2021 CALIFORNIA

The Continuing Impact of COVID-19 on Cancer Incidence, Early Detection, and Survival in California

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Acknowledgements and Disclaimer

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Executive Summary

- Due to highly contagious new variants and ongoing waves of infections, the COVID-19 pandemic continued to significantly disrupt cancer screening, access to in-person health care and cancer care in 2021.
- Using California Cancer Registry data and estimated cancer counts from the American Cancer Society, observed-to-expected incidence ratios were calculated for 21 common cancers.
 - Incidence was lower than expected for 15 cancers in 2021, suggesting missed early detection.
 - Lower than expected incidence was observed for four out of five screening-detectable cancers, including breast (97.9 percent), cervical (83.6 percent), lung (88.5 percent), and melanoma (94.8 percent).
- Changes in the age-adjusted incidence rate of screening-detectable cancers highlighted disparities by age, race/ethnicity, sex, and stage at diagnosis.
 - The incidence of cervical, colorectal, and lung cancer among those older than the recommended screening ages was higher in 2021 than 2020, but lower than 2019.
 - The incidence of breast, cervical, colorectal, and lung cancer among Black/African Americans and Hispanic/Latinos was higher in 2021 than 2020, but lower than 2019.
 - Similarly, the incidence of colorectal, lung, and melanoma cancer among Asian/Pacific Islanders was higher in 2021 than 2020, but lower than 2019.
 - The incidence of colorectal and lung cancers diagnosed at in situ/localized stage was higher in 2021 than 2020, but lower than 2019.
 - The incidence rate of breast cancer diagnosed regional/remote stage in 2021 was higher than the previous two years.

- The risk of death within one year of diagnosis was 13 to 40 percent higher for patients diagnosed during 2020 than 2018 for four out of five screening-detectable cancers, suggesting that patients diagnosed during the pandemic had worse survival outcomes.
- Findings from this report highlight the continued impact of the pandemic on cancer incidence, early detection, and survival in California in 2021. Potential strategies to mitigate the lasting impact of the COVID-19 pandemic on early cancer detection include public health campaigns to increase public awareness and access to screening, educating primary care providers on disparities in early cancer-detection and evidence-based interventions, and offering catchup screenings for those who aged out of cancer screening recommendations during the pandemic. Further research is needed to evaluate the long-term effects of the COVID-19 pandemic on cancer outcomes.

Introduction

Ongoing disruption in healthcare delivery continued to negatively impact the receipt of timely cancer care and outcomes in 2021[1-5]. The emergence of highly transmissible COVID-19 variants posed significant challenges to strained healthcare delivery systems and cancer screening uptake failed to return to pre-pandemic levels[6-8]. Cancer screening saves lives through early detection and treatment of cervical, colorectal, breast, lung, and melanoma cancers[9-13].

During the COVID-19 pandemic, many Americans lost employment, and therefore private health insurance[14]. However, as a result of California's State of Emergency which remained in effect throughout 2021, Medi-Cal, California's Medicaid program, implemented a "continuous coverage" policy. This allowed individuals to stay enrolled in Medi-Cal throughout the duration of the emergency, offering a safety net for those affected by the economic fallout of the pandemic. Therefore, Medi-Cal enrollment increased amid the COVID-19 pandemic, specifically among adults[2, 15]. Health insurance type can differentially impact access to regular health care, including earlier use of preventive care, earlier cancer diagnosis, and better access to cancer treatment and survivorship care. Studies have shown disparities in stage at cancer diagnosis and survival by health insurance type, with uninsured and Medicaid-insured patients diagnosed at later stages and experiencing shorter survival compared to privately insured patients[16].

The differential risk of death for cancer patients due to the COVID-19 pandemic is unclear. Prior studies have shown increased mortality among cancer patients infected by COVID-19 compared to the general population, as they are immunocompromised[17-19]. Additionally, limited access to inperson healthcare and cancer screening during the pandemic led to a widespread delay in cancer detection[20-23]. Those who are diagnosed with cancer after it metastasizes have fewer treatment options and poorer survival[24, 25]. We leveraged the population-based California Cancer Registry to quantify the overall one-year hazard of death of patients diagnosed during the COVID-19 pandemic in 2020 compared to those diagnosed pre-pandemic in 2018.

An initial assessment of the impact of COVID-19 on cancer incidence, early detection of screening-detectable cancers (female breast, cervical,

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colorectal, lung, and melanoma), and mortality among Californians was summarized in a previous report[20]. Key findings from the initial report showed lower than expected incidence in 17 of the 21 most common cancers and highlighted disparities in early detection and stage at diagnosis among vulnerable populations, such as those residing in the lowest socioeconomic status (SES) neighborhoods, historically marginalized races/ethnicities, and individuals older than the recommended screening age for all screeningdetectable cancers. The purpose of this report is to evaluate the continuing impact of the COVID-19 pandemic on cancer incidence and survival, as well as to examine disparities in the early detection of screening-detectable cancers among Californians in 2021.

This report is based on data obtained by the California Cancer Registry (CCR), the state mandated population-based cancer surveillance system in California. CCR has collected information on all reportable cancers diagnosed among California residents since 1988. The California Department of Public Health (CDPH) partners with the California Cancer Reporting and Epidemiologic Surveillance (CalCARES) Program, within the University of California Davis Comprehensive Cancer Center, to manage day-to-day operations of the CCR. Data on cancer incidence, diagnosis, treatment, and follow-up are gathered through a system of regional registries and provides the foundation for a wide array of research and cancer control initiatives throughout the state.

Methods

Population

Incidence

Incident cases of cancer diagnosed among California residents from 2006 to 2021 were included in this report. Tumors were classified based on primary site and histology according to the International Classification of Diseases for Oncology, third edition[26]. The analyses for screening-detectable cancers, include both *in situ* and invasive tumors. Screening-detectable cancers include female breast, cervical, colorectal, lung, and melanoma cancers. Lung cancer includes lung and bronchus, liver cancer includes liver and intrahepatic bile duct, and kidney cancer includes kidney and renal pelvis.

Mortality_

Cancer death data were obtained from CDPH, Center for Health Statistics and Informatics (CHSI). Cause of death was coded according to the International Classification of Diseases, Tenth Edition (ICD-10)[27]. All mortality analyses presented in this report are the responsibility of the authors and were not reviewed or endorsed by CHSI prior to publication.

Cohort Characteristics

Age at Diagnosis

Incidence trends were assessed by age at diagnosis among screeningdetectable cancers. Trends for ages inside the recommended screening criteria for colorectal (45-74 years), lung (50-79 years), breast (40-74 years), cervical cancer (20-64 years), and melanoma (at least 20 years) were assessed, as well as for the age ranges younger and older. No recommended screening criteria exists for melanoma by age. Therefore, trends were assessed separately for individuals 0-14 years, 15-39 years, 40-64 years, and 65 years and older.

Health Insurance Type

Health insurance was grouped into six categories: private, Medicaid, Medicare, other public, uninsured, and unknown. Private insurance included private insurance managed care and fee-for-service, health maintenance organization (HMO), preferred provider organization (PPO), Medicare with supplement, and TRICARE. The Medicaid category included Medicaid, Medicaid administered through a managed care plan, and Medicare with Medicaid eligibility. The Medicare classification included health insurance coverage of patients 65 years or older who were insured by Medicare without supplement or Medicare administered through a managed care plan. Insurance through the military, Veterans Affairs, Indian/public health service, county funded, or by Medicare for those under 65 years of age was categorized as other public insurance.

Marital Status

Marital status was defined as married, not married, or unknown. The unmarried category included individuals who were single, separated, divorced, widowed, unmarried, or in a domestic partnership.

Race/Ethnicity

Race/ethnicity was grouped into the following mutually exclusive categories: American Indian, Asian/Pacific Islander, Hispanic/Latino, non-Hispanic/Latino Black/African American (Black/African American), and non-Hispanic/Latino White. Race and ethnicity were reported as separate data items during data collection for both cases and deaths. American Indian race was assigned if there was any indication the patient identifies as American Indian regardless of Hispanic/Latino ethnicity. Hispanic/Latino ethnicity and Asian/Pacific Islander race were assigned using the North American Association of Central Cancer Registries' Hispanic and Asian/Pacific Islander Identification Algorithm (NHAPIIA). NHAPIIA uses information on a person's race, birthplace, last name, and maiden name to determine Hispanic/Latino ethnicity or Asian/Pacific Islander race. Hispanic/Latino ethnicity may be assigned to individuals of any race. Persons reported as White or Black race and non-Hispanic/Latino ethnicity were classified as non-Hispanic/Latino White and Black/African American, respectively.

Stage at Diagnosis

The determination of stage at diagnosis relied on the Summary Stage schema provided by The Surveillance, Epidemiology, and End Results (SEER) Program. Reassignment of cancers initially diagnosed with an unknown stage to in situ/localized or regional/remote stage was based on the five-year relative survival of each cancer type and stage. For breast cancer and

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melanoma, the five-year relative survival rate of patients with unknown stage at diagnosis closely resembled those of individuals diagnosed with in situ or localized stages, resulting in their reclassification as in situ/localized stage cancers. For cervical, colorectal, and lung cancer, the five-year relative survival rates of patients initially diagnosed at an unknown stage fell between those of patients diagnosed at regional and remote stages, leading to their reclassification as regional/remote stage cancers.

Neighborhood Socioeconomic Status

A neighborhood-level socioeconomic status (SES) measure was utilized in this report. This SES measure is a composite score created using principal component analysis and incorporates census tract-level measures of employment, income, housing characteristics, and education. An SES score was calculated for each census tract in California. A patient's SES is based on the census tract in which they resided at the time of their cancer diagnosis[28]. The SES score for all cancer patients was divided into tertiles representing low-, middle-, and high-SES.

Comorbidities_

Because comorbid conditions can affect a cancer patient's treatment and length of survival following a cancer diagnosis, the survival analysis was adjusted for the number of comorbid conditions that a patient had. Charlson Comorbidity Index categories of 0, 1, and more than 1 were used to describe patient comorbidities. The score was based on sixteen medical conditions, excluding cancer diagnoses, reported in hospital discharge data linked to CCR data[29].

Statistical Analyses

Age-Adjusted Rates

Incidence rates were calculated as the number of new cases in specific age groups per 100,000 persons each year and were age-adjusted to the 2000 United States standard population. Age-adjusted rates are weighted averages of age-specific rates, where the weights represent the age distribution of a standard population. Such adjustment eliminates differences in rates due to changes in the age of a population over time or due to differences in the age distribution between population groups. Rates in this report were calculated using the National Cancer Institute's Surveillance Research Program, SEER*Stat software version 8.4.3[30]. Minor changes in

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the number of cases or deaths within small populations can yield high variation in age-adjusted rates.

Observed-to-Expected Ratios

Given that cancer incidence data collected by population-based registries lags two years behind the current year, the American Cancer Society (ACS) annually estimates the number of expected new invasive cancers and deaths by state for 21 common cancers, including colorectal, urinary bladder, oropharyngeal, thyroid, liver, leukemia, melanoma, lung, cervical, stomach, breast, ovarian, pancreatic, corpus uteri, kidney, myeloma, laryngeal, non-Hodgkin lymphoma, brain and other nervous system (ONS), esophageal, and prostate[31-33]. These estimates were used as expected values to calculate observed-to-expected (O/E) ratios for cancer incidence in 2021. Invasive tumors diagnosed among California residents in 2021 were used as observed values. The O/E ratio was calculated by dividing the observed value by the expected value, then multiplying the quotient by 100 to create a percent. Ninety-five percent confidence intervals for O/E ratios were calculated by applying the Wilson and Hilferty approximation for chi-square percentiles[31, 34].

<u>Survival</u>

The CCR was used to identify 87,410 patients diagnosed with female breast, cervical, colorectal, lung, and melanoma cancers during the pre-pandemic era from January 1, 2018 to December 31, 2018 and 78,791 during the pandemic era from January 1, 2020 to December 31, 2020. Patients diagnosed in 2019 were not included in the pre-pandemic era, because the first year following their diagnosis overlapped with the first year of the COVID-19 pandemic in many cases. Flexible parametric models estimated the one-year relative hazard of death for patients diagnosed with screening-detectable cancers during the pandemic in 2020 versus pre-pandemic in 2018[35]. Hazard ratios and associated 95 percent confidence intervals are presented. Models were adjusted for age at diagnosis, race/ethnicity, marital status, stage at diagnosis, number of comorbidities, socioeconomic status, and health insurance type. A hazard ratio of 1.0 indicates that patients diagnosed in 2020 had the same estimated hazard of death within one year as patients diagnosed in 2018.

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Trends in Cancer Incidence

Joinpoint linear regression was used to calculate trends in age-adjusted incidence rates (AAIR) for screening-detectable cancers by age, race/ethnicity, stage at diagnosis, and sex. In this analysis, a statistical algorithm detects joinpoints, or points in time where the slope of the regression line significantly changes. Thus, the model describes trends during different time segments, with the annual percent change (APC) estimated for each segment. The Average Annual Percent Change (AAPC) is a summary measure of a trend over a pre-specified fixed interval. It allows the use of a single number to describe the average increase or decrease in rates over a period of multiple years. The AAPC is a valid measure even if there were changes in trends during the period considered. It is computed as a weighted average of the APCs from the joinpoint model, with the weights equal to the length of each APC interval. The overall, or total percent change in rates during the period was calculated as 100*(1 + AAPC/100)t - 100, where t is the number of years in the period. Joinpoint version 5.1.0 software was used for all trend analyses[36]. If a joinpoint is not detected, the APC equals the AAPC. The calculation of trends in this report excludes the 2020 incidence rate, which was an outlier due to the missed detection of many cancers during the COVID-19 pandemic[20, 37]. However, the 2020 incidence rate is shown in the figures. Only statistically significant increases and decreases in trends are reported. If a trend was not statistically significant, the trend is considered stable.

Limitations_

This report has limitations. Population denominators were not available for exact screening-recommended age ranges for all cancers. Therefore, trends in age were calculated using the closest possible age ranges available in SEER*Stat. For example, the screening-recommended age range for colorectal cancer is 45-75 years[38]. However, the trend analysis used 45-74 years. The cervical cancer recommended screening age is 20-64 years; ages 21-64 years were considered the screening-recommended ages for the trend analysis.

Results

Observed-to-Expected Ratios for Common Cancers in California in 2021

To evaluate the impact of the COVID-19 pandemic on new cancer diagnoses in California in 2021, observed-to-expected (O/E) incidence ratios and associated 95 percent confidence intervals (CI) were calculated for 21 common cancers (Table 1). For 15 cancers, the O/E incidence ratios were significantly less than 100 percent, indicating that fewer than expected cancers of these types were diagnosed in California in 2021. The lowest O/E incidence ratios were among cancers of the cervix, liver, and myeloma, all of which had approximately 15 percent fewer cancers diagnosed than expected. Four out of five screening-detectable cancers had fewer diagnoses than expected in 2021, including breast, cervical, lung, and melanoma. The O/E incidence ratio for stomach cancer was significantly higher than 100 percent, indicating that more cancers were diagnosed than expected in 2021.

Table 1. Observed-to-Expected (O/E) Incidence Ratios for CommonCancers in California, 2021

| | O/E Incidence Ratio |
|-----------------------|-----------------------------------|
| Cancer Site | (95 percent Confidence Intervals) |
| Brain & ONS | 98.1 (94.3, 102.0) |
| Breast | 97.9* (97.9, 99.0) |
| Cervix | 83.6* (79.3, 88.0) |
| Colorectal | 101.3 (99.8, 102.9) |
| Esophagus | 94.2* (89.6, 98.9) |
| Kidney | 92.0* (89.8, 94.2) |
| Larynx | 90.0* (83.6, 96.7) |
| Leukemia | 89.2* (86.8, 91.7) |
| Liver | 84.4* (81.9, 86.9) |
| Lung | 88.5* (87.1, 89.9) |
| Melanoma | 94.8* (93.0, 96.6) |
| Myeloma | 84.3* (81.2, 87.5) |
| Non-Hodgkin Lymphoma | 90.7* (88.7, 92.7) |
| Oral Cavity & Pharynx | 89.3* (86.8, 91.9) |
| Ovary | 97.3 (93.5, 101.1) |
| Pancreas | 94.6 (92.2, 97.1) |
| Prostate | 90.87* (89.7, 92.0) |
| Stomach | 104.5* (101.1, 108.0) |
| Thyroid | 102.3 (99.4, 105.1) |
| Urinary Bladder | 88.9* (86.8, 91.0) |
| Corpus Uterine | 88.2* (86.1, 90.4) |

*The O/E ratio is significantly different from 100 at alpha=0.05.

Female Breast Cancer

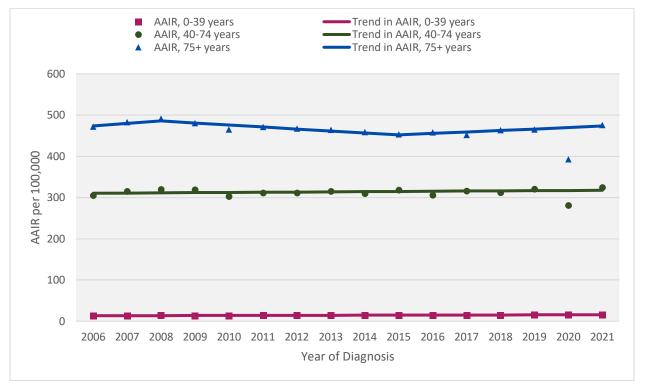
Most breast cancers are diagnosed among women who are 50 years or older. Common risk factors for breast cancer include, getting older, inheriting genetic mutations such as BRCA1 and BRCA2, having dense breasts, family or personal history of breast cancer, prior treatment with radiation therapy, and exposure to the drug diethylstilbestrol (DES)[39]. To reduce the risk of breast cancer, the Centers for Disease Control and Prevention (CDC) recommends exercising regularly, limiting alcohol consumption, and avoiding tobacco and other chemicals that cause cancer. The US Preventative Services Task Force (USPSTF) recommends that women who are 50 to 74 years old and are at average risk for breast cancer get a mammogram every two years. Women between 40 to 49 years old should talk to their health care provider about when to start and how often to get a mammogram[40].

In 2021, 36,411 breast cancers were diagnosed in California. The majority (73.3 percent) were diagnosed in situ/localized stage. The most common age of diagnosis was 40-74 years (77.2 percent), followed by 75 years and older (18.4 percent), and 0-39 years (4.4 percent). Most cases were diagnosed among non-Hispanic/Latina Whites (51.6 percent), followed by Hispanic/Latinas (22.0 percent), Asian/Pacific Islanders (18.2 percent), Black/African Americans (6.0 percent), other/unknown race/ethnicity (1.5 percent), and American Indians (0.7 percent). Most women diagnosed with breast cancer resided in the highest SES neighborhoods (42.3 percent), followed by middle (34.7 percent), and lowest (23.0 percent) SES neighborhoods. There were 2.1 percent fewer invasive breast cancer diagnoses than expected (30,070 versus 30,730) in 2021.

From 2006-2021, women 0-39 years of age had the lowest breast cancer incidence rates compared to women 40-74 years of age and those 75 years of age and older (Figure 1). During the study period, the age-adjusted incidence rate (AAIR) among women 0-39 years increased by 1.0 percent per year while it remained stable among women 40-74 years of age. From 2015-2021, the AAIR among women 75 years and older increased by 0.8 percent per year.

In 2021, the incidence per 100,000 of breast cancer among those 40-74 years of age (324.4) and 75 years and older (475.7) was higher than in 2020 (280.9 and 393.0, respectively) and 2019 (320.9 and 465.1, respectively). In 2021, the AAIR among those 0-39 years of age returned to the same rate as in 2019 (15.5) after a decrease in 2020 (14.9).

Figure 1. Trend in the Age-Adjusted Incidence Rate (AAIR) of Female Breast Cancer by Age Group, California, 2006-2021



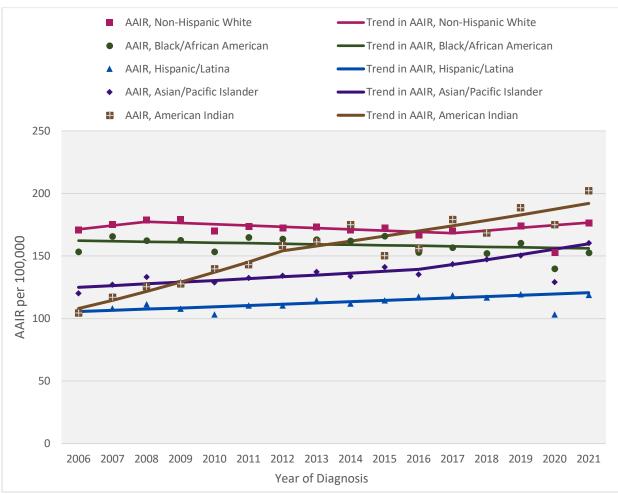
Source of Data: California Cancer Registry, California Department of Public Health.

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In 2021, the incidence of breast cancer was highest among American Indians and lowest among Hispanic/Latinas. The AAIR of breast cancer among non-Hispanic/Latina Whites increased by 1.2 percent per year from 2017-2021 (Figure 2). From 2006-2021, the AAIR of breast cancer among Black/African Americans remained stable while the AAIR among Hispanics/Latinas increased by 0.9 percent per year. The AAIR of breast cancer among Asian/Pacific Islanders increased by 2.8 percent per year from 2016-2021.The AAIR among American Indians remained stable from 2012-2021.

In 2021, the incidence per 100,000 of breast cancer among American Indians (202.2), Asian/Pacific Islanders (160.2) and non-Hispanic/Latina Whites (176.4) was higher than 2020 (175.0 among American Indians, 129.1 among Asian/Pacific Islanders, and 153.0 among non-Hispanic/Latina Whites) and 2019 (188.7, 150.3, 174.2, respectively). In contrast, breast cancer incidence in 2021 among Black/African Americans (152.5), and Hispanic/Latina (118.9) women was higher than 2020 (139.9 among Black/African Americans and 103.3 among Hispanic/Latinas), but lower than 2019 (160.3 among Black/African Americans, and 119.4 among Hispanic/Latinas).

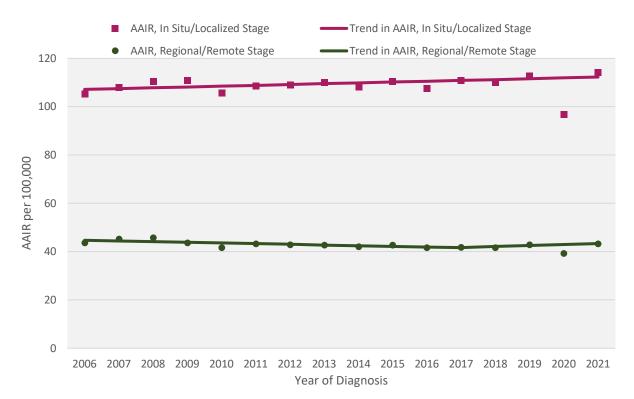




From 2006-2021, more breast cancers were diagnosed in situ/localized versus regional/remote stage (Figure 3). During the same period, the AAIR of breast cancers diagnosed in situ/localized stage increased by 0.3 percent per year. The AAIR of breast cancers diagnosed regional/remote stage remained stable from 2017-2021.

Breast cancer incidence rates increased in 2021 compared to 2020 and 2019 for both in situ/localized (114.2, 96.8, and 112.8 per 100,000, respectively) and regional/remote stages (43.3, 39.3, and 42.9 per 100,000, respectively).

Figure 3. Trend in the Age-Adjusted Incidence Rate (AAIR) of Female Breast Cancer by Stage at Diagnosis, California, 2006-2021



Cervical Cancer

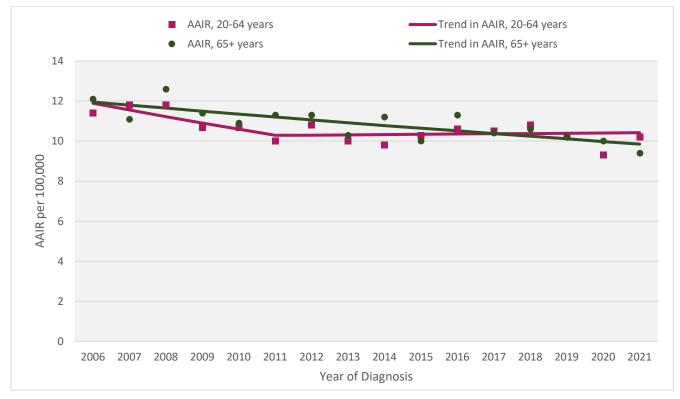
Although screening methods exist for cervical cancer, over half of cervical cancer diagnoses (13,253, 56.3 percent) from 2006-2021 in California were diagnosed at regional/remote stage. Nearly all cervical cancers are caused by persistent infection with high-risk strains of human papillomavirus (hrHPV). Other risk factors include tobacco use, human immunodeficiency virus (HIV) infection, obesity, and exposure to an anti-miscarriage drug called diethylstilbestrol in-utero[41, 42]. The USPSTF recommends cervical cancer screening for women ages 21-65 years. For those aged 21-29 years, Papanicolaou (Pap) testing every three years is recommended. For those aged 30-65, a Pap test every three years or a combined Pap and hrHPV (cotest) every 5 years is recommended.

In 2021, 1,438 cervical cancers were diagnosed in California. The majority were diagnosed at regional/remote stage (60.2 percent). Cervical cancer was most common among women ages 20-64 years (78.9 percent), followed by those 65 years and older (21.1 percent), and 0-19 years (less than 1 percent). Hispanic/Latina women made up 42.9 percent of cervical cancer diagnoses, followed by non-Hispanic/Latina White (31.6 percent), Asian/Pacific Islander (17.4 percent), Black/African American (5.6 percent), and American Indian (1.1 percent) women. Most cervical cancer cases were among women living in the lowest SES neighborhoods (40.3 percent), followed by the middle (33.2 percent), and highest (26.5 percent) SES neighborhoods. There were 16.4 percent fewer invasive cervical cancers diagnosed (1,438 versus 1,720 cases) than expected in 2021.

From 2016-2021, incidence among women 65 years of age and older was similar to women 20-64 years (Figure 4). Whereas cervical cancer incidence among women ages 65 years and older decreased by 1.3 percent per year during the study period, the incidence among women ages 20-64 years was stable from 2011-2021.

Among women ages 20-64 years, incidence dropped from 10.3 per 100,000 in 2019 to 9.3 per 100,000 in 2020, then returned to 10.2 per 100,000 in 2021. However, among women ages 65 years and older, incidence declined from 10.2 per 100,000 in 2019 to 10.0 per 100,000 in 2020 and 9.4 per 100,000 in 2021.

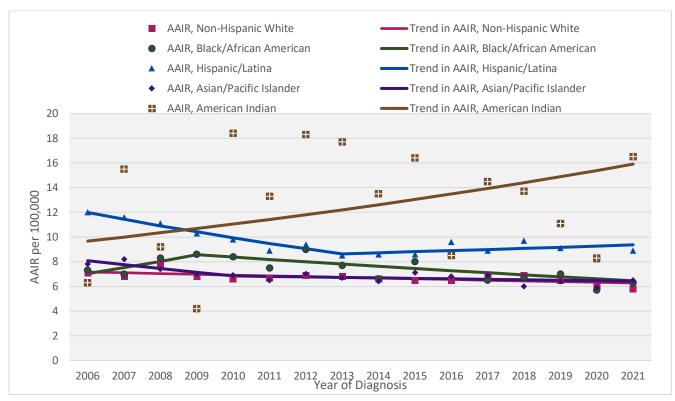
Figure 4. Trend in the Age-Adjusted Incidence Rate (AAIR) of Cervical Cancer by Age Group, California, 2006-2021



In 2021, incidence was highest among American Indians and lowest among non-Hispanic Whites, Black/African Americans, and Asian/Pacific Islanders (Figure 5). Throughout the study period, non-Hispanic/Latina Whites experienced a 0.9 percent decrease per year in incidence rates. Likewise, from 2009-2021, Black/African Americans' incidence decreased by 2.3 percent per year. Hispanic/Latinas' incidence remained stable from 2013 to 2021. Rates remained stable for Asian/Pacific Islanders throughout the study period. Although the trend among American Indians appeared to increase during the study period, the increase was not statistically significant.

Cervical cancer incidence rates per 100,000 in 2021 among Black/African Americans (6.3), Hispanic/Latinas (8.9), and American Indians (16.5) were higher than 2020 incidence rates (5.7, 8.2, and 8.3, respectively) but lower than 2019 incidence rates (7.0, 9.1, and 11.1, respectively). For non-Hispanic/Latina Whites the 2021 incidence rate (5.8 per 100,000) was lower than the 2020 (6.0 per 100,000) and 2019 (6.5 per 100,000) incidence rates. Among Asian/Pacific Islanders, the 2021 incidence rate (6.5 per 100,000) was higher than the 2020 rate (5.9 per 100,000) and similar to the 2019 rate (6.4 per 100,000).

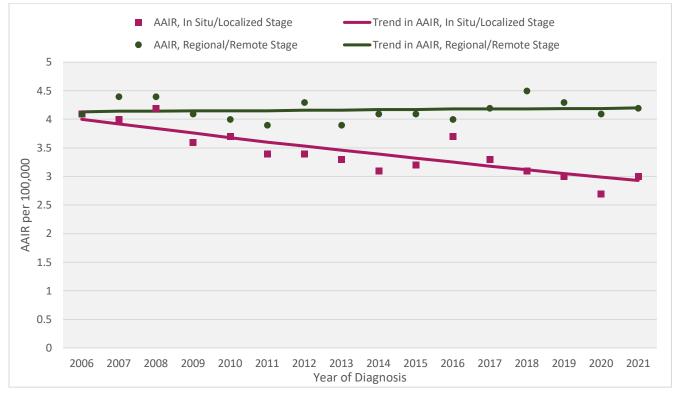
Figure 5. Trend in the Age-Adjusted Incidence Rate (AAIR) of Cervical Cancer by Race/Ethnicity, California, 2006-2021



Whereas incidence of in situ/localized cervical cancer decreased by 2.1 percent per year during the study period, incidence of regional/remote stage cervical cancer remained stable during the study period (Figure 6).

The incidence rate of cervical cancers diagnosed in situ/localized stage increased in 2021 compared to 2020 (3.0 versus 2.7 per 100,000) but was the same as 2019 (3.0 per 100,000). The incidence rate of cervical cancers diagnosed regional/remote stage increased in 2021 compared to 2020 (4.2 versus 4.1 per 100,000) but was lower than the 2019 rate of 4.3 per 100,000.

Figure 6. Trend in the Age-Adjusted Incidence Rate (AAIR) of Cervical Cancer by Stage at Diagnosis, California, 2006-2021



Colorectal Cancer

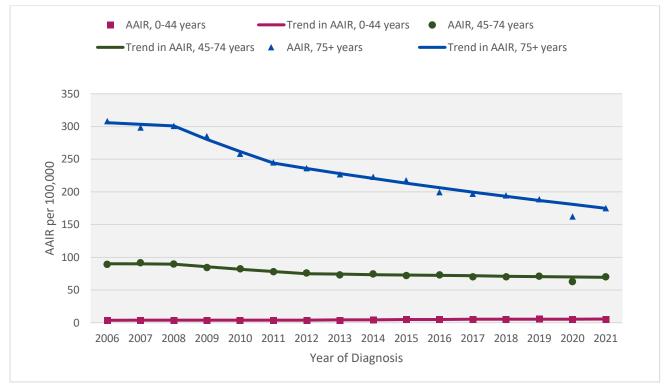
Colorectal cancer typically initiates as benign growths known as polyps within the colon or rectum. While the chance of polyps turning into cancer depends largely on the type of polyp, regular screening can detect and remove polyps before oncogenesis [43, 44]. Various factors contribute to the risk of colorectal cancer, including age greater than 50 years, family history of colorectal cancer or adenomatous polyps, inflammatory bowel disease, and certain genetic predispositions. Lifestyle choices, such as obesity, physical inactivity, smoking, excessive alcohol consumption, and diets high in red or processed meats, play significant roles in its development[45]. Despite the availability of screening methods including stool tests, sigmoidoscopy, colonoscopy, and CT colonography for early detection and intervention, 1 in 3 eligible adults in the United States have never been screened[44]. The USPSTF recommends regular screening for individuals aged 45-75 years, with screening methods such stool testing every 1-3 years, sigmoidoscopies every 5 years, colonoscopies every 10 years, or CT colonography every 5 years. However, screening is tailored to individual risk profiles[46].

In 2021, 1.3 percent more cases of invasive colorectal cancer were diagnosed in California than expected. Of the 15,387 cases, 52.7 percent were diagnosed among men and 47.2 percent were diagnosed among women. More cases were diagnosed regional/remote stage (63.2 percent) compared to in situ/localized stage and among those aged 45-74 years (63.4 percent) compared to older and younger ages. Individuals over 75 and 0-44 years comprised 28.5 percent and 8.0 percent of diagnoses, respectively. Most colorectal cancer patients were non-Hispanic/Latino White (49.3 percent), followed by Hispanic/Latino (26.0 percent), Asian/Pacific Islander (15.6 percent), Black/African American (6.8 percent), other/unknown races/ethnicities (2.0 percent), and American Indian (0.08 percent). The majority of colorectal cancer cases were among individuals living in middle SES neighborhoods (36.3 percent), followed by highest (34.5 percent), and lowest (29.2 percent) SES neighborhoods.

The incidence of colorectal cancer varied across age groups (Figure 7). Throughout the study period, incidence was highest among ages 75 years and older, followed by 45-74 years, and 0-44 years of age. The incidence of colorectal cancer among individuals aged 75 and above decreased by 3.3 percent per year from 2011 to 2021, while incidence among those aged 0-44 and 45-74 years remained stable during the study period.

In 2021, individuals aged 75 and above had the highest incidence rates, with 175.1 cases per 100,000, followed by those aged 45-74 with 70.1 cases per 100,000, and individuals aged 0-44 with 5.5 cases per 100,000. In 2021, incidence rates per 100,000 for all age groups were lower than those of 2019 (5.7 for 0-44 year olds, 71.2 for 45-74 year olds, and 188.8 for 75+) but higher than 2020 (5.1 for 0-44 year olds, 62.8 for 45-74 year olds, and 162.5 for 75+).



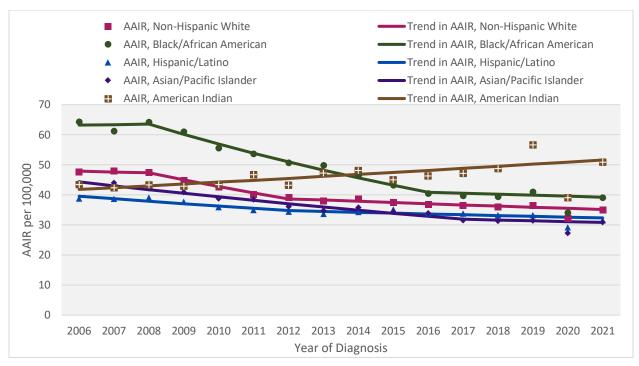


Source of Data: California Cancer Registry, California Department of Public Health.

The incidence rates of colorectal cancer among non-Hispanic/Latino Whites decreased by 1.1 percent per year from 2012-2021, while the AAIR among Hispanic/Latinos remained stable during the same period (Figure 8). The AAIR among Black/African Americans remained stable from 2016-2021. Similarly, the AAIR among Asian/Pacific Islanders remained stable from 2017-2021. In contrast, the AAIR among American Indians increased by 1.4 percent per year during the study period. Consequently, American Indians had the highest incidence rate of colorectal cancer in 2021.

In 2021, incidence rates per 100,000 for all races/ethnicities (35.0 among non-Hispanic/Latino Whites, 39.0 among Black/African Americans, 31.5 among Hispanic/Latinos, 30.9 among Asian/Pacific Islanders, and 50.8 among American Indians) were higher than 2020 (32.1 among non-Hispanic/Latino Whites, 34.0 among Black/African Americans, 29.1 among Hispanic/Latinos, 27.2 among Asian/Pacific Islanders, and 39.0 among American Indians) but lower than 2019 (36.4 among non-Hispanic/Latino Whites, 41.0 among Black/African Americans, 33.2 among Hispanic/Latinos, 31.4 among Asian/Pacific Islanders, and 56.6 among American Indians).

Figure 8. Trend in the Age-Adjusted Incidence Rate (AAIR) of Colorectal Cancer by Race/Ethnicity, California, 2006-2021

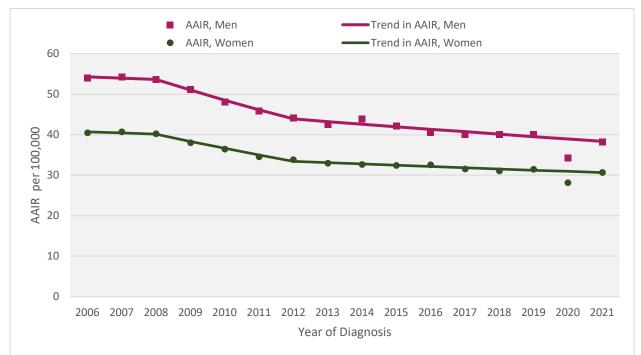


Source of Data: California Cancer Registry, California Department of Public Health.

The Continuing Impact of COVID-19 on Cancer Incidence, Early Detection, and Survival in California The AAIR of colorectal cancer was consistently higher among men compared to women, although it decreased for both sexes over the study period (Figure 9). Among men, the AAIR decreased by an average of 1.5 percent annually, while among women, it decreased by an average of 1.0 percent annually from 2012 to 2021.

In 2021, the incidence rate of colorectal cancer was 38.3 cases per 100,000 for men and 30.7 cases per 100,000 for women. Both men and women experienced higher incidence rates in 2021 compared to 2020 (34.4 among men and 28.2 among women). However, the AAIRs in 2019 (40.1 among men and 31.5 among women) were higher than those in 2021.

Figure 9. Trend in the Age-Adjusted Incidence Rate (AAIR) of Colorectal Cancer by Sex, California, 2006-2021



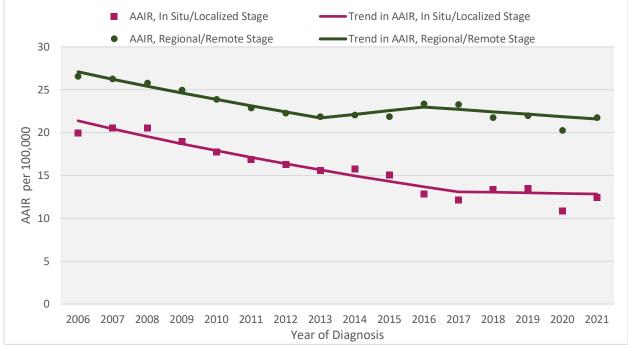
Source of Data: California Cancer Registry, California Department of Public Health.

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Throughout the study period, more colorectal cancers were diagnosed at a regional/remote versus in situ/localized stage (Figure 10). The AAIR of colorectal cancers diagnosed at a regional/remote stage decreased by an average of 1.2 percent per year from 2016 to 2021, while the incidence rate remained stable for those diagnosed in situ/localized.

The 2021 incidence per 100,000 of colorectal cancers diagnosed in situ/localized (12.5) and regional/remote (21.8) stage was higher than in 2020 (10.9 and 20.3, respectively) but lower than in 2019 (13.5 and 22.0, respectively).

Figure 10. Trend in the Age-Adjusted Incidence Rate (AAIR) of Colorectal Cancer by Stage at Diagnosis, California, 2006-2021



Lung Cancer

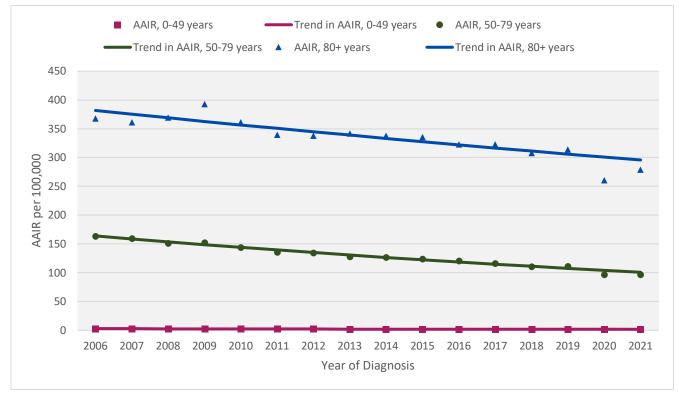
Smoking cigarettes is the leading cause of lung cancer and linked to 90 percent of lung cancer deaths in the United States[47]. Other risk factors include secondhand exposure to tobacco smoke, radon, asbestos, arsenic, diesel exhaust, silica, chromium, and high pollution. Annual lung cancer screening with low-dose computed tomography (CT) is recommended for individuals who are 50-80 years old, have a 20-pack year smoking history, and currently smoke or quit within the previous 15 years. A 20 pack-year smoking history means an individual has averaged one pack of cigarettes per day for 20 years. Someone who has smoked one pack per day for 20 years, two packs per day for 10 years, or 4 packs per day for 5 years would all have a 20 pack-year smoking history[48].

In 2021, 15,785 California residents were diagnosed with lung cancer. The majority (72.5 percent) were 50-79 years old, followed by 80 years and older (24.9 percent), and 0-49 years (2.5 percent). The majority of cases were diagnosed at regional/remote stage (73.1 percent) compared to in situ/localized stage (26.9 percent). Non-Hispanic/Latino Whites were diagnosed with 61.6 percent of lung cancers in 2021, followed by Asian/Pacific Islanders (16.2 percent), Hispanic/Latinos (13.5 percent), Black/African Americans (7.4 percent), and American Indians (0.6 percent). The most lung cancer diagnoses were among those living in medium SES neighborhoods (38.2 percent), followed by the highest (33.3 percent), and lowest (28.5 percent) SES neighborhoods. There were 11.5 percent fewer invasive lung cancers diagnosed in 2021 than expected (15,720 versus 17,760).

Incidence was highest for those 80 years and older, followed by 50-79 years, and 0-49 years during the entire study period (Figure 11). Incidence decreased by 3.2 percent per year for those 50-79 years and by 1.7 percent per year for those over 80 years. For those 0-49 years, incidence was stable from 2014-2021.

For those 0-49 years and 80 years and older, 2021 incidence rates (1.7 and 279.2 per 100,000, respectively) were greater than 2020 (1.6 and 261.0 per 100,000, respectively), but lower than 2019 (1.8 and 314.4 per 100,000, respectively). For those 50-79 years, incidence rates per 100,000 decreased from 2019 (111.2) to 2020 (97.1) to 2021 (96.7).

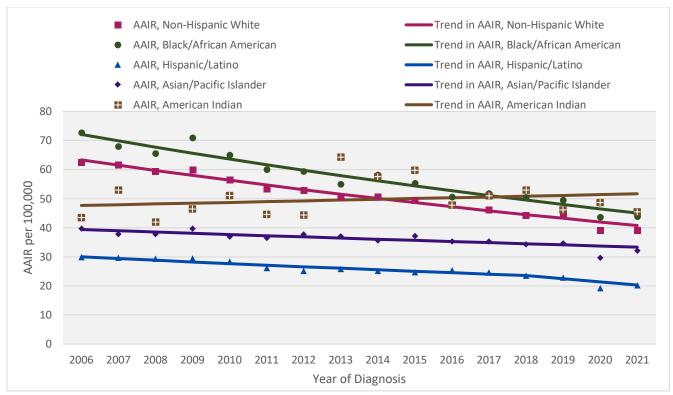
Figure 11. Trend in the Age-Adjusted Incidence Rate (AAIR) of Lung Cancer by Age Group, California, 2006-2021



In 2021, the highest incidence rates were among American Indians, at 45.4 per 100,000 people (Figure 12). Throughout the study period, rates were the lowest among Hispanic/Latinos. Incidence decreased by 2.9 percent per year for non-Hispanic/Latino Whites, 3.1 percent for Black/African Americans, and 1.1 percent for Asian/Pacific Islanders. Rates among Hispanic/Latinos decreased 4.9 percent per year from 2018-2021. Rates appeared to increase among American Indians during the study period, but the increase was not statistically significant.

For all races except American Indians, rates decreased from 2019 to 2020, then increased in 2021, but were less than 2019 levels. For non-Hispanic/Latino Whites, incidence fell from 44.9 per 100,000 in 2019 to 39.0 in 2020, then rose to 39.1 in 2021. For Black/African Americans, incidence fell from 49.4 per 100,000 in 2019 to 43.6 in 2020, then rose to 43.8 in 2021. Among Hispanic/Latinos, incidence fell from 22.8 per 100,000 in 2019 to 19.2 in 2020, then rose to 20.2 in 2021. Among Asian/Pacific Islanders, incidence fell from 34.6 per 100,000 in 2019 to 29.6 in 2020, then rose to 32.1 in 2021. Among American Indians, the incidence rate increased from 46.1 per 100,000 in 2019 to 48.6 in 2020, then decreased again to 45.4 in 2021.

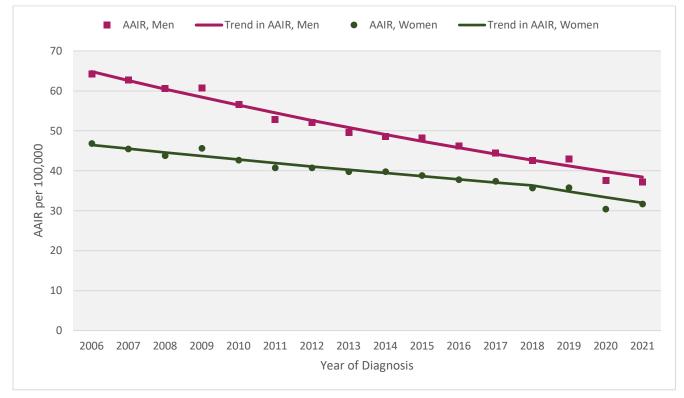
Figure 12. Trend in the Age-Adjusted Incidence Rate (AAIR) of Lung Cancer by Race/Ethnicity, California, 2006-2021



Lung cancer incidence was higher among men than women, but decreased during the study period for both sexes (Figure 13). Incidence decreased among men by 3.4 percent per year. Among women, incidence decreased by 4.1 percent per year from 2018 to 2021.

In 2021, the incidence per 100,000 for both sexes (37.2 among males and 31.7 among females) was higher than in 2020 (37.6 among males and 30.4 among females), but lower than 2019 (42.9 among males and 35.8 among females).

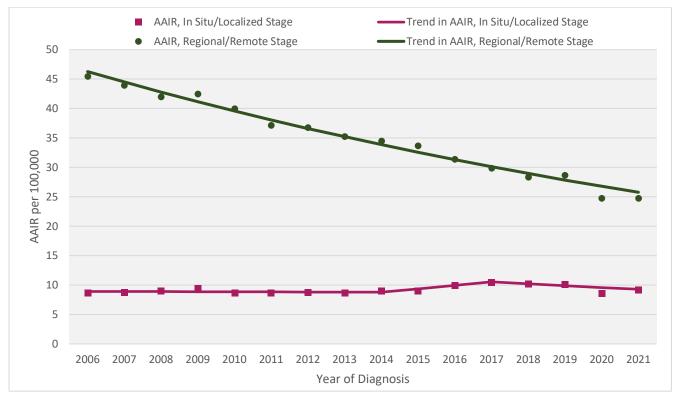
Figure 13. Trend in the Age-Adjusted Incidence Rate (AAIR) of Lung Cancer by Sex, California, 2006-2021



During the entire study period, more lung cancers were diagnosed at regional/remote versus in situ/localized stage (Figure 14). Regional/remote stage diagnoses decreased by 3.8 percent per year on average. In situ/localized stage diagnoses decreased by 3.1 percent per year from 2017 to 2021.

Incidence per 100,000 increased from 2020 to 2021 among in situ/localized stage tumors (8.6 and 9.2, respectively), but was lower than 2019 (10.1). Among regional/remote stage tumors, incidence per 100,000 was the same in 2021 as 2020 (24.8), but was lower than 2019 (28.7).

Figure 14. Trend in the Age-Adjusted Incidence Rate (AAIR) of Lung Cancer by Stage at Diagnosis, California, 2006-2021



Source of Data: California Cancer Registry, California Department of Public Health.

Melanoma

Melanoma, while comprising only 1.0 percent of all skin cancer cases, is the most dangerous type, as it is more likely to spread to other parts of the body[49, 50]. Various risk factors contribute to melanoma, including fair skin, freckles, numerous or atypical moles, family history of melanoma, dysplastic nevus syndrome (atypical mole syndrome), familial atypical multiple mole and melanoma syndrome (FAMM), and Xeroderma pigmentosum (XP)[51]. Ultraviolet (UV) light exposure, stemming from sources like sunlight and tanning beds, remains a major modifiable risk factor for melanoma[52].

USPSTF lacks an official screening guideline for melanoma due to insufficient evidence regarding the benefits and risks of screening, however methods such as self-examination and dermoscopy are available. Self-examination involves scrutinizing the entire body, including hard-to-reach areas, using a mirror in a well-lit room, while dermoscopy involves a medical professional assessing the characteristics of skin lesions to detect potential melanoma[53].

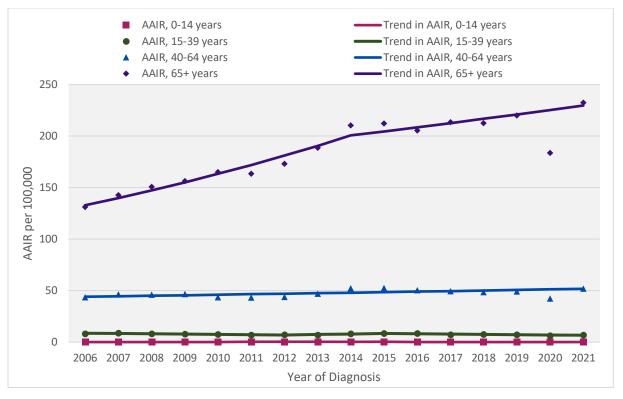
In 2021, 21,719 California residents were diagnosed with melanoma. Most cases (58.9 percent) were diagnosed among men. The majority of diagnoses were in situ/localized stage (93.7 percent). The most common age for melanoma diagnosis was over 65 years old (62.4 percent), followed by 40-64 years old (33.2 percent), and 15-39 years old (4.4 percent). Melanoma was most frequently diagnosed among non-Hispanic/Latino Whites (75.6 percent), followed by other/unknown race/ethnicity (18.5 percent), Hispanic/Latinos (4.8 percent), Asian/Pacific Islanders (0.5 percent), American Indians (0.3 percent), and Black/African Americans (0.2 percent). The majority of melanomas were diagnosed among those living in the highest SES neighborhoods (54.9 percent), followed by the middle (32.4 percent), and lowest (12.6 percent) SES neighborhoods. There were 5.2 percent fewer invasive melanomas diagnosed in 2021 than expected (10,850 versus 11,450).

Throughout the study period, individuals aged 65 and above experienced the highest incidence of melanoma compared to younger age groups, with a rate of 232.5 cases per 100,000 in 2021 (Figure 15). The incidence among those aged 40-64 was 51.8 cases per 100,000, while individuals aged 15-39 had

The Continuing Impact of COVID-19 on Cancer Incidence, Early Detection, and Survival in California an incidence of 7.0 cases per 100,000 in the same year. The AAIR among patients 65 years of age and older remained stable from 2014-2021. Meanwhile, the AAIR of melanoma for individuals aged 40-64 increased by an average of 1.1 percent annually throughout the study period. From 2014-2021, the AAIR among 0-14 year olds decreased by 13.6 percent per year. Similarly, the AAIR among those 15-39 years of age decreased by 3.6 percent per year from 2015-2021.

Individuals aged 0-14 years had the same incidence rate per 100,000 for 2019, 2020, and 2021 (0.1). Those who were 15-39 years and 65 years and over had greater incidence rates of melanoma per 100,000 in 2021 (7.0 and 232.5, respectively) than in 2020 (6.2 and 183.5, respectively) but lower than in 2019 (7.2 and 220.1, respectively). Those who were 40-64 years had higher incidence rates per 100,000 in 2021 (51.8) than in 2020 (42.2) and 2019 (49.0).

Figure 15. Trend in the Age-Adjusted Incidence Rate (AAIR) of Melanoma by Age Group, California, 2006-2021

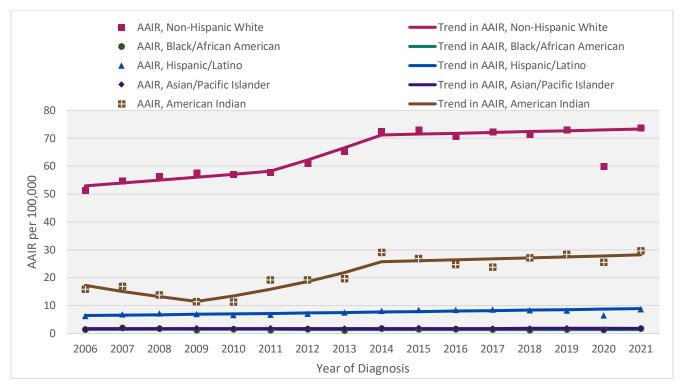


Source of Data: California Cancer Registry, California Department of Public Health.

The Continuing Impact of COVID-19 on Cancer Incidence, Early Detection, and Survival in California Throughout the study period, non-Hispanic/Latino Whites had the highest AAIR of melanoma among all racial/ethnic groups, followed by American Indians, Hispanic/Latinos, and Black/African Americans and Asian/Pacific Islanders (Figure 16). Non-Hispanic/Latino Whites experienced stable incidence from 2014 to 2021. Hispanic/Latinos and American Indians experienced their highest incidence rates in 2021, with rates of 8.9 and 28.2 cases per 100,000, respectively. Over the study period, the AAIR of melanoma for Hispanic/Latinos increased by an average of 2.2 percent per year. In contrast, the AAIR remained steady for both Asian/Pacific Islanders and Black/African Americans during the study period.

In 2021, the AAIR of melanoma per 100,000 among non-Hispanic/Latino Whites (73.7), Black/African Americans (1.7), Hispanic/Latinos (8.6), and American Indians (29.6) was greater than 2020 (59.8, 1.3, 6.5, and 25.4, respectively) and 2019 (73.0, 1.4, 8.2, and 28.3, respectively). The 2021 AAIR among Asian/Pacific Islanders (1.7 per 100,000) was greater than incidence in 2020 (1.2 per 100,000) but lower than incidence in 2019 (1.9 per 100,000).

Figure 16. Trend in the Age-Adjusted Incidence Rate (AAIR) of Melanoma by Race/Ethnicity, California, 2006-2021

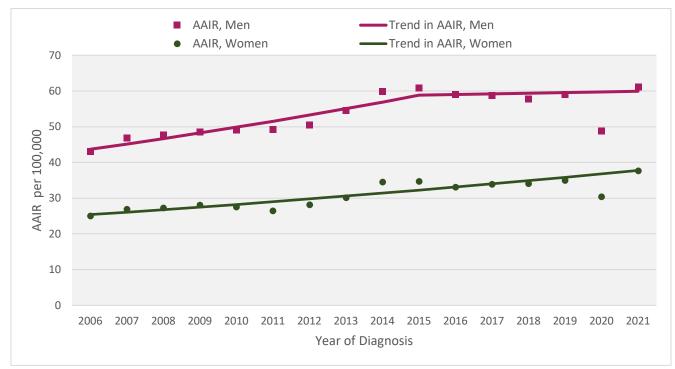


Source of Data: California Cancer Registry, California Department of Public Health.

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Throughout the study period, the incidence of melanoma was higher among men than women (Figure 17). In 2021, there were 61.2 cases per 100,000 among men and 37.7 cases per 100,000 among women. The AAIR increased for women by an average of 2.7 percent per year over the study period but remained steady for men from 2015-2021. Both men and women experienced a decline in melanoma incidence rates per 100,000 from 2019 (59.0 among men and 35.0 among women) to 2020 (48.8 among men and 30.4 among women). However, by 2021, the incidence rates had surpassed those of 2019 (61.2 among men and 37.7 among women).

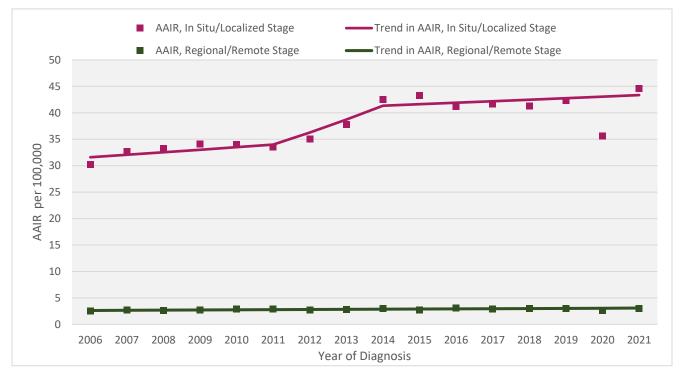




Source of Data: California Cancer Registry, California Department of Public Health.

Throughout the study period, more melanomas were diagnosed in situ/localized than regional/remote stage (Figure 18). In 2021, in situ/localized incidence was 44.6 cases per 100,000 and regional/remote was 3.08 cases per 100,000. From 2006 to 2021, the AAIR of regional/remote stage melanoma increased by an average of 1.1 percent per year, while remaining steady for in situ/localized stage. In 2021, the incidence rate per 100,000 for those diagnosed in situ/localized (44.6) was higher than in 2020 (35.6) and 2019 (42.3). Incidence rates for those diagnosed regional/remote were the same in 2019 and 2021 (3.0), decreasing slightly in 2020 (2.6).

Figure 18. Trend in the Age-Adjusted Incidence Rate (AAIR) of Melanoma by Stage at Diagnosis, California, 2006-2021



Source of Data: California Cancer Registry, California Department of Public Health.

One-Year Survival

To evaluate the impact of the COVID-19 pandemic on the length of time patients survived following the diagnosis of a screening-detectable cancer, adjusted one-year hazard ratios for 2020 versus 2018 cancer diagnosis and associated 95 percent confidence intervals were calculated for breast, cervix, colorectal, lung, and melanoma cancers respectively (Table 3, Figure 19). Estimates are adjusted to account for the differential one-year hazard of death due to age at diagnosis, race/ethnicity, marital status, stage at diagnosis, number of comorbidities, socioeconomic status, and health insurance type. For four out of five cancer sites, the hazard ratios were significantly higher than 1.0, indicating the hazard of dying within one year was higher for patients diagnosed during the pandemic than pre-pandemic. Among cervical cancer patients, the relative risk of dying within one year of diagnosis was 40 percent higher among those diagnosed during the pandemic compared to pre-pandemic. Among breast, colorectal, and melanoma patients, the relative risk of dying within one year of diagnosis was 16 percent, 15 percent, and 13 percent higher for those diagnosed during the pandemic versus pre-pandemic, respectively. The relative risk of dying within one year of diagnosis was stable among those diagnosed with lung cancer during the pandemic versus pre-pandemic.

Table 3: Adjusted^a one-year hazard ratios and associated 95 percent confidence interval (CI) for screening-detectable cancers during the pandemic (2020) versus pre-pandemic (2018)

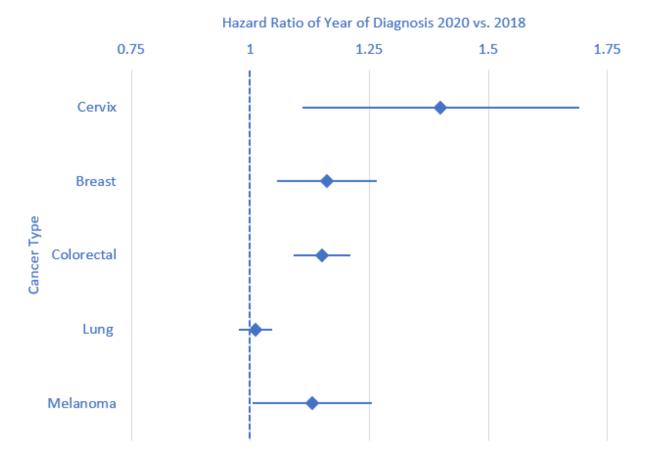
| Type of Cancer | Hazard Ratio | 95 percent CI |
|----------------|--------------|---------------|
| Cervix* | 1.40 | (1.14, 1.72) |
| Breast* | 1.16 | (1.06, 1.27) |
| Colorectal* | 1.15 | (1.09, 1.21) |
| Lung | 1.01 | (0.98, 1.05) |
| Melanoma* | 1.13 | (1.02, 1.27) |

^aModels were adjusted for age at diagnosis, race/ethnicity, marital status, stage at diagnosis, number of comorbidities, socioeconomic status, and health insurance type.

*The hazard ratio is significantly different from 1 at alpha=0.05

Source of data: California Cancer Registry, California Department of Public Health.

Figure 19: Adjusted^a one-year hazard ratios and associated 95 percent confidence interval (CI) for screening-detectable cancers during the pandemic (2020) versus pre-pandemic (2018)



^aModels were adjusted for age at diagnosis, race/ethnicity, marital status, stage at diagnosis, number of comorbidities, socioeconomic status, and health insurance type.

Source of Data: California Cancer Registry, California Department of Public Health.

Conclusion

This report analyzed the continued impact of the COVID-19 pandemic on cancer incidence, early detection, and survival in California in 2021. The COVID-19 pandemic has been linked to disruptions in the receipt of preventative care, including significant declines in cancer screening[20-22, 24]. Due to highly contagious new variants and ongoing waves of infections, the COVID-19 pandemic continued to disrupt the cancer care continuum in 2021 [20-22, 24].

Fifteen of 21 common cancers had lower than expected incidence, suggesting missed early-detection in 2021. Notably, only 83.6 percent of expected cervical cancers were diagnosed. Furthermore, between 84 to 98 percent of expected myeloma, liver, uterine, lung, urinary bladder, leukemia, oral cavity & pharynx, larynx, non-Hodkin lymphoma, prostate, kidney, esophagus, pancreas, melanoma, breast, and brain & ONS cancers were detected.

Striking disparities in the incidence of screening-detectable cancers were observed by age, race/ethnicity, and stage at diagnosis in 2021. The incidence of cervical, colorectal, and lung cancer among those older than the recommended screening ages was higher in 2021 than 2020, but lower than 2019. Disparities also persisted among historically marginalized racial/ethnic groups. The incidence of breast, cervical, colorectal and lung cancer among Black/African Americans and Hispanic/Latinos was higher in 2021 than 2020, but lower than 2019. Similarly, the incidence of colorectal, lung and melanoma cancer among Asian/Pacific Islanders was higher in 2021 than 2020, but lower than 2019. Finally, all screening-detectable cancers diagnosed in situ/localized stage exceeded their 2020 incidence rate in 2021. However, the 2021 incidence rate of colorectal and lung cancers diagnosed in situ/localized stage was lower than in 2019. The incidence rate of breast cancer diagnosed regional/remote stage in 2021 was higher than the previous two years.

The risk of death within one year of diagnosis was 13-40 percent higher for patients diagnosed during 2020 than 2018 for four out of five screening-detectable cancers, suggesting that patients diagnosed during the pandemic had worse survival outcomes compared to those diagnosed before the onset of the pandemic. Possible explanations include decreased early cancer

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detection, delayed or foregone cancer treatment during the pandemic, and overall increased mortality in the United States in 2020[54].

Findings from this report highlight the continued impact of the pandemic on cancer incidence, early detection, and survival in California in 2021. Potential strategies to mitigate the lasting impact of the COVID-19 pandemic on early cancer detection include public health campaigns to increase public awareness and access to screening, educating primary care providers on disparities in early cancer-detection and evidence-based interventions, and offering catch-up screenings for those who aged out of cancer screening recommendations during the pandemic. Policymakers should prioritize funding aimed to reduce barriers and increase equitable access to cancer screening through distributing stool tests for colorectal cancer via mail, offering transportation to and from cancer screening appointments, funding mobile mammography, and educational campaigns for primary care providers and the public regarding cancer screening guidelines and importance[55-57]. Health systems should educate staff regarding disparities in early cancer detection and implement evidence-based interventions to increase cancer screenings at their facilities [56]. Further research is needed to evaluate the long-term effects of the COVID-19 pandemic on cancer outcomes.

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