A Geospatiotemporal Exploration of Sociodemographic Correlates of US Autism: A Convergence of Ecological Sociocultural and Cannabinoid-Related Trends

Short Title:

Sociodemographics, Cannabinoid Use and Autism Spectrum Disorder

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Key Points

Question: Could increased cannabis consumption and its associated cultural trends be a principal driver of the otherwise unexplained rise in US autism rates?

Findings: Using panel and geospatiotemporal regression procedures to analyze nationally representative datasets we found in an ecological study that exposure to cannabis and the selected cannabinoids Δ9-tetrahydrocannabinol and cannabigerol were independently significantly related to the US autism rate after appropriate adjustment for other ethnic, income and drug use covariates.

Meaning: The possibility that increased cannabis use could be driving US autism rates needs to be seriously considered.

Abstract

Importance: Whilst cannabis is known to be toxic to brain function and brain development in many respects it is not known if its increasing availability is associated with the rising US autism rates, whether this contribution is sufficient to effect overall trends and if its effects persist after controlling for other major covariates.

Objective: To determine whether patterns of cannabis use account for US autism rates and the relative importance of identifiable covariates.

Design: An ecological longitudinal epidemiological study using nationally representative datasets covering 1991-2011. The present analysis was conducted in 2019 and based on national autism census data from the US Department of Education Individuals with Disabilities Act (IDEA) published in 2018.

Setting: IDEA dataset was supplemented with nationally representative survey data of the non-institutionalized US population obtained from the National Survey of Drug Use and Health and US Census and CDC Wonder population and birth data.

Participants: Non-institutionalized US population data.

Exposure: Five ethnicities: Caucasian-American, African-American, Hispanic-American, Asian-American and American Indians-Native Alaskans. Five drugs: cigarettes, alcohol abuse, analgesic, cocaine abuse and cannabis use monthly, daily and in pregnancy. Also median household income.

Main outcomes and measures: Hypothesis constructed prior to data analysis. Panel regression was performed for national covariates. Geospatiotemporal regression was conducted by state with state autism rate as the dependent variable. Data processed in R.

Results: At the national level after adjustment cannabis use was significantly related (β-est.=4.374, $P<2.2x10^{-16}$) as was cannabis exposure in the first trimester of pregnancy (β-est.=0.121, $P=1.7x10^{-12}$). At the state level following adjustment cannabis use was significant (from β-est.=8.406, P=0.002); after adjustment for varying cannabis exposure by ethnicity and other covariates (from β-est.=10.881, $P=1.4x10^{-5}$); cannabigerol was significant

(from β-est.=-13.769, P = $1.8x10^{-6}$) and Δ9-tetrahydrocannabinol (from β-est.=1.957, P=$4x10^{-4}$).

Conclusions and Relevance: These associational data support our hypothesis that cannabis use is associated with autism rates at state and national level, is powerful enough to affect overall trends, and persists after controlling for other socioeconomic and ethnic-related covariates. Further study is required to focus these results from the ecological-associational sphere to direct clinical importance. Meanwhile, as indicated by ACOG and AAP, caution is advisable.

Introduction

It is well known that autistic spectrum disorder is growing strongly in the USA at present with rates as high as 1.68% being reported nationwide by CDC [1]. Indeed up to 4.5% of 8 year old boys in New Jersey are said to have been diagnosed with this disorder [1]. For reasons which are unclear the syndrome is much more common in young boys than in young girls although it has been argued that this may relate to the many extra neurological genes on the X-chromosome which is randomly inactivated in females making them genetically mosaic and giving much wider range of spare genetic alleles from which to support neurological development [2].

Whilst the literature identifies several causes which contribute to the incidence of autism, including obesity, maternal diabetes, advanced parental age, links with twins, bleeding, having another autistic sibling, higher income, exposure to some drugs including cannabinoids [3-7], the primary drivers of the present surge have remained largely elusive.

Of concern all three longitudinal studies of brain development following prenatal cannabis exposure (PCE) have identified adverse neurological outcomes mimicking ADHD and autistic spectrum features [8]. At a time of major commercialization of the cannabis industry such findings must be of particular concern.

Because these syndromes are not usually identified prior to the age of 8 years of age there is inevitably a lengthy delay in reporting the current state of the epidemic.

At the time of conducting our analysis we were aware that drug exposure was highly correlated to ethnocultural factors and that PCE was known to be rising across USA. It was felt to be important to take such considerations into account in conducting our analysis.

Our primary hypothesis was that increasing substance- and / or cannabinoid- exposure might constitute a primary underlying driver of US autism. This hypothesis was formulated prior to data analysis. We wished to explore the effects and relative contribution of external demographic and socioeconomic covariates in a formal geotemporospatial framework.

Methods

Data Sources. State autism rates were derived from the US Department of Education Individuals with Disabilities (IDEA) database [9]. State population data from the US Census Bureau were used to calculate national rates. State population, ethnicity and median household income data was sourced from US Census via the tidycensus package in "R" from CRAN. Data on national age of child-bearing was sourced from the births registries of the CDC Wonder website [10]. Drug use data in various demographic subgroups and in pregnancy was taken from the nationally representative National Survey of Drugs and Health (NSDUH) conducted each year by the Substance Abuse and Mental Health Services Administration (SAMHSA) and particularly from the online interactive Substance Abuse and Mental Health Data Archive (SAMHDA [11]). Data on national cannabinoid concentrations was from Drug Enforcement Agency [12,13]. Missing data were casewise deleted except where otherwise described.

State cannabinoid exposure estimates were derived by multiplying the monthly cannabis use rate by state by the concentration of the various cannabinoids obtained in Federal seizures. Data on Δ9-tetrahydrocannabinol (Δ9THC), cannabinol, cannabidiol, cannabigerol, cannabichromene and tetrahydrocannabidivarin were available [12,13].

Ethnicity was defined by SAMHSA and US Census. These official definitions of ethnicity were used in analysis.

Statistics. This study was conducted in 2019. Data was processed using "R Studio" version 1.2.1335 based on "R" version 3.6.1. Variables were log transformed as guided by the Shapiro test. Graphs were drawn with R ggplot2 and bivariate graphs were drawn with colorplaner. For straightforward linear regression least squares regression was employed. Panel regression was conducted for space-time panel data using package plm. Spatiotemporal regression was conducted using functions from spdep and with the spml and spreml functions from R package splm by Millo [14,15]. Model specification was checked with Lagrange multiplier tests and models were compared by their Log Likelihood ratios at optimization using the spatial Hausman test (sphtest). $P<0.05$ was considered significant.

Ethics. All information used was de-identified and publicly available group data. The Human Research Ethics Committee of the University of Western Australia provided ethical approval for the study to be undertaken 7th June 2019 (No. RA/4/20/4724).

Results

National rate of autistic spectrum disorder was derived from the IDEA database combined with state population data obtained from US Census and used to compute national rates of autism. It was combined with other data as shown in Supplementary Table 1 and graphed in Supplementary Figure 1. Since the IDEA database began in 1991 and terminates in 2011 it was extended through to 2018 using conservative published projections [16] which are actually below the most recent CDC estimate (1.31% in 2014 v. 1.68% in [1]). Data on cannabis use by ethnic group, daily cannabis smoking and cannabis use in pregnancy was only available from SAMHSA at the national level which indicated that these variables needed to be analyzed at the national level.

The IDEA dataset for the fifty US states was almost complete for the 18 years 1994-2011. Only five datapoints were missing for this period being New Hampshire in 1994, Montana 2006, Vermont in 2007 and 2008, and Wyoming 2010 and these were filled by temporal kriging (mean substitution).

Figure 1 presents a sequential map series showing the progress of autism across USA 1992-2011. Supplementary Figure 2 presents a bivariate map series of the autism rate together with the cannabis use rate and one notes that both are elevated in the northeast and northwest of the country (pink and purple areas).

Supplementary Figure 3 presents a similar bivariate map of USA showing autism and cigarette use plotted together. As cigarettes decline in use this map appears to be "turning bluer" than the previous map.

Supplementary Figure 4 presents a geofacetted map with US states laid out in approximately their natural position, and shows cannabis use rates by ethnic group. The figure shows that most minority groups tend to use more than Caucasian-Americans with Asian-Americans a notable exception who generally use less.

The UN 2019 World Drug Report clearly demonstrates that recent American use of cannabis relates primarily to increased daily use [17]. SAMHSA provide data that stratify the monthly frequency of cannabis use into groups as non-user, 1-2 days, 3-5 days, 6-19 days and 20-30

days shown in Supplementary Figure 5. The confidence intervals are taken directly from SAMHDA. Again one notes that Asian-Americans smoke less cannabis 20-30 days per week and more are non-users. Using the midpoint of these daily intervals as a multiplicand it is possible to calculate the mean daily use of each ethnic group over time with the results shown in Figure 2. Clear differences in mean daily cannabis use by ethnicity are evident.

As disclosed by UNODP the pattern of cannabis use matters. SAMHDA data show that in 2017 about 92.6% of Americans smoked cannabis to a trivial extent ($\leq$ 3 days per month) and 7.35% smoked it more than that (Supplementary Table 2).

Supplementary Table 3 shows the results of linear regression of daily cannabis use rates by ethnicity in a model quadratic with time and confirms highly significant differences in cannabis use by ethnicity (from β-est.=1.219$\pm$0.106, $P<2.2x10^{-16}$; quadratic superior to linear model, Anova F = 2.147, df=13, P=0.019).

These data allow the calculation of an ethnic cannabis use index (RaceRateSum) which can be plotted against a State-Time index and against time (Supplementary Figure 6A and 6B). These data show that in the case of each state the ethnicity index rose across time. The red line in the centre of Panel B shows the median trajectory as a loess curve of best fit.

Figure 3 considers daily and near daily cannabis use and related indices. Panel A shows that high intensity cannabis use is falling amongst teenagers, but rising in older age groups. Panel B confirms this trend in the first trimester of pregnancy which shows more cannabis use than later trimesters. Panel C has been drawn from CDC birth data and confirms the trend of childbirth to be occurring at older maternal ages. In the light of the findings of Panel A this implies that these women are moving up into a higher cannabis use age bracket.

Panel D confirms that first trimester cannabis use is rising with time, a trend not seen at later trimesters. The SAMHSA data for 2015 is incomplete so this point has been filled by mean substitution (0.027). The correlation between time and the rising use of cannabis in pregnancy is R= 0.6115 (P=0.00118). The slope of the first trimester regression line is significantly different to that in the third trimester (β-est. = $-4.97x10^{-8}$, P = 0.007, model Adj. R^2 = 0.174, F = 4.31, df = 3,44, P = 0.009).

These data invite exploration by regression analysis. Panel regression was utilized as time is an implicit variable rather than an explicit one (important in small regression tables), and one can easily include both temporal lags and instrumental variables in the R package plm. Only a limited number of variables can be included because of the small number of the observations. A variable for cannabis exposure has been derived called the product_of_mean_days_of_cannabis_useage_with_THC_potency (MeanddPot) to quantify exposure to high intensity cannabis use. Cigarettes, the cannabis index, analgesics, three races and median household income (MHY) have been included as main effects. When the regression is performed for the national autism rate in this manner the results indicated in Table 1A are obtained. A very high level of statistical significance of all the variables is noted (all $P < 2.2x10^{-16}$).

When a similar exercise is conducted modelling the autism rate as a function of first trimester cannabis use and THC potency again very high levels of statistical significance are seen (Table 1B).

Naturally we were interested to explore if these relationships extended to an analysis at state level. Supplementary Figure 7 sets out the geospatial links and weights which were defined by the function poly2nb from R's spdep package with Alaska and Hawaii elided (moved) conceptually to Oregon and Washington and to California respectively.

Geospatial regression was performed using the splm::spreml function including both spatial autocorrelation errors and spatial lags and random effects using the error structure of Kapoor, Kelejian and Prucha [18]. As shown in Supplementary Table 4 five drugs – cigarettes, alcohol abuse, misuse of analgesics, cocaine - and the five US races - Caucasian-American, African-American, Hispanic-American, Asian-American and American Indians and Alaskan Natives – were considered as main effects, and instrumental variables were used for monthly cannabis use, Δ9THC and cannabigerol and the annual ethnic cannabis exposure index was used to control for cannabis exposure arising in relation to ethnic origin. A three way interaction term included cigarettes, cannabis and opioids. As shown in Supplementary Table 4 significant results for cannabis were obtained (from β-est. = 8.406 ± 2.719, P = 0.002) at two years lags.

Clearly in such a study one is concerned that ethnocultural factors relating to increased drug exposure in certain communities might be acting in addition to ethnopharmacogenomic factors relating to different responses to or processing of addictive drugs. In order to control at least in part for this effect we performed a further regression not with the states' racial composition but with the sum of the race rates for cannabis use described above (RaceRateSum). The instrumental variable list was similar to that described above. These results are shown in Supplementary Table 5 where terms including cannabis are noted to be significant (from β-est. = 10.881$\pm$2.505, P = 1.4×10^{-5}) at two years lag.

Finally we were interested to learn if the inclusion of specific cannabinoids in the model would be significant when race and median household income were included. The regression results from spatial two-stage and lagged models are shown in Table 2. Terms including cannabinoids are significant in an unlagged model (from β-est.= -13.770$\pm$2.884, P = 1.8×10^{-6}). The log likelihood values at model optimization are as shown. Spatial Hausman tests confirm that the un-lagged model is superior to the models lagged to two and four years (ChiSq. = 66.879, df = 9, P = 3.21×10^{-11} and ChiSq.= 626.46, df = 9, P = 8.744×10^{-129}).

Discussion

This study is an epidemiological study which uses panel and geospatial regression to analyze ecological covariates of childhood autism across a diverse range of domains including socioeconomic, ethnicity and drug exposure on a state and national basis. A particular focus of this report is on environmental exposure to cannabis and selected cannabinoids which have been noted to be neurotoxic with effects on foetal brain development including microcephaly, anencephaly and impaired child neurological development [8,19-22].

Spatiotemporal regression studies implicate both ethnic and drug exposure variables as being significantly associated with autism incidence with three ethnicities, Caucasian-American, Asian-American and American Indian and Alaskan Native Americans, three drugs, tobacco, alcohol abuse or dependence and two cannabinoids Δ9THC, and cannabigerol, remaining in final models with high level statistical significance. Of importance one notes that autism is rising whilst the use of the classical intoxicants tobacco and alcohol is falling. Since opioid and cocaine use only impact a small segment of the community this naturally impugns cannabis use which alone is rising dramatically.

However it is equally clear that within the present circumstance in the USA in recent years these various changes are not occurring independently but appear to be emerging as a confluent stream of broader sociocultural events which together appear to be conspiring to drive the autism rate. Women are having their children later and in so doing are moving into older cohorts with a longitudinal history of greater cumulative cannabis exposure. The US population is undergoing long term changes in ethnic population ratios with minority populations mostly growing faster than the majority Caucasian-American population, and with the notable exception of Asian-Americans, most of these minorities are now using more cannabis than the dominant ethnic group. The rate of cannabis exposure during the first trimester of pregnancy is growing steeply as cannabis use in the wider population increases. Whilst cannabis was only used more than three days per month by 7.35% of the population in 2017, high intensity cannabis use has grown dramatically across USA in the past decade with overall daily or near daily use doubling nationwide [17] and having increased from 0.38% to 1.5% in the >35 years cohort 2002-2017 (Figure 3 [11]).

In this sense therefore the present rapid increase in numbers presenting with child autism is occurring on a vortex driven by confluent and converging sociodemographic trends in the wider culture where high intensity cannabis use is becoming more common. It is noted that amongst regular smokers of cannabis first trimester exposure will occur almost inevitably even when the mother stops cannabis consumption upon receiving a diagnosis of pregnancy due to the long half-time of cannabis retention and excretion from body fat stores in regular cannabis smokers [23,24].

That cannabis potency and use is increasing, is retained in tissue for significant periods, and has been shown to have a number of severely neurotoxic activities particularly on the developing brain is pertinent. Several reports from CDC have linked cannabis exposure with anencephalus [20,21] with separate data linking it to spina bifida in Canada [19], microcephaly in Hawaii [22] and adverse child neurological outcomes in Pittsburgh, Toronto and Netherlands [8]. A generalized inhibitory effect on cell growth has been reported [25-28], as have interference with synapse formation by inhibition of neuroligin and neurexin, key partners in synapse formation and determination [7,29,30]; an uncoupling of neuronal mitochondrial oxidative phosphorylation [31,32] and of grey-white matter connections [33], and increase in astrogliosis [24], neuroinflammation [34] and thus brain aging [35], an inhibition of brain neurogenesis and thus plasticity [36,37] an adverse effect on the slit : robo ratio which is one of the key determinants of the formation of the exuberant cortex characterising human beings [38,39] along with numerous other genetic and epigenetic disruptions [40-43].

The present study has a number of strengths and weaknesses. Its strengths include the use of several nationally representative databases, the application of geospatial analytical techniques to these questions for the first time to our knowledge, the timeliness of the information presented, and the cultural and community-wide implications at a time when cannabis use is expanding rapidly. The limitations of the present study relate mainly to its ecological design which include the lack of individual participant-level data. The findings of this detailed statistical epidemiological exploration of these wide-ranging sociodemographic and pharmacological exposure studies are however strongly provocative and indicate further case-control and basic science research in the area.

Given that the data we have employed come from the USA, which by many metrics is the world's leading nation, we feel that the study findings are in all probability likely to be

generalizable to other nations and other scenarios. Whilst there are to our knowledge no other similar wide-ranging analyses of autism, adverse reports of neurological function following widespread cannabis use have issued from other countries such as Egypt, China, India and Morocco [17] and it is not inconceivable that adverse child neurological development is similarly caught up in these apparently community-wide accounts.

Our interpretation of the present investigations therefore accords with that expressed by CDC, ACOG and AAP that increased drug exposure during pregnancy is likely to adversely affect foetal development. Converging sociocultural trends relating to increased cannabis use by men and women in older age groups, and of non-Asian-American ethnic background and delayed child bearing conspire in an environment of increasing cannabis commercialization and high intensity use to create conditions conducive to disordered brain development in the young. Our results implicate both Δ9THC and cannabigerol in these associational studies which suggest that merely lowering the Δ9THC content of widely available cannabinoid preparations would not constitute a sufficient public health response. These data confirm at the ecological and associational level our opening hypothesis that increased cannabis use and its related socioethnodemographic trends is likely to be shown in time to be one of the primary principal drivers of US autism. In view of the present aggressive growth phase of the emerging cannabis industry further research on the factors identified in this ecological study, including higher definition spatiotemporal epidemiological studies, are indicated.

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ASR assembled the data, designed and conducted the analyses, and wrote the first manuscript draft. GKH provided technical and logistic support, co-wrote the paper, assisted with gaining ethical approval, provided advice on manuscript preparation and general guidance to study conduct.

Neither author has conflicts of interest to declare.

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Table 1.: National Panel Regression Model Results

Model Type	Dependent Variable	Instrumental Variables	Parameter	Parameter				Model		
				Estimate	Std. Error	t value	Pr(>|t|)	Chi.Squ.	dF	P
General Population Model										
2 Lags, 1 Interactions										
plm(AutRateNational) ~ cigmon * MeanddPot + MHY + anlyr + White + Black + Hispanic										
plm	AutRateNational	lag(mrjmon), 0:2	Cigarettes, Monthly	31.8300	1.0357	30.733	< 2.2e-16	48.2761	2	3.29E-11
		lag(d9THCRt), 0:2	African-American	11.1520	0.2820	39.546	< 2.2e-16			
		lag(CBGRt), 0:2	MeanddPot	4.3744	0.1589	27.529	< 2.2e-16			
		cocyr	Hispanic	0.8344	0.0307	27.223	< 2.2e-16			
			Median Household Income	0.0000	0.0000	37.588	< 2.2e-16			
			Non-medical use of Analgesics	-2.9764	0.1423	-20.921	< 2.2e-16			
			Caucasian-American	-14.7900	0.2553	-57.938	< 2.2e-16			
			cigmon:MeanddPot	-18.6450	0.6632	-28.114	< 2.2e-16			
Modelling the Effect of First Trimester Pregnancy Exposure										
2 Lags, 1 Interaction										
plm(AutRateNational) ~ cigmon * MeanddPot + MHY + anlyr + White + Black + Hispanic										
plm	AutRateNational	lag(TrimCanExp), 0:2	TrimCanExp:Potency	-0.0627	0.0064	-9.7767	< 2.2e-16	4109.61	4	<2e-319
		lag(Potency), 0:2	Caucasian-American	-6.1912	0.4521	-13.695	< 2.2e-16			
		lag(White), 0:2	TrimCanExp	0.1210	0.0172	7.0543	1.7E-12			
		lag(Hispanic), 0:2	Cocaine	0.2519	0.0459	5.4942	3.9E-08			

Abbreviations:		
	MeanddPot :	Mean Days of Cannabis Use by Ethnicity (RaceRateSum) x THC Potency
	TrimCanExp:	Trimester cannabis exposure
	d9THCRt:	Δ9-Tetrahydrocannabinol exposure
	CBGRt:	Cannabigerol exposure
	cocyr:	Annual cocaine exposure

Table 2.: Geospatial Regression of Autism Rate by Individual Cannabinoids Race and Income

General			Parameters					Model			
Model Type	**Technique**	**Instumental + Lagged Variables**	**Parameter**	**Estimate**	**Std. Error**	**t value**	**P-Value**	**LogLik**	**Parameters**	**Value**	**P-Value**
SEM2SRRE	spreml		***Interactive Models***								
SLAG	spatial.error=		***0 Lags***								
	"kkp"	mrjmon	***spreml(AutRt) ~ cigmon * ΔTHC * CBG * anlyr + Alcohol_Abuse + cocyr + MHY + 5_Races)***								
	random	Δ9THC	NHAsian	0.4330	0.0506	8.5611	< 2.2e-16	220.3128	phi	1.6E-07	NA
	Spatial lag	Cannabigerol	NHWhite	2.0050	0.2972	6.7466	1.5E-11		psi	0.9386	< 2.2e-16
	AR1 Serial	NHWhite_Score	CBG: Alcohol_Abuse	-13.7698	2.8838	-4.7749	1.8E-06		rho	-0.6020	2.2E-09
	Correlation	NHBlack_Score	Alcohol_Abuse	-44.3493	10.9914	-4.0349	5.5E-05		lambda	0.5000	< 2.2e-16
	Spatial Error	Hispanic_Score	CBG	0.8092	0.2437	3.3206	0.0009				
		NHAsian_Score	NHAIAN	-0.0438	0.0141	-3.1100	0.0019				
		NHAIAN_Score	cigmon: CBG: Alcohol_Abuse	8.9123	3.1168	2.8594	0.0042				
			d9THC	4.5891	1.6204	2.8321	0.0046				
			cigmon: d9THC	-16.2288	6.3303	-2.5637	0.0104				
			d9THC: CBG	0.9431	0.3710	2.5424	0.0110				
			cigmon: d9THC: CBG	-3.3925	1.4394	-2.3568	0.0184				
SEM2SRRE	spreml		***2 Lags***								
SLAG	spatial.error=	mrjmon,0:2	***spreml(AutRt) ~ cigmon * ΔTHC * CBG * anlyr + Alcohol_Abuse + cocyr + MHY + 5_Races)***								
	"kkp"	Δ9THC, 0:2	NHAsian	0.4211	0.0604	6.9754	3.1E-12	178.8988	phi	0.0000	1.0000
	random	Cannabigerol, 0:2	NHWhite	1.9476	0.3682	5.2895	1.2E-07		psi	0.9378	< 2.2e-16
	Spatial lag	NHWhite_Score, 0:2	Alcohol_Abuse	-43.9184	13.2900	-3.3046	0.0010		rho	-0.4350	0.0011

	AR1 Serial	NHBlack_Score, 0:2	NHAIAN	-0.0547	0.0166	-3.3014	0.0010		lambda	0.4158	5.4E-07
	Correlation	Hispanic_Score, 0:2	CBG: Alcohol_Abuse	-11.2444	3.5087	-3.2047	0.0014				
	Spatial Error	NHAsian_Score, 0:2	d9THC	1.1414	0.4042	2.8236	0.0047				
		NHAIAN_Score, 0:2	CBG	0.8095	0.2977	2.7193	0.0065				
			d9THC: CBG	0.2451	0.1079	2.2710	0.0231				
			NHAfrican-American	0.0818	0.0410	1.9928	0.0463				
SEM2SRRE	spreml		***4 Lags***								
SLAG	spatial.error=	mrjmon,0:4	***spreml(AutRt) ~ cigmon * ΔTHC * CBG * anlyr + Alcohol_Abuse + cocyr + MHY + 5_Races)***								
	"kkp"	Δ9THC, 0:4	NHAIAN	-0.1096	0.0141	-7.7528	9.0E-15	132.859	phi	7.3530	0.0002
	random	Cannabigerol, 0:4	NHAsian	0.3682	0.0707	5.2055	1.9E-07		psi	0.8793	< 2.2e-16
	Spatial lag	NHWhite_Score, 0:4	NHWhite	1.5197	0.3954	3.8432	0.0001		rho	-0.4960	0.0011
	AR1 Serial	NHBlack_Score, 0:4	CBG: Alcohol_Abuse	-22.6824	6.2318	-3.6398	0.0003		lambda	0.3196	0.0016
	Correlation	Hispanic_Score, 0:4	d9THC	1.9574	0.5530	3.5399	0.0004				
	Spatial Error	NHAsian_Score, 0:4	Alcohol_Abuse	-72.4519	21.3347	-3.3960	0.0007				
		NHAIAN_Score, 0:4	cigmon: CBG: Alcohol_Abuse	71.6493	23.5907	3.0372	0.0024				
			cigmon: d9THC	-6.4419	2.1347	-3.0177	0.0025				
			cigmon: Alcohol_Abuse	214.5583	80.3987	2.6687	0.0076				

Abbreviations:

NHAsian :	Non-Hispanic Asian-American
NHAIAN:	Non-Hispanic American Indian or Alaska Native
d9THC:	Δ9-Tetrahydrocannabinol
CBG:	Cannabigerol
anlyr:	Analgesic misuse in past year
cocyr:	Cocaine use in past year

cigmon:	Cigarettes use in past month
Alcohol_Abuse:	Alcohol dependence or misuse in the past year (coded as abodalc in NSDUH, SAMHSA).
MHY:	Median Household Income
5_Races:	Caucasian-American, African-American, Hispanic-American, Asian-American, NHAIAN.

Figure Captions

Figure 1.: Map-sequence of autism rates across USA 1992-2011. Data from IDEA Dataset in reference 4.

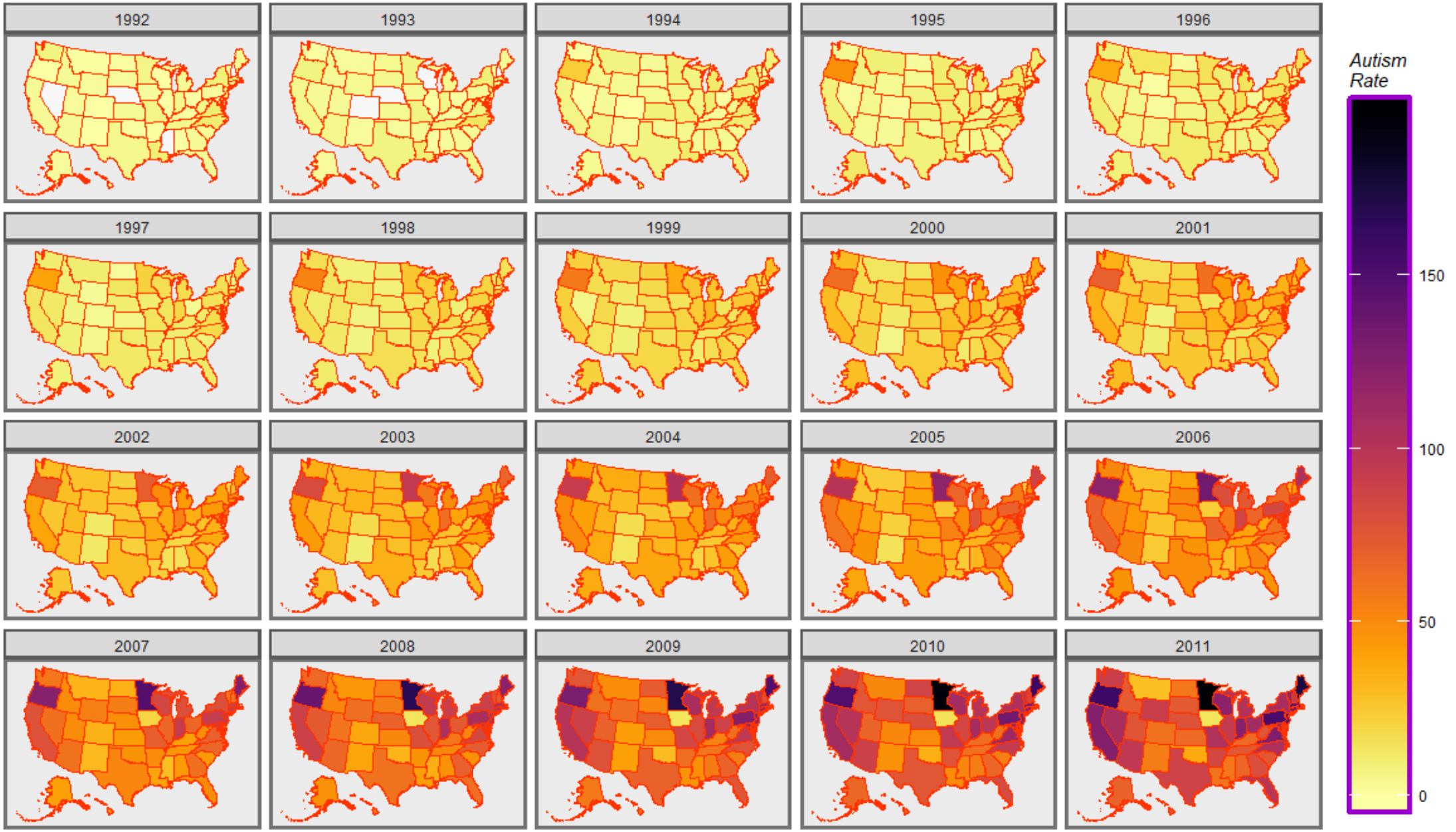
Figure 2.: Mean Cannabis Use by Ethnicity. Data from SAMHDA from SAMHSA.

Figure 3.: Major Relevant Cultural Trends. (A) Percentage of Daily or near daily cannabis use by age group, SAMHDA data; (B) Percentage of daily or near daily cannabis use by pregnancy trimester, SAMHDA data; (C) Age of maternal child-bearing, Data from CDC Wonder; (D) Overall Cannabis use rates in pregnancy by trimester, data from SAMHDA.

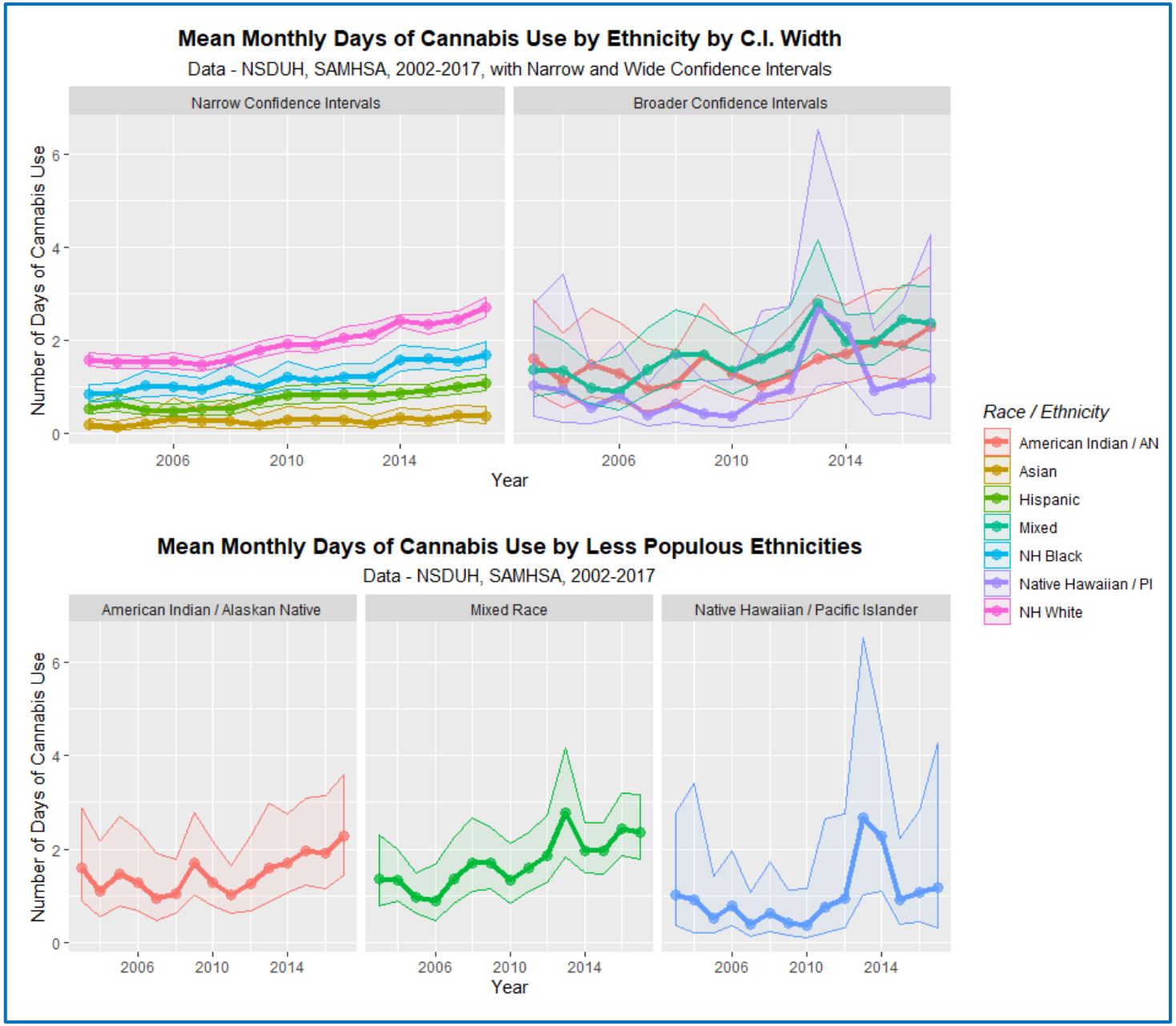
F1

Autism Spectrum Disorder Rate Across USA Over Time

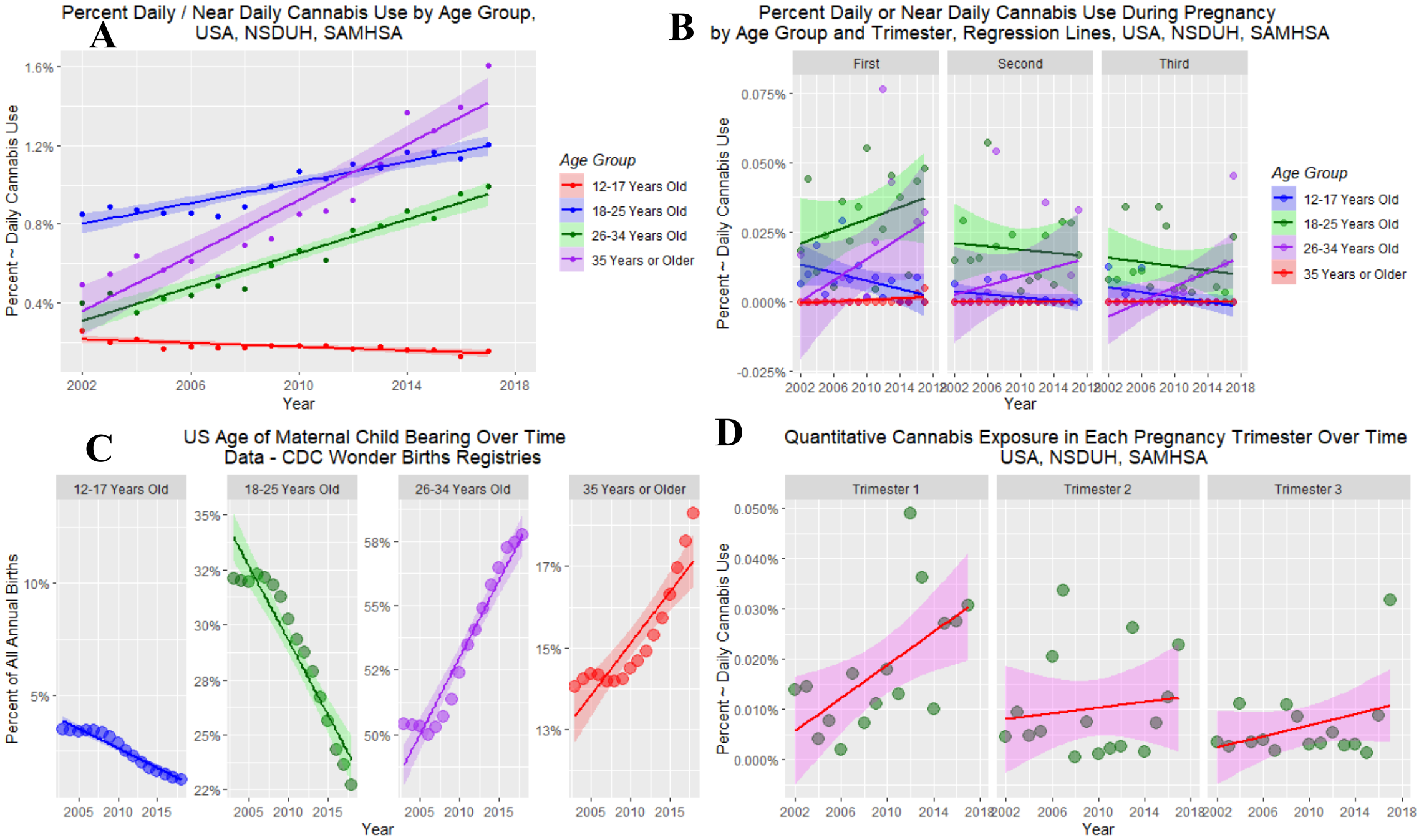
Data: IDEA Dataset, 1992-2011



F2 Mean Cannabis Use by Ethnicity



F3

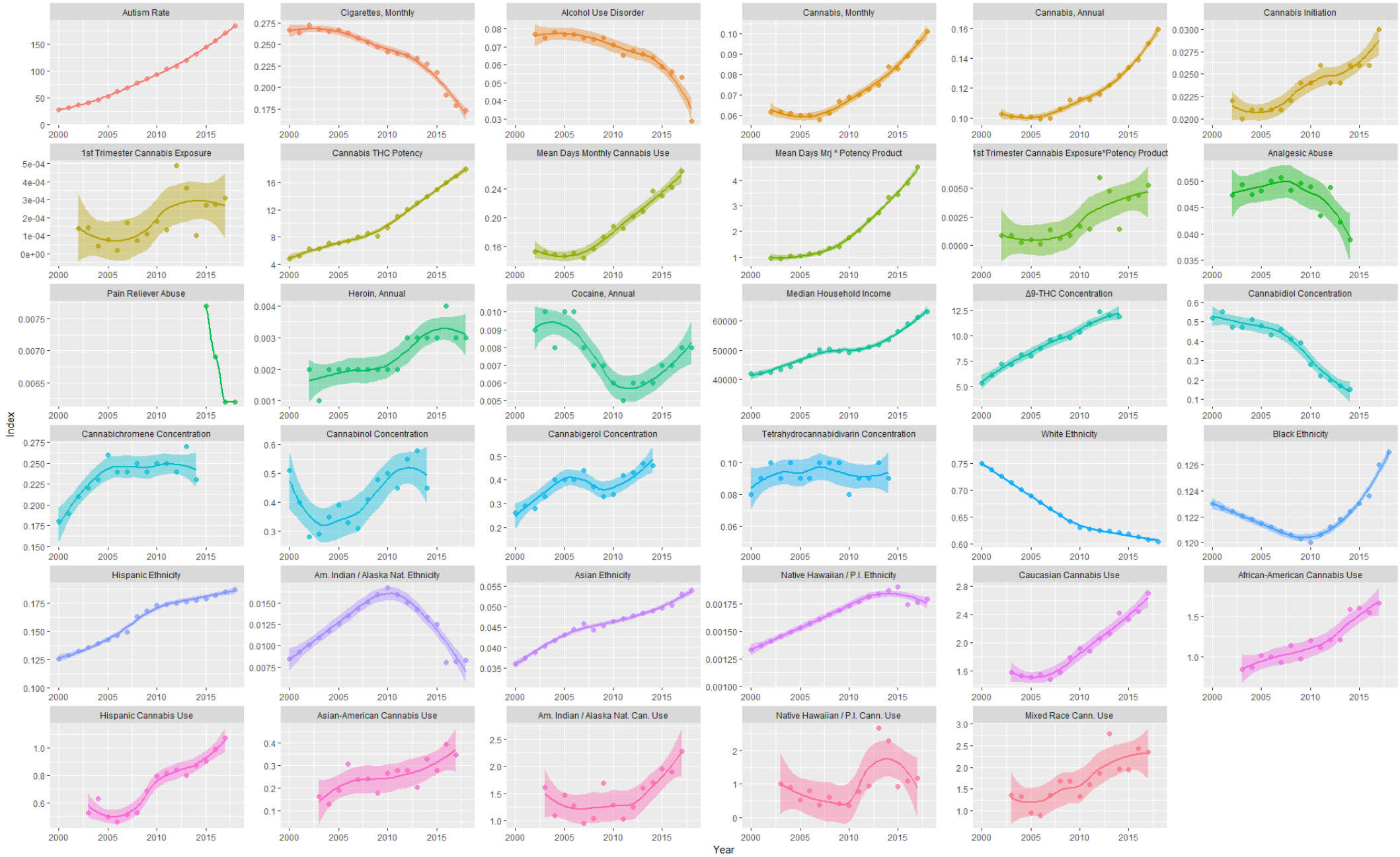

A
Percent Daily / Near Daily Cannabis Use by Age Group,
USA, NSDUH, SAMHSA
Percent ~ Daily Cannabis Use
1.6%
1.2%
0.8%
0.4%
2002
2006
2010
2014
2018
Year
Age Group
12-17 Years Old
18-25 Years Old
26-34 Years Old
35 Years or Older
B
Percent Daily or Near Daily Cannabis Use During Pregnancy
by Age Group and Trimester, Regression Lines, USA, NSDUH, SAMHSA
First
Second
Third
Percent ~ Daily Cannabis Use
0.075%
0.050%
0.025%
0.000%
-0.025%
2002 2006 2010 2014 2018
Year
Age Group
12-17 Years Old
18-25 Years Old
26-34 Years Old
35 Years or Older
C
US Age of Maternal Child Bearing Over Time
Data - CDC Wonder Births Registries
12-17 Years Old
18-25 Years Old
26-34 Years Old
35 Years or Older
Percent of All Annual Births
10%
5%
35%
32%
30%
28%
25%
22%
58%
55%
52%
50%
17%
15%
13%
2005 2010 2015
Year
D
Quantitative Cannabis Exposure in Each Pregnancy Trimester Over Time
USA, NSDUH, SAMHSA
Trimester 1
Trimester 2
Trimester 3
Percent ~ Daily Cannabis Use
0.050%
0.040%
0.030%
0.020%
0.010%
0.000%
2002 2006 2010 2014 2018
Year

SF1

Input Parameters

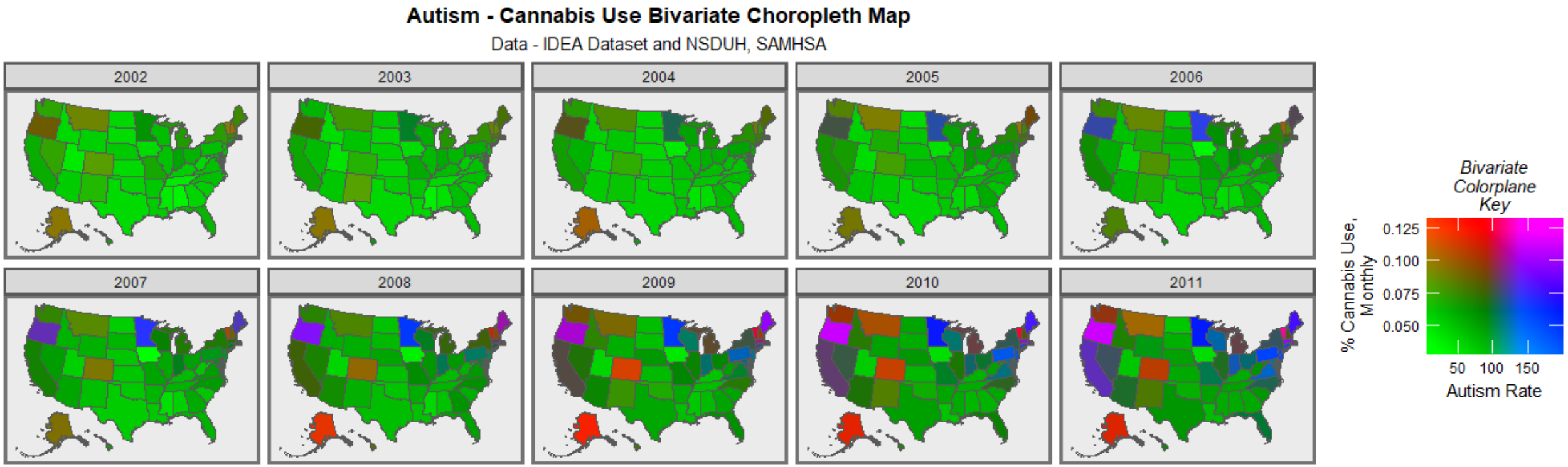
Major Drug, Ethnic and Income Paramaters, USA, 2000-2018

Data: DEA, US Census Bureau, NSDUH, SAMHSA



SF2

Bivariate Autism-Cannabis

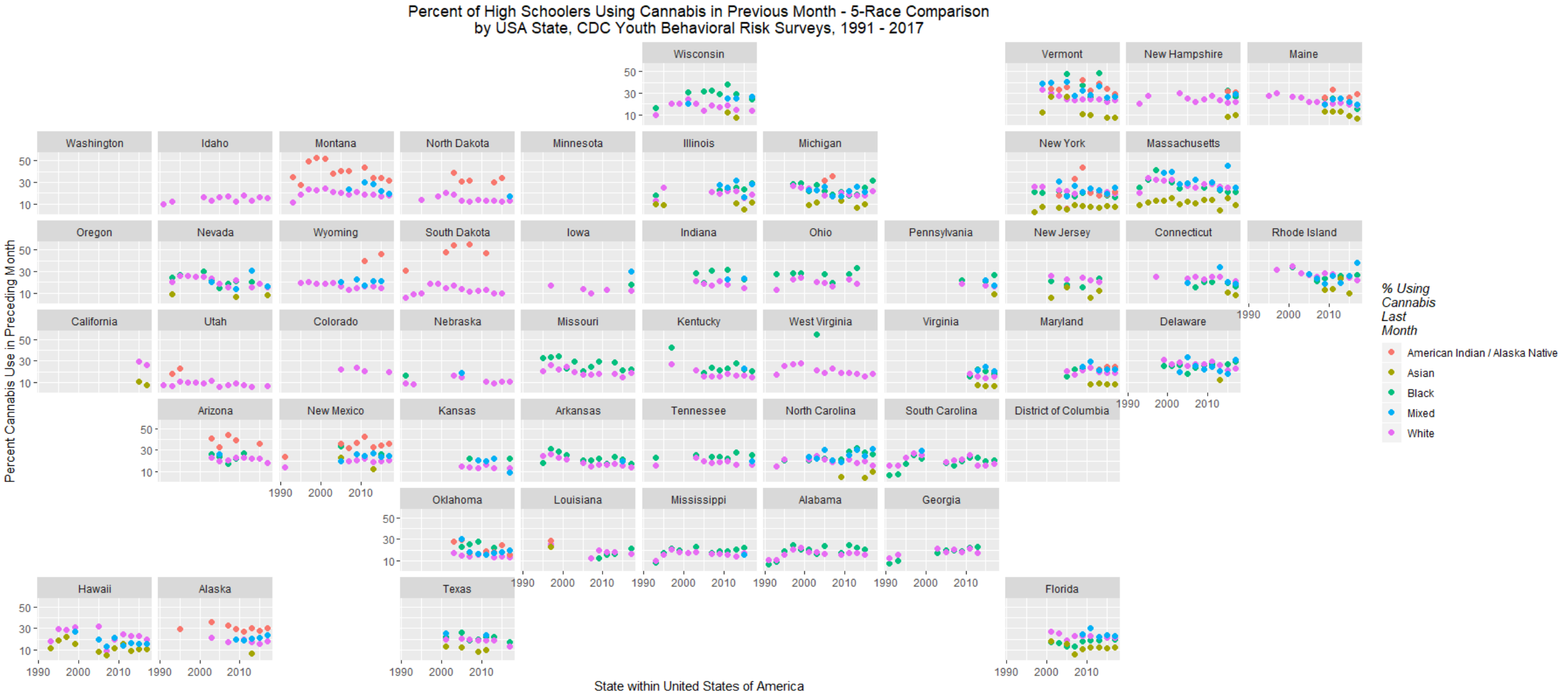


SF3

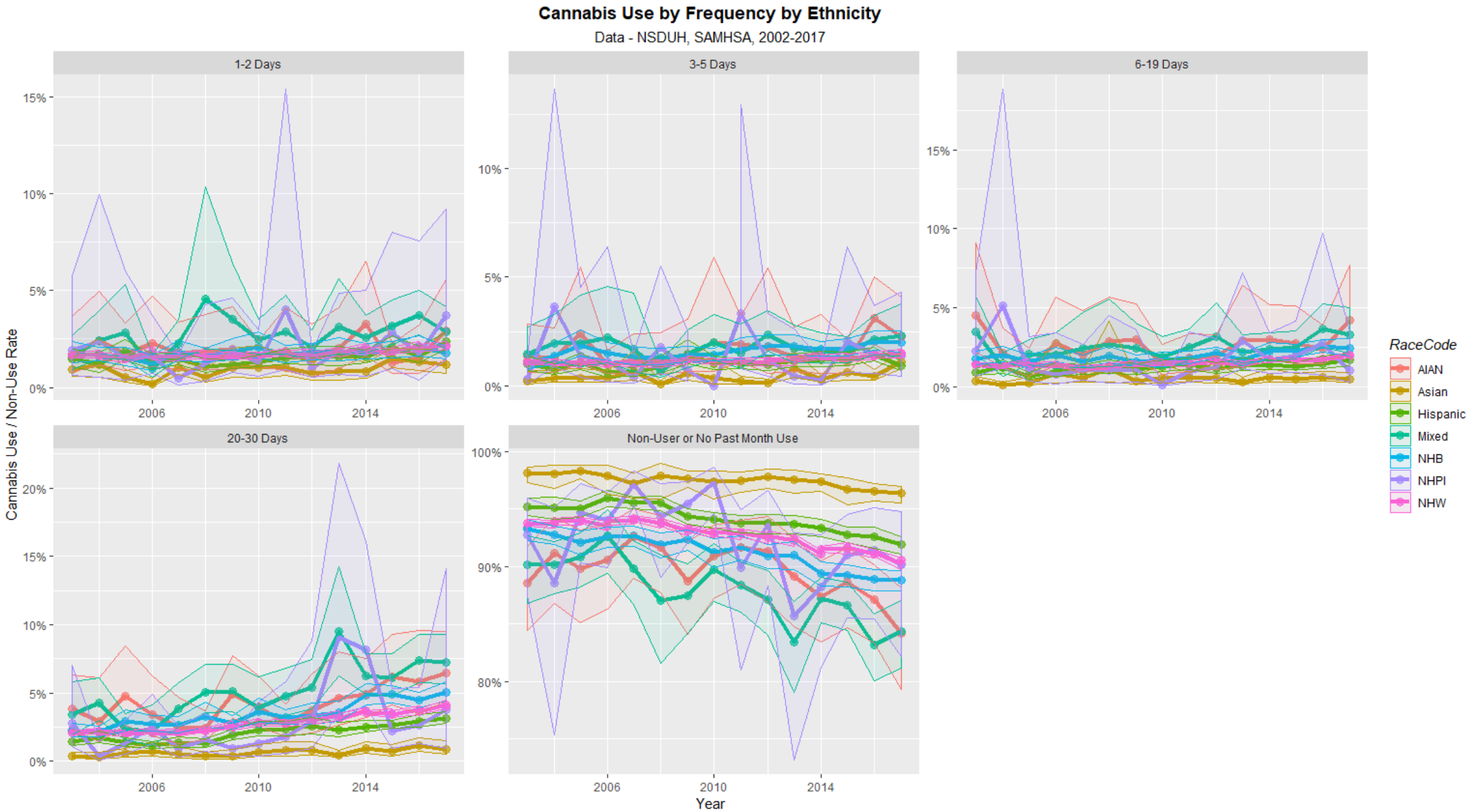
Bivariate Autism-Cigarettes

SF4

5 Races

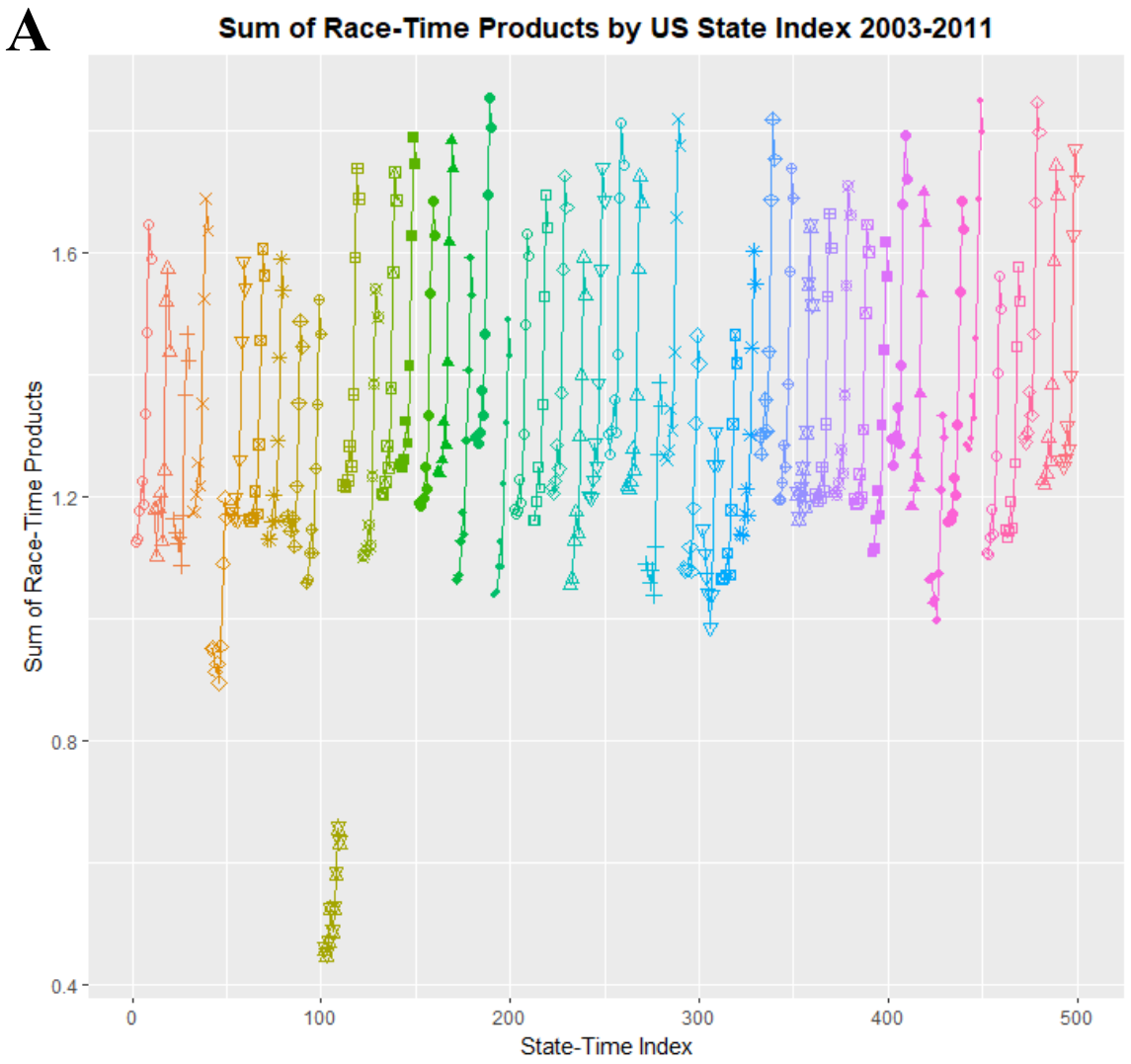

Percent of High Schoolers Using Cannabis in Previous Month - 5-Race Comparison
by USA State, CDC Youth Behavioral Risk Surveys, 1991 - 2017
Percent Cannabis Use in Preceding Month
State within United States of America
% Using Cannabis Last Month
American Indian / Alaska Native
Asian
Black
Mixed
White
Wisconsin
Vermont
New Hampshire
Maine
Washington
Idaho
Montana
North Dakota
Minnesota
Illinois
Michigan
New York
Massachusetts
Oregon
Nevada
Wyoming
South Dakota
Iowa
Indiana
Ohio
Pennsylvania
New Jersey
Connecticut
Rhode Island
California
Utah
Colorado
Nebraska
Missouri
Kentucky
West Virginia
Virginia
Maryland
Delaware
Arizona
New Mexico
Kansas
Arkansas
Tennessee
North Carolina
South Carolina
District of Columbia
Oklahoma
Louisiana
Mississippi
Alabama
Georgia
Hawaii
Alaska
Texas
Florida

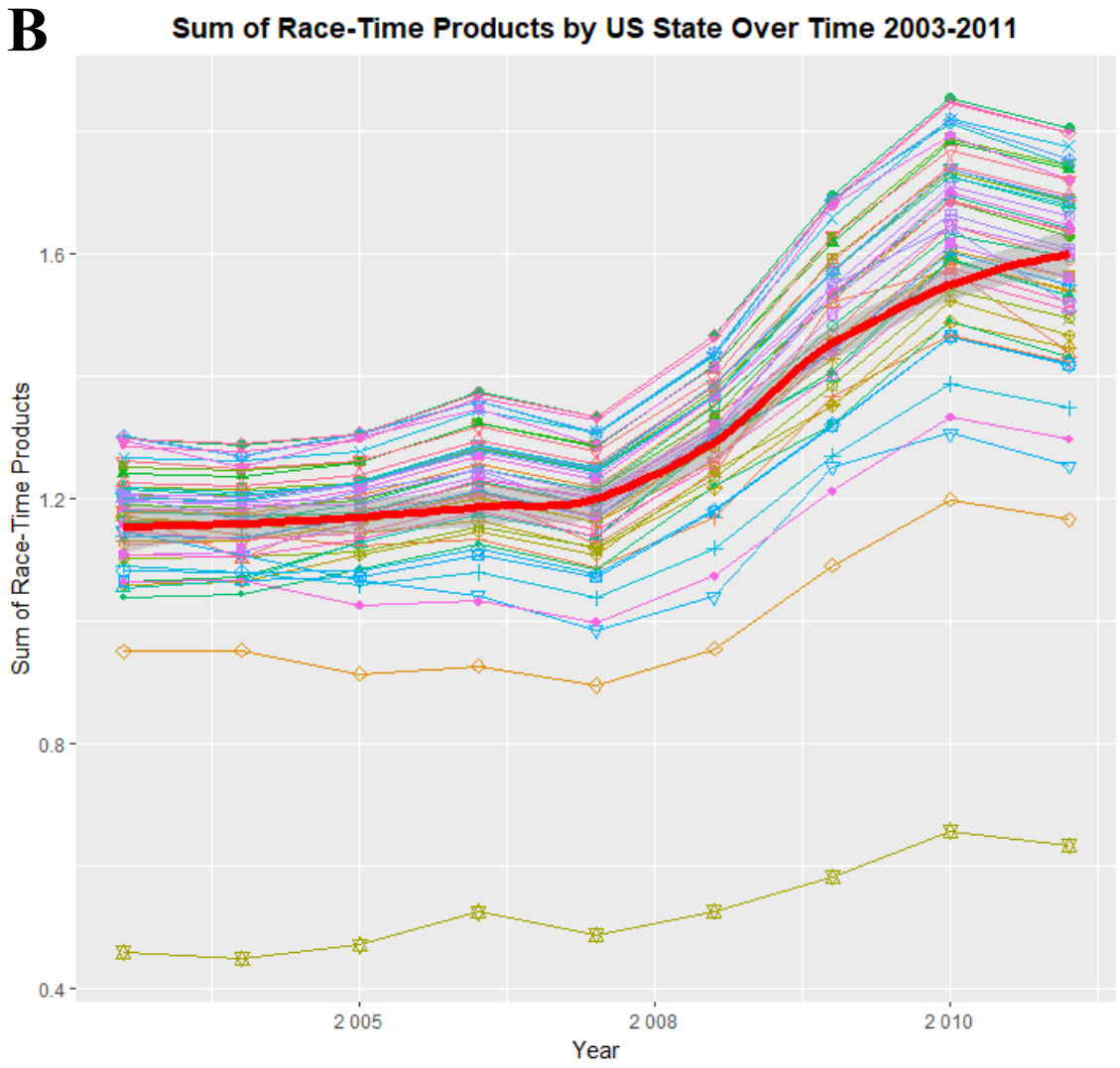
SF5 Cannabis Use Frequency by Ethnicity



SF6

Effect of Race on Monthly Days Cannabis Used





USA State

Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming

SF7

Geospatial Weights