Associations of cannabis use and body mass index–The Coronary Artery Risk Development in Young Adults (CARDIA) study

Jakob, Julian; Schwerdtel, Fiona; Sidney, Steve; Rodondi, Nicolas; Pletcher, Mark J.; Reis, Jared P.; Muniyappa, Ranganath; Clair, Carole; Tal, Kali; Bancks, Michael P.; Rana, Jamal S.; Collet, Tinh-Hai; Auer, Reto

How to cite

JAKOB, Julian et al. Associations of cannabis use and body mass index–The Coronary Artery Risk Development in Young Adults (CARDIA) study. In: European journal of internal medicine, 2024, p. S0953–6205(24)00289–9. doi: 10.1016/j.ejim.2024.07.007

This publication URL: https://archive-ouverte.unige.ch/unige:179127

Publication DOI: 10.1016/j.ejim.2024.07.007

European Journal of Internal Medicine xxx (xxxx) xxx

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

Associations of cannabis use and body mass index–The Coronary Artery Risk Development in Young Adults (CARDIA) study

Julian Jakob[a,b,*], Fiona Schwerdtel[a], Steve Sidney[c], Nicolas Rodondi[a,d], Mark J. Pletcher[e,f], Jared P. Reis[g], Ranganath Muniyappa[h], Carole Clair[i], Kali Tal[a], Michael P. Bancks[j], Jamal S. Rana[k], Tinh-Hai Collet[l,m], Reto Auer[a,i]

[a] Institute of Primary Health Care (BIHAM), University of Bern, Mittelstrasse 43, Bern 3012, Switzerland
[b] Department of Paediatrics, University Hospital Bern, Inselspital, Bern, Switzerland
[c] Division of Research, Kaiser Permanente Northern California, Oakland, CA, USA
[d] Department of General Internal Medicine, Inselspital, Bern University Hospital, Bern, Switzerland
[e] Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, USA
[f] Department of Medicine, University of California San Francisco, San Francisco, CA, USA
[g] National Heart, Lung, and Blood Institute, Bethesda, USA
[h] Diabetes, Endocrinology, and Obesity Branch, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, USA
[i] Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland
[j] Department of Epidemiology & Prevention, Wake Forest University School of Medicine, Winston-Salem, NC, USA
[k] Department of Cardiology, Kaiser Permanente Northern California, Oakland, CA, USA
[l] Service of Endocrinology, Diabetology, Nutrition and Therapeutic Education, Department of Medicine, Geneva University Hospitals, Geneva, Switzerland
[m] Diabetes Centre, Faculty of Medicine, University of Geneva, Geneva, Switzerland

ARTICLE INFO

Keywords:
Cannabis
BMI
Weight

ABSTRACT

Background: With increasing use of cannabis, we need to know if cannabis use and Body Mass Index (BMI) are associated.

Methods: The Coronary Artery Risk Development in Young Adults Study followed Black and White adults over 30 years with assessments every 2 to 5 years in four centers in the USA. We assessed self-reported current and computed cumulative cannabis exposure at every visit, and studied associations with BMI, adjusted for relevant covariables in mixed longitudinal models. We also applied marginal structural models (MSM) accounting for the probability of having stopped cannabis over the last 5 years.

Results: At the Year 30 visit, 1,912 (58 %) identified as women and 1,600 (48 %) as Black, mean age was 56 (SD 2) years. While 2,849 (85 %) had ever used cannabis, 479 (14 %) currently used cannabis. Overall, participants contributed to 35,882 individual visits over 30 years. In multivariable adjusted models, mean BMI was significantly lower in daily cannabis users (26.6 kg/m^2, 95 %CI 26.3 to 27.0) than in participants without current use (27.7 kg/m^2, 95 %CI 27.5 to 27.9, $p < 0.001$). Cumulative cannabis use was not associated with BMI. The MSM showed no change in BMI when stopping cannabis use over a 5-year period (β=0.2 kg/m^2 total, 95 %CI -0.2 to 0.6).

Conclusions: Current cannabis use was associated with lower BMI, but cumulative cannabis use and cessation were not. This suggests that recreational cannabis use may not lead to clinically relevant changes in BMI and that the association between current cannabis use and lower BMI is likely due to residual confounding.

Funding source: The Coronary Artery Risk Development in Young Adults Study (CARDIA) is supported by contracts 75N92023D00002, 75N92023D00003, 75N92023D00004, 75N92023D00005, and 75N92023D00006 from the National Heart, Lung, and Blood Institute (NHLBI).Study type: Cohort study.Disclaimer: The views expressed in this manuscript are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institutes of Health; or the U.S. Department of Health and Human Services. We used no AI in this study.Data sharing statement: Data is available upon request. See CARDIA website for more information: https://www.cardia.dopm.uab.edu/scientific-resources-landing-page2.STROBE guidelines: see Supplement Document.

* Corresponding author at: Institute of Primary Health Care (BIHAM), University of Bern, Mittelstrasse 43, Bern 3012, Switzerland.
E-mail address: julian.jakob@unibe.ch (J. Jakob).

https://doi.org/10.1016/j.ejim.2024.07.007
Received 7 May 2024; Received in revised form 3 July 2024; Accepted 5 July 2024

1. Introduction

In the US in 2020, 18 % of the population reported use of cannabis in the past year. Use among middle and older-aged people is rising [1,2]; from 2016 to 2018 the percentage of US adults ≥55 years old who reported using cannabis at least once a month increased for women and men with the greatest absolute increases for those 60–69 years [3]. As more jurisdictions regulate the use, sale and production of cannabis for recreational use, health care professionals, consumers, the public, and policy makers need to be better informed about the health effects of recreational cannabis use typical of the general population, in early adulthood and in a middle-aged population [4].

Several longitudinal studies suggested that *current* cannabis use (i.e. short-term effects) is associated with lower BMI [5–11], while others have not [12,13]. Few studies have examined the effects of *cumulative* cannabis use over lifetime (i.e. long-term effects) on BMI. These studies found no association between cumulative use of cannabis and BMI [6–10,13,14]. Associations between *cumulative* exposure to cannabis from early adulthood until late middle-age and BMI have never been studied. Associations between current and cumulative cannabis are obviously hard to disentangle, as they are closely correlated. If *current* cannabis exposure was a cause of lower BMI, with a direct effect of cannabis on BMI, one would expect a lower BMI in current users, with a gain in weight once people stop using it, similarly to tobacco smoking. The scientific evidence on the association between tobacco use and BMI is clearer than for cannabis and BMI. Current tobacco smoking (i.e. short-term effects) is associated with lower BMI in adults [15–17], but smoking cessation, and cumulative tobacco exposure (i.e. long-term effects), are both associated with weight gain: long-term smokers and ex-smokers tend to gain more weight over time than never-smokers, possibly due to disturbances in metabolism [16–18]. Disentangling exposure to tobacco and cannabis is also a challenge. Cannabis smokers may also smoke tobacco or mix tobacco with cannabis in joints ("mulling"). Data from a cohort in the USA, where a large proportion of cannabis users are not exposed to tobacco, represents a unique opportunity to study the association between cannabis and BMI.

We aimed to determine the association between current and cumulative cannabis use and BMI in a large community-based cohort followed over three decades, with multiple assessments of cannabis exposure, BMI, and a rich set of assessed covariables in multiple statistical modelling approaches. We further explored whether associations may differ by sex and race and whether changes in current cannabis use leads to changes in BMI, applying statistical approaches aiming at estimating causal effects, such as marginal structural models. We finally contrast these findings on cannabis use with those from tobacco use. We hypothesized that current and cumulative cannabis smoking was associated with lower BMI and that cannabis cessation was associated with weight gain.

2. Methods

2.1. Population

We used data from the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a cohort of 5115 self-identified Black and White women and men, aged between 18 and 30 years at baseline in four study sites in the USA (Birmingham, AL, Chicago, IL, Minneapolis, MI, Oakland, CA) over 30 years. The study strove for an approximately balanced sampling of participants by race, sex, education, and age at each site. Participants were examined in up to nine clinic visits over the study period (Year 0 was 1985/86; Year 30 was 2015/2016). All participants granted informed consent before entering the study and at each follow-up visit. All study protocols were approved by the institutional review boards at each site.

2.2. Cannabis exposure

Multiple cannabis use variables are available for all nine visits (baseline, and follow-up Years 2, 5, 7, 10, 15, 20, 25, and 30). Current cannabis use was assessed by the following survey question: "During the last 30 days, on how many days did you use cannabis?" Direct self-reported lifetime exposure was assessed by the question: "About how many times in your lifetime have you used cannabis?" We computed current use and baseline lifetime use as cannabis-years: 1 year of exposure was equivalent to 365 days of cannabis use. We assumed that current use at each visit (the number of days of cannabis use in the month before the visit) reflected the average number of days of use during the months before and after each visit. We imputed values for missing visits from the closest visit to the missing value, if the participant was not definitely lost to follow-up. We estimated cumulative lifetime use by totaling the number of days the participant used cannabis during follow-up. We adjusted our estimate upwards whenever participants self-reported higher lifetime use than we computed for each visit [19–22]. Cannabis use in the 24 h before the visit was queried at baseline and at the Years 2, 5, and 30 visits: "Did you use cannabis in the last 24 h?" (See online Appendix for a more detailed explanation of computing cannabis exposure).

2.3. BMI measures

Participants were weighed in light clothing without shoes on a calibrated balance beam scale (to the nearest 0.2 kg). Height was measured with a vertical ruler (to the nearest 0.5 cm), without shoes as well [23]. BMI was calculated as weight (in kg) divided by height squared (in m).

2.4. Covariables

We used the number of daily smoked tobacco cigarettes at every visit, enriched by yearly phone follow-ups, and cumulative lifetime exposure to tobacco cigarettes in pack-years [24]. Occasional smoking was not queried in CARDIA. Education (in years) was the highest educational grade the participant reached by each visit. Physical activity was measured at every visit; participants were asked how much time per week they spent in 13 categories of leisure, occupational, and household physical activities over the past 12 months [25]. We included use of corticosteroids, current and cumulative alcohol use (1 drink-year corresponding to 365 days/year x 1 drink/day, see online Appendix) [19], binge drinking episodes, and current exposure to cocaine and amphetamine. These variables were collected at each CARDIA examination. At three visits (Years 0, 7, 20), CARDIA collected information on total caloric intake (self-reported) [26].

2.5. Statistical analyses

For each visit, we used descriptive statistics to compare participants' BMI at different levels of current and cumulative cannabis use. We used linear mixed models with correlated random participant-specific intercepts and slopes to account for within-individual correlation of repeated measures and to model individual departures from the trajectories determined by the fixed effects. Age and visit were modeled as fixed effects and included in our multivariable adjusted model as random effects to identify time-dependent trends.

Firstly, we fitted unadjusted models with fixed effects separately for current cannabis use (days of cannabis use within the last month), or cumulative cannabis use (cannabis-years of exposure) excluding current use (thus including only participants with past cannabis use). Secondly, we fitted minimally adjusted models, including fixed effects for the covariables used in CARDIA to achieve balanced sampling (age, race, sex, study site, years of education). Thirdly, we fitted fully adjusted models. We added fixed effects for cumulative cannabis and tobacco use to models on current cannabis use, current tobacco, alcohol, physical activity, use of corticosteroids, and current cocaine and amphetamines use and tested the interaction between cannabis and tobacco and BMI. To confirm results and explore causality, we applied marginal structural models that accounted for the probability of stopping cannabis use in a counterfactual statistical approach, adjusted for all variables previously mentioned [27]. We used inverse probability of attrition weights (IPAWs) accounting for lost to follow-up and censoring due to death separately to minimize potential bias by informative censoring related to cannabis use and BMI [21,22,24].

We conducted sensitivity analyses. First, we ran models excluding current tobacco smokers or ever tobacco smokers. Second, we stratified analyses by sex and race. Third, we included caloric intake in the multivariable adjusted model for current cannabis use (available for visit Years 0, 7, and 20).

We conducted secondary analyses. We aimed at replicating the methods used for cannabis exposure to assess the association between tobacco use and BMI in CARDIA. If we can replicate results from the existing literature when modeling the association between tobacco use and BMI in CARDIA, this would support findings of our analyses on cannabis and BMI. We created models with current tobacco smoking (cigarettes per day) and cumulative tobacco use (tobacco pack-years) that excluded current smokers as main predictors, using similar covariables as in the cannabis models. To confirm our results and assess causality, we applied marginal structural models that accounted for the probability of stopping smoking tobacco in a counterfactual design [27].

Table 1
Baseline characteristics of 3351 CARDIA participants with BMI measurement at Year 30 visit, overall and by never/ever tobacco smoking.

	Overall	Never Tobacco Smoker *N* = 1708 (51 %)			Ever Tobacco Smoker *N* = 1643 (49 %)			p-value[g]
Year 30 Characteristic		Never cannabis use[b]	Past cannabis use[b]	Current cannabis use[b]	Never cannabis use[b]	Past cannabis use[b]	Current cannabis use[b]	
N (row%)	3351	433 (13)	1159 (35)	116 (3)	69 (2)	1211 (36)	363 (11)	
Demographics Age, median (Q1; Q3), years	56 (52;58)	54 (51; 58)	56 (53; 58)	55 (52; 58)	57 (53; 59)	56 (53; 58)	55 (52; 58)	0.001
Race/sex, N (col%)[a] - Black women	956 (29)	156 (36)	314 (27)	16 (14)	33 (48)	338 (28)	99 (27)	<0.001
- Black men	644 (19)	70 (16)	186 (16)	25 (22)	11 (16)	245 (20)	107 (29)	
- White women	956 (29)	105 (24)	363 (31)	19 (16)	15 (22)	378 (31)	76 (21)	
- White men	795 (24)	102 (24)	296 (26)	56 (48)	10 (14)	250 (21)	81 (22)	
Educational attainment, median (Q1; Q3), years	16.0 (14.0; 18.0)	16.0 (14.0; 18.0)	16.0 (15.0; 18.0)	16.0 (15.0; 17.0)	16.0 (13.0; 18.0)	15.0 (14.0; 17.0)	14.0 (12.0; 16.0)	<0.001
Study center, N (col%) - Birmingham, AL	753 (22)	185 (43)	221 (19)	10 (9)	36 (52)	258 (21)	43 (12)	<0.001
- Chicago, IL	744 (22)	113 (26)	243 (21)	22 (19)	14 (20)	292 (24)	60 (17)	
- Minneapolis, MI	860 (26)	82 (19)	254 (22)	25 (22)	12 (17)	357 (29)	130 (36)	
- Oakland, CA	994 (30)	53 (12)	441 (38)	59 (51)	7 (10)	304 (25)	130 (36)	
Substance use exposure Lifetime cannabis exposure among ever cannabis users, median (Q1; Q3), cannabis-years[c]	0.2 (0; 1.8)	–	0.2 (0; 0.2)	5.4 (1.5; 13.1)	–	0.8 (0.2; 1.9)	6.8 (2.5; 12.2)	<0.001
Tobacco smoking, N (col%)								<0.001
- Never smokers	1708 (51)	433 (100)	1159 (100)	116 (100)	-	-	-	
- Former smokers	1154 (34)	-	-	-	59 (86)	876 (72)	219 (60)	
- Current smokers	489 (15)	-	-	-	10 (14)	335 (28)	144 (40)	
Lifetime tobacco exposure among ever smokers, median (Q1; Q3), pack-years[d]	0 (0; 7)	–	–	–	1 (0; 12)	7 (1; 17)	10 (2; 21)	<0.001
Alcohol use - Cumulative alcohol use among ever drinkers, median (Q1, Q3), drink-years[e]	10 (2; 27)	1 (0; 5)	7 (1; 20)	27 (7; 43)	2 (0; 11)	15 (5; 34)	25 (10; 51)	<0.001
Current amphetamine and/or cocaine use, N (col%)	69 (2)	0 (0)	10 (1)	7 (6)	1 (1)	22 (2)	29 (8)	<0.001
Physical activity Physical activity score, median (Q1; Q3), exercise units[f]	259 (121; 465)	211 (85; 406)	277 (141; 493)	388 (191.7; 637.2)	148 (49; 361.5)	247 (110; 441)	261 (142; 486)	<0.001
Drug use Corticosteroids, N (col%)	23 (1)	5 (1)	3 (0)	0 (0)	1 (1)	9 (1)	5 (1)	0.140
BMI, median (Q1; Q3), kg/m^2	29.4 (25.4; 34.2)	31.4 (26.9; 36.2)	29.1 (25.3; 34.0)	28.9 (25.5; 33.2)	28.1 (25.0; 35.9)	29.3 (25.3; 33.8)	28.9 (25.1; 32.6)	<0.001

Abbreviations: BMI, body mass index (weight in kilograms divided by height in meters squared); CARDIA, Coronary Artery Risk Development in Young Adults study;; N, number of participants; Q1, Q3: 1st and 3rd quartile (percentile 25 and 75); SD, standard deviation; y, years.

[a] The CARDIA study sampled roughly equal numbers of self-identified white men, white women, Black men, and Black women [1].

[b] Based on the answer to these questions: "Have you ever used marijuana?" and "During the last 30 days, on how many days did you use marijuana?".

[c] Cumulative lifetime cannabis use in cannabis -years: 1 cannabis -year of exposure is equivalent to 365 days of cannabis use (1 year x 365 days per year) [2].

[d] Cumulative lifetime tobacco smoking in pack-years: 1 pack-year of exposure equivalent to 7300 cigarettes (1 year x 365 days/y x 1 pack/d x 20 cigarettes/pack) [2].

[e] Cumulative alcohol use in terms of drink-years: 1 drink-year is the total amount of ethanol consumed by a person who had 1 alcoholic drink per day for 1 year (1 drink-year = 17.24 ml of ethanol/drink x 1 drink/d x 365 days/y = 6292.6 ml of ethanol).

[f] Physical activity measured with the CARDIA Physical Activity History questionnaire, which asks how much time per week was spent in 13 categories of leisure, occupational, and household physical activities over the past 12 months [3]. The Physical activity score is based on the following equation: Sum over (moderate, heavy or all) activities of intensity x (number of month of infrequent activity + 3 x number of months of frequent activity). female/male: low physical activity Score: <149/<278; high physical activity Score: >468/>700.

[g] P-values are from Kruskal-Wallis rank test for age, years of education, cannabis-years, pack-years, drink-years, physical activity, and from a $\chi 2$ test for race and sex, study site, current cannabis and smoking status, illicit drug use categories, and current corticosteroids use.

Tests of statistical significance were two-tailed; alpha level was 0.05. All analyses were conducted with Stata version 14.2 (StataCorp LP, College Station, TX, USA).

2.6. Role of the funding source

The National Heart, Lung and Blood Institute contributed to the design and conduct of the CARDIA Study. The CARDIA P&P committee reviewed and approved this manuscript and its scientific content prior to submission.

3. Results

3.1. Population

The 5115 participants at baseline provided data for 35,882 participant-visits over 30 years. Of the 3351 participants with available data on BMI and current and cumulative cannabis use and tobacco smoke at the Year 30 follow-up visit, 1912 (58 %) were women and 1600 (48 %) were Black; 2849 (85 %) participants declared they had ever used cannabis, and 479 (14 %) currently used cannabis (Table 1). For participant's characteristics at baseline, see Appendix Table 1. For distribution of cannabis use over time, see Appendix Fig. 1.

3.2. Association between current and cumulative cannabis use and BMI

The mean BMI over all visits in never cannabis user and never smokers was 26.1 kg/m^2. In unadjusted models that included all participant-visits, the mean BMI was 26.7(95 % Confidence Interval: 26.5 to 26.8) in never or past cannabis users (no use in last 30 days) and 24.8 (95 % CI: 24.5 to 25.1, overall $p < 0.001$) in daily cannabis users. After full multivariable adjustment, the mean BMI was 27.7 (95 % CI: 27.5 to 27.9) in never or past cannabis users (no use in last 30 days) and 26.6 (95 % CI: 26.3 to 27.0, overall $p < 0.001$) in daily users (Table 2). In multivariable adjusted models that excluded current users, cumulative cannabis use was not associated with BMI (Table 2). The associations between current or cumulative cannabis use and BMI as continuous outcomes are presented in Fig. 1.

3.3. Exploratory analysis examining the association of cannabis cessation on BMI

The outputs from an MSM showed no change in BMI when participants reported no current cannabis use at subsequent visits (β=0.2 kg/m^{2}over 5 years, 95 % CI −0.2 to 0.6 kg/m^2). This corresponds to an average weight difference of 0.6 kg (95 % CI −0.6 to 1.8 kg) for a person 1.75 m tall.

3.4. Sensitivity analyses

We found current tobacco use to significantly interact on the association between current cannabis and BMI ($p < 0.001$). In models that excluded current tobacco smokers, our results were similar to the models that included current tobacco smokers. In models excluding current tobacco smokers, the mean BMI was 27.4 (95 % CI: 27.3 to 27.6) in those not currently using cannabis and 26.7 (95 % CI: 26.3 to 27.2, overall $p = 0.001$) in those using cannabis daily (30 days/month, Appendix Table 2). In models excluding ever tobacco smokers (N participant-visits included=18,967), the mean BMI was 27.4 (95 % CI: 27.1 to 27.6) in those not currently using cannabis and 26.9 (95 % CI: 26.1 to 27.7, overall $p = 0.22$) in those using cannabis daily (30 days/month, Appendix Table 2). The tests for interaction terms between sex, race, or across the four sex-race strata (Black women/Black men/White women/White men) on the association between cannabis and BMI were not statistically significant. We found no qualitative difference in the measure of association between cannabis use and BMI in stratified analyses. We observed that current cannabis use was associated with lower BMI in analyses stratified by women and men, or Black and White participants (Appendix Table 3). Cumulative cannabis use was not associated with BMI in any sex-race strata (Appendix Table 3). We found that adjusting models for caloric intake (available for three visits) did not alter results (Appendix Table 4).

Table 2
Association between BMI and current and cumulative exposure to cannabis.

Cannabis exposure	BMI, unadjusted*(95 % CI)	p-value[d]	BMI, adjusted for demographics *(95 % CI)	p-value[d]	BMI, fully adjusted and IPAW* (95 % CI)	p-value[d]
Current cannabis exposure (days of cannabis use within the last 30 days)[a] $N = 35{,}882$[b]						
- At 0 days/month	26.7 (26.5 to 26.8)	<0.001	27.0 (26.8 to 27.1)	<0.001	27.7 (27.5 to 27.9)	<0.001
- At 5 days/month	26.4 (26.2 to 26.5)		26.8 (26.7 to 27.0)		27.5 (27.3 to 27.7)	
- At 15 days/month	25.7 (25.5 to 25.9)		26.5 (26.3 to 26.7)		27.2 (26.9 to 27.4)	
- At 30 days/month	24.8 (24.5 to 25.1)		26.0 (25.7 to 26.3)		26.6 (26.3 to 27.0)	
Cumulative exposure to **cannabis** (in cannabis-years)[c], excluding current users $N = 29{,}668$[b]						
- At 0 cannabis-years	27.7 (27.6 to 27.9)	0.007	27.6 (27.5 to 27.8)	0.009	28.4 (28.2 to 28.6)	0.9
- At 0.5 cannabis-years	27.7 (27.5 to 27.9)		27.6 (27.4 to 27.8)		28.4 (28.2 to 28.6)	
- At 1 cannabis-year	27.6 (27.5 to 27.8)		27.5 (27.4 to 27.7)		28.4 (28.2 to 28.6)	
- At 5 cannabis-years	27.2 (26.9 to 27.6)		27.2 (26.8 to 27.5)		28.4 (27.8 to 29.0)	
- At 10 cannabis-years	26.8 (26.1 to 27.4)		26.7 (26.0 to 27.4)		28.4 (27.2 to 29.5)	

[a] Current exposure to cannabis assessed through the question, "During the last 30 days, on how many days did you use cannabis?".
[b] Composite number of participant-visits used in the mixed model.
[c] Cumulative exposure to cannabis expressed in cannabis-years, with 1 cannabis-year of exposure equivalent to 365 days of cannabis use.
[d] P-values are from a Wald test.
* Main predictors (current cannabis use, cumualtive cannabis use) modeled flexibly. The unadjusted model includes visit as covariable, as our mixed model pooled multiple participant-visits. With increasing visit number, participant got older, and thus accumulated a higher amount of cannabis-years, while also increasing their BMI, thus creating a spurious association. We then present results adjusted for demographics (sex, race, age, education years, study center) and finally, for current and cumulative alcohol and tobacco use, current use of amphetamines and/or cocaine, total physical activity score, and exposure to corticosteroids. Use of inverse probability of attrition weights (IPAW) in the multivariable adjusted model in oder to account for potential informative censoring during follow-up from lost to follow-up and death, separately.

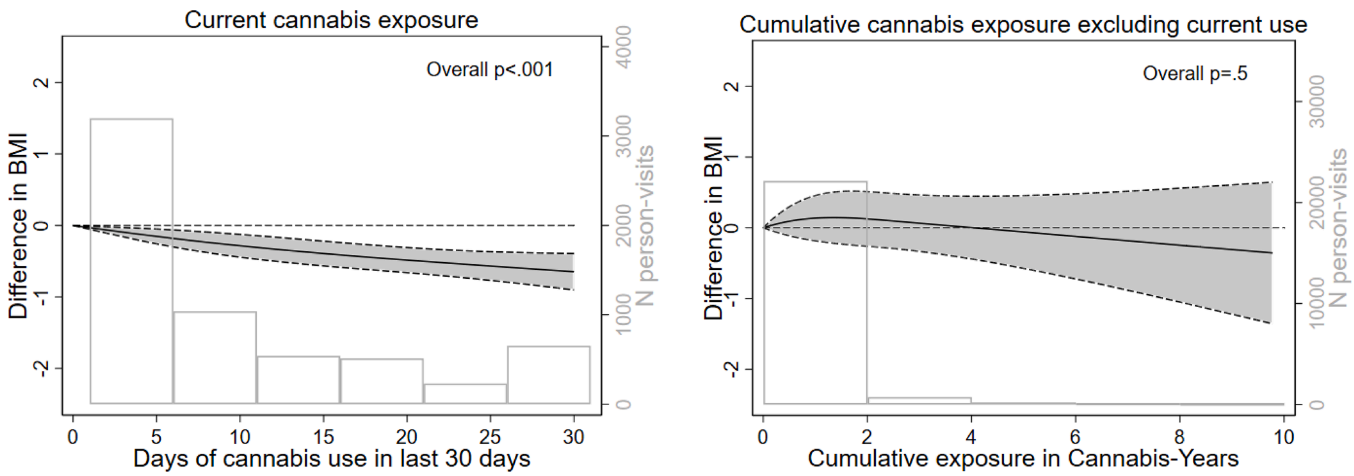

Fig. 1. Association between BMI and current and cumulative cannabis use (current users omitted for the cumulative exposure analysis due to collinearity). Results from multivariable adjusted mixed longitudinal models, using splines with three knots, and censoring participants with incident cardiovascular disease for current and future visits. Adjusted for demographics (sex, race, age, education years, study center), current and cumulative alcohol and tobacco use, cumulative alcohol use and binge-drinking episodes, current cocaine and amphetamine use, total physical activity score, and exposure to statins. Use of inverse probability of censoring weights in oder to account for missing follow-up data. Cumulative exposure to cannabis expressed in cannabis-years, with 1 cannabis-year of exposure equivalent to 365 days of cannabis use, adjusting for current cannabis use. N included person-visits = 35,882.

3.5. Association between current and cumulative tobacco use and BMI

At Year 30, 489 participants (15 %) reported smoking tobacco. In multivariable adjusted models, the mean BMI was 27.4 (95 % CI: 27.2 to 27.5) in those not smoking tobacco and 26.5 (95 % CI: 26.3 to 26.8, overall $p < 0.001$) in those smoking 20 cigarettes per day (Appendix Table 5). Cumulative exposure to tobacco was associated with higher BMI (28.4; 95 % CI: 27.7 to 29.1 for 20 packyears) than never smoking (BMI 27.3; 95 % CI: 27.1 to 27.5, overall $p < 0.013$) in multivariable adjusted analyses that excluded current smokers. The associations between tobacco smoking and BMI as continuous outcome are presented in Appendix Fig. 2.

3.6. Exploratory analysis examining the association of tobacco cessation on changes in BMI

The outputs from an MSM showed higher BMI when participants stopped smoking tobacco (β=1.32 kg/m^2, 95 % CI 0.7 to 1.9).

4. Discussion

Current cannabis use was associated with lower BMI, but cumulative cannabis exposure was not. The difference in BMI between daily cannabis users and never-users was low (−1.1 kg/m^2), corresponding to *a* < 5 % difference. Cessation of cannabis use during follow-up left BMI unchanged, suggesting that our finding of lower BMI in current users may have been at least partly due to residual confounding from comparing current or past cannabis users to never users, who diverge on a range of socio-demographic and behavioral covariables. Comparing current users over multiple visits to participants who reported not currently using cannabis anymore enables to provides a more reliable sample of participants for analyses on the associations between current cannabis use and BMI. The association between cannabis and lower BMI was similar in Black and White participants, and men and women. Additionally adjusting for caloric intake did not change results. In contrast, as expected from the existing literature, current tobacco use was associated with lower BMI, cumulative tobacco exposure with increased BMI, and tobacco cessation appeared to lead to increased BMI.

Several studies of adult cohorts also found that BMI was lower in current cannabis users compared to never users. A 2019 study included 650 current cannabis users in the US and found their BMI was 0.35 kg/m^2 lower than the BMI of non-users [6]. In an all-male US study (253 participants followed prospectively from age 7 to 32), authors found BMI was lower in participants with higher cumulative exposure to cannabis, but the study did not factor in current cannabis use [7]. A Swedish study of 18,000 study participants followed over 8 years showed that past cannabis users gained more weight than participants continuing to use cannabis, but no more than never cannabis users [8]. A study within the Dunedin birth cohort (1037 participants, followed to age 38 in New Zealand) found cumulative cannabis use was associated with lower BMI, but also did not factor in current use [14]. A US cohort study from 2013 including 4657 participants showed smaller waist circumference in cumulative users with the last cannabis use at least 1 month ago [28]. A birth cohort in Australia (2566 participants followed until age 21) found those who had used cannabis were less likely to have a BMI >25 kg/m^2 than never users [9], but an earlier analysis of the CARDIA cohort that included 15 years of follow-up found no association between cumulative cannabis use and BMI [13]. Another CARDIA analysis after the 25-year follow up showed no association between either cumulative or current cannabis use and total abdominal, visceral, subcutaneous or intermuscular adipose tissue [20].

Many studies tried to find explanatory factors when finding or refuting an association between cannabis use and BMI in observational settings [6,7,29]. We noted that BMI did not increase more over time in participants who stopped using cannabis compared to ongoing cannabis users, which suggests that the association between current cannabis use and lower BMI might not be causal; it is likely due to residual confounding. In their all-male study, Meier et al. showed that people with lower BMI as children were not more likely to start using cannabis, and did not have a healthier lifestyle (measured as consumption of more fruit and vegetables or lower alcohol intake) [7]. Though it is likely that people who use cannabis regularly differ from non-users in further aspects, we could not account for all potential factors, as is the case in many, if not all observational studies, in our multivariable adjusted models. To compare people who used cannabis in the past to those who currently use cannabis (as we did in our marginal structural model) is less likely to introduce bias than comparing never users with current users (as most other researchers have done in their regression models). Given the complexity of disentangling the predictors of cannabis use with the potential covariables confounding the association between cannabis and BMI, we argue that researchers should refrain from trying to find simple and clear explanatory models to test the potential association of cannabis on BMI when analyzing data from observational cohorts. Such explanatory models should be reserved for studies able to adequately measure exposure to cannabis and then test its potential association with BMI, as is the case in randomized controlled trials.

Because some studies show lower BMI levels among cannabis users, the pharmaceutical industry developed and tested rimonabant, a Cannabinoid-1 receptor (CB1) agonist that mimics Δ9-tetrahydrocannabinol (THC), the psychoactive substance in cannabis [30]. Chronic stimulation of CB1 receptors with rimonabant downregulates the CB1 receptor, apparently reducing energy storage and increasing metabolic rates, which appears to result in weight loss [29–33]. Rimonabant was designed as a therapy for weight loss and though users averaged a 10 % reduction in weight in a large RCT, major adverse psychological events led to having rimonabant withdrawn from the European market in 2008 [34]. Unlike giving rimonabant to participants in the context of an RCT, where the effects of rimonabant can be modeled and carefully studied, the study of the effects of cannabis use on BMI not within the context of an RCT in the general population is highly challenging.

Our study has several limitations. We did not have data collected on the type of cannabis or cannabis derived product used by participants, its potency, and the mode of use, any of which could affect outcomes [34]. We restricted the analyses to data collected in CARDIA up to year 30 in order to limit the potential change in availability of alternative cannabis delivery methods. At year 35, CARDIA collected the mode of use for cannabis, where 82 % reported smoking cannabis. CARDIA measures cannabis use through self-reports and does not biochemically validate participants' claims, so especially where cannabis remains illegal, participants may under-report use. Nevertheless, CARDIA presented the illicit drug form in a closed folder and staff were instructed not to look inside the filled-out form. Furthermore, CARDIA participants reported substantial amounts of recreational drug use on this form, as they have become well acquainted with the form and the fact that it is kept completely private at the individual level. We could confirm known effects of current, cumulative and cessation of tobacco on BMI with our modeling approach, which we believe gives credibility to our estimates on the association between current cannabis use and BMI. Since cumulative exposure to cannabis was extrapolated from information provided every 2 to 5 years, it may not have been accurate, but seems to be representative of the typical distribution of cannabis use intensity in the USA.

5. Conclusion

Current cannabis use was associated with lower BMI, but cumulative cannabis exposure was not. BMI did not increase with cannabis cessation, suggesting that recreational cannabis use may not result in clinically relevant changes in BMI and that the association between current cannabis use and lower BMI can likely be explained by residual confounding. We were able to confirm the known association between tobacco exposure and BMI when applying our methods used to examine the association between cannabis and BMI to tobacco. This should reassure health authorities, medical professionals, and the public, that increases in cannabis use in the general population might not lead to higher BMI, but also dampen enthusiasm that cannabis use might be solution to the obesity epidemic.

CRediT authorship contribution statement

Julian Jakob: Conceptualization, Visualization, Funding acquisition, Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **Fiona Schwerdtel:** Funding acquisition, Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **Steve Sidney:** Funding acquisition, Formal analysis, Data curation, Writing – review & editing. **Nicolas Rodondi:** Funding acquisition, Formal analysis, Data curation, Writing – review & editing. **Mark J. Pletcher:** Funding acquisition, Formal analysis, Data curation, Writing – review & editing. **Jared P. Reis:** Funding acquisition, Formal analysis, Data curation, Writing – review & editing. **Ranganath Muniyappa:** Funding acquisition, Formal analysis, Data curation, Writing – review & editing. **Carole Clair:** Funding acquisition, Formal analysis, Data curation, Writing – review & editing. **Kali Tal:** Funding acquisition, Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **Michael P. Bancks:** Funding acquisition, Formal analysis, Data curation, Writing – review & editing. **Jamal S. Rana:** . **Tinh-Hai Collet:** Conceptualization, Visualization, Funding acquisition, Formal analysis, Data curation, Writing – review & editing. **Reto Auer:** Conceptualization, Visualization, Funding acquisition, Formal analysis, Data curation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

None reported. All authors had access to the data.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2024.07.007.

References

[1] Center for Behavioral Health Statistics and Quality SAaMHSA, Rockville, MD. Substance abuse and mental health services administration, Key substance use and mental health indicators in the United States: results from the 2019 national survey on drug use and health,. 2020.
[2] Hasin DS, Saha TD, Kerridge BT, et al. Prevalence of Marijuana use disorders in the United States between 2001-2002 and 2012-2013. JAMA Psychiatry 2015;72(12):1235–42.
[3] Maxwell CJ, Jesdale BM, Lapane KL. Recent trends in cannabis use in older Americans. Ann Intern Med 2020.
[4] Kaufman TM, Fazio S, Shapiro MD. Brief Commentary: marijuana and cardiovascular disease–what should we tell patients?Marijuana and cardiovascular disease. Ann Intern Med 2019;170(2):119–20.
[5] YorkWilliams SL, Gibson LP, Gust CJ, Giordano G, Hutchison KE, Bryan AD. Exercise intervention outcomes with cannabis users and nonusers aged 60 and older. Am J Health Behav 2020;44(4):420–31.
[6] Alshaarawy O, Anthony JC. Are cannabis users less likely to gain weight? Results from a national 3-year prospective study. Int J Epidemiol 2019;48(5):1695–700.
[7] Meier MH, Pardini D, Beardslee J, Matthews KA. Associations between cannabis use and cardiometabolic risk factors: a longitudinal study of men. Psychosom Med 2019;81(3):281–8.
[8] Danielsson AK, Lundin A, Yaregal A, Östenson CG, Allebeck P, Agardh EE. Cannabis use as risk or protection for type 2 diabetes: a longitudinal study of 18 000 Swedish men and women. J Diabetes Res 2016;2016:6278709.
[9] Hayatbakhsh MR, O'Callaghan MJ, Mamun AA, Williams GM, Clavarino A, Najman JM. Cannabis use and obesity and young adults. Am J Drug Alcohol Abuse 2010;36(6):350–6.
[10] Vázquez-Bourgon J, Setién-Suero E, Pilar-Cuéllar F, et al. Effect of cannabis on weight and metabolism in first-episode non-affective psychosis: results from a three-year longitudinal study. J Psychopharmacol (Oxf Engl) 2019;33(3):284–94.
[11] Scheffler F, Kilian S, Chiliza B, et al. Effects of cannabis use on body mass, fasting glucose and lipids during the first 12 months of treatment in schizophrenia spectrum disorders. Schizophr Res 2018;199:90–5.
[12] Jin LZ, Rangan A, Mehlsen J, Andersen LB, Larsen SC, Heitmann BL. Association between use of cannabis in adolescence and weight change into midlife. PLoS ONE 2017;12(1):e0168897.
[13] Rodondi N, Pletcher MJ, Liu K, Hulley SB, Sidney S. Marijuana use, diet, body mass index, and cardiovascular risk factors (from the CARDIA study). Am J Cardiol 2006;98(4):478–84.
[14] Meier MH, Caspi A, Cerdá M, et al. Associations between cannabis use and physical health problems in early midlife: a longitudinal comparison of persistent cannabis vs tobacco users. JAMA Psychiatry 2016;73(7):731–40.
[15] Huot I, Paradis G, Ledoux M. Factors associated with overweight and obesity in Quebec adults. Int J Obes Relat Metab Disord J Int Assoc Study Obes 2004;28(6):766–74.
[16] Chiolero A, Faeh D, Paccaud F, Cornuz J. Consequences of smoking for body weight, body fat distribution, and insulin resistance. Am J Clin Nutr 2008;87(4):801–9.
[17] Wang X, Dong JY, Cui R, et al. Smoking cessation, weight gain and risk of cardiovascular disease. Heart 2022;108(5):375–81.
[18] Wang X, Qin LQ, Arafa A, Eshak ES, Hu Y, Dong JY. Smoking cessation, weight gain, cardiovascular risk, and all-cause mortality: a meta-analysis. Nicotine Tob Res Off J Soc Res Nicotine Tob 2021;23(12):1987–94.

[19] Auer R, Vittinghoff E, Yaffe K, et al. Association between lifetime marijuana use and cognitive function in middle age: the Coronary Artery Risk Development in Young Adults (CARDIA) study. JAMA-Intern Med 2016. In Press.
[20] Bancks M.P., Auer R., Carr J.J., et al. Self-reported marijuana use over 25 years and abdominal adiposity: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Addiction (Abingdon, England). 2018;113(4):689–98.
[21] Reis JP, Auer R, Bancks MP, et al. Cumulative lifetime marijuana use and incident cardiovascular disease in middle age: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Am J Public Health 2017;107(4):601–6.
[22] Auer R, Sidney S, Goff D, et al. Lifetime marijuana use and subclinical atherosclerosis: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Addiction 2018;113(5):845–56 (Abingdon, England).
[23] Rodondi N, Pletcher MJ, Liu K, Hulley SB, Sidney S. Coronary artery risk development in young adults S. Marijuana use, diet, body mass index, and cardiovascular risk factors (from the CARDIA study). Am J Cardiol 2006;98(4):478–84.
[24] Auer R, Vittinghoff E, Kiefe C, et al. Change in physical activity after smoking cessation: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Addiction 2014;109(7):1172–83 (Abingdon, England).
[25] Jacobs Jr DR, Hahn LP, Haskell WL, Pirie P, Sidney S. Validity and reliability of short physical activity history: cardia and the minnesota heart health program. J Cardiopulm Rehabil 1989;9(11):448–59.
[26] McDonald A, Van Horn L, Slattery M, et al. The CARDIA dietary history: development, implementation, and evaluation. J Am Diet Assoc 1991;91(9):1104–12.
[27] Robins JM, Hernán MÁ, Brumback B. Marginal structural models and causal inference in epidemiology. Epidemiology 2000;11(5).
[28] Penner EA, Buettner H, Mittleman MA. The impact of marijuana use on glucose, insulin, and insulin resistance among US adults. Am J Med 2013;126(7):583–9.
[29] Clark TM, Jones JM, Hall AG, Tabner SA, Kmiec RL. Theoretical explanation for reduced body mass index and obesity rates in cannabis users. Cannabis Cannabinoid Res 2018;3(1):259–71.
[30] Hirsch S, Tam J. Cannabis: from a plant that modulates feeding behaviors toward developing selective inhibitors of the peripheral endocannabinoid system for the treatment of obesity and metabolic syndrome. Toxins 2019;11(5).
[31] Hirvonen J, Goodwin RS, Li CT, et al. Reversible and regionally selective downregulation of brain cannabinoid CB1 receptors in chronic daily cannabis smokers. Mol Psychiatry 2012;17(6):642–9.
[32] Murphy T, Le Foll B. Targeting the endocannabinoid CB1 receptor to treat body weight disorders: a preclinical and clinical review of the therapeutic potential of past and present CB1 drugs. Biomolecules 2020;10(6).
[33] https://www.aerzteblatt.de/archiv/62095/Rimonabant-vom-Markt-genommen. Last accessed on 08-18-2023.
[34] Bielawiec P, Harasim-Symbor E, Chabowski A. Phytocannabinoids: useful drugs for the treatment of obesity? Special focus on cannabidiol. Front Endocrinol 2020;11:114.