

# Emerging evidence links cannabis use to increased risk of breast and testicular cancer in young Americans

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## Abstract

**Introduction:** The aim of this study was to test the a priori hypothesis that the increasing incidence of testis and breast cancer in adolescent and young adult (AYA) Americans correlates with their increasing cannabis use. **Methods:** The overall study design involved comparing breast and testis cancer incidence trends in jurisdictions that had or had not legalized cannabis use. Cancer incidence was assessed for the U.S. using the U.S. Surveillance, Epidemiology, and End Results (SEER) data, and for Canada, using Institute for Health Metrics and Evaluation data. **Results:** In the U.S., both breast carcinoma in 20- to 34-year-old females and testis cancer in 15- to 39-year-old males had annual incidence rate increases that were highly correlated (Pearson's  $r = 0.95$ ) with the increase in the number of cannabis-legalizing jurisdictions during the period 2000–2019. Both were significantly greater during the period 2000–2019 in the SEER registries of cannabis-legalizing than non-legalizing states (Joinpoint-derived average annual percent change, AAPC<sub>1.3</sub>,  $p < 0.001$  vs. 0.7,  $p < 0.001$ , respectively, for breast cancer, and AAPC<sub>1.2</sub>,  $p < 0.001$  vs. no increase during the period 2000–2011 for testis cancer). During the period 2000–2019, registries in cannabis-legalizing versus non-legalizing states had a 26% versus 17% increase in breast carcinoma and 24% versus 14% increase in testis cancer. In the same age groups, Canada had a greater increase in both breast and testis cancer incidence than the U.S., and in both countries, breast and cancer trends were both correlated with the country's cannabis use disorder prevalence by age. **Conclusions:** North America shows evidence that cannabis is a potential etiologic factor contributing to the rising incidence of breast carcinoma and testis cancer in young adults. Canada's greater increases than in the U.S. are consistent with its earlier and broader cannabis legalization. Given the increasing use and potency of cannabis facilitated by jurisdiction legalization and expanded availability, cannabis' potential as a cause of breast and testis cancer merits national consideration.

**Keywords:** breast cancer, testis cancer, incidence, cannabis, adolescents and young adults

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## 1. Introduction

The incidence of breast, testis, and other cancers has been increasing in adolescent and young adults (AYAs) [1–6]. Explanations have included obesity, sedentary lifestyle, chest radiation (especially CT scans), alcohol consumption, hereditary predisposition due to improved survival rates in subsequent generations, pregnancy at an older age, and breast density [1–6]. In February 2025, a report from the American Cancer Society (ACS) identified non-seminoma testis cancer as the cancer type most closely linked to cannabis use [7]. The ACS also cited evidence of an increased risk of other types of cancer, including breast, oral, hepatic, cervical, laryngeal, pancreatic, thyroid, lung, head/neck, and childhood cancer [7]. Their review also identified the need for the replication of previous studies for additional epidemiological investigations, rigorous study designs, and data collection protocols free from the biases of major confounders, misclassification, and measurement error in assessing cannabis exposure [7].

Australian researchers have recently reported that, in the United States (U.S.) and Europe, multiple types of cancer are associated with cannabis use, including the breast and the reproductive organs of the testis, ovary, and prostate [8–10]. For breast cancer, they found a direct correlation of incidence with the extent of cannabis exposure [9]. In multivariate models including sociodemographic, socioeconomic, and hormonal risk factors, they found that cannabis was “a more important carcinogen than tobacco and alcohol” [8, 10]. AYAs are distinguished from the general population by their unique psychosocial needs and risk factor exposures. Whether a cannabis-cancer correlation exists in AYAs remains to be described.

Having previously reported increasing breast cancer incidence in young females [11, 12] and also a testis cancer–cannabis association in AYAs [13], we compared the rise in incidence rates of breast and

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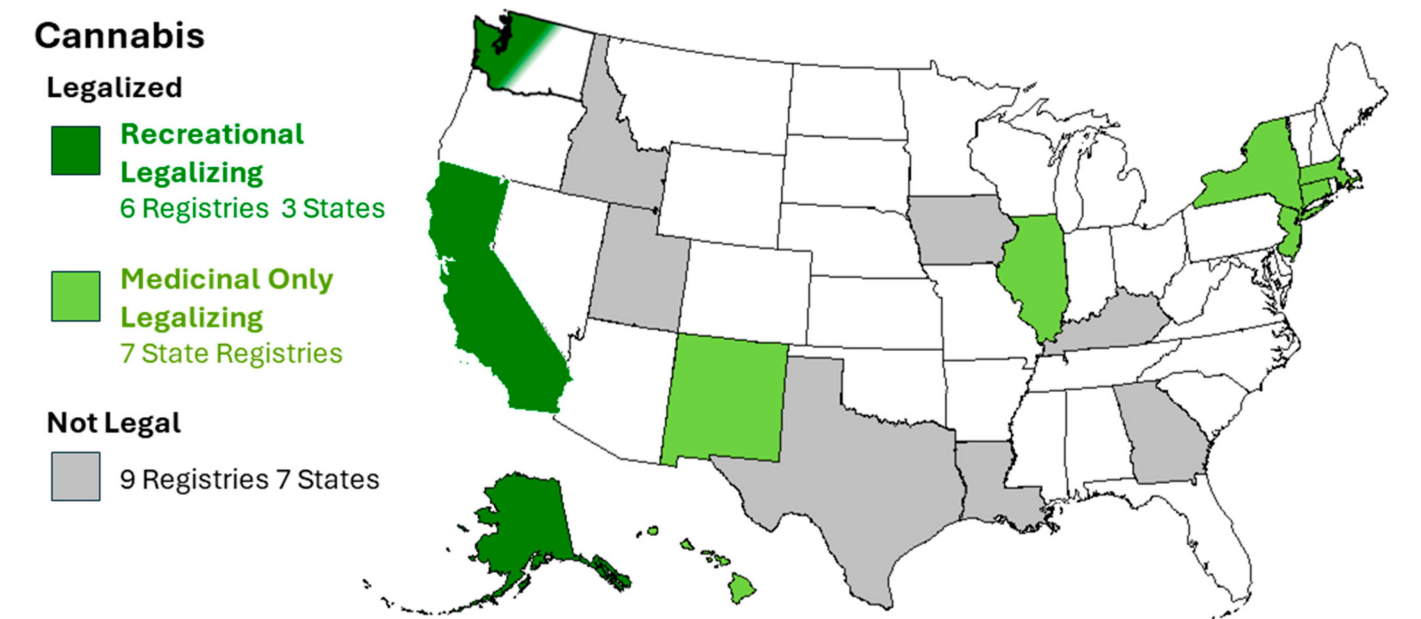
testis cancer in AYAs with the implementation of cannabis legalization, which, to our knowledge, has not been previously reported. Additionally, because Canada is U.S.’s closest neighbor both topographically and in cannabis use, and because Canada has legalized cannabis more than the U.S., we included Canada in our assessment.

2. Materials and methods

Annual cancer incidence data during the period 2000–2019 for the U.S. were obtained from the U.S. National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program SEER\*Stat Database [14] and, for Canada, from the Institute for Health Metrics and Evaluation (IHME) Global Health Burden resource [15]. National U.S. estimates were obtained from the National Vital Statistics System of the Centers for the Disease Control and Prevention (CDC), National Center for Health Statistics [16]. 2019 was the latest year evaluated, since the start of the COVID-19 pandemic showed lapses in diagnoses [17, 18]. Cannabis use disorder prevalence data were obtained from the IHME [15]. Alcohol consumption data were obtained from the National Institute on Alcohol Abuse and Alcoholism Division of Epidemiology and Prevention

Research Alcohol Epidemiologic Data System [19]. Tetrahydrocannabinol [THC] potency was obtained from National Institute on Drug Abuse [20]. Obesity prevalence was obtained from the CDC [21]. Average annual percent change (AAPC) and the associated statistical significance (*p*-value, 2-sided) and 95% confidence interval (CI) were provided by the SEER\*Stat AAPC program [14]. Ethical approval was not required since individual subjects were not assessed.

SEER22 registries (**Figure 1**) representing 48% to 50% of the U.S. population were considered the most applicable for cancer incidence evaluation because of their accuracy and detail, including biologic subtype of cancer and races/ethnicities and long-term follow-up of patients, and geographical locations that are representative of the entire U.S. The SEER registry system has been capturing cancer data for more than 50 years [22] and is regarded as one of the best such systems, with cancer incidence, mortality, and survival data derived therefrom that are analyzed by investigators around the world. Also, the SEER database specifically provides breast carcinoma data whereas the CDC and other systems have breast cancer data in general, including non-carcinoma types. The registries and their location in the U.S., total population, and population by race/ethnicity are listed in Table S1 [23] according to their cannabis legalization implementation status as of January 2019.

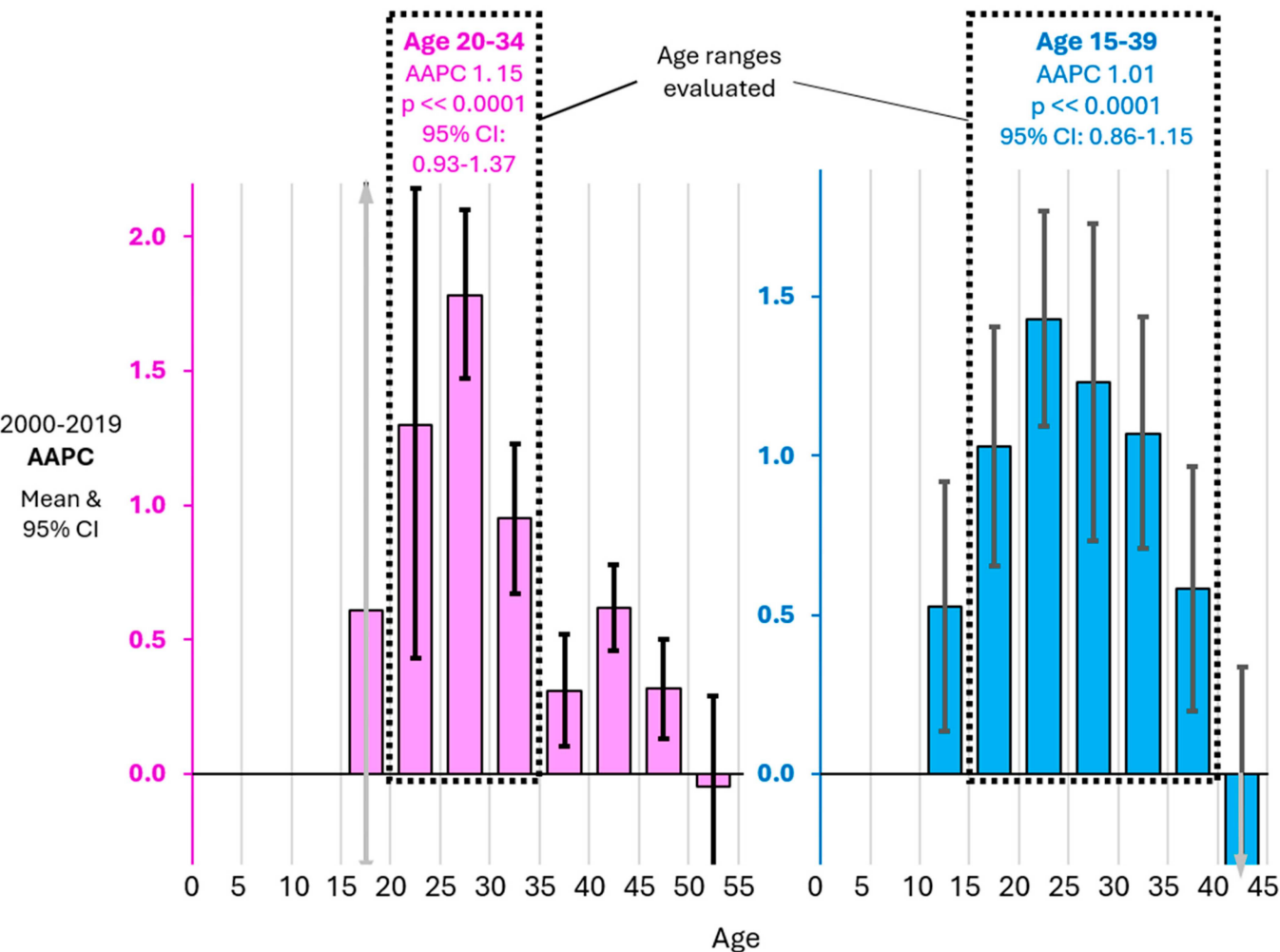


**Figure 1 •** SEER22 Registry cannabis legalization implementation status as of January 2019. Washington’s registries encompass 13 counties in its western region, including Seattle. Alaska’s registry is of Natives only. Data sources: SEER22 [14]; jurisdiction legalization: Bleyer A et al. [24].

The overall study design involved comparing breast and testis cancer incidence trends in registries that had or had not legalized cannabis use. Each registry was classified according to its state’s cannabis legalization implementation status as of January 2019. Seven registries were states that had implemented cannabis legalization for medicinal use only: Connecticut, Hawaii, Illinois, Massachusetts, New Jersey, New Mexico, and New York. Six registries in three states had both legal recreational and medicinal use implemented: California (Los Angeles, San Francisco–Oakland, San Jose–Monterey, and the rest of California), Washington (Seattle–Puget Sound Registries), and Alaska (limited to Alaska Natives).

Nine registries in seven states had not legalized cannabis: Georgia (Metropolitan Atlanta, Greater Georgia, and Rural Georgia registries), Idaho, Iowa, Kentucky, Louisiana, Texas, and Utah [24].

After evaluating the cancer incidence AAPC and its statistical significance as a function of 5-year age intervals (**Figure 2**), we selected ages 20 to 34 and 15 to 39 years to evaluate breast and testis cancer, respectively. Although 10- to 14-year-old males exhibited a statistically significant increase in testis cancer (**Figure 2**), we did not include this age group because it included boys not yet adolescent.



**Figure 2 •** Average annual percent change (AAPC) in incidence of breast carcinoma in young females and testis cancer in young males, 2000–2019, by age. AAPC was provided by the SEER\*Stat AAPC program [14]. The I bars are 95% CIs. Data source: SEER22 (49% of U.S.) [14].

3. Results

3.1. U.S. cancer incidence age trend

Since 2000, the breast and testis cancer incidence has been steadily increasing in AYA Americans, especially for breast carcinoma in 20- to 34-year-old females and for testis cancer in 15- to 39-year-old AYA males (Figure 2). The 2000–2019 AAPC in SEER22 was 1.15 (96% CI, 0.93 to 1.37;  $p < 0.001$ ) for breast carcinoma incidence in 20- to 34-year-old females and 1.01 (96% CI, 0.86 to 1.1;  $p < 0.001$ ) for testis cancer in 15- to 39-year-old males (Figure 2). Nationwide, according to the CDC [16], the number of newly diagnosed Americans in the aforementioned age groups increased 26% from 3622 in 2000 to 4868 in 2019 for breast cancer and 21% from 5111 in 2000 to 6181 in 2019 for testis cancer.

The Joinpoint analysis of the SEER22 data indicates that the incidence of breast cancer accelerated in 20- to 34-year-old females, from an AAPC of 0.61 (pNS) during the period 2000–2010 to 1.73 (95% CI, 1.29 to 3.47,  $p = 0.0004$ ) during the period 2010–2019, a 182% increase and a 24% incidence increase from 2000 to 2019 (Figure 3, pink data). For testis cancer, the increase in the 15- to 39-year-old males was continuous, without an inflection, at an AAPC of 1.6 (95% CI, 0.89 to 1.23,  $p < 0.001$ ), with an increase of 21% from 2000 to 2019 (Figure 3, blue data).

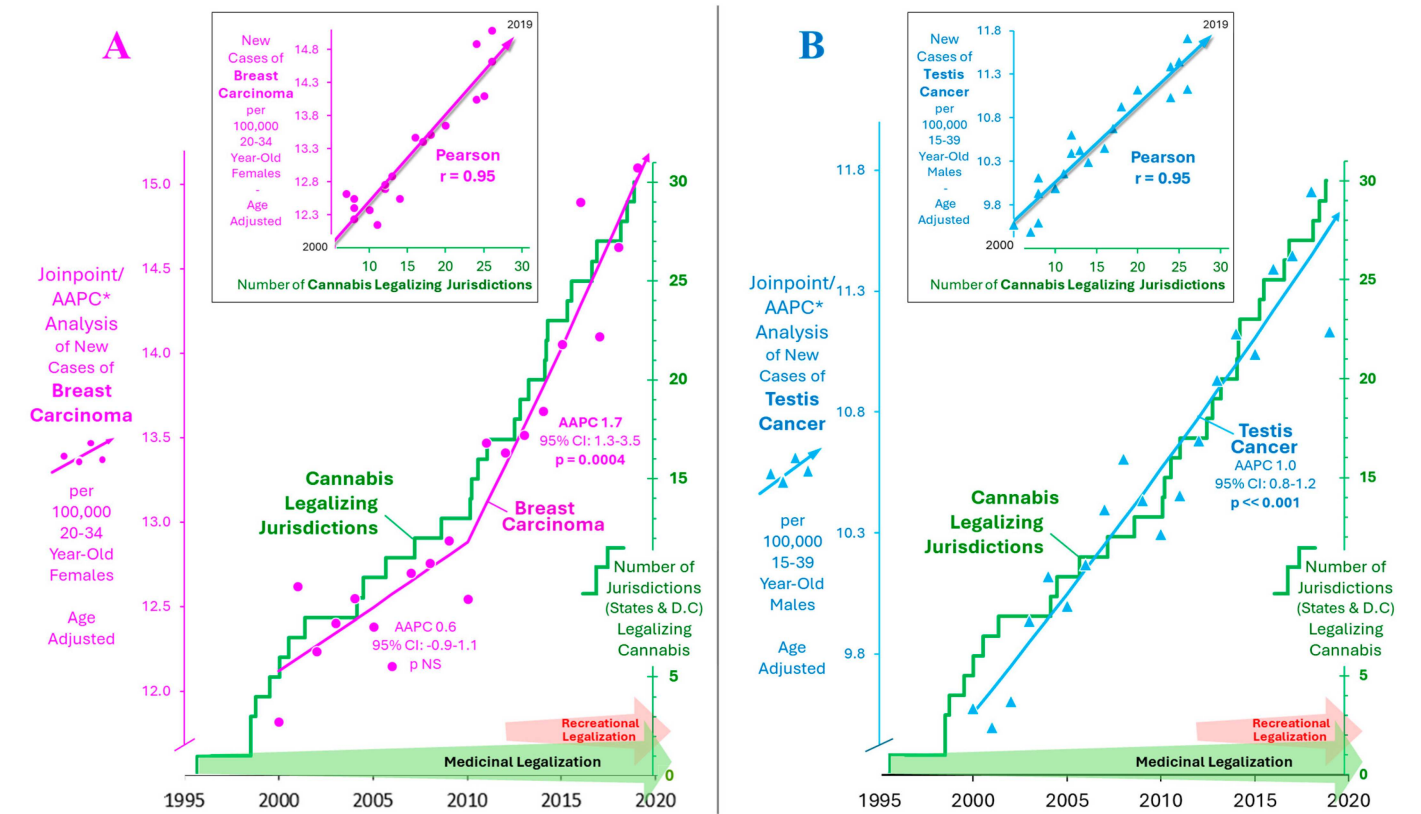
3.2. U.S. cancer incidence trends vs. cannabis legalization

The cancer incidence trends correlate with the temporal implementation of cannabis legalization in U.S. jurisdictions and the progressive implementation of medicinal cannabis legalization during the period 2000–2019 (Figure 3, green data and arrow) and, subsequently, with recreational legalization since 2014 (Figure 3 red arrow). Both annual breast carcinoma and testis cancer incidence during the period 2000–2019 are highly correlated with the number of cannabis-legalizing jurisdictions: Pearson’s  $r = 0.95$  for both breast and testis cancer (Figure 3A,B insets).

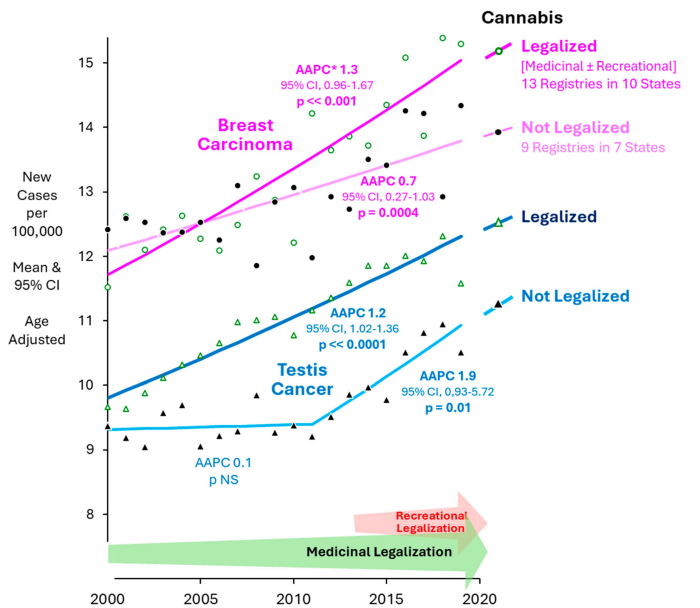
During the period 2000–2019, the SEER registries in U.S. states that had legalized cannabis showed greater increases in new cases of breast carcinoma cases in 20- to 34-year-old females and in testis cancer in 15- to 39-year-old males than shown in the registries located in states that had not legalized cannabis (Figure 4). Breast carcinoma increased more rapidly in legalizing state registries (AAPC 1.3,  $p < 0.001$ ) than in registries in non-legalizing states (AAPC 0.7,  $p = 0.004$ ) such that, by 2019, the incidence was greater in legalizing state registries (Figure 4, pink data). The testis cancer incidence continuously increased during the period 2000–2019 in legalizing state registries (AAPC 1.2,  $p < 0.001$ ) in comparison to registries in non-legalizing states, which had no increase during the

period 2000–2011 and a less statistically significant subsequent increase thereafter ( $p = 0.01$ ) (Figure 4, blue data). According to the Joinpoint regressions, the increases from 2000 to 2019 were a 26% increase in legalizing and 13% in non-legalizing regions for

breast carcinoma and 24% and 17%, respectively, for testis cancer. The 95% CIs in legalizing and non-legalizing AAPCs overlapped but the AAPCs were statistically more significant in the legalizing cohorts for both breast carcinoma and testis cancer (Figure 4).



**Figure 3 •** Number of jurisdictions (states and D.C.) legalizing cannabis, 1997–2019, U.S. and Joinpoint/average annual percent change (AAPC) of annual incidence, 2000–2019, SEER22, of breast carcinoma in 20- to 34-year-old females (A) and testis cancer in 15- to 39-year-old males (B). Insets: The breast carcinoma and testis cancer incidences vs. number of cannabis-legalizing jurisdictions, calendar year. AAPC per the SEER\*Stat AAPC program [14]. Data sources: carcinoma incidence: SEER22 [14]; jurisdiction legalization: Bleyer A et al. [24].



**Figure 4 •** Joinpoint/AAPC\* analysis of annual incidence of breast carcinoma in 20- to 34-year-old females and testis cancer in 15- to 39-year-old males, 2000–2019, in SEER22 registries of states that had or had not implemented cannabis legalization by January 2019. \*AAPC—average annual percent change, per the SEER\*Stat AAPC program [14]. Data source: SEER22 [14].

### 3.3. Breast cancer type vs. cannabis legalization in the U.S.

The breast cancer subtype that was the most strongly correlated with recent cannabis legislation was hormone-receptor-negative cancer (HR-/HER2-, triple-negative), with the AAPC from 2014 (the first year hormone receptor and HER2 status were reported) to 2019 being 5.6 (95% CI, 2.7 to 8.6) ( $p = 0.006$ ) in registries of legalizing states and 2.5 (95% CI, -3.0 to 8.5) in registries of non-legalizing states (Figure 5). The other subtypes either increased or decreased, in the same direction, in both legalizing and non-legalizing state registries (Figure 5).

### 3.4. U.S. race/ethnicity correlations

In five of the ten comparisons of race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, American Indian and Alaska Native, Hispanic), the AAPC incidence increases were significantly more rapid in the legalizing states (Figure 6A–C,H,J). There were no significant comparative AAPC changes in the other groups (Figure 6D–G,I). The greatest race/ethnicity increases associated with cannabis legalization were breast carcinoma in non-Hispanic White and non-Hispanic Black females (Figure 6A,B), and testis cancer in Hispanic and in American Indian and Alaska Native males (Figure 6H,J). The



difference in the White population proportions in legalizing and non-legalizing states was only 0.7% and the proportion of the Black population had an absolute difference of 5.1% smaller in legalizing vs. non-legalizing states (Table S1), the latter difference strengthening the cannabis–breast cancer correlation. For testis cancer, an absolute difference of 5.1% greater in legalizing states may be contributing to the testis cancer incidence increase in legalizing states. The other race and ethnicity population proportion differences were too small in either absolute or relative differences to significantly alter the cancer–cannabis correlations.

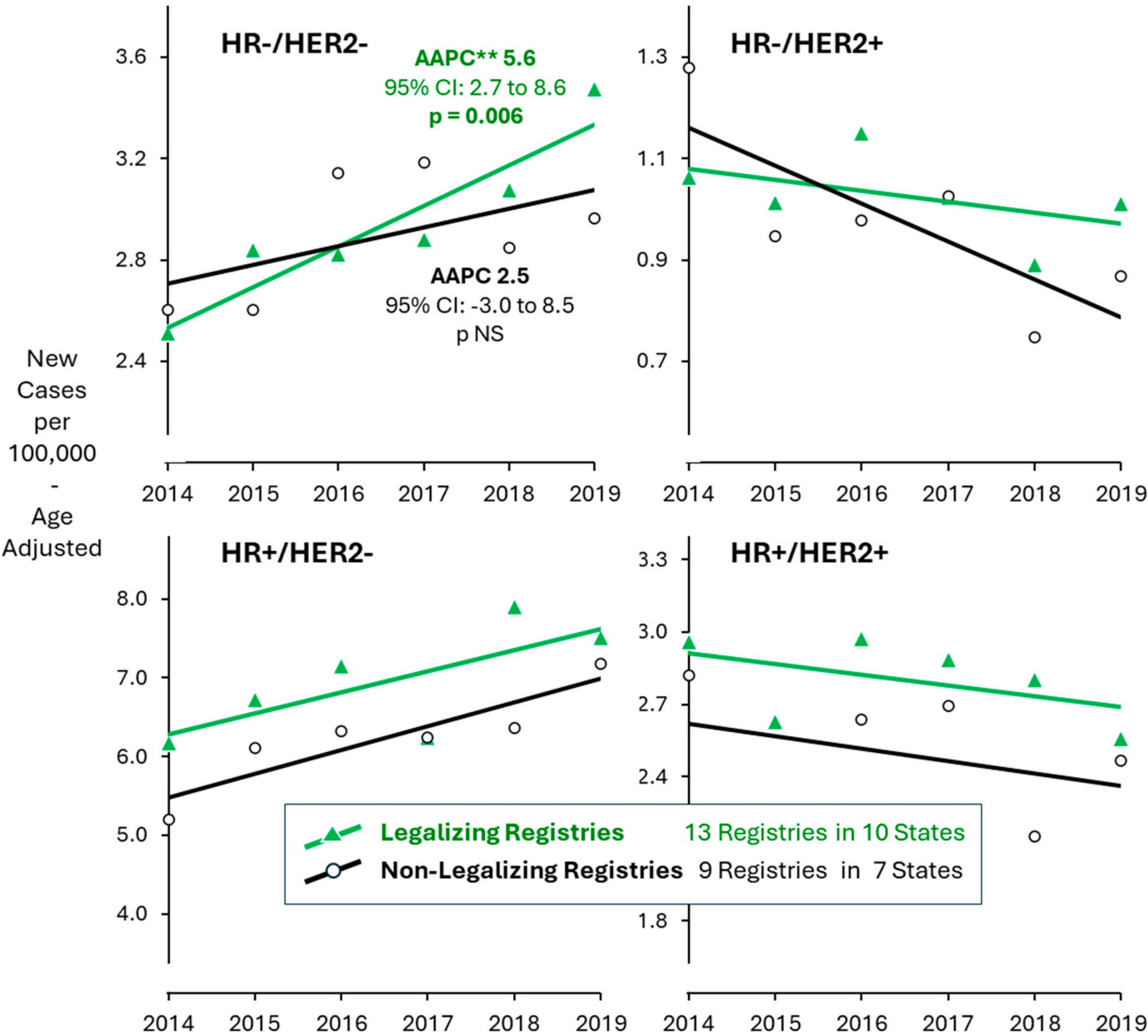
3.5. Cancer incidence trends vs. alcohol consumption

Given the recent emphasis on alcohol [25] and its known status

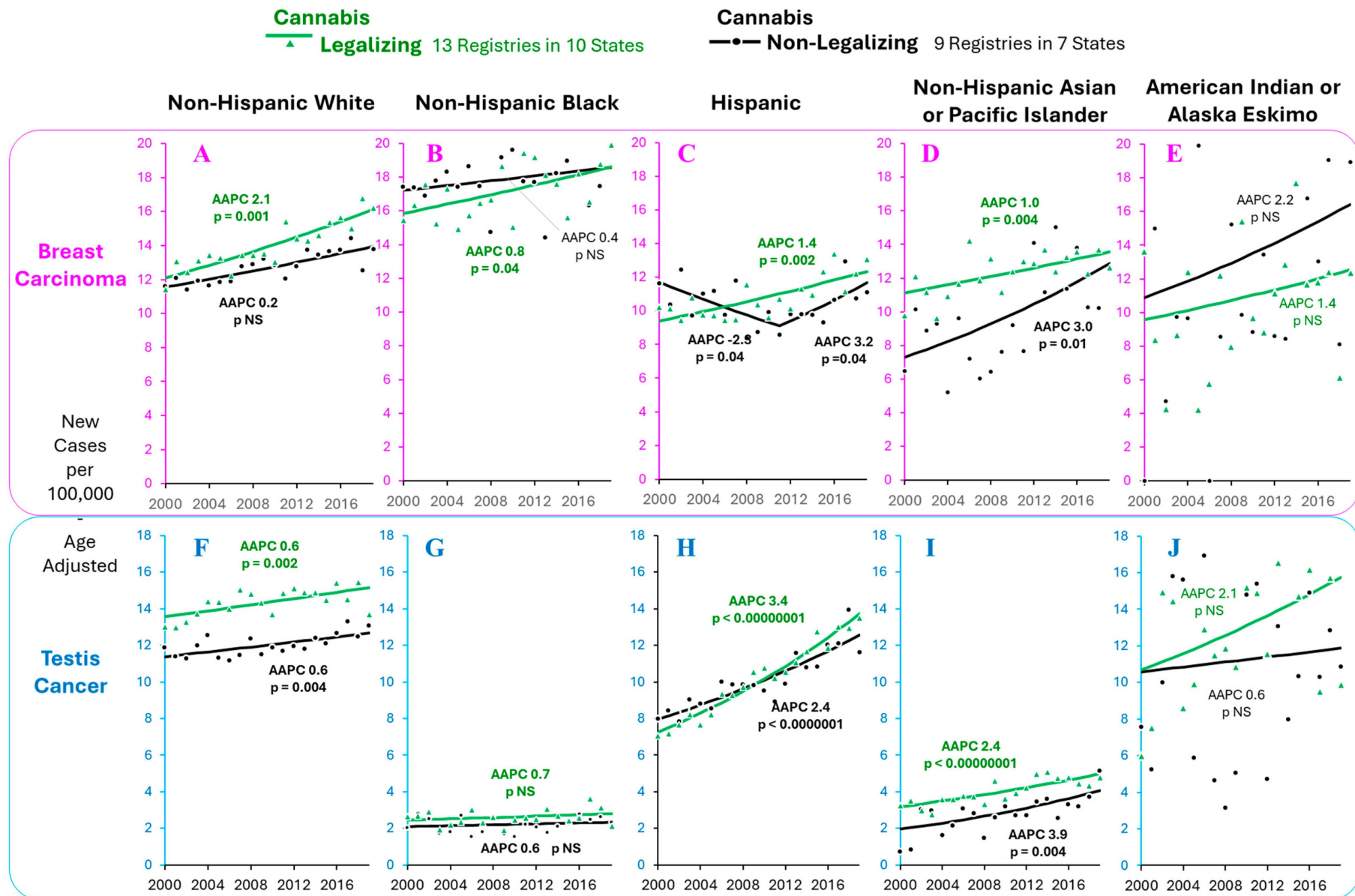
as a breast carcinogen [26], we compared the states’ alcohol consumption with cannabis legalization (Figure 7) [19]. In contrast to cannabis legalization correlations, there was no significant difference between high and low alcohol consumption for either breast carcinoma incidence in 20- to 34-year-old females or testis cancer in 15- to 39-year-old males (Figure 7).

3.6. Cancer incidence trends vs. THC potency

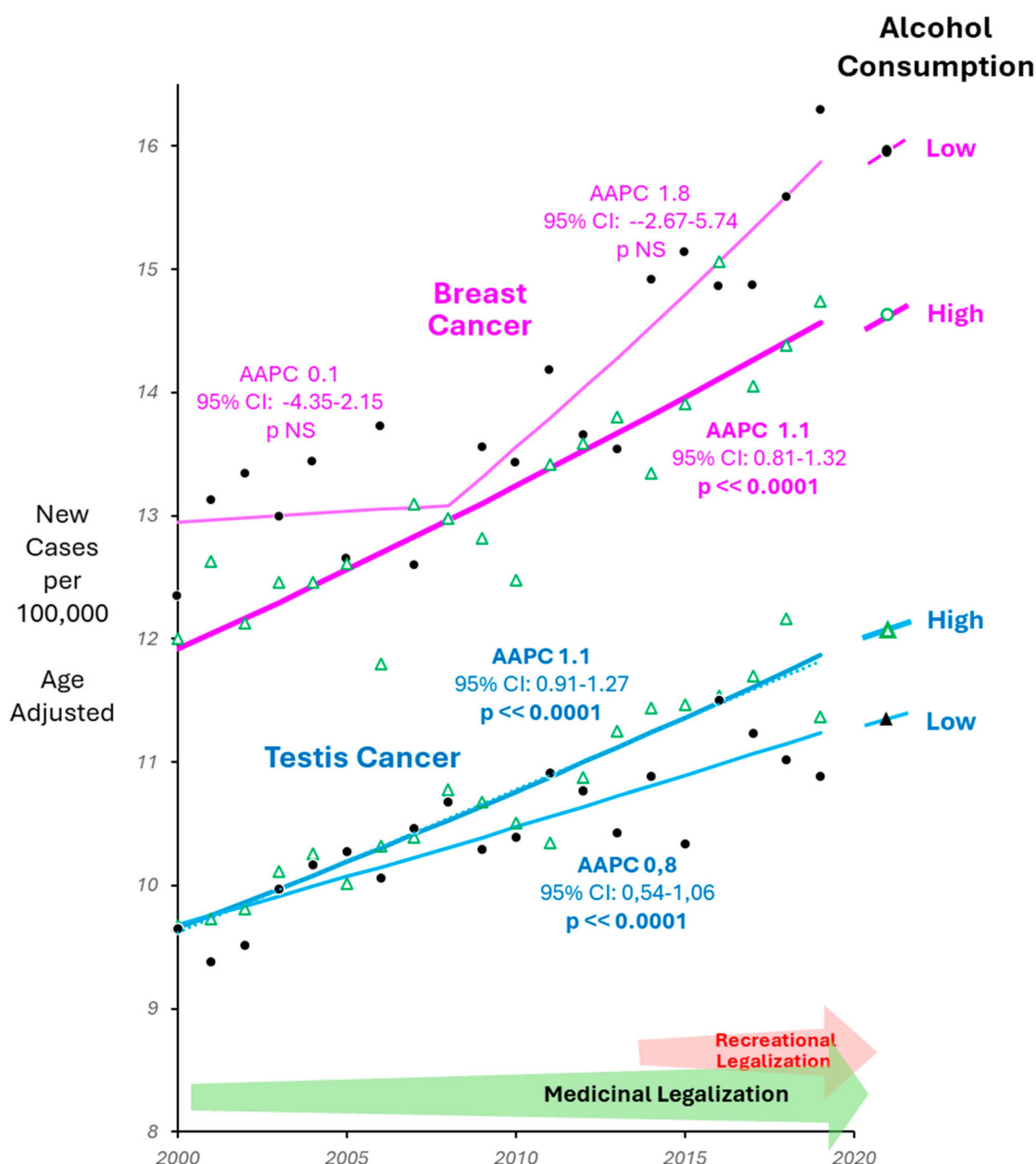
The temporal incidence trends of breast carcinoma and testis cancer in the AYA age groups analyzed were also strongly correlated for both cancers with the THC potency of samples seized and analyzed by the NIDA [20] during the period 2000–2029 (Pearson’s  $r = 0.85$  and  $0.94$ , respectively) (Figure 8).



**Figure 5 •** Annual age-adjusted incidence of breast carcinoma hormonal subtype in females, 2014 \*–2019, age 20–34, in SEER registries that were in states that had (green data) and had not (black data) implemented cannabis legalization as of January 2019. \* 2014, the 1st calendar year that hormonal type data became available \*\*AAPC—average annual percent change, per the SEER\*Stat AAPC program [14]. Data source: SEER22 [14].



**Figure 6 •** Joinpoint/average annual percent change (AAPC) analysis of annual breast carcinoma in 20- to 34-year-old females (upper panel A–E) and testis cancer in 15- to 39-year-old males (lower panel F–J), 2000–2019, by race/ethnicity in SEER22 registries of states that had (green data) and had not (black data) implemented cannabis legalization as of January 2019. AAPC per the SEER\*Stat AAPC program [14]. Data source: SEER22 [14].



**Figure 7 •** Joinpoint/AAPC\* analysis of breast carcinoma in age 20- to 34-year-old females, and testis cancer incidence in 15- to 39-year-old males in SEER22 registries of states with high or low alcohol consumption, 2019. \*AAPC—average annual percent change, per the SEER\*Stat AAPC program [14]. High consumption: >8.74 liters per capita: 14 registries in 11 states: Alaska, California, Connecticut, Hawaii, Illinois, Iowa, Louisiana, Massachusetts, New Jersey, New Mexico, Texas. Low consumption: <8.74 liters per capita: 8 registries in 6 states: Georgia, Idaho, Kentucky, New York, Utah, Washington. Data source: SEER22 [14]; alcohol consumption: National Institute on Alcohol Abuse and Alcoholism [19].

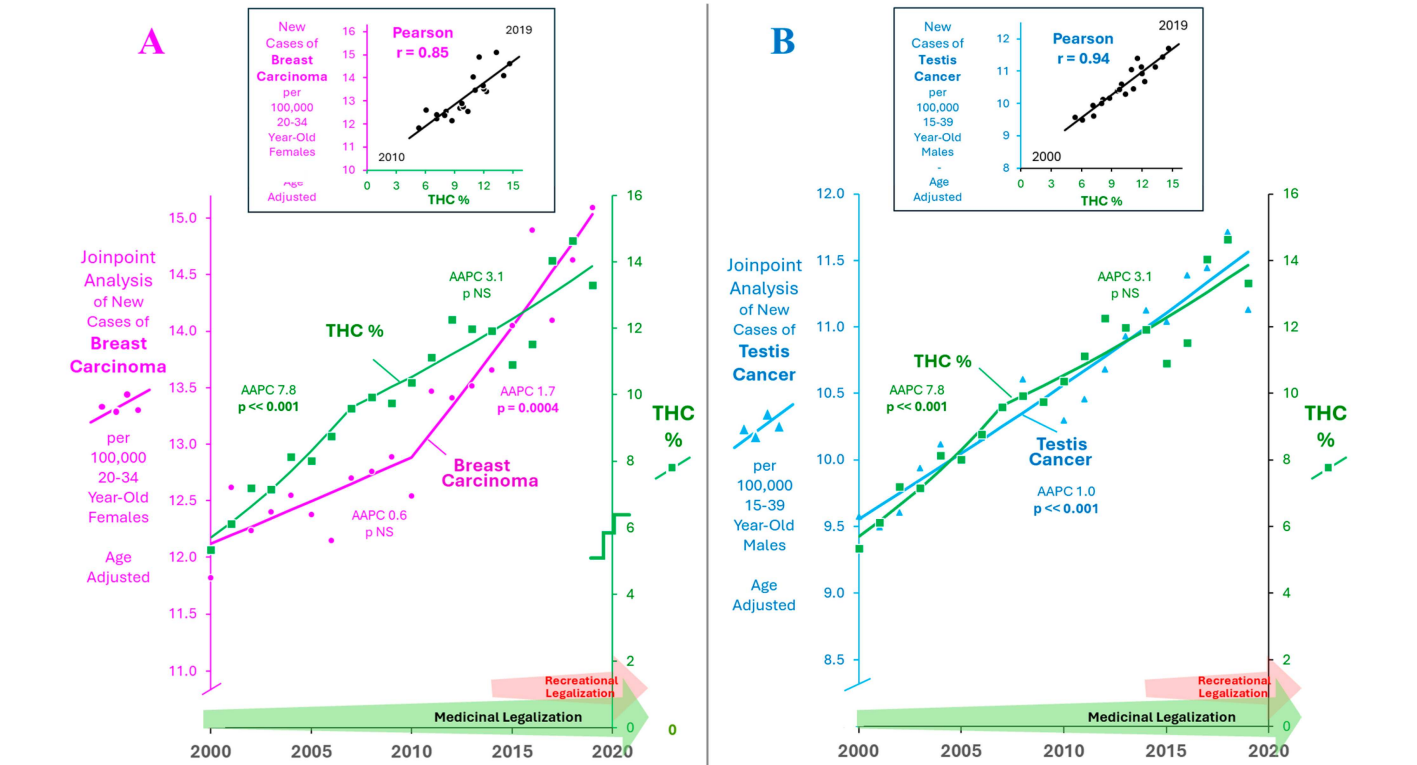
### 3.7. Cancer incidence trends vs. self-reported obesity

As of 2020, the legalizing jurisdictions had a statistically significant lower self-reported mean obesity prevalence, at 29.9% (95% CI, 28.6% to 31.2%), than that in the non-legalizing jurisdictions, 35.1% (95% CI, 33.8% to 36.4%).

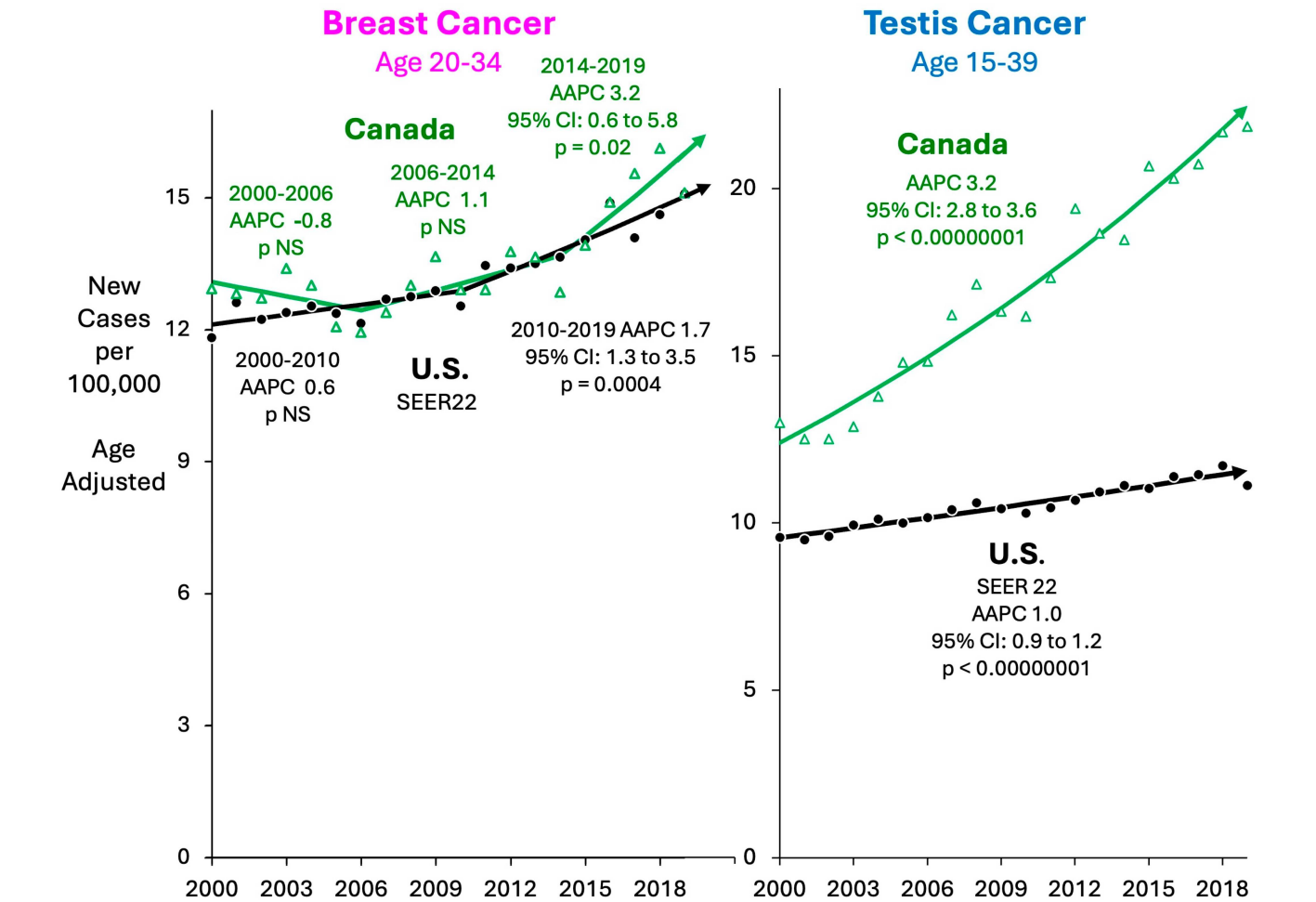
### 3.8. Cancer incidence trends vs. cannabis use disorder in Canada and U.S.

According to the IHME [15], the number of females in Canada who were newly diagnosed with breast carcinoma while 20 to 34 years of age increased by 35% (95% CI, 27% to 39%) from 399 (95% CI, 313 to 504) in 2000 to 537 (95% CI, 397 to 698) in 2019. The increase among 15- to 39-year-old males with newly diagnosed testis cancer

was 83% (95% CI, 77% to 87%), from 703 (95% CI, 581 to 847) to 1289 (95% CI, 1088 to 1499). The incidence increase for breast cancer among 20- to 34-year-old females was similar in Canada and the U.S. until 2014, after which the rate in Canada (AAPC 3.2 [95% CI, 0.6 to 5.9,  $p = 0.02$ ]) was greater than in the U.S. (AAPC 1.7 [95% CI, 1.3 to 3.5,  $p < 0.001$ ]) (Figure 9). The Joinpoint analysis also identified Canada as having switched from a decreasing breast cancer rate during the period 2000–2006 to an increasing rate thereafter, whereas the U.S. had a continuous increase (Figure 9). The testis cancer increase was more pronounced in Canada (AAPC 3.2 [95% CI, 2.8 to 3.6,  $p < 0.001$ ]) than in the U.S. (SEER 22 AAPC 1.0 [95% CI, 0.9 to 1.2,  $p < 0.001$ ]), resulting in an increase in incidence from one-third higher in the early 2000s to twice as high by 2019 (Figure 9).



**Figure 8 •** Joinpoint/AAPC(average annual percent change) analysis of breast carcinoma in females, age 20–34 (A), and testis cancer in males, SEER22 (B) and tetrahydrocannabinol (THC) potency of samples seized in the U.S. by FDA, 2000–2019. Insets: Pearson's correlation of cancer incidence vs. THC potency. Data sources: SEER22 [14] and NIDA [20].

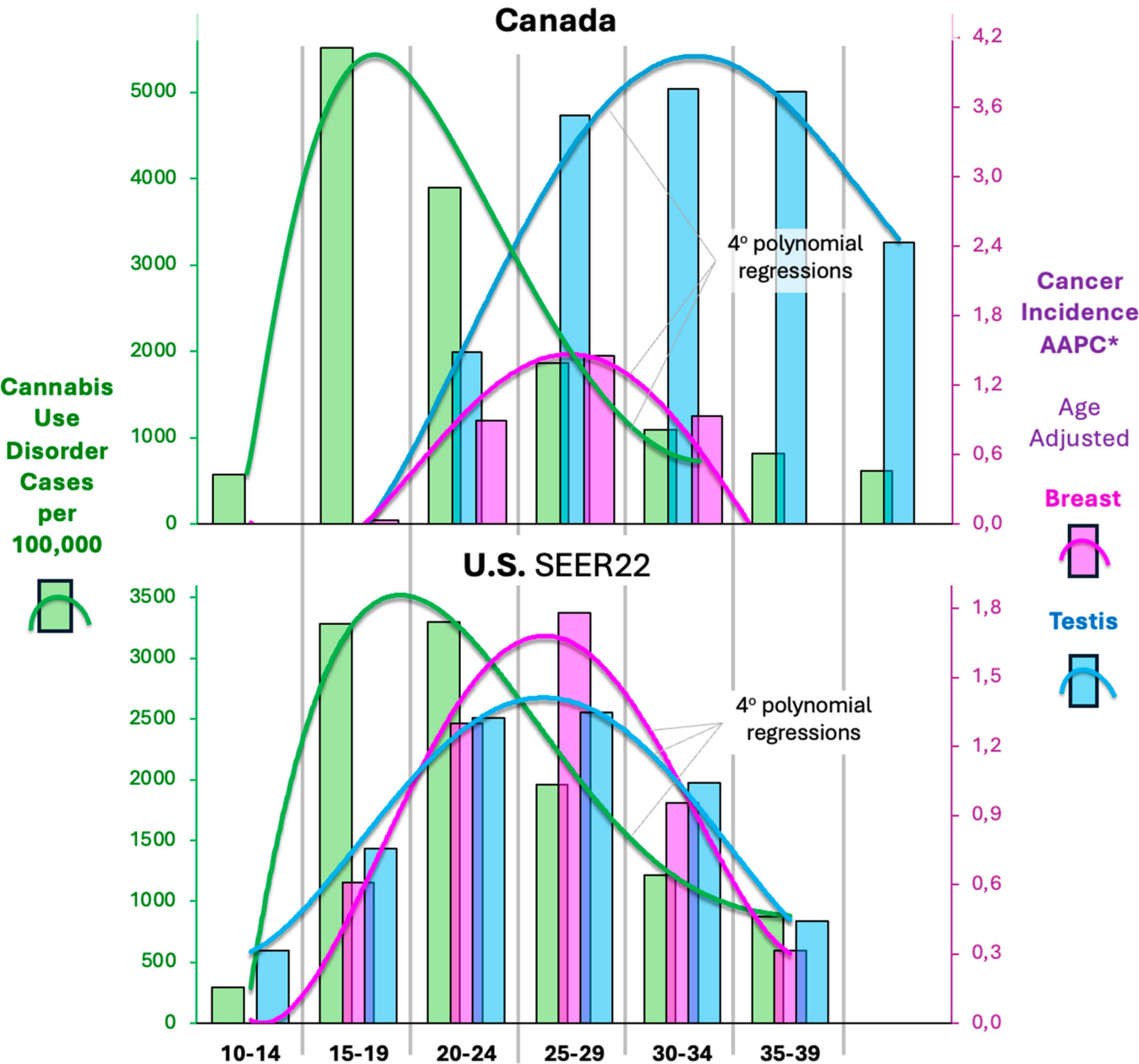


**Figure 9 •** Joinpoint and average annual percent change (AAPC) analysis of breast and testis cancer age-adjusted incidence, 2000–2019, in Canada and U.S. SEER registries. AAPC per the SEER\*Stat AAPC program [14]. Data sources: Canada data: IHME [15]; U.S. data: SEER22 [14].



The prevalence of cannabis use disorder in Canada during 2019 was greatest in 15- to 19-year-olds, next greatest in 20–24-year-olds, and inversely proportional to age in all older age groups. (Figure 10, upper panel, green data). In the U.S., the cannabis use disorder prevalence was lower than that in Canada but also highest in 15- to 24-year-olds and 20- to 24-year-olds (Figure 10, lower panel, green data). Whereas the U.S. has had comparable increases for breast and testis cancer in AAPCs and age peaks (Figure 10,

lower panel), Canada has had a much greater testis cancer increase, which peaked at a later (5 to 10 years older) age than in the U.S. (Figure 10). Both countries have similar age trends for breast and testis cancer increases that occur in residents 5 to 15 years older than the cannabis use disorder age peak (Figure 10). The temporal pattern of peaks in cannabis use disorder and breast and testis incidence AAPCs suggests that the cancers occur clinically within 5 to 15 years after cannabis exposure.



**Figure 10 •** Cannabis use disorder prevalence, 2019, and AAPC in breast and testis cancer incidence, 2000–2019, Canada (top panel) and U.S. SEER registries (lower panel), at ages 15–44 in 5-year intervals. Data sources: U.S. Cancer incidence: SEER22 [14]; cannabis use disorder prevalence and Canada cancer incidence: IHME [15]. \*AAPC—average annual percent change, per the SEER\*Stat AAPC program [14].

#### 4. Discussion

The American Cancer Society currently lists breast and testis cancer as the second and third most rapidly increasing cancers in AYAs, preceded only by thyroid cancer [27]. Compared to older females, those in their 20s have the most rapidly increasing rate of

breast carcinoma [28, 29]. Our U.S. data support the results of Australian researchers [8–10] and their conclusion that increasingly widespread cannabis use is accelerating breast and testis cancer incidence in both the U.S. and Europe. Whereas the Australian studies did not analyze patient age as a variable, our focus was on AYAs, who use cannabis more frequently than all other age

groups; in the U.S, cannabis use is highest among 18- to 25-year-olds) [30, 31]. Our results also indicate that most races and ethnicities in the U.S. show evidence for a cannabis–cancer connection among AYAs. Our previous conclusion that the testis correlation was greater in Hispanic people [13] persists in the current dataset. In this investigation, the cannabis–breast carcinoma correlation was greatest in non-Hispanic White and Black people and the cannabis–testis cancer correlation greatest in Hispanic and Native American people. Our breast cancer correlation is consistent with reports of cannabis use among female adolescents in the U.S. being greatest in non-Hispanic Whites [32].

Canada and the U.S. have similar breast and testis cancer incidence trends in young people and also several potentially important differences relative to the possible effect of cannabis. The greater incidence increase in both breast and testis cancer in Canada compared to the U.S. is consistent with the earlier and nationwide cannabis legalization in Canada in comparison with the more recent and slower, state by state, legalization in the U.S. That both Canada and the U.S. have cannabis use disorder prevalences that are similarly inversely proportional to age also supports the cannabis causation hypothesis. The age pattern (**Figure 10**) suggests that if cannabis is accelerating the incidence of breast and testis cancers, it is doing so in less than 10 years and probably less than 5 years.

Reports other than those by Australian investigators [8–10] have implicated cannabis as a potential cause of cancer [33–35], including breast cancer [34, 35]. Other reports have suggested that cannabis may prevent or slow the progression of breast cancer [36–42] and that cannabis use disorder is not associated with an increased incidence of cancer [43]. The cytotoxic effects of cannabinoids most likely depend not only on the nature of cannabinoids and the presence of other phytochemicals but also on the type of breast cancer [39, 42], as well as on age, genetic inheritance, cannabis potency, and other factors. That both breast and testis cancer incidence were temporally correlated with the THC potency of cannabis products in the U.S. also supports the cannabis–cancer connection hypothesis. It also raises the possibility that legalizing jurisdictions may have had a greater increase in THC potency if the cannabis industry focused on manufacturing such products where it was legal.

That testis cancer incidence increases were found in the same young adult age group and geographical locations of cannabis legislations strengthens the cannabis–breast cancer hypothesis in that testis cancer incidence has previously been associated with cannabis use in multiple reports [44–51], with one exception [52]. Head and neck cancer, especially oral, oropharyngeal, and laryngeal, has been associated with cannabis use disorder [33].

A connection of cannabis with breast cancer is biologically feasible in that epithelial cells and adipocytes in breasts have endocannabinoid receptors [53, 54], especially cannabidiol receptor 1 (CB-1) [41, 55]. In adolescent mice, the number and size of adipocytes in breasts have been shown to decrease after cannabis exposure [56]. If true in humans, developing breast tissue in AYAs may be more vulnerable to a cannabidiol-mediated effect than mature breasts of older human females, in whom the cannabis would have less effect in binding to adipocytes and mediating this effect in the breast. Obesity, which is currently epidemic in U.S. AYAs, could increase breast adipocytes and the associated number of cannabinoid receptors, and thereby further escalate the risk of cannabis-induced breast carcinoma.

Cannabis is also an endocrine disruptor that decreases luteinizing hormone and its activation of several types of gonadotropin receptors. Breasts and testes also have gonadotropin receptors [40, 41, 54, 57, 58] that can be affected by cannabis' biologic effects. The activation of gonadotropin-releasing hormone 2 has been shown to prevent or eliminate early breast cancer [59]. By disrupting gonadotropin-releasing hormone 2, cannabis' inactivation of gonadotropin receptor 2 may therefore be another potential mechanism of breast carcinogenesis. This possibility is supported by environmental breast carcinogens that are endocrine-disrupting chemicals [60]. That our results show triple-negative breast cancer to be the most correlated with cannabis legalization may or may not be consistent with a gonadotropin-mediated mechanism.

Although obesity at the AYA age has been reported to lower the breast cancer risk before menopause [61], central obesity in AYAs has been associated with early-onset triple-negative (hormone-receptor-negative) breast cancer [62]. Our finding of a cannabis–cancer connection with hormone-receptor-negative breast cancer is consistent with this distinction. Also, obesity as a cause of the cancer incidence increase is countered by our observation that the obesity prevalence was significantly lower in the legalizing than non-legalizing jurisdictions. Our cannabis connection hypothesis was also strengthened by the lack of a correlation of alcohol consumption with cannabis legalization.

Cannabis may also reduce treatment effectiveness after cancer occurs. A prospective observational study of newly diagnosed patients with metastatic breast cancer showed a statistically significantly shorter median time to cancer progression (3.4 vs. 13.1 months) and median overall survival (6.4 versus 28.5 months,  $p = 0.0025$ ) [63] for users versus nonusers. Among colon cancer patients, a pre-existing diagnosis of cannabis use disorder was associated with significantly increased odds of five-year mortality (OR = 24.4, 95% CI: 11.4–52.3,  $p < 0.001$ ) [64]. Breast cancer is a common second malignant neoplasm (SMN), both in the contralateral breast in breast cancer survivors [65] and among female AYAs diagnosed with other types of cancer [66, 67]. Half of the AYA females surviving 5 years after a diagnosis of another type of cancer are subsequently diagnosed with breast cancer as an SMN [68]. AYAs diagnosed with breast cancer or with another type of cancer may specifically want to avoid cannabis use.

The legalization progression and potential reclassification of cannabis in the U.S. and other countries considering cannabis legalization may benefit from considering the additional potential risk outlined here. Given cannabis' increasing use in cancer patients, whether or not it is legal in their state [69], and the ongoing federal legislative effort to move cannabis from Schedule I to Schedule III despite adequate science [70], the need to ascertain the carcinogenicity risk of cannabis is even more urgent. The lack of laboratory research to assess the carcinogenicity of cannabis and its myriad biochemical components is apparent to us and should be more adequately pursued.

## 5. Limitations

The primary limitation of our study is its ecologic/correlative nature and the fact that there are many other demonstrated and suspected causes of breast and testis cancer. The only confounding variables that we included were race/ethnicity, THC potency, alcohol consumption, and obesity prevalence. This study is not a

case-control study and we were not able to analyze the amount or frequency of cannabis consumption (as risk factors) on an individual level. Other potential confounding factors not evaluated were how different jurisdictions' cannabis policies influence public health outcomes and overall cancer incidence rates, tobacco habits, hormonal/contraceptive use, socioeconomics, and the familial risk of cancer. Our study was not designed to directly evaluate the future risk of cancers in young adults consuming cannabis products.

Another limitation is that we used SEER data based on half of the U.S. and not the entire country. SEER\*Stat represents locations that were selected to be racially, ethnically, geographically, and socioeconomically representative of the U.S. and has more accurate and extensive incidence data than the national CDC database. We also did not evaluate recreational legalization per se, which began to be implemented in 2013 (as shown in **Figure 3** and **Figure 4**), and by 2019, had six SEER registries in three states, one of which was Natives-only (Alaska) (**Figure 1**). The accuracy of a recreational versus medicinal only comparison was, therefore, considered limiting and not assessed.

## 6. Conclusions

North America has evidence that implicates cannabis as a potential etiologic factor contributing to the increasing incidence of breast carcinoma in young females and testis cancer in older adolescent and young adult males, and in most races and ethnicities. Temporal correlations suggest that a carcinogenic effect of cannabis is rapid, leading to cancer within a few years after cannabis exposure. Given the increasing use and potency of cannabis in the U.S. facilitated by jurisdiction legalization and increasing availability, further research into the role of cannabis as a causative factor of breast and other cancers is warranted. Future analyses of possible cannabis connections should focus on the age group that most uses cannabis, AYAs.

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## Author contributions

A.B. acquired and analyzed the data, generated the figures, and drafted the manuscript; R.H.J. and F.C. analyzed the data and edited the manuscript; R.H.J., A.S. and F.C. reviewed and edited the manuscript; R.H.J. presented some of the content at the 6th Global Adolescent and Young Adult Cancer Congress in December 2024. All authors have read and agreed to the published version of the manuscript.

## Conflict of interest

The authors declare no conflict of interest.

## Data availability statement

The data associated statistical analyses, and figure derivations will be available on a public website: [www.comedsoc.org/2025/01/02/aya-cancer-incidence-increase-artifact/](http://www.comedsoc.org/2025/01/02/aya-cancer-incidence-increase-artifact/).

## Institutional review board statement

Not applicable to this research.

## Informed consent statement

Not applicable to this research.

## Supplementary materials

The supplementary materials are available at <https://doi.org/10.20935/AcadOnco7758>.

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