1.14)	1.00 (0.96, 1.04)	1.05 (0.90, 1.22)	1.11 (0.88, 1.40)
Q4	0.91 (0.77, 1.07)	0.93 (0.87, 0.99)	0.99 (0.95, 1.02)	0.95 (0.80, 1.12)	1.14 (0.93, 1.39)
Q5	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
	Colorectal**				
Exposure	**Medicare (alone) n=345,924**	**Medicaid (including dual Medicare/Medicaid) n=104,209**	**Commercial Insurance n=1,623,109**	**Uninsured n=41,380**	**Multiple n=501,265**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Rural urban commuting area***					
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)		1.00 (ref)
Micropolitan	0.97 (0.82, 1.13)	0.87 (0.62, 1.21)	0.94 (0.88, 0.99)		1.02 (0.95, 1.09)
Small rural town	0.67 (0.49, 0.91)	0.62 (0.36, 1.04)	0.93 (0.85, 1.01)		1.07 (0.91, 1.26)
Isolated small rural town	0.96 (0.80, 1.16)	1.01 (0.66, 1.55)	1.01 (0.93, 1.11)		1.11 (1.03, 1.19)
Rural urban commuting area					
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Rural****	0.92 (0.82, 1.05)	0.84 (0.66, 1.07)	0.95 (0.91, 0.99)	0.72 (0.41, 1.26)	1.06 (0.99, 1.12)
Yost Quintiles					
Q1	0.68 (0.65, 0.71)	0.69 (0.65, 0.74)	0.72 (0.70, 0.73)	0.96 (0.89, 1.04)	0.70 (0.68, 0.73)
Q2	0.86 (0.82, 0.87)	0.88 (0.83, 0.93)	0.77 (0.76, 0.79)	0.96 (0.88, 1.05)	0.78 (0.76, 0.80)
Q3	0.88 (0.86, 0.91)	0.91 (0.86, 0.96)	0.82 (0.80, 0.83)	1.00 (0.91, 1.10)	0.81 (0.79, 0.83)
Q4	0.93 (0.90, 0.95)	0.96 (0.91, 1.01)	0.89 (0.88, 0.90)	0.95 (0.87, 1.04)	0.88 (0.86, 0.90)
Q5	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)

*Adjusted for birth year, pregnancy, race and ethnicity, cohort entry year
** Adjusted for birth year, sex, race and ethnicity, cohort entry year
***Urban or metropolitan (50,000 or more), micropolitan or large town (10,000-49,999), small rural town (2,000-9,999), isolated small rural town (under 2,500)
****Rural consists of micropolitan or large town, small rural town, and isolated small rural town
Abbreviations: OR – odds ratio, CI – confidence interval, Q – quintile

Supplemental Table 5. Adjusted associations between neighborhood socioeconomic status and up-to-date cancer screening for cervical and colorectal cancer among screening eligible participants by screening modality

	Cervical*		Colorectal**	
Exposure	**Pap Test**	**Cotest**	**Colonoscopy**	**FIT**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Rural urban commuting area***				
Urban			1.00 (ref)	1.00 (ref)
Micropolitan			0.78 (0.73, 0.84)	1.20 (1.13, 1.28)
Small rural town			0.72 (0.69, 0.77)	1.28 (1.16, 1.42)
Isolated small rural town			0.86 (0.78, 0.95)	1.19 (1.09, 1.30)
Rural urban commuting area				
Urban	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Rural****	0.73 (0.57, 0.93)	1.24 (1.11, 1.38)	0.79 (0.75, 0.83)	1.21 (1.16, 1.27)
Yost Quintiles				
Q1	1.77 (1.66, 1.89)	0.33 (0.29, 0.38)	0.82 (0.79, 0.86)	0.87 (0.84, 0.90)
Q2	1.27 (1.16, 1.40)	0.66 (0.58, 0.75)	0.90 (0.87, 0.93)	0.91 (0.89, 0.94)
Q3	1.03 (0.96, 1.12)	0.89 (0.81, 0.97)	0.90 (0.87, 0.93)	0.95 (0.93, 0.98)
Q4	0.94 (0.89, 0.98)	0.98 (0.92, 1.03)	0.92 (0.89, 0.94)	1.00 (0.97, 1.03)
Q5	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)

*Adjusted for birth year, race and ethnicity, pregnancy, cohort entry year

**Adjusted for birth year, sex, race and ethnicity, cohort entry year

***Urban or metropolitan (50,000 or more), micropolitan or large town (10,000-49,999), small rural town (2,000-9,999), isolated small rural town (under 2,500)

****Rural consists of micropolitan or large town, small rural town, and isolated small rural town

Abbreviations: OR – odds ratio, CI – confidence interval, Q – quintile

Supplemental Table 6. Variables by race and ethnicity

	Cervical					
	Non-Hispanic White n=175,916	**Black n=48,209**	**Hispanic n=124,826**	**API n=31,209**	**AIAN n=927**	**Multiple n=7,050**
Rural urban commuting area*						
Urban	174,974 (99.5)	48,201 (99.9)	124,771 (99.9)	31,171 (99.9)	916 (98.8)	7,002 (99.3)
Micropolitan	660 (0.4)	4 (0.01)	44 (0.04)	29 (0.09)	7 (0.8)	40 (0.6)
Small rural town	125 (0.07)	3 (0.01)	7 (0.01)	4 (0.01)	1 (0.1)	3 (0.04)
Isolated small rural town	157 (0.09)	1 (0.0)	4 (0.0)	5 (0.02)	3 (0.3)	5 (0.07)
Yost Quintiles						
Q1	6,809 (3.9)	19,114 (39.7)	62,642 (50.2)	2,093 (6.7)	85 (9.2)	350 (5.0)
Q2	14,150 (8.0)	9,807 (20.3)	26,115 (20.9)	4,454 (14.3)	161 (17.4)	955 (13.6)
Q3	22,040 (12.5)	7,665 (15.9)	14,150 (11.3)	5,026 (16.1)	224 (24.2)	1,315 (18.7)
Q4	46,901 (26.7)	6,869 (14.3)	10,927 (8.8)	8,004 (25.7)	267 (28.8)	1,984 (28.1)
Q5	85,164 (48.4)	3,852 (8.0)	6,982 (5.6)	11,327 (36.3)	183 (19.7)	2,417 (34.3)
Providing Site						
KPWA	65,612 (37.3)	5,296 (11.0)	7,703 (6.2)	15,969 (51.2)	674 (72.7)	3,533 (50.1)
PH-UTSW	9,308 (5.3)	30,496 (63.3)	94,482 (75.7)	3,926 (12.6)	140 (15.1)	187 (2.7)
MGB	100,996 (57.4)	12.417 (25.8)	22,641 (18.1)	11,314 (36.3)	113 (12.2)	3,330 (47.2)
	Colorectal					
	White n=1,258,575	**Black n=227,305**	**Hispanic n=677,025**	**API n=412,530**	**AIAN n=7,883**	**Multiple n=23,739**
Rural urban commuting area*						
Urban	1,234,000 (98.1)	226,463 (99.6)	670,208 (99.0)	411,450 (99.7)	7,737 (98.2)	23,583 (99.3)
Micropolitan	12,839 (1.0)	498 (0.2)	4,509 (0.7)	666 (0.2)	85 (1.1)	94 (0.4)
Small rural town	4,679 (0.4)	157 (0.07)	1,119 (0.2)	208 (0.05)	22 (0.3)	23 (0.1)
Isolated small rural town	7,057 (0.6)	187 (0.08)	1,109 (0.2)	206 (0.05)	39 (0.5)	39 (0.2)
Yost Quintiles						
Q1	48,322 (3.8)	46,419 (20.4)	126,584 (18.7)	20,025 (4.9)	589 (7.5)	1,632 (6.9)

Q2	107,229 (8.5)	45,793 (20.2)	141,424 (20.9)	36,357 (8.8)	1,022 (13.0)	2,974 (12.5)
Q3	188,478 (15.0)	40,038 (17.6)	145,241 (21.5)	58,029 (14.1)	1,488 (18.9)	4,055 (17.1)
Q4	344,792 (27.4)	49,007 (21.6)	143,560 (21.2)	110,536 (26.8)	2,177 (27.6)	6,136 (25.9)
Q5	565,299 (44.9)	44,254 (19.5)	117,324 (17.3)	185,326 (44.9)	2,573 (32.6)	8,832 (37.2)
Providing Site						
KPWA	85,993 (6.8)	5,077 (2.2)	5,226 (0.8)	13,079 (3.2)	726 (9.2)	1,993 (8.4)
UTSW	8,304 (0.7)	23,041 (10.1)	33,112 (4.9)	3,330 (0.8)	99 (1.3)	104 (0.4)
KPNC	656,902 (52.2)	88,406 (38.9)	204,111 (30.2)	243,487 (59.0)	4,380 (55.6)	5,878 (24.8)
KPSC	507,376 (40.3)	110,781 (48.7)	434,576 (64.2)	152,634 (37.0)	2,678 (34.0)	15,764 (66.4)

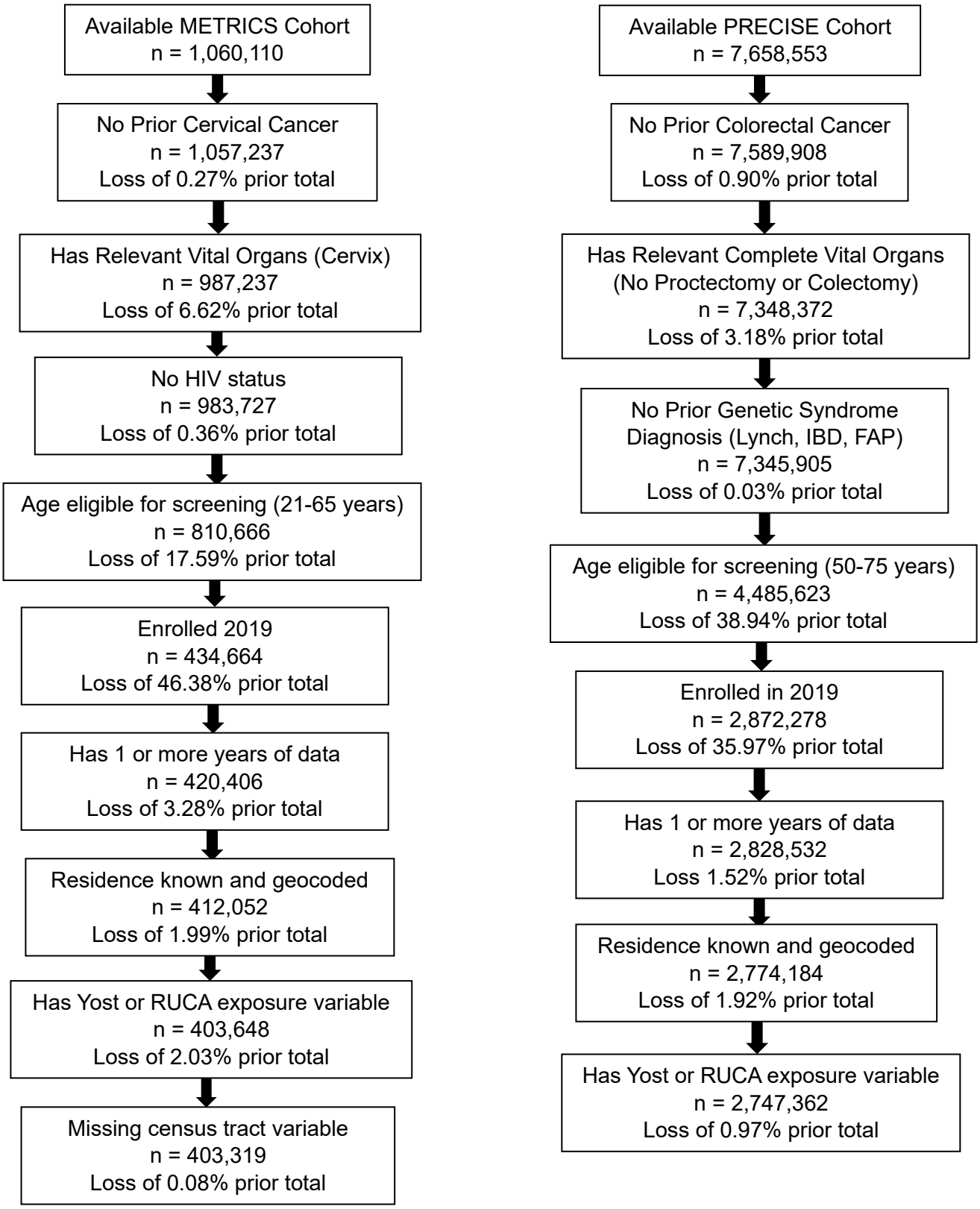
*Urban or metropolitan (50,000 or more), micropolitan or large town (10,000-49,999), small rural town (2,000-9,999), isolated small rural town (under 2,500)

Abbreviations: OR – odds ratio, CI – confidence interval, Q – quintile, API – Asian & Pacific Islander & Native Hawaiian, AIAN – American Indian & Alaska Native

Supplemental Table 7. Providing site by screening modality

	Cervical			Colorectal	
Providing Site	**Pap Test**	**Co-Test**	**Providing Site**	**Colonoscopy**	**FIT**
KPWA	14,864 (13.5)	55,982 (50.9)	KPWA	43,184 (35.2)	35,338 (28.8)
PH-UTSW	66,777 (48.0)	17,673 (12.7)	UTSW	15,017 (22.0)	15,668 (22.9)
MGB	28,983 (26.2)	79,615 (51.7)	KPNC	363,786 (28.7)	566,164 (44.7)
			KPSC	556,326 (56.9)	378,332 (29.3)

Supplemental Figure 1. CONSORT diagram



Aim 2

COVID-19 effects on colorectal and cervical cancer screening in the Kaiser Permanente Research Bank

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ABSTRACTS

Background

The coronavirus disease 2019 (COVID-19) pandemic negatively impacted multiple forms of cancer screenings in the United States due to restrictions placed on non-urgent and elective procedures, particularly in the earlier phase of the pandemic. Our study aims to evaluate the impact of the COVID-19 pandemic on colorectal cancer (CRC) and cervical cancer screening over time and by COVID-19 patient characteristics in the Kaiser Permanente healthcare system.

Methods

Health data from the Kaiser Permanente Research Bank (KPRB) cohort were analyzed to assess changes and trends in CRC and cervical cancer screening counts due to the COVID-19 pandemic, as well as associations of behaviors surrounding the COVID-19 guidelines and screening one year after the pandemic start. KPRB routinely collects data on demographics, procedures and test codes via electronic health records and collected information regarding experiences during the COVID-19 pandemic via questionnaires. We utilized an interrupted time series analysis to evaluate baseline levels and overall trend changes in CRC and cervical cancer screening. We also utilized logistic regression to calculate odds ratios (ORs) and 95% confidence intervals of CRC and cervical cancer screening associated with behaviors surrounding the COVID-19 pandemic (e.g., willingness to receive the COVID-19 vaccine, quarantining and masking behaviors, employment).

Results

There were 60,942 and 44,806 participants who were eligible for CRC and cervical cancer screenings in this analysis. We observed statistically significant decreases in CRC (60.6%) and cervical cancer (98.9%) screening trends after April 1st, 2020. However, after the initial decrease

due to the pandemic, we observed a recovery in screening rates with increasing trends and counts in CRC and cervical cancer screening. Behaviors related to the COVID-19 pandemic were also associated with cancer screening. Willingness to get the COVID-19 vaccine, quarantining from friends, avoiding crowded places, and avoiding travel were associated with higher odds of cancer screening after the pandemic start. Participants with concerns about acquiring COVID-19 at the clinic, those who were prepared to stay at home without leaving for 15 days, and those only leaving home for essential reasons had lower odds of cancer screening.

Conclusion

Our results suggest that there were significant, immediate decreases in CRC and cervical cancer screening due at the onset of the pandemic. However, since then, there has been a rise in cancer screening returning to pre-pandemic levels. We also found associations of behaviors related to the COVID-19 pandemic with screening practices.

INTRODUCTION

The emergence of the coronavirus disease 2019 (COVID-19) pandemic in 2020 has posed a significant threat to public health, in ways that go far beyond physiologic effects of the SARS-CoV-2 virus itself.[1-3] One example is the significant impacts it has on cancer screening and early detection of cancer.[4-6] Policy mandates restricting access to non-emergency medical services in the early phase of the pandemic limited the spread of infection, prompting the downscaling of clinical activities in order to reallocate resources to combatting the virus.[7] Health care providers delayed or canceled non-urgent and elective procedures to preserve capacity for COVID-19 patients. Rates of tests and procedures used for cancer screening and diagnosis decreased substantially from December 2019 to September 2020, ranging from 60-80% decline across cancer sites.[6] In March and April 2020 alone, sharp decreases were estimated to be 80-90% for cervical cancer and colorectal cancer (CRC) screening volumes.[6,8]

The impact of the COVID-19 pandemic on cancer care delivery is still being investigated and not yet fully understood. To prepare for future emerging pandemic events, it is important to investigate if the disruptions to clinical care in the early phase of the COVID-19 pandemic were shouldered disproportionately across communities in ways that adversely affect underserved populations. Postponing cancer screening may negatively affect cancer outcomes through diagnoses of later-stage cancer, subsequent cancer-related deaths, and additional cancer screening burden.[9-11] Our study aims to evaluate the impact of the COVID-19 pandemic on CRC and cervical cancer screening according to time and COVID-19 patient characteristics in the Kaiser Permanente health care system.

METHODS

Study Population

The Kaiser Permanente Research Bank (KPRB) is a population-based data repository that spans Northern California, Southern California, Colorado, Georgia, Hawaii, Mid-Atlantic States (Maryland, Virginia, Washington DC), Northwest (Oregon, southwest Washington), and Washington, drawing from 8 regional healthcare systems consisting of approximately 12.5 million members with varying insurance products and care delivery. KPRB began new recruitment in 2015, building on an existing cohort from the Research Program on Genes, Environment and Health.[12-14] Participants are 18 years or older with standardized data across all sites, including comprehensive data on medical procedures, health behaviors, and COVID-19 diagnoses for all cohort members. All KPRB participants provided written informed consent for survey completion, electronic health record (EHR) access, and biospecimen collection. Study protocols and human subjects considerations were reviewed and approved by the Institutional Review Boards at the University of Washington, Fred Hutchinson Cancer Center, and Kaiser Permanente of the Mid-Atlantic States.

We identified 128,846 individuals who completed the COVID-19 questionnaires. We identified 60,942 individuals who were eligible for CRC screening after exclusions based on incomplete vital organs (colon or rectum) (n=148), prior CRC diagnosis (n=1,425), and age (45-75 years) (n=32,079). We also excluded individuals who were not due for any screening during January, 1st, 2019 through June 1st, 2021 (colonoscopy: 10 years, virtual colonoscopy: 5 years, sigmoidoscopy: 5 years) (n=33,952).[15] For analysis of uptake on screening during the pandemic, we also excluded those who ended enrollment prior to April 1st, 2020 (n=39). We identified 44,806 individuals who were eligible for cervical cancer screening after exclusions based on incomplete vital organs (cervix) (n=970), prior cervical cancer diagnosis (n=785), age (21-65 years) (n=59,966), female sex at birth (n=21,387). We also excluded individuals who

were not due for any screening during January 1st, 2019 through June 1st, 2021 (Pap test: 3 years) (n=632).[16] For analysis of uptake on screening during the pandemic, we also excluded those who ended enrollment prior to April 1st, 2020 (n=52).

COVID-19 Questionnaire

Beginning in April 2020, surveys aimed at assessing impacts and behaviors of the COVID-19 pandemic were sent to all KPRB participants who were enrolled in the Kaiser Permanente health plan as of April 1st, 2020. An initial COVID-19 pandemic survey collected information on SARS-CoV-2 infection and potential COVID-related risk factors.[17-20] Among those who completed the initial survey, 11 follow-up surveys were sent between May 2020 and January 2021 every 2-4 weeks to collect up-to-date information and assess changes over time. Completion for all 11 follow-up questionnaires was not required for inclusion in our study. These questionnaires assessed factors that relate to the COVID-19 pandemic, such as willingness to receive the COVID-19 vaccine, concerns about contracting COVID-19, beliefs regarding COVID-19, employment, and individual protective measures (e.g., masking, quarantining).

Cancer Screening

Data on cancer screening was obtained through EHRs. For each patient, procedure codes and lab data were utilized to identify date and receipt of CRC and cervical cancer screening (**Supplemental Table 4**).[21-23] Data from EHRs were utilized to obtain incident cancer screening occurrence. We utilized the United States Preventive Services Task Force recommendations to determine eligibility for cancer screening as of January 1st, 2019.[15,16] For CRC screening, we ascertained in-clinic colonoscopy and at-home fecal immunochemical tests (FITs). For cervical

cancer screening, we also ascertained human papillomavirus (HPV) tests and pap tests (both in-clinic only).

Statistical Analysis

We used descriptive statistics to evaluate patient demographics. We calculated means and standard deviations (SDs) for continuous variables and frequencies and percentages for categorical variables. We also present patient characteristics and behaviors during the COVID-19 pandemic.

We used interrupted time series analysis to evaluate trend changes in incident screenings from January 1st, 2019 through April 30th, 2021. The primary outcome was defined as the monthly number of CRC and cervical cancer screenings. The interruption time point of April 1st, 2020 was utilized to assess significant level changes and trends corresponding to COVID-19 restrictions. We utilized segmented regression analysis to estimate levels and trends of outcomes before, at the start of, and after the pandemic start period. The trend before the pandemic was added to the pandemic as the control variable. We also used a lag of 12 months to account for monthly trends within a year-long period. Autocorrelation was assessed by examining the plot of residuals; an autoregressive error model was subsequently used to correct for autocorrelation. The segmented regression interrupted time series analysis was used to measure parameter estimates and 95% confidence intervals (CIs) for changes in outcome and trend (slope).[24-26] We assessed patterns with overall CRC screening and overall cervical cancer screening, as well as with individual screening modalities. In sensitivity analyses, we also utilized an interruption of March 15th, 2020 when evaluating the trend changes in incident screening.

We used logistic regression to calculate unadjusted and adjusted odds ratios (ORs) and 95% CIs to compare the odds of CRC and cervical cancer screening during the pandemic (after April 1st, 2020) according to characteristics related to the COVID-19 pandemic for willingness to receive the COVID-19 vaccine, concern about contracting COVID-19, beliefs about COVID-19, employment, and precautions surrounding the pandemic (e.g., quarantining, masking). All estimates of association were adjusted for *a priori*-determined confounders of age (years) and race and ethnicity (non-Hispanic White; Black or African American; Asian, Native Hawaiian, or Pacific Islander; American Indian or Alaska Native, multiple, other). Analyses for CRC screening were additionally adjusted for sex (male, female). In sensitivity analyses, we examined the odds of CRC and cervical cancer screening modalities and patient characteristics related to the COVID-19 pandemic. We also examined the association between odds of CRC and cervical cancer screening stratified by race and ethnicity.

All statistical analyses were two-sided and a p-value of <0.05 was considered statistically significant. All analyses were conducted using SAS (Version 9.4, SAS Institute, Inc., Cary, NC, USA).

RESULTS

A total of 60,942 and 44,806 KPRB participants were eligible for colorectal and cervical cancer screening, respectively, between January 1st, 2019 and May 31st, 2021. Participants eligible for CRC screening were, on average, aged 62.3 years (SD: 8.1). A majority identified as female (63.4%) and non-Hispanic White (79.5%). Participants eligible for cervical cancer screening were, on average, aged 52.5 years (SD: 10.9). A majority also identified as non-Hispanic White (71.7%) (**Table 1**).

Cancer Screening Trends

Segmented regression interrupted time series analysis results are shown in **Table 2**. The baseline level before the COVID-19 pandemic was 3,430 counts (95% CI: 2,973, 3,887) of overall CRC screening per month. The trend before the pandemic was not statistically significant (11.8 count decrease monthly, 95% CI: -75.0, 51.5). The immediate change in overall CRC screenings at the pandemic start of April 1st, 2020, was a decrease by 2,079 counts (95% CI: -2,809, -1,348) or 60.6%. Following that time point, there was a statistically significant upward trend in overall CRC screening (326.9 count, 95% CI: 209.2, 444.6). By the end of June 2020, overall screening numbers were similar to those prior to the pandemic. When assessing colonoscopy and FIT modalities separately, results were similar. In sensitivity analyses, when assessing March 15th, 2020 as the interruption time point, there was not a significant decrease in FIT testing (76.4 count increase, 95% CI: -1,170, 1,323). We also see that there are significant decreases in FIT (-138.5 count, 95% CI: -243.2, -23.8 prior to March 15th, 2021. Results for colonoscopy and overall CRC screening were similar.

For cervical cancer screening, the baseline level before the COVID-19 pandemic was 623.2 counts (95% CI: 585.5, 661.0) per month. The trend before the pandemic was significantly decreasing by a small amount per month (-19.7, 95%: -24.9, -14.6). The immediate change in cervical cancer screening count at the pandemic start of April 1st, 2020, was a decrease of 616.5 (95% CI: -540.3, -692.7) counts or 98.9% in screenings. Since then, there is also a statistically significant rise in cervical cancer screenings (104.8 count, 95% CI: 99.5, 110.0). By the end of October 2020, cervical cancer screening numbers were similar to those pre-pandemic. In sensitivity analyses, when assessing March 15th, 2020 as the interruption start, we see similar results for cervical cancer screening.

COVID-19 Patient Characteristics & Cancer Screening

Of the examined COVID-19 characteristics, a majority of KPRB participants were willing to get the COVID vaccine (89.1-92.6%, were not concerned about getting to a clinic for a vaccine (93.9-94.6%), and were not concerned about contracting COVID-19 from a clinic (81.0-81.8%) (**Table 1**). A majority of participants (89.0-91.8%) felt mistrust regarding the COVID-19 vaccine, but did not report receiving negative information or did not claim religious or other beliefs against vaccines. A majority of participants (95.1-96.2%%) did not lose their job or have an essential service job during the pandemic. Most participants (94.4-95.0%) did not quarantine from in-home family, but a majority did quarantine from out-of-home family (53.1-60.6%). Most participants quarantined from their friends (70.0-75.8%) and community (52.9-60.9%), but reported not quarantining from coworkers (55.9-70.4%). Over half of participants avoided crowded (69.3-76.2%) and public places (62.8-68.7%), and reported only leaving home for essential reasons (61.7-61.8%). When outside of their home, most individuals reported staying 6 feet away from people (89.4-90.2%) and not attending gatherings of more than 10 people, whether indoor (88.4%) or outdoor (78.1-79.7%). A majority of participants also reported masking in both indoor (95.5-96.1%) and outdoor spaces (77.2-77.7%).

We also assessed the associations between incident colorectal and cervical cancer screening and COVID-related patient characteristics (**Table 3**). After adjustment, we found that willingness to receive the COVID-19 vaccine was associated with higher odds of receiving colorectal (1.25, 95% CI: 1.15, 1.36) and cervical (1.18, 95% CI: 1.04, 1.34) cancer screening between April 1st, 2020 and May 31st, 2021. Concern about contracting COVID-19 at the clinic was associated with 22% lower odds of CRC screening (95% CI: 0.64, 0.95). Having an essential service job was associated with lower odds of CRC screening (OR: 0.91, 95% CI: 0.86, 0.96) and higher odds of cervical cancer screening (OR: 1.09, 95% CI: 1.02, 1.17). Those who quarantined from

in-home family had lower odds of CRC screening, but those who quarantined from friends had higher odds of CRC screening. Meanwhile, participants who quarantined from in-home family, coworkers, and their community had higher odds of cervical cancer screening. Individuals who also avoided crowded places were more likely to be screened after April 1st, 2020. Avoiding traveling in-state was associated with higher odds of being screened for CRC, while avoiding traveling out-of-state was associated with higher odds of both colorectal and cervical cancer. Individuals who were prepared to stay at home without leaving for 15 days (CRC only) or only leaving home for essential reasons (CRC and cervical cancer) had lower odds of being screened for after April 1st, 2020. Those who did not attend any gatherings (indoor or outdoor) were more likely to receive CRC screening, while those who did not attend outdoor gatherings were less likely to receive cervical cancer screening. Other COVID-related characteristics were not found to be associated with colorectal or cervical cancer screening. In sensitivity analyses where we assessed individual modalities, we found that masking in outdoor spaces was associated with lower odds of and pap test (OR: 0.66, 95% CI: 0.59, 0.74) screenings. Quarantining from out-of-home family also had higher odds of HPV tests (OR: 1.12, 95% CI: 1.05, 1.17) and lower odds of pap tests (OR: 0.87, 95% CI: 0.78, 0.96). Staying 6 people away from people was also found to be associated with increased odds of HPV tests (OR: 1.11, 95% CI: 1.02, 1.21). Other findings when stratified were similar to the aggregated screening measure. When stratified by race and ethnicity, statistically significant associations between COVID-related characteristics and colorectal and cervical cancer screening were more common in non-Hispanic White populations.

DISCUSSION

The results of our study illustrate the impact of the COVID-19 pandemic on CRC and cervical cancer screening in the United States (US). Lockdowns and pandemic mandates and

restrictions mitigated the spread of the virus; however, they also adversely affected cancer care. Of the states covered by KP, California was the first to impose a stay-at-home order and the earliest of our regions to impose a shutdown.[27] All other states (Colorado, Hawaii, Maryland, Oregon, Virginia, Washington) in our KP system imposed a shutdown in April.[27] Maryland was the earliest to reopen and Virginia was the latest, with all other states reopening in May.[27] Mask mandates also varied by state, with Hawaii and Maryland in May, California in June, and Colorado, Washington, and Oregon in July.[27] Virginia did not have a mask mandate.[27] In our health care system-based study conducted in the KPRB cohort, we observed changes in CRC and cervical cancer screening due to the COVID-19 pandemic. We found that while there were statistically significant monthly trends of cancer screening prior to the pandemic start, they were small in scale. However, the immediate change due to the pandemic was statistically significant, resulting in decreases of 60.6% and 98.9% in CRC and cervical cancer screening counts, respectively. However, screening counts recovered after the pandemic start, which was observed in the statistically significant upward trend of screening counts after April 1st, 2020.

We also found that behaviors surrounding the COVID-19 pandemic were associated with whether a participant was screened for CRC or cervical cancer after the pandemic start of April 1st, 2020. Individuals who were willing to receive the COVID-19 vaccine had higher odds of being screened for CRC and cervical cancer. This result could be indicative of healthy screenee bias, as those who are more willing to uptake other health-related behaviors are more willing to uptake screening.[28] This can also reflect overall health-seeking behavior, such as following recommendations on masking and limiting travel). Quarantining from individuals outside of the home also were behaviors that were associated with higher odds of screening, while those who were prepared to stay at home without leaving for 15 days and reported only leaving the home for essential reasons were associated with lower odds. These factors may reflect COVID-19 fears and may imply concerns around immune-compromised patient conditions. These results

suggest that specific COVID-related avoidance behaviors are correlated with patient willingness to receive cancer screening.

Prior studies have shown that the COVID-19 pandemic negatively affected cancer screening counts. One study in Italy also found that in the first (March-May) of the pandemic in 2020, rates of CRC screening were lower compared to 2019, suggesting that the pandemic may have important implications for CRC screening reduction.[29] Another study in the US found that at the peak of the pandemic in April 2020, there was a decrease of colon cancer screenings by 75%.[30] A US study found that compared to 2018, 2020 resulted in colonoscopy prevalence decreasing by 16%, whereas the prevalence of stool testing increased by 7%.[31] Similar results were found in a study (US) that found that past-year stool testing increase by 3.3% offset declines in colonoscopies of 1.7%.[32] These findings suggest that the potential at-home testing may have maintained population-wide screening rates during this major health care disruption. However, these results may differ depending on the health care institution due the capacity to follow-up with colonoscopies. For example, most Kaiser Permanente sites paused mailing FIT kits home to members during the beginning of the COVID-19 pandemic due to reduced access for follow-up colonoscopies. Thus, our results for FIT may be more reflective of patterns related to institution-wide changes in FIT outreach due to the pandemic rather than of patient personal choice. However, prior commentaries have suggested that at-home FIT tests could be beneficial during times of the pandemic.[33,34]

In terms of cervical cancer screening, screening rates declined by 78% and 29% during and after state stay-at-home mandates compared to 2019 in the US, respectively.[35] A study (US) also found that after years of stable cervical cancer screening prevalence, screening in 2020 compared to 2018 were 11% lower, with 4.47 million fewer women reporting receiving cervical cancer screening.[31] Our results align with those found in prior studies. Perhaps similar to CRC

screening, once approved, at-home screening could be utilized to offset decreased screening due to limited health care resources. While our results do not address at-home HPV testing because HPV testing was done in the clinic at KP and there are mixed results of at-home HPV testing, this method could be further investigated to support the needs of cervical cancer screening during events like the pandemic pending Food & Drug Administration approval.[36] A survey of clinicians showed that 92% felt that screening using HPV self-sampling would be very or somewhat helpful to addressing screening decreases due to the pandemic.[37]

Prior studies have also shown that public interest in cancer screenings may have decreased due to the onset of the COVID-19 pandemic. A study found that Google Trends estimated the decrease in colon cancer screening usage was 9.7%.[38] A study also found that among those who delayed cancer screening during the pandemic, the most common reasons were due to COVID-19 exposure (45.8%), not having seen a doctor during the pandemic (21.1%), and not having thought about cancer screening (15.5%).[39] Perhaps behaviors and concerns related to COVID-19 could be alleviated to encourage cancer screening, such as letters from health care providers about it being safe to return in-person.[40] Tele-health is also an option, as well as at-home testing, which could assist cancer early detection campaigns post-pandemic. A study has shown that past telehealth use was associated with higher likelihood of cancer screening.[41] Telehealth allows for “forward triage” that could assist in recommendations for screening and urgency for in-clinic procedures.[42]

Some limitations should be considered in interpreting our results. Although our study is large overall, there may be limited statistical power in analyses stratifying by race and ethnicity as sample sizes for Black, Hispanic, Asian, Native Hawaiian, Pacific Islander, American Indian, and Alaska Native participants may be too small to detect associations. In addition, our study population includes participants in KPRB, who all have the KP health plan. As such, we are

unable to account for patients that may have lost insurance as a result of unemployment during the pandemic. However, we can expect that disparities will be greater for those suffering from loss of employment during the pandemic. KPRB is also considered a closed healthcare system that is membership-based and pre-paid. Results from KPRB studies may not be fully generalizable to other healthcare delivery environments and institutions. Nevertheless, the differences observed across settings provide data to gauge the impacts of the COVID-19 pandemic. We also may have incomplete data on up-to-date screening due to limited or missing data on prior screening procedures. Therefore, our population may include some individuals who were not due for screening and could bias logistic regression results. While we also adjust for available relevant covariates, there may be confounders that are not accessible through our datasets (e.g., socioeconomic status, neighborhood-level characteristics); their exclusion may result in residual confounding. However, our study is a large healthcare system-based study, spanning multiple geographic regions that allows us to evaluate multiple patient factors.

In conclusion, our results suggest that the COVID-19 pandemic resulted in a large, immediate negative impact on CRC and cervical cancer screening. However, colorectal and cervical screening counts rebounded quickly after the pandemic start. We also found that various factors of the pandemic were associated with whether a participant had a screening one year after the pandemic start. Based on these results, we suggest that efforts should be focused on developing a plan for events that disrupt healthcare systems similar to the pandemic. We propose that future studies also assess these effects among subgroups that have previously experienced disparities in cancer screening, as they may have been disproportionately affected due to the pandemic.

REFERENCES

1. Zhang L, Zhu F, Xie L, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Annals of Oncology*. 2020/07/01/ 2020;31(7):894-901. doi:https://doi.org/10.1016/j.annonc.2020.03.296

2. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol*. Mar 2020;21(3):335-337. doi:10.1016/s1470-2045(20)30096-6

3. Dai M, Liu D, Liu M, et al. Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multicenter Study during the COVID-19 Outbreak. *Cancer Discov*. Jun 2020;10(6):783-791. doi:10.1158/2159-8290.Cd-20-0422

4. Riera R, Bagattini Â M, Pacheco RL, Pachito DV, Roitberg F, Ilbawi A. Delays and Disruptions in Cancer Health Care Due to COVID-19 Pandemic: Systematic Review. *JCO Glob Oncol*. Feb 2021;7:311-323. doi:10.1200/go.20.00639

5. Issaka RB, Taylor P, Baxi A, Inadomi JM, Ramsey SD, Roth J. Model-Based Estimation of Colorectal Cancer Screening and Outcomes During the COVID-19 Pandemic. *JAMA Network Open*. 2021;4(4):e216454-e216454. doi:10.1001/jamanetworkopen.2021.6454

6. Bakouny Z, Paciotti M, Schmidt AL, Lipsitz SR, Choueiri TK, Trinh Q-D. Cancer Screening Tests and Cancer Diagnoses During the COVID-19 Pandemic. *JAMA oncology*. 2021;7(3):458-460. doi:10.1001/jamaoncol.2020.7600

7. Hick JL, Biddinger PD. Novel Coronavirus and Old Lessons — Preparing the Health System for the Pandemic. *New England Journal of Medicine*. 2020/05/14 2020;382(20):e55. doi:10.1056/NEJMp2005118

8. DeGroff A, Miller J, Sharma K, et al. COVID-19 impact on screening test volume through the National Breast and Cervical Cancer early detection program, January–June 2020, in the United States. *Preventive medicine*. 2021/10/01/ 2021;151:106559. doi:https://doi.org/10.1016/j.ypmed.2021.106559

9. Meester RG, Zauber AG, Doubeni CA, et al. Consequences of Increasing Time to Colonoscopy Examination After Positive Result From Fecal Colorectal Cancer Screening Test. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. Oct 2016;14(10):1445-1451.e8. doi:10.1016/j.cgh.2016.05.017

10. Maringe C, Spicer J, Morris M, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. *Lancet Oncol*. Aug 2020;21(8):1023-1034. doi:10.1016/s1470-2045(20)30388-0

11. van den Puttelaar R, Lansdorp-Vogelaar I, Hahn AI, et al. Impact and Recovery from COVID-19-Related Disruptions in Colorectal Cancer Screening and Care in the US: A Scenario Analysis. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. Jan 9 2023;32(1):22-29. doi:10.1158/1055-9965.Epi-22-0544

12. Kvale MN, Hesselson S, Hoffmann TJ, et al. Genotyping Informatics and Quality Control for 100,000 Subjects in the Genetic Epidemiology Research on Adult Health and Aging (GERA) Cohort. *Genetics*. Aug 2015;200(4):1051-60. doi:10.1534/genetics.115.178905

13. Feigelson HS, Clarke CL, Van Den Eeden SK, et al. The Kaiser Permanente Research Bank Cancer Cohort: a collaborative resource to improve cancer care and survivorship. *BMC cancer*. Feb 25 2022;22(1):209. doi:10.1186/s12885-022-09252-6

14. Hedderson MM, Ferrara A, Avalos LA, et al. The Kaiser Permanente Northern California research program on genes, environment, and health (RPGEH) pregnancy cohort: study design, methodology and baseline characteristics. *BMC Pregnancy Childbirth*. Nov 29 2016;16(1):381. doi:10.1186/s12884-016-1150-2

15. Force USPST. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *Jama*. 2021;325(19):1965-1977. doi:10.1001/jama.2021.6238

16. Force USPST. Screening for Cervical Cancer: US Preventive Services Task Force Recommendation Statement. *Jama*. 2018;320(7):674-686. doi:10.1001/jama.2018.10897

17. Kelly C, White LL, Scott SG, Feigelson HS, Burnett-Hartman AN. Social risk factors among individuals with a history of cancer during the COVID-19 pandemic. *J Cancer Surviv*. Apr 2023;17(2):309-317. doi:10.1007/s11764-022-01235-7

18. White LL, Goldberg SR, Spencer Feigelson H, Burnett-Hartman AN. Depression, anxiety, & loneliness among cancer survivors during the COVID-19 pandemic. *J Psychosoc Oncol*. 2024;42(2):242-255. doi:10.1080/07347332.2023.2238192

19. White LL, Burnett-Hartman AN, Ichikawa LE, et al. SARS-CoV-2 Infection and Related Hospitalization among Cancer Survivors. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. Mar 1 2024;33(3):442-444. doi:10.1158/1055-9965.Epi-23-1303

20. Young DR, Hong BD, Lo T, Inzhakova G, Cohen DA, Sidell MA. The longitudinal associations of physical activity, time spent outdoors in nature and symptoms of depression and anxiety during COVID-19 quarantine and social distancing in the United States. *Preventive medicine*. Jan 2022;154:106863. doi:10.1016/j.ypmed.2021.106863

21. Fisher DA, Princic N, Miller-Wilson L-A, Wilson K, Fendrick AM, Limburg P. Utilization of a Colorectal Cancer Screening Test Among Individuals With Average Risk. *JAMA Network Open*. 2021;4(9):e2122269-e2122269. doi:10.1001/jamanetworkopen.2021.22269

22. Longstreth GF, Anderson DS, Zisook DS, Shi JM, Lin JC. Low Rate of Cancer Detection by Colonoscopy in Asymptomatic, Average-Risk Subjects with Negative Results From Fecal Immunochemical Tests. *Clinical Gastroenterology and Hepatology*. 2020/12/01/ 2020;18(13):2929-2936.e1. doi:https://doi.org/10.1016/j.cgh.2020.01.029

23. Hirth JM, Tan A, Wilkinson GS, Berenson AB. Compliance with cervical cancer screening and human papillomavirus testing guidelines among insured young women. *American Journal of Obstetrics and Gynecology*. 2013/09/01/ 2013;209(3):200.e1-200.e7. doi:https://doi.org/10.1016/j.ajog.2013.05.058

24. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *International journal of epidemiology*. 2017;46(1):348-355. doi:10.1093/ije/dyw098

25. Xiao H, Augusto O, Wagenaar BH. Reflection on modern methods: a common error in the segmented regression parameterization of interrupted time-series analyses. *International journal of epidemiology*. Jul 9 2021;50(3):1011-1015. doi:10.1093/ije/dyaa148

26. Turner SL, Karahalios A, Forbes AB, Taljaard M, Grimshaw JM, McKenzie JE. Comparison of six statistical methods for interrupted time series studies: empirical evaluation of 190 published series. *BMC Medical Research Methodology*. 2021/06/26 2021;21(1):134. doi:10.1186/s12874-021-01306-w

27. Zhang X, Warner ME. COVID-19 Policy Differences across US States: Shutdowns, Reopening, and Mask Mandates. *Int J Environ Res Public Health*. Dec 18 2020;17(24)doi:10.3390/ijerph17249520

28. Weiss NS, Rossing MA. Healthy Screenee Bias in Epidemiologic Studies of Cancer Incidence. *Epidemiology*. 1996;7(3):319-322.

29. D'Ovidio V, Lucidi C, Bruno G, Lisi D, Miglioresi L, Bazuro ME. Impact of COVID-19 Pandemic on Colorectal Cancer Screening Program. *Clinical colorectal cancer*. Jul 30 2020;doi:10.1016/j.clcc.2020.07.006

30. Patt D, Gordan L, Diaz M, et al. Impact of COVID-19 on Cancer Care: How the Pandemic Is Delaying Cancer Diagnosis and Treatment for American Seniors. *JCO Clin Cancer Inform*. Nov 2020;4:1059-1071. doi:10.1200/cci.20.00134

31. Fedewa SA, Star J, Bandi P, et al. Changes in Cancer Screening in the US During the COVID-19 Pandemic. *JAMA Network Open*. 2022;5(6):e2215490-e2215490. doi:10.1001/jamanetworkopen.2022.15490

32. Star J, Bandi P, Siegel RL, et al. Cancer Screening in the United States During the Second Year of the COVID-19 Pandemic. *Journal of clinical oncology : official journal of the*

American Society of Clinical Oncology. Sep 20 2023;41(27):4352-4359. doi:10.1200/jco.22.02170

33. Jaklevic MC. Pandemic Spotlights In-home Colon Cancer Screening Tests. *Jama*. Dec 23 2020;doi:10.1001/jama.2020.22466

34. Issaka RB, Somsouk M. Colorectal Cancer Screening and Prevention in the COVID-19 Era. *JAMA Health Forum*. May 2020;1(5)doi:10.1001/jamahealthforum.2020.0588

35. Miller MJ, Xu L, Qin J, et al. Impact of COVID-19 on Cervical Cancer Screening Rates Among Women Aged 21-65 Years in a Large Integrated Health Care System - Southern California, January 1-September 30, 2019, and January 1-September 30, 2020. *MMWR Morb Mortal Wkly Rep*. 2021;70(4):109-113. doi:10.15585/mmwr.mm7004a1

36. Arbyn M, Smith SB, Temin S, Sultana F, Castle P. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. *BMJ (Clinical research ed)*. Dec 5 2018;363:k4823. doi:10.1136/bmj.k4823

37. Fuzzell L, Lake P, Brownstein NC, et al. Examining the perceived impact of the COVID-19 pandemic on cervical cancer screening practices among clinicians practicing in Federally Qualified Health Centers: A mixed methods study. *eLife*. 2023/09/04 2023;12:e86358. doi:10.7554/eLife.86358

38. Greiner B, Tipton S, Nelson B, Hartwell M. Cancer screenings during the COVID-19 pandemic: An analysis of public interest trends. *Current problems in cancer*. Feb 2022;46(1):100766. doi:10.1016/j.currproblcancer.2021.100766

39. Schoenborn NL, Boyd CM, Pollack CE. Impact of the COVID-19 pandemic on cancer screening attitudes, intentions, and behaviors in older adults. *J Am Geriatr Soc*. Jan 2022;70(1):67-69. doi:10.1111/jgs.17449

40. Janda M, Paul C, Horsham C. Changes in cancer preventive behaviours, screening and diagnosis during COVID-19. *Psychooncology*. Feb 2021;30(2):271-273. doi:10.1002/pon.5575

41. Peng W, Huang Q, Mao B. Evaluating variations in the barriers to colorectal cancer screening associated with telehealth use in rural U.S. Pacific Northwest. *Cancer Causes & Control*. 2024/04/01 2024;35(4):635-645. doi:10.1007/s10552-023-01819-3

42. Knudsen KE, Willman C, Winn R. Optimizing the Use of Telemedicine in Oncology Care: Postpandemic Opportunities. *Clinical Cancer Research*. 2021;27(4):933-936. doi:10.1158/1078-0432.CCR-20-3758

Table 1. Population characteristics

Characteristic	Colorectal Cancer n=60,942	Cervical n=44,806
Age (years)	62.3 ± 8.1	51.5 ± 11.2
Sex		
Male	22,282 (36.6)	
Female	38,658 (63.4)	44,806 (100.0)
Race and ethnicity		
Non-Hispanic White	48,458 (79.5)	32,104 (71.7)
Black	2,342 (3.8)	2,254 (5.0)
Hispanic	4,052 (6.7)	4,732 (10.6)
Asian and Native Hawaiian or Pacific Islander	4,010 (6.6)	3,788 (8.5)
American Indian or Alaska Native	152 (0.3)	120 (0.3)
Multiple	1,013 (1.7)	1,152 (2.6)
Other	65 (0.1)	65 (0.2)
Willing to get COVID vaccine*		
Yes	34,538 (92.6)	20,977 (89.1)
No	2,764 (7.4)	2,567 (10.9)
Concern about getting to a clinic for vaccine*		
Yes	146 (5.4)	153 (6.1)
No	2,540 (94.6)	2,361 (93.9)
Concern about getting COVID at the clinic*		
Yes	510 (19.0)	457 (18.2)
No	2,177 (81.0)	2,060 (81.8)
Mistrust of the COVID vaccine*		
Yes	2,437 (89.0)	2,340 (91.8)
No	402 (11.0)	209 (8.2)
Negative information of the COVID vaccine*		
Yes	1,010 (37.4)	955 (37.8)
No	1,693 (62.6)	1,572 (62.2)
Religions or other beliefs against vaccines*		
Yes	205 (7.6)	227 (9.0)
No	2,487 (92.4)	2,287 (91.0)
Lost a job*		
Yes	2,329 (3.8)	2,206 (4.9)
No	58,509 (96.2)	42,558 (95.1)
Essential service job*		
Yes	7,318 (12.0)	9,518 (21.3)
No	53,520 (88.0)	35,246 (78.7)
Quarantined from in-home family*		
Yes	2,359 (5.0)	1,875 (5.6)

No	45,087 (95.0)	31,401 (94.4)
Quarantined from out-of-home family*		
Yes	25,175 (53.1)	20,179 (60.6)
No	22,271 (46.9)	13,097 (39.4)
Quarantined from friends*		
Yes	33,195 (70.0)	25,214 (75.8)
No	14,251 (30.0)	8,062 (24.2)
Quarantined from coworkers*		
Yes	14,028 (29.6)	14,663 (44.1)
No	33,418 (70.4)	18,613 (55.9)
Quarantined from community*		
Yes	25,087 (52.9)	20,255 (60.9)
No	22,359 (47.1)	13,021 (39.1)
Avoided crowded places*		
Yes	32,854 (69.3)	25,358 (76.2)
No	14,592 (30.8)	7,918 (23.8)
Avoided public places*		
Yes	29,772 (62.8)	22,852 (68.7)
No	17,674 (37.3)	10,424 (31.3)
Avoided traveling in-state*		
Yes	23,979 (50.5)	19,233 (57.8)
No	23,467 (49.5)	14,043 (42.2)
Avoided traveling out-of-state*		
Yes	23,698 (50.0)	13,822 (41.5)
No	23,758 (50.1)	19,454 (58.5)
Prepared to stay at home without leaving for 15 days*		
Yes	24,815 (54.4)	16,880 (43.9)
No	20,825 (45.6)	13,192 (43.9)
Only leave home for essential reasons*		
Yes	28,223 (61.8)	18,545 (61.7)
No	17,415 (38.2)	11,528 (38.3)
Stay 6 feet away from people*		
Yes	41,168 (90.2)	26,887 (89.4)
No	4,479 (9.8)	3,192 (10.6)
Do not attend indoor gatherings more than 10 people*		
Yes	40,350 (88.4)	26,569 (88.4)
No	5,286 (11.6)	3,502 (11.7)
Do not attend outdoor gatherings more than 10 people*		
Yes	36,361 (79.7)	23,475 (78.1)
No	9,284 (20.3)	6,601 (22.0)

Mask in a public indoor space*		
Yes	43,588 (95.5)	28,892 (96.1)
No	2,051 (4.5)	1,183 (3.9)
Mask in a public outdoor space*		
Yes	35,219 (77.2)	23,369 (77.7)
No	10,424 (22.8)	6,709 (22.3)
Screened for cancer	36,158 (59.3)	5,888 (13.1)

Percentages may not add up to 100 due to rounding and missing values.

*Percentage based on those who answered question

Table 2. Interrupted time series regression analysis of colorectal and cervical cancer screening and by screening modality

	Level Before Pandemic (95% CI)	**Trend before April 1st, 2020 (95% CI)**	**Immediate Change on April 1st, 2020 (95% CI)**	**Change in Trends after April 1st, 2020 (95% CI)**
Colorectal Cancer Screening	3,430 (2,973, 3,887)	-11.8 (-75.0, 51.5)	-2,079 (-2,809, -1,348)	326.9 (209.2, 444.6)
Colonoscopy	407.0 (395.4, 418.6)	0.6 (-1.0, 2.1)	-283.4 (-302.6, -264.3)	24.1 (21.6, 26.5)
FIT	3,022 (2,617, 3,426)	-10.9 (-66.9, 45.2)	-1,818 (-2,421, -1,215)	306.3 (207.7, 404.8)
Overall (no FIT)	411.2 (403.0, 419.3)	0.1 (-1.0, 1.1)	-283.7 (-298.6, -268.7)	25.6 (24.3, 26.9)
Cervical Cancer Screening	623.2 (585.5, 661.0)	-19.7 (-24.9, -14.6)	-616.5 (-692.7, -540.3)	104.8 (99.5, 110.0)

*Values of screening modalities listed may not add up to overall screening due to other unlisted screening types

Figure 1-4. Monthly numbers of colorectal cancer screening (overall, colonoscopy, FIT) from January 1st, 2019 to April 30th, 2021

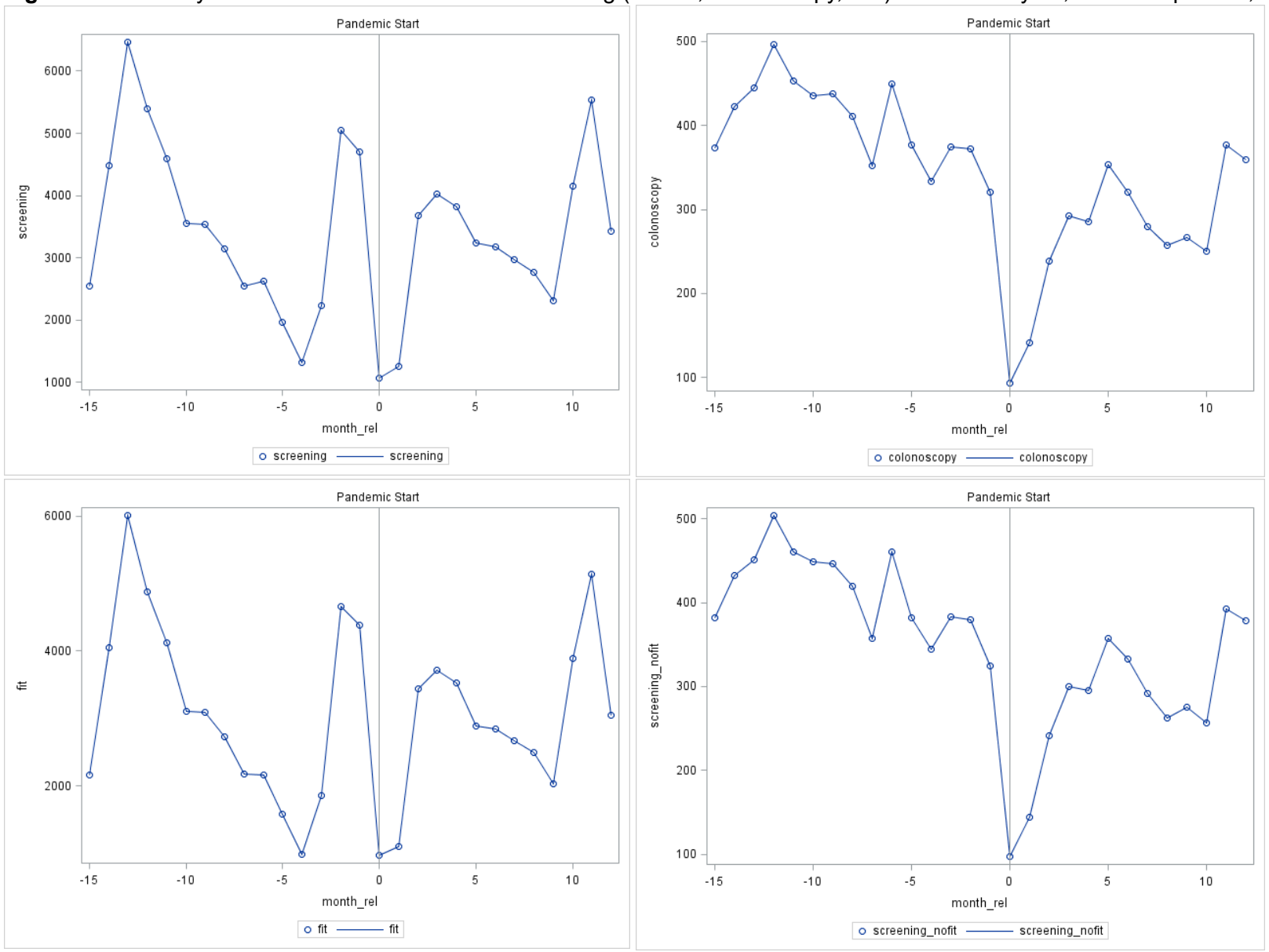


Figure 5. Monthly numbers of cervical cancer screening from January 1st, 2019 to April 30th, 2021

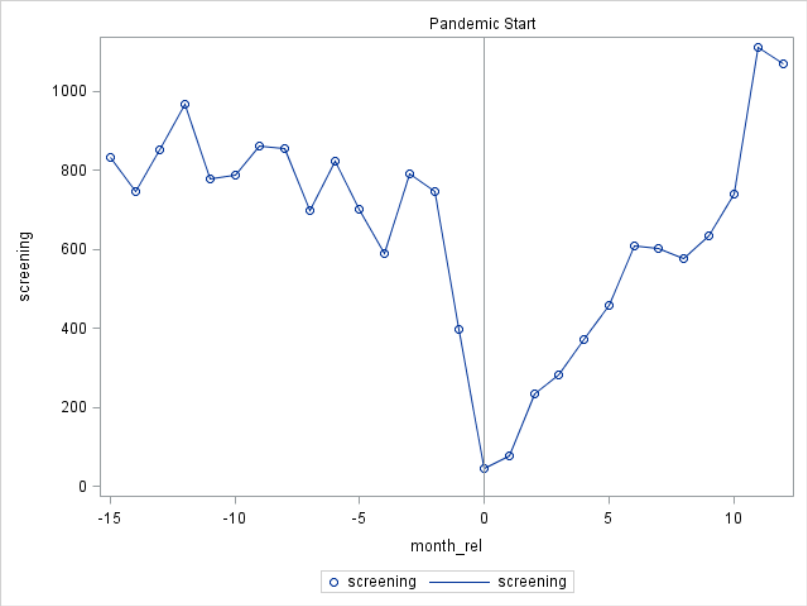


Table 3. Associations between COVID-related patient characteristics and cancer screening

	Colorectal Cancer Screening n=60,903		Cervical Cancer Screening n=44,754	
	Unadjusted	**Adjusted***	**Unadjusted**	**Adjusted****
Characteristics	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Willing to get COVID vaccine	1.05 (0.97, 1.14)	1.25 (1.15, 1.36)	1.07 (0.95, 1.22)	1.18 (1.04, 1.34)
Concern about getting to a clinic for vaccine	0.84 (0.60, 1.18)	0.84 (0.60, 1.19)	0.84 (0.49, 1.42)	0.79 (0.46, 1.35)
Concern about getting COVID at the clinic	0.77 (0.63, 0.93)	0.78 (0.64, 0.95)	0.87 (0.63, 1.20)	0.88 (0.64, 1.22)
Mistrust of the COVID vaccine	1.01 (0.85, 1.39)	1.02 (0.80, 1.31)	1.01 (0.66, 1.57)	0.96 (0.62, 1.50)
Negative information of the COVID vaccine	0.85 (0.72, 0.99)	0.85 (0.73, 1.00)	1.06 (0.83, 1.36)	1.09 (0.85, 1.41)
Religions or other beliefs against vaccines	1.13 (0.84, 1.51)	1.13 (0.84, 1.52)	1.03 (0.68, 1.56)	0.92 (0.60, 1.41)
Lost a job	1.11 (1.01, 1.20)	1.00 (0.92, 1.09)	1.02 (0.89, 1.15)	0.96 (0.84, 1.09)
Essential service job	1.29 (1.23, 1.36)	0.91 (0.86, 0.96)	1.34 (1.26, 1.43)	1.09 (1.02, 1.17)
Quarantined from in-home family	0.82 (0.75, 0.89)	0.82 (0.75, 0.89)	1.15 (1.01, 1.32)	1.17 (1.02, 1.34)
Quarantined from out-of-home family	1.03 (0.99, 1.07)	0.98 (0.94, 1.02)	1.13 (1.06, 1.21)	1.06 (0.99, 1.13)
Quarantined from friends	1.14 (1.09, 1.18)	1.08 (1.03 1.12)	1.18 (1.09, 1.27)	1.08 (1.00, 1.17)
Quarantined from coworkers	1.27 (1.22, 1.32)	0.96 (0.92, 1.00)	1.47 (1.38, 1.57)	1.16 (1.08, 1.24)
Quarantined from community	1.08 (1.04, 1.12)	1.00 (0.97, 1.04)	1.19 (1.11, 1.27)	1.12 (1.04, 1.19)
Avoided crowded places	1.16 (1.11, 1.20)	1.06 (1.02, 1.10)	1.27 (1.18, 1.38)	1.15 (1.06, 1.24)
Avoided public places	1.08 (1.04, 1.12)	1.03 (0.99, 1.07)	1.15 (1.07, 1.23)	1.06 (0.99, 1.14)
Avoided traveling in-state	1.13 (1.09, 1.18)	1.06 (1.02, 1.10)	1.16 (1.09, 1.24)	1.07 (1.00, 1.15)
Avoided traveling out-of-state	1.14 (1.10, 1.18)	1.05 (1.01, 1.09)	1.24 (1.16, 1.33)	1.16 (1.08, 1.24)
Prepared to stay at home without leaving for 15 days	0.94 (0.90, 0.98)	0.95 (0.91, 0.98)	0.89 (0.83, 0.96)	0.93 (0.87, 1.00)
Only leave home for essential reasons	0.85 (0.82, 0.88)	0.88 (0.84, 0.91)	0.81 (0.75, 0.86)	0.85 (0.79, 0.91)
Stay 6 feet away from people	0.99 (0.93, 1.06)	1.04 (0.98, 1.11)	0.92 (0.83, 1.03)	1.01 (0.90, 1.13)
Do not attend indoor gatherings more than 10 people	1.10 (1.03, 1.16)	1.13 (1.06, 1.20)	1.01 (0.91, 1.12)	1.03 (0.92, 1.14)
Do not attend outdoor gatherings more than 10 people	0.99 (0.95, 1.05)	1.07 (1.02, 1.12)	0.84 (0.78, 0.91)	0.92 (0.85, 0.99)

Mask in a public indoor space	1.06 (0.97, 1.16)	1.02 (0.93, 1.12)	1.05 (0.88, 1.25)	0.95 (0.79, 1.13)
Mask in a public outdoor space	0.94 (0.91, 0.99)	0.98 (0.94, 1.03)	0.94 (0.87, 1.02)	0.98 (0.90, 1.07)

*Adjusted for sex (male, female), age (years), race and ethnicity (Non-Hispanic White, Black or African American, Asian or Native Hawaiian or Pacific Islander, American Indian or Alaska Native, multiple, other)

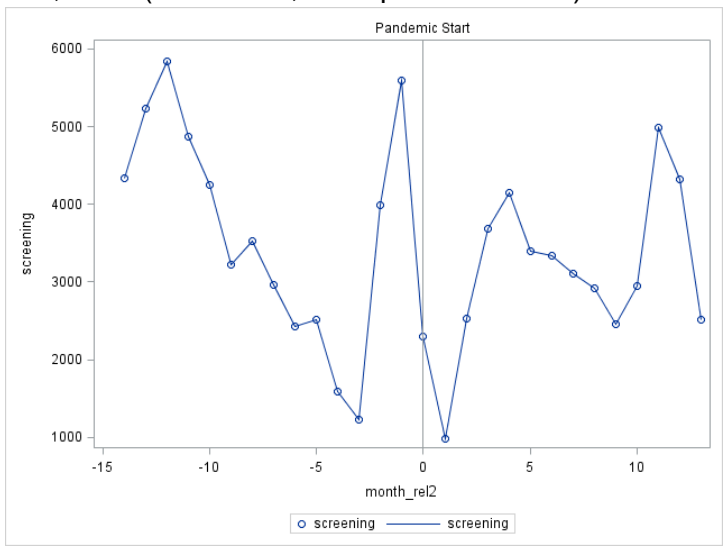
**Adjusted for age (years), race and ethnicity (Non-Hispanic White, Black or African American, Asian or Native Hawaiian or Pacific Islander, American Indian or Alaska Native, multiple, other)

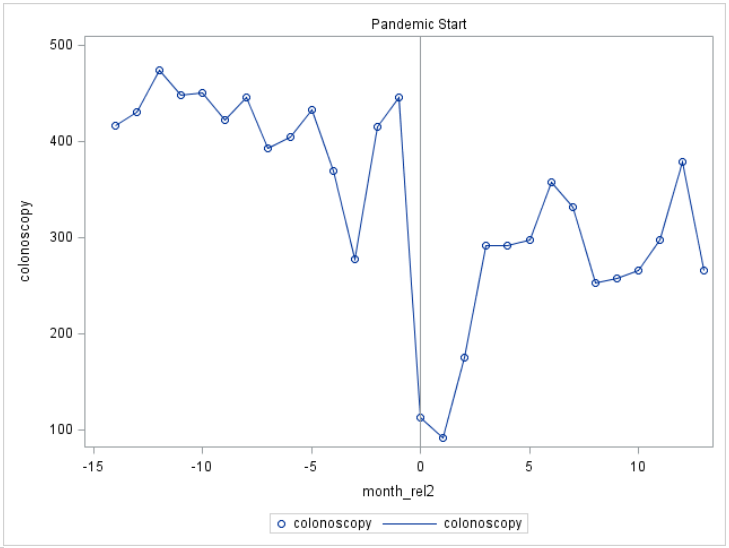
Supplemental Table 1. Interrupted time series regression analysis of colorectal and cervical cancer screening and by screening modality with March 15th

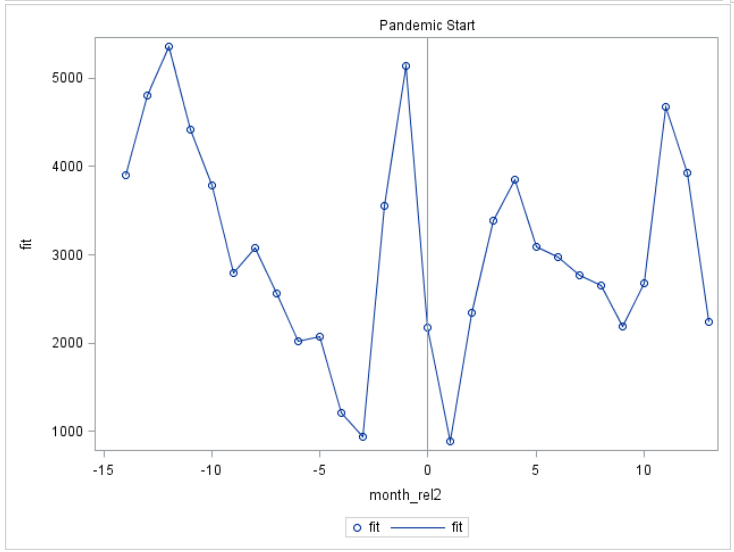
	Level Before Pandemic (95% CI)	Trend before March 15th, 2020 (95% CI)	Immediate Change on March 15th, 2020 (95% CI)	Change in Trends after March 15th, 2020 (95% CI)
Colorectal Cancer Screening	3,924 (3,095, 4,752)	43.5 (-68.4, 155.4)	-2,696 (-4,022, -1,369)	254.0 (120.9, 387.2)
Colonoscopy	444.9 (378.4, 511.4)	4.5 (-4.3, 13.3)	-304.0 (-420.3, -187.7)	13.3 (5.3, 21.3)
FIT	2,097 (1,289, 2,905)	-138.5 (-253.2, -23.8)	76.4 (-1,170, 1,323)	261.0 (110.2, 411.8)
Overall (no FIT)	439.3 (367.0, 511.5)	2.7 (-6.8, 12.2)	-280.8 (-407.1, -154.5)	13.6 (4.9, 22.4)
Cervical Cancer Screening	669.2 (663.8, 674.5)	-16.6 (-17.4, -15.7)	-628.5 (-637.3, -619.6)	89.5 (88.6, 90.3)

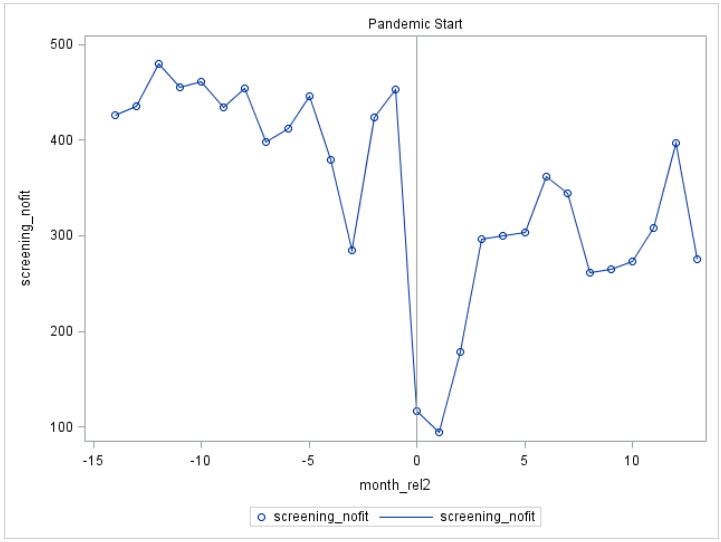
*Values of screening modalities listed may not add up to overall screening due to other unlisted screening types

Supplemental Figure 1-4. Monthly numbers of colorectal cancer screening (overall, colonoscopy, FIT) from January 1st, 2019 to May 15th, 2021 (March 15th, 2020 pandemic start)

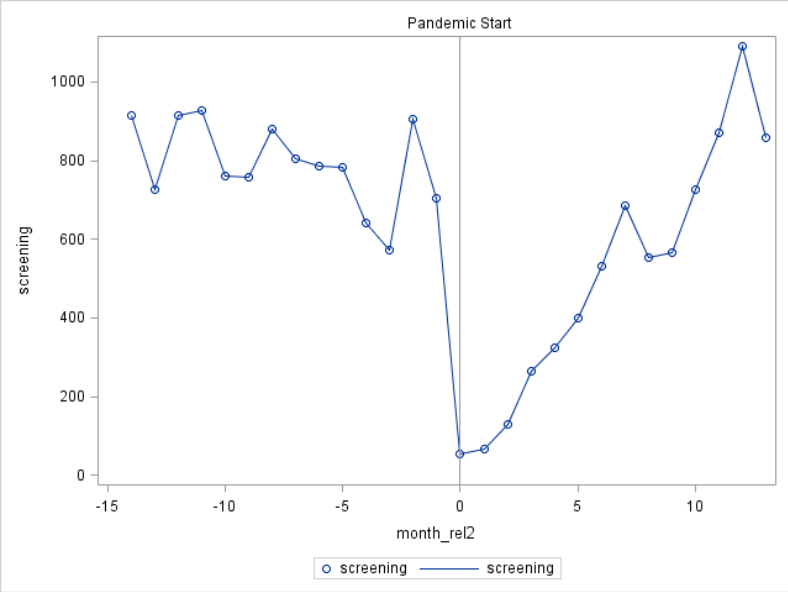








Supplemental Figure 5. Monthly numbers of cervical cancer screening from January 1st, 2019 to May 15th, 2021 (March 15th, 2020 pandemic start)



Supplemental Table 2. Adjusted* associations between COVID-related patient characteristics and cancer screening by screening modality

	Colorectal Cancer Screening		Cervical Cancer Screening	
	Colonoscopy	FIT	HPV Test	Pap Test
Characteristics	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Willing to get COVID vaccine	1.28 (1.12, 1.46)	1.15 (1.06, 1.26)	1.14 (1.04, 1.26)	1.22 (0.99, 1.49)
Concern about getting to a clinic for vaccine	0.50 (0.23, 1.08)	0.94 (0.65, 1.35)	0.79 (0.55, 1.16)	
Concern about getting COVID at the clinic	0.71 (0.49, 1.03)	0.90 (0.73, 1.10)	0.93 (0.74, 1.17)	
Mistrust of the COVID vaccine	0.94 (0.63, 1.42)	1.08 (0.84, 1.40)	0.87 (0.63, 1.18)	
Negative information of the COVID vaccine	1.14 (0.87, 1.49)	0.87 (0.73, 1.03)	0.94 (0.78, 1.12)	
Religions or other beliefs against vaccines	1.01 (0.62, 1.66)	1.19 (0.86, 1.64)	1.09 (0.81, 1.46)	
Lost a job	1.04 (0.91, 1.18)	1.04 (0.95, 1.14)	1.01 (0.92, 1.11)	0.87 (0.70, 1.08)
Essential service job	0.98 (0.90, 1.06)	0.93 (0.88, 0.99)	1.13 (1.08, 1.19)	0.96 (0.86, 1.07)
Quarantined from in-home family	1.12 (0.99, 1.27)	0.83 (0.76, 0.91)	1.00 (0.90, 1.11)	1.10 (0.89, 1.37)
Quarantined from out-of-home family	1.06 (1.00, 1.12)	0.98 (0.94, 1.02)	1.12 (1.06, 1.17)	0.87 (0.78, 0.96)
Quarantined from friends	1.09 (1.02, 1.16)	1.06 (1.01, 1.11)	1.20 (1.13, 1.27)	1.01 (0.89, 1.14)
Quarantined from coworkers	0.97 (0.91, 1.04)	0.95 (0.91, 0.99)	1.22 (1.16, 1.28)	1.24 (1.11, 1.38)
Quarantined from community	1.10 (1.03, 1.16)	0.99 (0.95, 1.03)	1.18 (1.12, 1.24)	1.07 (0.96, 1.19)
Avoided crowded places	1.06 (0.99, 1.12)	1.05 (1.01, 1.10)	1.22 (1.15, 1.29)	1.29 (1.13, 1.48)
Avoided public places	1.03 (0.98, 1.07)	0.99 (0.96, 1.04)	1.11 (1.05, 1.17)	1.04 (0.93, 1.17)
Avoided traveling in-state	1.01 (0.95, 1.07)	1.06 (1.02, 1.10)	1.17 (1.11, 1.23)	0.79 (0.71, 0.88)
Avoided traveling out-of-state	1.03 (0.98, 1.10)	1.02 (0.98, 1.06)	1.13 (1.08, 1.19)	1.14 (1.02, 1.26)
Prepared to stay at home without leaving for 15 days	1.06 (1.00, 1.13)	0.92 (0.88, 0.96)	0.91 (0.86, 0.95)	1.09 (0.98, 1.22)
Only leave home for essential reasons	1.01 (0.95, 1.07)	0.89 (0.86, 0.93)	0.86 (0.82, 0.91)	0.70 (0.63, 0.78)
Stay 6 feet away from people	1.07 (0.97, 1.18)	1.04 (0.97, 1.11)	1.11 (1.02, 1.21)	0.86 (0.73, 1.01)
Do not attend indoor gatherings more than 10 people	1.03 (0.94, 1.13)	1.10 (1.03, 1.17)	1.18 (1.09, 1.28)	0.70 (0.60, 0.81)
Do not attend outdoor gatherings more than 10 people	0.99 (0.93, 1.07)	1.07 (1.02, 1.13)	1.01 (0.95, 1.08)	0.71 (0.63, 0.80)

Mask in a public indoor space	1.03 (0.89, 1.18)	1.02 (0.93, 1.12)	1.07 (0.94, 1.22)	1.22 (0.89, 1.67)
Mask in a public outdoor space	0.95 (0.89, 1.02)	0.96 (0.91, 1.00)	0.99 (0.93, 1.05)	0.65 (0.58, 0.73)

*Adjusted for sex (male, female), age (years), race and ethnicity (Non-Hispanic White, Black or African American, Asian or Native Hawaiian or Pacific Islander, American Indian or Alaska Native, multiple, other)

Supplemental Table 3. Adjusted* associations between COVID-related patient characteristics and cancer screening by race and ethnicity

	Colorectal Cancer Screening			
	Non-Hispanic White	**Black**	**Hispanic**	**Asian, Native Hawaiian, or Pacific Islander**
Characteristics	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Willing to get COVID vaccine	1.31 (1.19, 1.44)	0.98 (0.70, 1.36)	1.31 (0.99, 1.74)	0.79 (0.53, 1.15)
Concern about getting to a clinic for vaccine	0.72 (0.48, 1.08)	2.62 (0.52, 13.21)	0.70 (0.21, 2.40)	0.91 (0.23, 3.59)
Concern about getting COVID at the clinic	0.69 (0.55, 0.87)	0.70 (0.33, 1.48)	1.50 (0.72, 3.14)	0.98 (0.41, 2.36)
Mistrust of the COVID vaccine	0.95 (0.71, 1.26)	0.64 (0.26, 1.59)	2.68 (0.98, 7.35)	1.51 (0.48, 4.77)
Negative information of the COVID vaccine	0.76 (0.63, 0.92)	1.08 (0.56, 2.07)	1.27 90.73, 2.23)	1.56 (0.71, 3.42)
Religions or other beliefs against vaccines	1.23 (0.87, 1.74)	1.07 (0.32, 3.58)	1.01 (0.37, 2.74)	0.77 (0.14, 4.18)
Lost a job	1.01 (0.92, 1.12)	1.11 (0.73, 1.68)	0.88 (0.65, 1.19)	0.90 (0.64, 1.26)
Essential service job	0.91 (0.86, 0.97)	0.95 (0.75, 1.21)	1.02 (0.86, 1.21)	0.79 (0.65, 0.96)
Quarantined from in-home family	0.79 (0.72, 0.88)	0.80 (0.56, 1.14)	1.10 (0.83, 1.46)	0.78 (0.56, 1.10)
Quarantined from out-of-home family	0.98 (0.94, 1.02)	1.02 (0.83, 1.25)	1.09 (0.94, 1.26)	0.85 (0.73, 0.99)
Quarantined from friends	1.07 (1.02, 1.12)	1.05 (0.85, 1.31)	1.27 (1.09, 1.48)	1.00 (0.85, 1.18)
Quarantined from coworkers	0.95 (0.91, 0.99)	1.09 (0.88, 1.36)	1.03 (0.88, 1.21)	0.86 (0.72, 1.03)
Quarantined from community	1.01 (0.97, 1.05)	0.90 (0.74, 1.11)	1.18 (1.02, 1.36)	0.85 (0.73, 0.99)
Avoided crowded places	1.05 (1.01, 1.10)	1.00 (0.81, 1.24)	1.24 (1.06, 1.44)	0.97 (0.83, 1.14)
Avoided public places	1.02 (0.98, 1.06)	1.04 (0.85, 1.28)	1.14 (0.98, 1.32)	0.97 (0.83, 1.13
Avoided traveling in-state	1.07 (1.03, 1.12)	0.90 (0.74, 1.10)	1.26 (1.09, 1.46)	0.87 (0.75, 1.02)
Avoided traveling out-of-state	1.05 (1.01, 1.10)	0.88 (0.72, 1.07)	1.17 (1.01, 1.35)	0.96 (0.82, 1.12)
Prepared to stay at home without leaving for 15 days	0.94 (0.90, 0.98)	1.05 (0.85, 1.30)	0.99 (0.85, 1.17)	1.06 (0.90, 1.25)
Only leave home for essential reasons	0.88 (0.84, 0.92)	0.92 (0.72, 1.18)	1.02 (0.86, 1.21)	0.76 (0.63, 0.91)

Stay 6 feet away from people	1.04 (0.97, 1.12)	1.11 (0.75, 1.63)	0.97 (0.74, 1.28)	1.16 (0.88, 1.53)
Do not attend indoor gatherings more than 10 people	1.16 (1.09, 1.24)	0.85 (0.60, 1.22)	1.10 (0.87, 1.38)	0.96 (0.73, 1.26)
Do not attend outdoor gatherings more than 10 people	1.07 (1.01, 1.13)	1.07 (0.80, 1.45)	1.14 (0.94, 1.37)	0.93 (0.75, 1.16)
Mask in a public indoor space	1.05 (0.95, 1.16)	1.27 (0.80, 2.00)	0.80 (0.55, 1.15)	0.75 (0.50, 1.12)
Mask in a public outdoor space	0.98 (0.93, 1.03)	1.04 (0.75, 1.44)	0.99 (0.80, 1.22)	0.86 (0.68, 1.09)
	Cervical Cancer Screening			
	Non-Hispanic White	**Black**	**Hispanic**	**Asian, Native Hawaiian, or Pacific Islander**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Willing to get COVID vaccine	1.17 (1.00, 1.36)	1.29 (0.76, 2.17)	1.06 (09.73, 1.54)	1.51 (0.86, 2.63)
Concern about getting to a clinic for vaccine	0.72 (0.36, 1.41)		1.09 (0.29, 4.12)	0.86 (0.10, 7.18)
Concern about getting COVID at the clinic	0.93 (0.63, 1.39)	0.54 (0.15, 1.90)	1.28 (0.57, 2.86)	0.50 (0.11, 2.31)
Mistrust of the COVID vaccine	1.16 (0.67, 2.00)	0.37 (0.11, 1.25)	0.69 (0.18, 2.58)	0.53 (0.11, 2.69)
Negative information of the COVID vaccine	1.29 (0.96, 1.73)	0.52 (0.18, 1.47)	0.88 (0.43, 1.80)	0.27 (0.07, 0.99)
Religions or other beliefs against vaccines	1.09 (0.69, 1.74)	0.60 (0.08, 4.75)	0.76 (0.21, 2.72)	
Lost a job	0.97 (0.84, 1.13)	0.60 (0.27, 1.33)	0.92 (0.64, 1.34)	0.96 (0.61, 1.50)
Essential service job	1.10 (1.02, 1.19)	1.20 (0.89, 1.61)	1.17 (0.97, 1.41)	1.00 (0.80, 1.25)
Quarantined from in-home family	1.12 (0.94, 1.32)	1.17 (0.68, 2.01)	1.37 (0.96, 1.96)	1.46 (0.94, 2.26)
Quarantined from out-of-home family	1.05 (0.97, 1.13)	1.39 (0.96, 1.99)	0.96 (0.77, 1.21)	1.12 90.88, 1.43)
Quarantined from friends	1.10 (1.01, 1.21)	1.33 (0.89, 2.00)	0.91 (0.72, 1.16)	0.95 (0.72, 1.24)
Quarantined from coworkers	1.16 (1.07, 1.25)	1.43 (1.02, 2.02)	1.02 (0.82, 1.26)	1.18 (0.92, 1.51)
Quarantined from community	1.13 (1.05, 1.22)	1.22 (0.86, 1.75)	1.07 (0.85, 1.33)	1.02 (0.81, 1.30)
Avoided crowded places	1.19 (1.08, 1.31)	1.11 (0.75, 1.65)	1.00 (0.78, 1.28)	0.98 (0.74, 1.28)
Avoided public places	1.07 (0.99, 1.17)	0.89 (0.63, 1.25)	1.06 (0.85, 1.33)	0.99 (0.78, 1.28)
Avoided traveling in-state	1.09 (1.01, 1.18)	1.20 (0.86, 1.69)	0.87 (0.70, 1.08)	1.11 (0.87, 1.41)
Avoided traveling out-of-state	1.17 (1,08, 1.26)	1.17 (0.83, 1.66)	1.13 (0.91, 1.41)	1.11 (0.87, 1.42)

Prepared to stay at home without leaving for 15 days	0.95 (0.88, 1.03)	0.94 (0.65, 1.36)	0.82 (0.65, 1.04)	1.01 (0.79, 1.31)
Only leave home for essential reasons	0.84 (0.78, 0.91)	0.79 (0.53, 1.20)	0.79 (0.61, 1.01)	1.06 (0.80, 1.40)
Stay 6 feet away from people	1.02 (0.90, 1.15)	1.86 (0.87, 3.98)	0.87 (0.59, 1.27)	1.06 (0.70, 1.61)
Do not attend indoor gatherings more than 10 people	0.99 (0.89, 1.13)	1.01 (0.54, 1.87)	1.02 (0.72, 1.45)	1.30 (0.83, 2.02)
Do not attend outdoor gatherings more than 10 people	0.90 (0.83, 0.99)	0.80 (0.50, 1.29)	0.88 (0.67, 1.15)	1.17 (0.84, 1.63)
Mask in a public indoor space	0.94 (0.76, 1.15)	1.05 (0.44, 2.53)	0.67 (0.40, 1.13)	1.33 (0.66, 2.68)
Mask in a public outdoor space	0.99 (0.90, 1.08)	1.03 (0.56, 1.90)	0.90 (0.67, 1.22)	1.06 (0.72, 1.57)

*Adjusted for sex (male, female), age (years)

Supplemental Table 4. Procedure codes to identify cancer screening

Colorectal Cancer Screening	Cervical Cancer Screening
0066T	56820
0067T	56821
44388	57420
44389	57421
44390	57452
44391	57454
44394	57455
44401	57456
44403	57460
44404	57461
45300	87620
45303	87621
45305	87623
45307	87624
45309	87625
45315	88141
45317	88142
45320	88143
45330	88148
45331	88150
45332	88164
45333	88174
45334	88175
45335	G0101
45337	G0123
45338	G0124
45339	G0143
45340	G0145
45341	G0476
45342	Q0091
45346	
45347	
45349	
45350	
45355	
45378	
45379	
45379	
45380	
45381	
45382	
45383	
45384	
45385	
45386	
45388	
45389	

45390	
45391	
45392	
45393	
74261	
74262	
74263	
74270	
74280	
81528	
82270	
82271	
82272	
82273	
82274	
G0102	
G0104	
G0105	
G0106	
G0107	
G0120	
G0121	
G0122	
G0328	
G0464	
G6024	

Aim 3

Association of diagnosis-to-treatment interval and patient characteristics and survival among colorectal cancer patients

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ABSTRACT

Background

Disparities in cancer care can result from differences across diagnosis-to-treatment interval (DTI). Prolonged time to treatment can result in further progression of disease as well as negatively affecting psychological well-being and quality of life.

Methods

Our population-based study included colorectal cancer (CRC) patients (n=1,652) diagnosed from 1998-2018 using questionnaire and cancer registry data on CRC diagnosis, demographics, risk factors, cancer characteristics, and vital status. To calculate DTI, we used diagnosis and treatment dates available through Surveillance, Epidemiology, and End Results (SEER) and medical record abstraction. Linear regression was used to calculate change in DTI (days) and standard errors (SEs), and logistic regression to calculate odds of a DTI greater than 30 days using odds ratios (ORs) and 95% confidence intervals (CIs). Cox proportional hazards regression was used to calculate hazard ratios (HRs) and 95% CIs the associations between DTI and mortality.

Results

Of the 1,652 CRC patients in the study population, 444 (26.9%) had a DTI of greater than 30 days. Older age at diagnosis (70+ vs. <50 years, OR: 1.67, 95% CI: 1.10, 2.51) and rectal tumor site (OR vs. proximal colon cancer: 3.68, 95% CI: 2.71, 4.98) were associated with greater risk of DTI >30 days. Cancer stage was inversely associated with a DTI >30 days: regional (OR: 0.63, 95% CI: 0.48, 0.82) stage was more likely to have shorter DTI than localized cancer. There was no association between DTI and CRC-specific and all-cause mortality.

Conclusion

Our results suggest that there are associations with patient and cancer characteristics (age, cancer site, cancer stage) and DTI. Associations between DTI and survival were not observed, which may be relevant for future quality-metrics analyses of delivered cancer care.

INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed cancer, as well as the third most common cause of cancer death in the United States (US).[1] CRC incidence and mortality can be preventable through regular cancer screening, surveillance, and adequate treatment.[1] Specifically, CRC mortality has decreased since 1970, but that decrease has slowed more recently.[1] Trends vary widely by age and race and ethnicity. Incidence and mortality are highest in Alaska Native populations, as well as non-Hispanic Black populations.[1,2] Incidence of and mortality from CRC also differ by socioeconomic status (SES): those with the lowest SES are 40% more likely to be diagnosed with CRC than highest SES individuals.[3]

Disparities in the cancer continuum can include differences in outcome consequent upon differences in time to treatment. Studies have indicated that shorter time to diagnosis and time to treatment are associated with more favorable outcomes.[4] However, these relationships have been particularly unclear for racial and ethnic subgroups, as well as across levels of SES, factors which have been associated with prolonged DTI.[5] Members of racial and ethnic subgroups and those with lower SES may experience medical mistrust, language barriers, and systematic barriers that may increase DTI.

We examined whether DTI was associated with patient factors, including tumor characteristics, race and ethnicity, and SES, and explored the association of DTI and mortality in a large prospective study of CRC patients.

METHODS

Study Population and Design

We conducted a population-based study of CRC cases who were ages 18 to 74 years old at the time of diagnosis and were diagnosed between January 1st, 1998 and December 31st, 2018. CRC cases were identified through the Cancer Surveillance System (CSS), a subset of the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) cancer registries. CSS is a population-based cancer registry that collects information on cancer cases in the 13-county Puget Sound region of western Washington State.[6,7] Among the cases in the registry, International Classification of Diseases, Oncology, Version 3 (ICD-O-3) codes were used to identify individuals diagnosed with primary incident invasive CRC. Excluded from this study were cancer cases with non-sharable contact information, out-of-date contact information, research opt-out, and those who were identified as deceased prior to contact. Study participants were recruited through mail and telephone to become a part of the Colon Cancer Family Registry (CCFR) and Advanced Study of Colorectal Cancer of the Serrated Subtype (ACCESS) cohorts. Study population and recruitment procedures have been described previously for these studies.[8,9]

Study protocols and human subject considerations were reviewed and approved by the Institutional Review Board at the University of Washington and Fred Hutchinson Cancer Center.

Patient Characteristics

Consenting participants completed a questionnaire on patient demographics, medical history, and CRC risk factors. Baseline questionnaires were conducted via telephone interview, online-portal, or self-administered on paper following receipt of cancer diagnosis from CSS (1998-2018). The questionnaire included items on known and suspected risk factors for CRC and sociodemographic factors, including education and income.

Tumor Characteristics

Tumor site was obtained for all participants from pathology reports in the CSS registry. Colon cancer was defined as ICD-O-3 codes C180 and C182-189; rectal cancer was defined as ICD-O-3 codes C199 and C209. Colon cancer was further subdivided into proximal (C180, C182-C184) and distal (C185-C187) colon cancer. Cancer stage at diagnosis was obtained from the CSS registry, categorized as localized, regional, and distant.

Diagnosis-to-Treatment Interval (DTI) Assessment

DTI was estimated using information in the CSS registry and information derived from medical record abstraction. Diagnosis dates were obtained through the CSS registry. In the case of uncertain dates, diagnosis dates were abstracted from medical records. Treatment dates were obtained through medical abstraction only by a trained abstractor. When the abstractor had questions regarding the interpretation of information, they met with the study team to reach a consensus. A second abstractor performed quality control on 10% of the records. If data conflicted during that quality control data review, the records were reviewed by the study team to reach a decision. Due to potential uncertainty and discrepancies in date of diagnosis and treatment, individuals who had fewer than 0 days and more than 365 days of DTI were excluded from the analysis (n=108). Individuals who also did not have any treatment data were excluded from the study (n=2).

Guidelines for time from DTI have been shown to range between and within countries.[10,11] Internationally, Dutch recommendations are that CRC should be treated within 5 weeks.[11] In the UK, it is recommended that surgery in 94% of patients be within 31 days from the decision to

treat.[11] Although there are no common standards in the US nor clinically recommended intervals for categorizing delay, some international guidelines recommend treatment within one month of diagnosis.[12] Thus, there is no standard timeframe when care should be initiated and this may vary by center and logistic difficulty (e.g., scheduling) in implementing an agreed-upon treatment plan.[12] Chemotherapy often starts within 2 weeks, thus >4 weeks DTI would be considered long.[13] For surgery, center size may affect the time to surgery and this can range widely from days to weeks. For radiation, simulation scans need to be scheduled before treatment can be planned, resulting in a 3-4 week start time. Taking these recommendations into consideration, we utilized the DTI categorization of greater than 30 days and less than or equal to 30 days based on prior studies and reflective of practice patterns.[5,14-16]

Survival Ascertainment

Vital status, death date, and cause of death were obtained through linkage to the CSS registry and the National Death Index. Mortality was categorized into CRC-specific and all-cause mortality. All-cause mortality encompassed all causes of death, whereas CRC-specific deaths included causes of death attributed to International Classification of Diseases, 10th Revision (ICD-10) codes C18.0, C18.2-C18.9, C20.0, C20.9, or C26.0. The latest linkage for vital status was completed in April 2022. Participants who were alive at the latest linkage were censored at that date.

Statistical Analysis

We used descriptive statistics to evaluate patient demographics and tumor characteristics. We estimated means and standard deviation (SDs) for continuous variables and frequencies and

percentages for categorical variables. Descriptive statistics were estimated for the overall sample and according to categories for DTI >30 days and ≤30 days.

To assess the association between DTI and patient and cancer characteristics, we used linear and logistic regression: linear regression was used to assess changes in DTI (days) and logistic regression to assess associations with a DTI greater than 30 days. Multivariable-adjusted regressions were run with the following variables as covariates: age (<50 years, 59-59 years, 60-69 years, 70+ years), sex at birth (male, female), race and ethnicity (non-Hispanic White, Black, Hispanic, Asian and Native Hawaiian or Pacific Islander, other), cancer site (proximal, distal, rectal), cancer stage (localized, regional, distant), education (less than high school or high school graduate, some college, college graduate or higher), and income (less than $30,000, $30,000-$69,000, and greater than $70,000). Unadjusted and adjusted analyses were run for both regressions.

To assess the association between mortality and DTI, we used Cox proportional hazards regression to evaluate the differences in survival among patients with DTI >30 days and DTI ≤30 days (referent group). Left truncation was used to account for immortal time between cancer diagnosis and study enrollment/questionnaire completion (median: 5.6 months for ACCESS). Unadjusted and adjusted analyses were run for both CRC-specific and all-cause mortality; adjusted analyses included sex, age, race and ethnicity, education, income, cancer site, cancer stage, and year of diagnosis. Sensitivity analyses including stratification by cancer site (proximal, distal, rectal), cancer stage (localized, regional, distant), education (less than high school or high school graduate, some college, college graduate or higher), and income (less than $30,000, $30,000-$69,000, $70,000) as well as DTI cut-offs of 45 and 60 days.

All covariates in adjusted models were selected *a priori*. All statistical analyses were two-sided and a p-value of <0.05 was considered statistically significant. All analyses were conducted using SAS (Version 9.4, SAS Institute, Inc., Cary, NC, USA).

RESULTS

Descriptive statistics for the overall study population (n=1,652) are reported in **Table 1**. Of the overall study population, 444 (26.9%) had a DTI greater than 30 days. The study population had an average age of 55.5 years (SD: 11.7 years). The majority of participants were male (50.4%) and/or non-Hispanic White (90.6%). The majority of study participants were diagnosed with a colon cancer (35.5% proximal colon and 30.2% distal colon cancer). Patients experiencing a DTI >30 days tended to be slightly older at the time of diagnosis, were more likely to have rectal cancers, and/or to have a localized cancer stage at diagnosis.

When assessing associations between DTI and patient characteristics, older age was associated with increased DTI. Those aged 60-69 years experienced a DTI approximately 5 days (SE: 1.5) longer than those diagnosed at age 50 and younger (**Table 2**). Individuals diagnosed with rectal cancer also experienced a DTI of almost 15 days (SE: 1.4) longer than those with proximal colon cancer. Regional cancer stage at diagnosis was associated with a shorter DTI than localized cancer stage (-4 days, SE: 1.3). Participants who were diagnosed at 50-59, 69-69 years, and 70+ years were, respectively, 1.43 (95% confidence interval (CI): 1.03, 1.99); 1.61 (1.17, 2.23), and 1.67 (1.10, 2.51) times as likely to have a DTI >30 days than those diagnosed at age <50 years. Participants diagnosed with rectal cancer were 3.7 times (2.71-4.98) as likely as those diagnosed with proximal colon cancer to have a DTI >30 days. Those with regional cancer stage were 0.63 (0.48, 0.82) times as likely as those with localized cancer

stage to have a DTI >30 days. No statistically significant associations were observed between DTI and sex, race and ethnicity, education, or income.

DTI was not associated with survival for either CRC-specific or all-cause mortality. When stratified by cancer site, cancer stage (**Supplemental Table 1**), education, and income (**Supplemental Table 2**), results were similar. Similar findings were observed when using a DTI threshold of >45 days and >60 days (**Supplemental Table 3**).

DISCUSSION

Our study found that older age at diagnosis, cancer site, and earlier cancer stage were associated with longer DTI. Older age may equate to being more medically frail, which may prolong time to treatment. Rectal cancer may be associated with a longer DTI due to the complexity of the multimodality approach to treatment that is often required; initiating therapy can be more logistically complicated, requiring more diagnostic tests, such magnetic resonance imaging (MRI) of the pelvis and/or flexible sigmoidoscopy, as well as coordination of care. Similarly, regional stage cancer may require more urgent treatment.

Although our sample size was limited across racial and ethnic minority subgroups, we observed no statistically significant associations of race and ethnicity with DTI. In contrast, one prior US study found that racial and ethnic minority subgroups were statistically significantly more likely to have prolonged DTI than non-Hispanic White patients.[5] These differences were most pronounced in lower SES strata; Hispanic patients with low SES had 78% higher odds (95% CI: 1.69-1.88) of prolonged DTI (categorized as greater than 1 month) than non-Hispanic White patients with low SES.[5] However, this relationship is also found among those with higher SES: Hispanic patients with high SES had 26% higher odds (95% CI: 1.17-1.36) for prolonged DTI

than non-Hispanic White patients with high SES.[5] Similar patterns were found for Asian and Pacific Islanders and American Indian and Alaska Native populations in that study.[5] A study in Canada also found that sex and CRC site were associated with a longer time from presentation of symptoms to diagnosis.[17] Additionally, Zarcos-Petrinaci et al. found that predictors of DTI are rectal cancer diagnosis, low level of education, small tumor size, former-smoker status, asymptomatic at diagnosis, and following a cancer screening in Spain.[18] Another US study found that delay of over 30 days was associated with non-hospital work-up.[16] Compared to our results, we only found that rectal cancer diagnosis was associated with delayed treatment. This result is replicated in other studies that found that rectal cancer patients have a longer DTI.[19] Thus, our results could indicate differential treatment plans that may or may not extend DTI. Colon cancer tends to have the following treatments: surgery, chemotherapy, radiation therapy, targeted therapy, and immunotherapy.[20] Colon cancers stages I-III tend to be treated with surgery, with stage III may be followed by chemotherapy.[20] Rectal cancer tends to have the following treatments: surgery, radiation therapy, chemotherapy, chemoradiation therapy, active surveillance, targeted therapy, and immunotherapy.[21] Rectal cancer stage I tends to treated with just surgery, with stages II and III involves chemoradiation or chemotherapy followed by surgery, which may be followed up with more chemotherapy.[21]

Our study found no association between DTI and mortality. A systematic review found mixed results. Among 26 studies, 20 found no association, 4 found that delay was associated with a better prognosis, and 2 with a poorer prognosis.[22] A follow-up meta-analysis on this systematic review found that, overall, delay in colorectal cancer treatment was not associated with survival.[23] However, when separating colon and rectal cancer, later stage at diagnosis was associated with a longer delay.[23] Another updated systematic review reported inconsistency in the literature, but noted that more studies found that shorter time to diagnosis was associated with more favorable outcomes.[4] The mixed results in these studies may be a result of specific

limitations, including analyzing colon and rectal cancers together and small sample sizes. Pruitt et al. found that when stratified by cancer site, colon cancer patients with the shortest delays had higher odds of all-cause mortality.[14] However, all other associations were not significant.[14] Another study found that DTI greater than 31 days was associated with increased risk of death (HR: 1.51, 95% CI: 1.43-1.59) compared to DTI less than 30 days.[15] Studies have also shown that when stratified by cancer stage, there is an association between 5-year mortality among stage III colon cancer (38.9% for 61-120 days vs. 47.8% for 181-365 days delay).[24] This relationship has more recently been studied among early-onset CRC patients (younger than 50 years); there were no associations between time to treatment and survival.[25] Finally, one study reported a U-shaped association between diagnostic intervals and mortality: patients with the shortest diagnostic interval and those with the longest diagnostic interval had higher mortality than the rest of the patients.[26]

The strengths of the current study include the large, well-characterized study population and the ability to access CSS, National Death Index data, and medical record abstraction. However, there are some limitations. Calculation of DTI relied on CSS data sometimes with incomplete information on diagnosis date, reducing the size of the study population. In addition, due to the racial and ethnic make-up of our study, we were unable to stratify by race and ethnicity to assess the effects of DTI and mortality. Our study may have benefited from considering other factors that may affect DTI, such as distance to healthcare facilities and healthcare utilization. We also lacked some information regarding first treatment plan and presentation to oncology clinic. Although our models have accounted for numerous potential confounders, residual confounding may still be present.

In conclusion, our study showed that there was a longer DTI among specific subgroups of CRC patients, but that there was no association between DTI and worse outcomes. The relationship

between DTI and mortality should be explored further among various racial and ethnic groups. Furthermore, with the changing CRC trends in incidence and mortality of early-onset CRC, assessing DTI among this younger age group may be beneficial in addressing potential disparities, particularly considering race and ethnicity and SES, as lack of poor access to healthcare may lead to excessive delay in treatment among some subgroups of early-onset patients. Future studies could also include more information regarding treatment data and plans, as well as factors that may affect delays in treatment, such as healthcare access and utilization. Studies should also include other outcomes, such as increased anxiety due to an extended DTI.

REFERENCES

1. Siegel RL, Wagle NS, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2023. *CA: a cancer journal for clinicians*. May-Jun 2023;73(3):233-254. doi:10.3322/caac.21772

2. Melkonian SC, Jim MA, Haverkamp D, et al. Disparities in Cancer Incidence and Trends among American Indians and Alaska Natives in the United States, 2010-2015. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. Oct 2019;28(10):1604-1611. doi:10.1158/1055-9965.Epi-19-0288

3. Doubeni CA, Laiyemo AO, Major JM, et al. Socioeconomic status and the risk of colorectal cancer: an analysis of more than a half million adults in the National Institutes of Health-AARP Diet and Health Study. *Cancer*. Jul 15 2012;118(14):3636-44. doi:10.1002/cncr.26677

4. Neal RD, Tharmanathan P, France B, et al. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. *British journal of cancer*. Mar 31 2015;112 Suppl 1(Suppl 1):S92-107. doi:10.1038/bjc.2015.48

5. Bui A, Yang L, Myint A, May FP. Race, Ethnicity, and Socioeconomic Status Are Associated With Prolonged Time to Treatment After a Diagnosis of Colorectal Cancer: A Large Population-Based Study. *Gastroenterology*. Oct 12 2020;doi:10.1053/j.gastro.2020.10.010

6. Park HS, Lloyd S, Decker RH, Wilson LD, Yu JB. Overview of the Surveillance, Epidemiology, and End Results database: evolution, data variables, and quality assurance. *Current problems in cancer*. Jul-Aug 2012;36(4):183-90. doi:10.1016/j.currproblcancer.2012.03.007

7. Enewold L, Parsons H, Zhao L, et al. Updated Overview of the SEER-Medicare Data: Enhanced Content and Applications. *JNCI Monographs*. 2020;2020(55):3-13. doi:10.1093/jncimonographs/lgz029

8. Newcomb PA, Baron J, Cotterchio M, et al. Colon Cancer Family Registry: an international resource for studies of the genetic epidemiology of colon cancer. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. Nov 2007;16(11):2331-43. doi:10.1158/1055-9965.Epi-07-0648

9. Newcomb PA, Ton M, Malen RC, et al. Cannabis use is associated with patient and clinical factors in a population-based sample of colorectal cancer survivors. *Cancer causes & control : CCC*. Jul 14 2021;doi:10.1007/s10552-021-01468-4

10. Molenaar CJL, Winter DC, Slooter GD. Contradictory guidelines for colorectal cancer treatment intervals. *The Lancet Oncology*. 2021;22(2):167-168. doi:10.1016/S1470-2045(20)30738-5

11. Molenaar CJL, Janssen L, van der Peet DL, Winter DC, Roumen RMH, Slooter GD. Conflicting Guidelines: A Systematic Review on the Proper Interval for Colorectal Cancer Treatment. *World J Surg*. Jul 2021;45(7):2235-2250. doi:10.1007/s00268-021-06075-7

12. Cancer waiting times. Cancer Research UK. 2024. https://www.cancerresearchuk.org/about-cancer/worried-about-cancer/cancer-waiting-times

13. Hanna TP, King WD, Thibodeau S, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. *BMJ (Clinical research ed)*. 2020;371:m4087. doi:10.1136/bmj.m4087

14. Pruitt SL, Harzke AJ, Davidson NO, Schootman M. Do diagnostic and treatment delays for colorectal cancer increase risk of death? *Cancer Causes & Control*. 2013/05/01 2013;24(5):961-977. doi:10.1007/s10552-013-0172-6

15. Lee Y-H, Kung P-T, Wang Y-H, Kuo W-Y, Kao S-L, Tsai W-C. Effect of length of time from diagnosis to treatment on colorectal cancer survival: A population-based study. *PloS one*. 2019;14(1):e0210465-e0210465. doi:10.1371/journal.pone.0210465

16. Kalam A, Arientyl V, Schriner JB, et al. Examining patterns of and reasons for delays to treatment in colon cancer. *Journal of Clinical Oncology*. 2021/01/20 2021;39(3_suppl):52-52. doi:10.1200/JCO.2021.39.3_suppl.52

17. Castelo M, Paszat L, Hansen BE, et al. Comparing Time to Diagnosis and Treatment Between Younger and Older Adults With Colorectal Cancer: A Population-Based Study. *Gastroenterology*. Jun 2023;164(7):1152-1164. doi:10.1053/j.gastro.2023.02.024

18. Zarcos-Pedrinaci I, Fernández-López A, Téllez T, et al. Factors that influence treatment delay in patients with colorectal cancer. *Oncotarget*. May 30 2017;8(22):36728-36742. doi:10.18632/oncotarget.13574

19. Langenbach MR, Schmidt J, Neumann J, Zirngibl H. Delay in Treatment of Colorectal Cancer: Multifactorial Problem. *World Journal of Surgery*. 2003/03/01 2003;27(3):304-308. doi:10.1007/s00268-002-6678-9

20. Board PDQATE. Colon Cancer Treatment (PDQ®): Patient Version. *PDQ Cancer Information Summaries*. National Cancer Institute (US); 2002.

21. Board PDQATE. Rectal Cancer Treatment (PDQ®): Patient Version. *PDQ Cancer Information Summaries*. National Cancer Institute (US); 2002.

22. Ramos M, Esteva M, Cabeza E, Campillo C, Llobera J, Aguiló A. Relationship of diagnostic and therapeutic delay with survival in colorectal cancer: a review. *European journal of cancer (Oxford, England : 1990)*. Nov 2007;43(17):2467-78. doi:10.1016/j.ejca.2007.08.023

23. Ramos M, Esteva M, Cabeza E, Llobera J, Ruiz A. Lack of association between diagnostic and therapeutic delay and stage of colorectal cancer. *European journal of cancer (Oxford, England : 1990)*. Mar 2008;44(4):510-21. doi:10.1016/j.ejca.2008.01.011

24. Cone EB, Marchese M, Paciotti M, et al. Assessment of Time-to-Treatment Initiation and Survival in a Cohort of Patients With Common Cancers. *JAMA Network Open*. 2020;3(12):e2030072-e2030072. doi:10.1001/jamanetworkopen.2020.30072

25. Castelo M, Paszat L, Hansen BE, et al. Analysis of Time to Treatment and Survival Among Adults Younger Than 50 Years of Age With Colorectal Cancer in Canada. *JAMA Network Open*. 2023;6(8):e2327109-e2327109. doi:10.1001/jamanetworkopen.2023.27109

26. Tørring ML, Frydenberg M, Hamilton W, Hansen RP, Lautrup MD, Vedsted P. Diagnostic interval and mortality in colorectal cancer: U-shaped association demonstrated for three different datasets. *Journal of clinical epidemiology*. Jun 2012;65(6):669-78. doi:10.1016/j.jclinepi.2011.12.006

Table 1. Population characteristics (N=1,652)

Characteristic	**Overall N=1,652**	**DTI > 30 days n=444**	**DTI ≤ 30 days n=1,208**
DTI (days)	23.1 ± 25.2	54.7 ± 27.5	11.5 ± 9.5
Age at Diagnosis (years)	55.5 ± 11.7	56.9 ± 10.7	55.0 ± 12.1
Age at Diagnosis			
<50 years	571 (34.6)	117 (26.4)	454 (37.6)
50-59 years	386 (23.4)	121 (27.3)	265 (21.9)
60-69 years	475 (28.8)	146 (32.9)	329 (27.2)
70+ years	220 (13.3)	60 (13.5)	160 (13.3)
Sex			
Male	832 (50.4)	242 (54.5)	590 (48.8)
Female	820 (49.6)	202 (45.5)	618 (51.2)
Race and ethnicity			
Non-Hispanic White	1,496 (90.6)	392 (88.3)	1,104 (91.4)
Black	41 (2.5)	10 (2.3)	31 (2.6)
Hispanic	20 (1.2)	7 (1.6)	13 (1.1)
Asian and Native Hawaiian or Pacific Islander	40 (2.4)	18 (4.1)	22 (1.8)
Other	39 (2.4)	15 (3.4)	24 (2.0)
Missing	16 (1.0)	2 (0.5)	14 (1.2)
Cancer Site			
Proximal	587 (35.5)	108 (24.3)	479 (39.7)
Distal	498 (30.2)	111 (25.0)	387 (32.0)
Rectal	567 (34.3)	225 (50.7)	342 (28.3)
Cancer Stage			
Localized	671 (40.6)	207 (46.6)	464 (38.4)
Regional	769 (46.6)	177 (39.9)	592 (49.0)
Distant	204 (12.4)	56 (12.6)	148 (12.3)
Missing	8 (0.5)	4 (0.9)	4 (0.3)
Education			
Less than HS or HS graduate	379 (22.9)	96 (21.4)	283 (23.4)
Some college	528 (32.0)	136 (30.6)	392 (32.5)
College graduate or higher	742 (44.9)	212 (47.8)	530 (43.9)
Income			
Less than $30,000	469 (28.4)	113 (25.5)	356 (29.5)
$30,000-$69,000	409 (24.8)	106 (23.9)	303 (25.1)
$70,000+	683 (41.3)	204 (46.0)	479 (39.7)
Diagnosis Year			
1998-2004	814 (49.3)	109 (24.6)	705 (58.4)
2005-2011	139 (8.4)	26 (5.9)	113 (9.4)
2012-2018	699 (42.3)	309 (69.6)	390 (32.3)

Percentages may not add up to 100 due to rounding and missing values.

Table 2. Associations between DTI and patient characteristics

	DTI (days)				DTI (>30 days)	
	Unadjusted		Adjusted*		Unadjusted	Adjusted*
	β (SE)	p-value	β (SE)	p-value	OR (95% CI)	OR (95% CI)
Age at Diagnosis						
<50 years	ref		ref		ref	ref
50-59 years	3.32 (1.66)	0.045	1.34 (1.56)	0.390	1.77 (1.32, 2.38)	1.43 (1.03, 1.99)
60-69 years	5.31 (1.56)	0.001	4.82 (1.50)	0.001	1.72 (1.30, 2.28)	1.61 (1.17, 2.23)
70+ years	1.48 (2.00)	0.458	3.43 (1.93)	0.075	1.46 (1.02, 2.08)	1.67 (1.10, 2.51)
Sex						
Male	ref		ref		ref	ref
Female	-3.72 (1.24)	0.003	-2.69 (1.16)	0.020	0.80 (0.64, 0.99)	0.85 (0.67, 1.08)
Race and ethnicity						
Non-Hispanic White	ref		ref		ref	ref
Black	-0.11 (3.99)	0.978	0.70 (3.70)	0.850	0.91 (0.44, 1.87)	1.01 (0.45, 2.27)
Hispanic	-0.06 (5.68)	0.991	-3.76 (5.27)	0.475	1.52 (0.60, 3.83)	1.06 (0.38, 2.97)
Asian and Native Hawaiian or Pacific Islander	9.84 (4.04)	0.015	3.03 (3.76)	0.421	2.30 (1.22, 4.34)	1.28 (0.64, 2.55)
Other	0.93 (4.09)	0.820	2.36 (3.79)	0.534	1.76 (0.91, 3.39)	2.51 (1.21, 5.21)
Cancer Site						
Proximal	ref		ref		ref	ref
Distal	3.49 (1.49)	0.019	3.55 (1.43)	0.013	1.27 (0.95, 1.71)	1.37 (0.99, 1.89)
Rectal	14.39 (1.44)	<0.001	14.77 (1.41)	<0.001	2.92 (2.23, 3.82)	3.68 (2.71, 4.98)
Cancer Stage						
Localized	ref		ref		ref	Ref
Regional	-5.27 (1.33)	<0.001	-4.85 (1.25)	<0.001	0.67 (0.53, 0.85)	0.63 (0.48, 0.82)
Distant	-1.16 (2.01)	0.563	-2.31 (1.91)	0.228	0.85 (0.60, 1.20)	0.70 (0.47, 1.03)
Education						
Less than HS or HS Graduate	-1.30 (1.59)	0.414	1.96 (1.50)	0.191	0.85 (0.64, 1.12)	1.17 (0.85, 1.61)
Some college	0.39 (1.44)	0.788	1.00 (1.34)	0.455	0.87 (0.67, 1.12)	0.89 (0.67, 1.18)
College graduate or higher	ref		ref		ref	ref
Income						
Less than $30,000	-1.59 (1.51)	0.294	3.19 (1.56)	0.041	0.75 (0.57, 0.97)	1.22 (0.88, 1.71)
$30,000-$69,000	-1.09 (1.58)	0.490	1.71 (1.52)	0.259	0.82 (0.62, 1.08)	1.10 (0.80, 1.51)
$70,000+	ref		ref		ref	ref

*Adjusted for sex (male, female), age (<50 years, 50-59 years, 60-69 years, 70+ years), race and ethnicity (Non-Hispanic White, Black, Hispanic, Asian and Native Hawaiian or Pacific Islander, Other), education (less than high school or high school graduate,

some college, college graduate or higher), cancer site (proximal, distal, rectal), cancer stage (localized, regional, distant), diagnosis year

Table 3. Association between DTI and CRC-specific and all-cause mortality

	CRC-Specific		All-Cause Mortality	
	Unadjusted	**Adjusted***	**Unadjusted**	**Adjusted***
DTI >30 days	0.96 (0.66, 1.38)	1.01 (0.69, 1.50)	1.10 (0.85, 1.42)	1.05 (0.80, 1.37)

*Adjusted for sex (male, female), age (years), race and ethnicity (Non-Hispanic White, Black, Hispanic, Asian and Native Hawaiian or Pacific Islander, Other), education (less than high school or high school graduate, some college, college graduate or higher), cancer site (proximal, distal, rectal), cancer stage (localized, regional, distant), diagnosis year

Supplemental Table 1. Association between DTI (>30 days) and CRC-specific and all-cause mortality stratified by cancer site and stage

	CRC-Specific		All-Cause Mortality	
	Unadjusted	**Adjusted***	**Unadjusted**	**Adjusted***
Site				
Proximal	1.34 (0.70, 2.57)	1.68 (0.84, 3.37)	1.50 (0.96, 2.35)	1.52 (0.95, 2.43)
Distal	0.37 (0.13, 1.03)	0.50 (0.17, 1.44)	0.67 (0.38, 1.16)	0.64 (0.36, 1.15)
Rectal	1.02 (0.61, 1.72)	0.90 (0.52, 1.56)	1.22 (0.82, 1.81)	1.05 (0.70, 1.57)
Stage				
Localized	2.03 (0.88, 4.69)	1.92 (0.80, 4.61)	1.10 (0.72, 1.68)	0.97 (0.62, 1.50)
Regional	1.20 (0.71, 2.02)	0.91 (0.52, 1.60)	1.51 (1.04, 2.19)	1.13 (0.77, 1.68)
Distant	0.71 (0.35, 1.43)	0.89 (0.42, 1.88)	0.73 (0.37, 1.42)	0.90 (0.44, 1.84)

*Adjusted for sex (male, female), age (years), race and ethnicity (Non-Hispanic White, Black, Hispanic, Asian and Native Hawaiian or Pacific Islander, Other), education (less than high school or high school graduate, some college, college graduate or higher), cancer site (proximal, distal, rectal), cancer stage (localized, regional, distant), diagnosis year

Supplemental Table 2. Association between DTI (>30 days) and CRC-specific and all-cause mortality stratified by race and ethnicity and socioeconomic status

	CRC-Specific		All-Cause Mortality	
	Unadjusted	**Adjusted***	**Unadjusted**	**Adjusted***
Education				
Less than HS or HS graduate	0.88 (0.45, 1.74)	0.93 (0.46, 1.91)	1.03 (0.67, 1.59)	0.99 (0.63, 1.56)
Some college	1.16 (0.64, 2.13)	1.43 (0.75, 2.71)	1.25 (0.80, 1.94)	1.16 (0.73, 1.83)
College graduate or higher	0.83 (0.43, 1.59)	0.74 (0.36, 1.49)	0.99 (0.62, 1.56)	0.99 (0.60, 1.65)
Income				
Less than $30,000	1.17 (0.67, 2.05)	1.26 (0.68, 2.32)	1.20 (0.84, 1.71)	1.36 (0.93, 1.98)
$30,000-$69,000	0.80 (0.39, 1.62)	0.71 (0.33, 1.54)	0.97 (0.59, 1.61)	0.87 (0.51, 1.50)
$70,000+	0.65 (0.29, 1.43)	0.80 (0.34, 1.92)	0.72 (0.38, 1.35)	0.80 (0.41, 1.58)

*Adjusted for sex (male, female), age (years), race and ethnicity (Non-Hispanic White, Black, Hispanic, Asian and Native Hawaiian or Pacific Islander, Other), education (less than high school or high school graduate, some college, college graduate or higher), cancer site (proximal, distal, rectal), cancer stage (localized, regional, distant), diagnosis year

Supplemental Table 3. Association between DTI and CRC-specific and all-cause mortality

	CRC-Specific		All-Cause Mortality	
	Unadjusted	**Adjusted***	**Unadjusted**	**Adjusted***
DTI >45 days	1.14 (0.69, 1.87)	1.06 (0.63, 1.76)	1.12 (0.76, 1.63)	1.04 (0.71, 1.54)
DTI >60 days	1.69 (0.96, 2.97)	1.39 (0.78, 2.48)	1.42 (0.90, 2.25)	1.33 (0.83, 2.14)

*Adjusted for sex (male, female), age (years), race and ethnicity (Non-Hispanic White, Black, Hispanic, Asian and Native Hawaiian or Pacific Islander, Other), education (less than high school or high school graduate, some college, college graduate or higher), cancer site (proximal, distal, rectal), cancer stage (localized, regional, distant), diagnosis year