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SUPPLEMENTARY MATERIAL

Title: Marijuana Use and Estimated Glomerular Filtration Rate in Young Adults

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Appendix 1: Supplemental Methods

Cumulative marijuana use (marijuana-years): Current marijuana use was assessed with the

following question: “During the last 30 days, on how many days did you use marijuana?”

Lifetime marijuana use was assessed with the following question: “About how many times in

your lifetime have you used marijuana?” Current and lifetime marijuana use were used to

calculate cumulative marijuana use in marijuana-years. The number of days of marijuana use

during each study visit year was estimated by multiplying the number of days of marijuana use

reported within the 30 days prior to each study visit by a factor of approximately 12 (365 days/30

days). The number of days of marijuana use during the intervening years between study visits

was estimated by forwards and backwards imputation of the number of days of marijuana use

during the most proximal study visit years; in the case of an uneven number of yearly intervals

between study visits, forward imputation was applied arbitrarily. Lifetime marijuana use reported

at baseline (year 0) was used to estimate the number of days of marijuana use prior to year 0, and

the number of days of marijuana use during each subsequent year (as calculated above) was

added to this year 0 value in order to calculate the cumulative number of days of marijuana use.

Finally, the cumulative number of days of marijuana use was divided by 365 in order to obtain

the cumulative number of years of marijuana use expressed in marijuana-years (one marijuana-

year is equivalent to 365 days of marijuana use). We adjusted our estimate upwards if self-

reported lifetime marijuana use was higher than our computed estimates.

Cumulative marijuana use (joint-years): Until study year 10, the quantity of marijuana use per

day was assessed using the following question: “During the last 30 days, if you used marijuana,

what was the usual number of joints or pipe fulls you smoked per day?” Cumulative marijuana

use in joint-years was calculated in a similar manner as described above for marijuana-years. The

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number of joints or filled pipe bowls smoked during each study year was estimated by multiplying the number of days of marijuana use reported within the 30 days prior to each study visit by the number of joints or filled pipe bowls smoked per day, and the product was multiplied by a factor of approximately 12 (365 days/30 days). The number of joints or filled pipe bowls smoked in the intervening years between study visits was estimated by imputation as described above. The cumulative number of joints or filled pipe bowls smoked was divided by 365 in order to obtain cumulative marijuana use expressed in joint-years (one joint-year is equivalent to 365 joints or filled pipe bowls smoked). Given that the question asking about quantity of marijuana smoked was only available through year 10, for patients reporting continued marijuana use beyond year 10, we imputed joint-years at years 15, 20, and 25 based on the assumption that the number of joints or filled pipe bowls smoked per day reported at year 10 remained constant for the remainder of follow-up.

Supplemental Table 1: Percent Difference in eGFR_{cys} at Year 10 (Calendar Years 1995-1996) among Current Marijuana Users compared to Non-Users

Current Use (last 30 days) at Year 10	Participants (n)	eGFR _{cys} , mean (SD)	Unadjusted		Multivariable-adjusted	
			% difference eGFR _{cys} (95% CI)	p-value ^a	% difference eGFR _{cys} (95% CI)	p-value ^a
Overall cohort						
No use	3221	111 (13)	referent		referent	
1-10 days	388	111 (12)	0.7 (-0.7 to 2.2)	0.33	1.0 (-0.5 to 2.4)	0.20
11-29 days	109	108 (13)	-2.5 (-5.0 to 0.1)	0.06	-2.2 (-4.7 to 0.3)	0.09
30 days (daily)	47	107 (15)	-3.8 (-7.5 to 0.1)	0.06	-4.5 (-8.1 to -0.7)	0.02
p-value trend ^b				0.02		0.006
Race^c						
White						
No use	1689	109 (12)	referent		referent	
1-10 days	171	109 (11)	-0.2 (-2.3 to 2.0)	0.86	0.2 (-1.9 to 2.3)	0.84
11-29 days	57	105 (14)	-4.7 (-8.1 to -1.1)	0.01	-4.5 (-7.7 to -1.1)	0.009
30 days (daily)	26	100 (14)	-8.7 (-13 to -3.7)	0.001	-7.9 (-13 to -2.9)	0.002
p-value trend ^b				0.0002		0.0004
Black						
No use	1532	112 (14)	referent		referent	
1-10 days	217	113 (13)	0.9 (-1.0 to 2.9)	0.35	1.6 (-0.3 to 3.6)	0.10
11-29 days	52	112 (12)	-0.2 (-3.9 to 3.6)	0.91	0.5 (-3.2 to 4.3)	0.81
30 days (daily)	21	115 (12)	2.4 (-3.4 to 8.7)	0.43	-0.4 (-5.8 to 5.4)	0.89
p-value trend ^b				0.52		0.80

Abbreviations: eGFR_{cys}, estimated glomerular filtration rate as calculated with the CKD-EPI cystatin C equation (mL/min/1.73 m²); SD, standard deviation; CI, confidence interval

Multivariable model adjusted for age, race, sex, study site, income, education, employment, systolic blood pressure, diastolic blood pressure, diabetes, hyperlipidemia, body mass index, physical activity, and cumulative years of tobacco smoking, heavy and binge alcohol use, and cocaine, amphetamine, and heroin use.

The results can be interpreted as the percent difference in eGFR_{cys} at year 10 compared to the referent category. For example, in the multivariable-adjusted model, compared to participants with no marijuana use, those with daily current use had a 4.5% lower eGFR_{cys}, and this difference was statistically significant (p = 0.02).

^ap-values for percent difference in eGFR_{cys} compared to the referent (no use).

^bp-values for test for trend across categories of marijuana use.

^cp-value for test for interaction by race = 0.04.

p-values bolded if <0.05.

Supplemental Table 2: Percent Difference in eGFR_{cys} at CARDIA Year 10 (Calendar Years 1995-1996) among Participants with Cumulative Marijuana Use (in Joint-Years) compared to Never-Users

Cumulative Marijuana Use at Year 10 (joint-years)	Participants (n)	eGFR _{cys} , mean (SD)	Unadjusted		Multivariable-adjusted	
			% difference eGFR _{cys} (95% CI)	p-value ^a	% difference eGFR _{cys} (95% CI)	p-value ^a
Overall cohort						
Never used	634	111 (13)	referent		referent	
>0-5	2827	111 (13)	0.0 (-1.2 to 1.1)	0.94	0.4 (-0.8 to 1.6)	0.50
>5-10	153	110 (13)	-0.9 (-3.3 to 1.5)	0.45	-0.8 (-3.2 to 1.7)	0.52
>10	151	108 (17)	-3.8 (-6.1 to -1.4)	0.002	-3.7 (-6.1 to -1.3)	0.003
p-value trend ^b				0.002		0.002
Race^c						
White						
Never used	284	110 (12)	referent		referent	
>0-5	1543	109 (12)	-0.8 (-2.5 to 0.9)	0.34	-0.9 (-2.6 to 0.8)	0.29
>5-10	60	107 (11)	-3.3 (-6.9 to 0.5)	0.09	-3.6 (-7.1 to 0.1)	0.05
>10	56	102 (17)	-8.6 (-12 to -4.9)	<0.001	-8.0 (-12 to -4.4)	<0.001
p-value trend ^b				<0.001		<0.001
Black						
Never used	350	112 (14)	referent		referent	
>0-5	1284	113 (14)	1.1 (-0.5 to 2.7)	0.19	1.5 (-0.1 to 3.1)	0.07
>5-10	93	112 (14)	0.3 (-2.8 to 3.5)	0.85	1.3 (-1.8 to 4.5)	0.42
>10	95	111 (16)	-1.2 (-4.3 to 1.9)	0.45	-0.7 (-3.7 to 2.5)	0.68
p-value trend ^b				0.38		0.67

Abbreviations: eGFR_{cys}, estimated glomerular filtration rate as calculated with the CKD-EPI cystatin C equation (mL/min/1.73 m²); SD, standard deviation; CI, confidence interval

Multivariable model adjusted for age, race, sex, study site, income, education, employment, systolic blood pressure, diastolic blood pressure, diabetes, hyperlipidemia, body mass index, physical activity, and cumulative years of tobacco smoking, heavy and binge alcohol use, and cocaine, amphetamine, and heroin use.

The results can be interpreted as the percent difference in eGFR_{cys} at year 10 compared to the referent category. For example, in the multivariable-adjusted model, compared to participants who never used marijuana, those with >10 joint-years of use had a 3.7% lower eGFR_{cys}, and this difference was statistically significant (p = 0.003).

^ap-values for percent difference in eGFR_{cys} compared to the referent (never use).

^bp-values for test for trend across categories of marijuana use.

^cp-value for test for interaction by race = 0.007.

p-values bolded if <0.05.

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Supplemental Table 3: Percent Difference in eGFR_{cys} Change per Year during CARDIA Years 10-15 (Calendar Years 1995-1996 to 2000-2001) and 15-20 (Calendar Years 2000-2001 to 2005-2006) among Participants with Cumulative Marijuana Use (in Joint-Years) compared to Never-Users

Cumulative Marijuana Use (joint-years) ^a	5-Year Person-Intervals (n)	eGFR _{cys} Change per Year, mean (SD)	Unadjusted		Multivariable-adjusted	
			% difference eGFR _{cys} (95% CI)	p-value ^b	% difference eGFR _{cys} (95% CI)	p-value ^b
Never used	1011	-0.7 (4.3)	referent		referent	
>0-5	4402	-0.7 (5.5)	-0.1 (-0.4 to 0.1)	0.36	-0.2 (-0.5 to 0.1)	0.15
>5-10	200	-0.7 (2.2)	-0.1 (-0.7 to 0.4)	0.65	-0.1 (-0.7 to 0.5)	0.70
>10	202	-0.7 (2.3)	0.02 (-0.5 to 0.6)	0.93	0.1 (-0.5 to 0.7)	0.78
p-value trend ^c				0.94		0.72

Abbreviations: eGFR_{cys}, estimated glomerular filtration rate as calculated with the CKD-EPI cystatin C equation (mL/min/1.73 m²); SD, standard deviation; CI, confidence interval

Multivariable model adjusted for age, race, sex, study site, income, education, employment, systolic blood pressure, diastolic blood pressure, diabetes, hyperlipidemia, body mass index, physical activity, and cumulative years of tobacco smoking, heavy and binge alcohol use, and cocaine, amphetamine, and heroin use.

The results can be interpreted as the percent difference in change in eGFR_{cys} per year during years 10-15 and 15-20 compared to the referent category. For example, in the multivariable-adjusted model, compared to participants who never used marijuana, the annualized change in eGFR_{cys}, relative to the value at the beginning of each 5-year interval, was larger by 0.1% per year among those with >10 joint-years of use, but this difference was not statistically significant (p = 0.78).

^aCumulative marijuana use was evaluated at CARDIA years 10 (calendar years 1995-1996) and 15 (calendar years 2000-2001).

^bp-values for percent difference in eGFR_{cys} change per year compared to the referent (never use).

^cp-values for test for trend across categories of marijuana use.

Supplemental Table 4: Kidney Outcomes Measured during CARDIA Year 10 (Calendar Years 1995-1996) through Year 20 (Calendar Years 2005-2006) or Year 25 (Calendar Years 2010-2011) among Participants with Cumulative Marijuana Use (in Joint-Years) compared to Never-Users

Cumulative Marijuana Use (joint-years) ^a	Events (n)	5-Year Person-Intervals or Visits (n) ^b	Urine ACR, median (IQR)	Unadjusted		Multivariable-adjusted	
				PRR (95% CI)	p-value ^c	PRR (95% CI)	p-value ^c
<i>Rapid eGFR_{cys} decline^d</i>							
Never used	95	995		1.00 (referent)		1.00 (referent)	
>0-5	376	4375		0.90 (0.73 to 1.11)	0.32	1.01 (0.80 to 1.28)	0.94
>5-10	23	213		1.11 (0.73 to 1.69)	0.62	1.19 (0.74 to 1.92)	0.46
>10	24	232		1.04 (0.68 to 1.58)	0.87	0.95 (0.60 to 1.52)	0.84
p-value trend ^e					0.63		0.98
<i>Prevalent albuminuria^f</i>							
Never used	134	1995	5 (3-8)	1.00 (referent)		1.00 (referent)	
>0-5	431	9111	4 (3-7)	0.72 (0.56 to 0.93)	0.01	0.78 (0.60 to 1.01)	0.06
>5-10	34	534	4 (3-7)	0.91 (0.56 to 1.47)	0.70	0.87 (0.54 to 1.41)	0.57
>10	41	617	4 (3-7)	0.96 (0.62 to 1.48)	0.84	0.87 (0.53 to 1.41)	0.56
p-value trend ^e					0.89		0.68

Abbreviations: eGFR_{cys}, estimated glomerular filtration rate as calculated with the CKD-EPI cystatin C equation; ACR, urine albumin-to-creatinine ratio (mg/g); IQR, interquartile range; PRR, prevalence rate ratio; CI, confidence interval

Definitions: Rapid eGFR_{cys} decline = $\geq 3\%$ /year; albuminuria = ACR ≥ 30 mg/g

Multivariable model adjusted for age, race, sex, study site, income, education, employment, systolic blood pressure, diastolic blood pressure, diabetes, hyperlipidemia, body mass index, physical activity, and cumulative years of tobacco smoking, heavy and binge alcohol use, and cocaine, amphetamine, and heroin use.

^aCumulative marijuana use was evaluated at CARDIA years 10 (calendar years 1995-1996) and 15 (calendar years 2000-2001) for rapid eGFR_{cys} decline and years 10 (calendar years 1995-1996), 15 (calendar years 2000-2001), 20 (calendar years 2005-2006), and 25 (calendar years 2010-2011) for prevalent albuminuria.

^b5-year person-intervals for rapid eGFR_{cys} decline and visits for prevalent albuminuria.

^cp-values for prevalence rate of outcome compared to the referent (never use).

^dMeasured between CARDIA years 10-15 and 15-20.

^ep-values for test for trend across categories of marijuana use.

^fMeasured at CARDIA years 10, 15, 20, and 25.

p-values bolded if <0.05 .

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Supplemental Table 5: Percent Difference in eGFR_{cys} at CARDIA Year 10 (Calendar Years 1995-1996) among Participants with Cumulative Marijuana Use (in Marijuana-Years) compared to Never-Users (Inverse Probability of Censoring Weighting)

Cumulative Marijuana Use at Year 10 (marijuana-years)	Participants (n)	eGFR _{cys} , mean (SD)	Unadjusted		Multivariable-adjusted	
			% difference eGFR _{cys} (95% CI)	p-value ^a	% difference eGFR _{cys} (95% CI)	p-value ^a
Never used	634	111 (13)	referent		referent	
>0-<0.5	1744	111 (13)	0.1 (-1.3 to 1.5)	0.88	0.2 (-1.3 to 1.8)	0.76
0.5-<2	930	111 (13)	-0.1 (-1.6 to 1.4)	0.88	1.1 (-0.7 to 3.0)	0.25
2-<5	330	110 (14)	-0.6 (-2.7 to 1.5)	0.57	0.4 (-2.1 to 2.9)	0.77
≥5	127	108 (15)	-2.9 (-5.6 to 0.0)	0.05	-2.8 (-5.7 to 0.2)	0.07
p-value trend ^b				0.03		0.10

Abbreviations: eGFR_{cys}, estimated glomerular filtration rate as calculated with the CKD-EPI cystatin C equation (mL/min/1.73 m²); SD, standard deviation; CI, confidence interval

Multivariable model adjusted for age, race, sex, study site, income, education, employment, systolic blood pressure, diastolic blood pressure, diabetes, hyperlipidemia, body mass index, physical activity, and cumulative years of tobacco smoking, heavy and binge alcohol use, and cocaine, amphetamine, and heroin use.

The results can be interpreted as the percent difference in eGFR_{cys} at year 10 compared to the referent category. For example, in the multivariable-adjusted model, compared to participants who never used marijuana, those with ≥5 marijuana-years of use had a 2.8% lower eGFR_{cys}, and this difference was not statistically significant (p = 0.07).

^ap-values for percent difference in eGFR_{cys} compared to the referent (never use).

^bp-values for test for trend across categories of marijuana use.

p-values bolded if <0.05.

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Supplemental Table 6: Percent Difference in eGFR_{cys} at CARDIA Year 10 (Calendar Years 1995-1996) among Participants with Cumulative Marijuana Use (in Joint-Years) compared to Never-Users (Inverse Probability of Censoring Weighting)

Cumulative Marijuana Use at Year 10 (joint-years)	Participants (n)	eGFR _{cys} , mean (SD)	Unadjusted		Multivariable-adjusted	
			% difference eGFR _{cys} (95% CI)	p-value ^a	% difference eGFR _{cys} (95% CI)	p-value ^a
Never used	634	111 (13)	referent		referent	
>0-5	2827	111 (13)	0.1 (-1.3 to 1.4)	0.94	0.5 (-1.1 to 2.1)	0.55
>5-10	153	110 (13)	-0.8 (-3.1 to 1.6)	0.52	-0.7 (-3.2 to 1.9)	0.59
>10	151	108 (17)	-3.4 (-6.5 to -0.2)	0.04	-3.5 (-6.9 to 0.1)	0.06
p-value trend ^b				0.03		0.04

Abbreviations: eGFR_{cys}, estimated glomerular filtration rate as calculated with the CKD-EPI cystatin C equation (mL/min/1.73 m²); SD, standard deviation; CI, confidence interval

Multivariable model adjusted for age, race, sex, study site, income, education, employment, systolic blood pressure, diastolic blood pressure, diabetes, hyperlipidemia, body mass index, physical activity, and cumulative years of tobacco smoking, heavy and binge alcohol use, and cocaine, amphetamine, and heroin use.

The results can be interpreted as the percent difference in eGFR_{cys} at year 10 compared to the referent category. For example, in the multivariable-adjusted model, compared to participants who never used marijuana, those with >10 joint-years of use had a 3.5% lower eGFR_{cys}, and this difference was not statistically significant (p = 0.06).

^ap-values for percent difference in eGFR_{cys} compared to the referent (never use).

^bp-values for test for trend across categories of marijuana use.

p-values bolded if <0.05.