

Supplemental Material: Meier et al.

eTable 1. Longitudinal studies with objective, laboratory-based indices and physical examinations of cannabis users' long-term physical health.

eTable 2. Physical health measures at age 38.

eTable 3. Associations between tobacco and cannabis use from ages 18 to 38 and age-38 physical health are similar for continuous and categorical health outcomes and are similar before and after accounting for childhood health and SES.

eTable 4. Associations between tobacco and cannabis use from ages 18 to 38 and lung function at age 38.

eTable 5. Associations between persistent regular cannabis use from ages 18 to 38 and age 38 physical health measures.

eTable 6. Descriptive summary of findings presented in Table 2 and eTable 3.

eTable 7. Description of additional covariates.

eTable 8. Associations between tobacco and cannabis use from ages 18 to 38 and age-38 periodontal health.

eTable 9. Within-individual change in lung function from ages 26 to 38: associations between tobacco and cannabis use from ages 26 to 38 and lung function at age 38, controlling for baseline lung function at age 26.

eTable 10. Within-individual change in health from ages 26 to 38: associations between tobacco and cannabis use from ages 18 to 38 and age-38 physical health are similar for continuous and categorical health outcomes.

eTable 1. Longitudinal studies with objective, laboratory-based indices and physical examinations of cannabis users' long-term physical health.

Study	Analysis Sample	Age (or Age Range) at Baseline	Age (or Age Range) at Follow-up	Outcomes	Finding
Periodontal Health					
Thomson et al. ¹	Dunedin Multidisciplinary Health and Development Study: 903 men and women	18	32	Periodontal attachment loss	Cannabis use was associated with attachment loss, even after adjusting for tobacco use, sex, SES, dental service use, and plaque.
Lung Function ^a					
Pletcher et al. ²	Coronary Artery Risk Development in Young Adults (CARDIA): 5,016 men and women	18-30 (M=25)	Participants were followed up to 20 years from baseline	Forced expiratory volume (FEV ₁) and forced vital capacity (FVC)	In adjusted analyses (covariates included, but were not limited to, demographic factors and tobacco exposure), there was a non-linear association of cannabis exposure with FEV ₁ and FVC. At low levels of cannabis exposure, FEV ₁ and FVC increased. At higher levels of cannabis exposure, associations reversed (FEV ₁) or leveled (FVC).

eTable 1 Continued.

Study	Analysis Sample	Age (or Age Range) at Baseline	Age (or Age Range) at Follow-up	Outcomes	Finding
Hancox et al. ³	Dunedin Multidisciplinary Health and Development Study: 779 men and women	15	32	Forced expiratory volume (FEV ₁), forced vital capacity (FVC), and airflow obstruction (FEV ₁ /FVC)	In adjusted analyses (covariates included, but were not limited to, demographic factors, tobacco use, and baseline level of the outcome), cannabis use was associated with higher FVC but was not associated with FEV ₁ or FEV ₁ /FVC.
Taylor et al. ⁴	Dunedin Multidisciplinary Health and Development Study: 859-930 men and women	18	26	Forced expiratory volume (FEV ₁) and airflow obstruction (FEV ₁ /FVC)	In adjusted models (covariates included, but were not limited to, demographic factors and tobacco use), cannabis exposure was associated with reduced FEV ₁ but was not associated with FEV ₁ /FVC.
Tashkin et al. ⁵	255 men and women	M=33	Up to 8 years from baseline	Forced expiratory volume (FEV ₁)	Cannabis use was not associated with decline in FEV ₁ .

eTable 1 Continued.

Study	Analysis Sample	Age (or Age Range) at Baseline	Age (or Age Range) at Follow-up	Outcomes	Finding
Sherrill et al. ⁶	Tucson longitudinal study of airways obstructive disease: 856 men and women with pulmonary data from at least two assessments	15-60	Up to 6 years from baseline	Forced expiratory volume (FEV ₁) and airflow obstruction (FEV ₁ /FVC)	In adjusted models (covariates included, but were not limited to, demographic factors), previous cannabis use was associated with reduced FEV ₁ and FEV ₁ /FVC, whereas current cannabis use was associated with a non-significant increase in FEV ₁ and was not associated with FEV ₁ /FVC.
Systemic Inflammation					
Costello et al. ⁷	Great Smoky Mountains Study: 1334 boys and girls	9-16	21	C-reactive protein	Cannabis use was not associated with later C-reactive protein, controlling for past C-reactive protein. C-reactive protein predicted later cannabis use and cannabis use disorder controlling for previous cannabis use and cannabis-use disorder, but not after controlling for age, sex, race, body mass index, SES,

health, medications, and
psychiatric disorder.

eTable 1 Continued.

Study	Analysis Sample	Age (or Age Range) at Baseline	Age (or Age Range) at Follow-up	Outcomes	Finding
Metabolic Health					
Rodondi et al. ⁸	Coronary Artery Risk Development in Young Adults (CARDIA): 3,617 men and women	18-30	Participants were followed to 15 years from baseline.	Body mass index, waist circumference, systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, fasting plasma glucose	In unadjusted analyses, cannabis use was associated with larger waist circumference, higher systolic blood pressure, and higher triglycerides. In adjusted analyses (covariates included, but were not limited to, demographic factors; tobacco, alcohol, and illicit drug use; and baseline level of the outcome variable), all associations became non-significant.

Note. ^aWe report on spirometry measures (FEV₁, FVC, and FEV₁/FVC ratio). These are the most commonly reported measures of lung function in longitudinal studies, and FEV₁/FVC is the most sensitive measure for assessing airway remodeling in a large cohort. A few longitudinal studies of cannabis also included other measures of respiratory health. For a recent report from the Dunedin Study on cannabis and respiratory symptoms (e.g., morning cough, sputum production, wheeze), see Hancox et al.⁹

eTable 2. Physical health measures at age 38.

Measure	Description of Measure	Continuous Outcome: Mean and Standard Deviation	Categorical Outcome: Clinical Cutoffs and Prevalence for Females, Males
Periodontal Health	Examinations were conducted in all 4 quadrants using calibrated dental examiners; 3 sites (mesiobuccal, buccal, and distolingual) per tooth were examined, and gingival recession (the distance in millimeters from the cemento-enamel junction to the gingival margin) and probing depth (the distance from the gingival margin to the base of the pocket) were recorded using a PCP-2 probe. The attachment loss for each site was computed by summing gingival recession and probing depth (third molars were not included).	Mean attachment loss across all sites (combined attachment loss in millimeters): M=1.61, SD=0.74	Periodontal Disease: 1+ site(s) with 5 or more mm of attachment loss; ¹ 18%, 28%
Lung Function	Spirometry was performed before and after 200 mcg salbutamol inhaled via large-volume spacer. The best FEV ₁ (forced expiratory volume) and FVC (forced vital capacity) values from three acceptable and reproducible maneuvers were used. ¹⁰	Post-bronchodilator FEV ₁ /FVC ratio after 200 mg salbutamol: M=79.95, SD=6.46	Chronic obstructive pulmonary disease (airflow obstruction): FEV ₁ /FVC ratio < 0.70; ¹¹ 5%, 9%
Systemic Inflammation	Elevation in inflammation was assessed by assaying high-sensitivity C-reactive protein (mg/L). C-reactive protein level is thought to be one of the most reliable measured indicators of vascular inflammation and has been recently endorsed as an adjunct to traditional risk factor screening for cardiovascular risk. High-sensitivity C-reactive protein was measured on a Modular P analyzer (Roche Diagnostics, GmbH, D-68298, Mannheim, Germany) using a particle-enhanced immunoturbidimetric assay.	C-Reactive Protein Level (mg/L): M=2.43, SD=3.82	High C-reactive Protein: > 3 mg/L; ¹² 26%, 15%

eTable 2 Continued.

Measure	Description of Measure	Continuous Outcome: Mean and Standard Deviation	Categorical Outcome: Clinical Cutoffs and Prevalence for Females, Males
Metabolic Syndrome	Metabolic syndrome was assessed with five risk factor biomarkers: (i) high waist circumference, (ii) low high density lipoprotein cholesterol, (iii) high triglycerides, (iv) high blood pressure, and (v) high glycated hemoglobin. Study members with 3+ risk factors were defined as having the metabolic syndrome, per ATPIII guidelines (http://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf). ¹³ Categorical clinical cutoffs for the five biomarkers for metabolic syndrome are provided below.	-	Metabolic Syndrome: 3+ risks; 11%, 21%
Waist Circumference	Waist circumference (in centimeters).	Waist circumference in centimeters: M=86.41, SD=12.65	High Waist Circumference (Biomarker for Metabolic Syndrome): >88 cm for women or >102 cm for men; 25%, 16% ^a
High Density Lipoprotein (HDL)	Measured via blood in units of mmol/L using colorimetric assay on a Modular P analyzer.	HDL level (mmol/L): M=1.44, SD=0.42	Low HDL (Biomarker for Metabolic Syndrome): <1.3 mmol/L (50 mg/dL) for women or <1.04 mmol/L (40 mg/dL) for men; 25%, 26% ^{a,b}

eTable 2 Continued.

Measure	Description of Measure	Continuous Outcome: Mean and Standard Deviation	Categorical Outcome: Clinical Cutoffs and Prevalence for Females, Males
Triglyceride	Measured via blood in units of mmol/L using colorimetric assay on a Modular P analyzer.	Triglyceride level (mmol/L): M=2.06, SD=1.45	High Triglycerides (Biomarker for Metabolic Syndrome): ≥2.26 mmol/L (200 mg/dL); 14%, 50% ^{a,b}
Blood Pressure	Assessed according to standard protocols with a Hawksley random-zero sphygmomanometer with a constant deflation valve. ¹⁴	Systolic: M=120.26, SD=12.14; Diastolic: M=78.16, SD=9.93	High Blood Pressure (Biomarker for Metabolic Syndrome): ≥ 130 mm Hg for systolic or ≥ 85 mm Hg for diastolic; 16%, 38% ^a
Glycated Hemoglobin Concentration (HbA1c)	Glycated hemoglobin concentrations (expressed as a percentage of total hemoglobin) were measured by ion exchange high-performance liquid chromatography (Variant II; Bio-Rad, Hercules, CA) (coefficient of variation, 2.4%), a method certified by the U.S. National Glycohemoglobin Standardization Program (NGSP; http://www.ngsp.org/).	HbA1c (% of total hemoglobin): M=5.41, SD=0.54	High Glycated Hemoglobin (Biomarker for Metabolic Syndrome): Scores ≥ 5.7%; 14%, 23% ^c
Body Mass Index (BMI)	Height was measured to the nearest millimeter using a portable stadiometer. Weight was recorded to the nearest 0.1 kg using calibrated scales. Body mass index was measured as weight in kilograms divided by height in meters squared.	BMI: M=27.19, SD=5.31	Obese: BMI ≥ 30; 25%, 23%

eTable 2 Continued.

Measure	Description of Measure	Continuous Outcome: Mean and Standard Deviation	Categorical Outcome: Clinical Cutoffs and Prevalence for Females, Males
Self-Reported Health	Study members were asked: “In general, would you say your health is excellent, very good, good, fair, or poor?” Responses range from 5=excellent, to 1=poor.	Self-Reported Health Mean Rating: M=3.82, SD=0.85	Bad Health: Self ratings of fair or poor health; 5%, 8%

Note. ^aOn the basis of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). See <http://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf> ^bWe controlled the diets of all study members and obtained non-fasting lipids. Recent research suggests that fasting is unnecessary for lipids tests.¹⁵⁻¹⁹ We used the American Heart Association’s recommended cutoff of 200 mg/dL for non-fasting triglycerides. ^cOn the basis of the NGSP clinical advisory committee 2010 recommendation. See <http://www.ngsp.org/cac2010.asp>

eTable 3. Associations between tobacco and cannabis use from ages 18 to 38 and age-38 physical health are similar for continuous and categorical health outcomes and are similar before and after accounting for childhood health and SES.

		% or Mean As a Function of Use, Adjusted for Sex ^b					Model 1: Bivariate ^c			Model 2 ^d : + Control for Joint-Years (or Pack-Years)			Model 3 ^e : + Control for Childhood Health and SES		
Age 38 Health ^a	Exposure	Never Used	<5y/ No Dx	5 to <10 y/1Dx	10 to <15 y/2Dx	15+ y/3+ DX	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
A. Periodontal Health															
Categorical: % with 1+ Sites of >5mm Attachment Loss	Pack-years	12.26	16.00	20.74	36.29	52.89	1.63	1.51, 1.77	<.001	1.53	1.38, 1.70	<.001	1.49	1.34, 1.65	<.001
	Joint-Years	13.53	21.21	51.45	51.23	55.61	1.36	1.27, 1.46	<.001	1.11	1.02, 1.22	.020	1.11	1.01, 1.21	.024
	Cannabis Dependence	13.53	21.30	32.62	47.89	59.72	1.44	1.32, 1.57	<.001	1.13	1.02, 1.26	.024	1.12	1.01, 1.24	.031
Continuous: Mean Attachment Loss Across Sites (mm)	Pack-years	1.37	1.44	1.63	1.79	2.32	0.50	0.45, 0.56	<.001	0.45	0.38, 0.51	<.001	0.43	0.37, 0.50	<.001
	Joint-Years	1.41	1.57	2.08	2.21	2.51	0.33	0.26, 0.39	<.001	0.12	0.05, 0.18	<.001	0.12	0.05, 0.18	<.001
	Cannabis Dependence	1.41	1.57	1.75	2.06	2.58	0.33	0.27, 0.39	<.001	0.09	0.02, 0.16	.011	0.09	0.02, 0.16	.012

eTable 3 Continued.

		% or Mean As a Function of Use, Adjusted for Sex ^b					Model 1: Bivariate ^c			Model 2 ^d : + Control for Joint-Years (or Pack-Years)			Model 3 ^e : + Control for Childhood Health and SES		
Age 38 Health ^a	Exposure	Never Used	<5y/ No Dx	5 to <10 y/1Dx	10 to <15 y/2Dx	15+ y/3+ DX	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
B. Lung Function															
Categorical: % with COPD (FEV ₁ /FVC < 70)	Pack-years	5.06	7.93	6.54	7.80	10.55	1.30	1.06, 1.59	.010	1.26	1.01, 1.56	.038	1.18	0.95, 1.46	.147
	Joint-Years	5.26	6.81	11.33	10.81	9.75	1.18	0.98, 1.42	.075	1.06	0.87, 1.29	.58	1.10	0.90, 1.33	.36
	Cannabis Dependence	5.24	6.68	9.05	9.01	12.73	1.23	1.00, 1.52	.053	1.09	0.85, 1.40	.48	1.16	0.91, 1.47	.24
Continuous: FEV ₁ /FVC [±]	Pack-years	80.98	79.74	79.78	79.67	77.58	-0.19	-0.26, -0.13	<.001	-0.15	-0.22, -0.08	<.001	-0.14	-0.21, -0.06	<.001
	Joint-Years	80.72	80.15	77.95	78.09	76.43	-0.17	-0.23, -0.11	<.001	-0.10	-0.17, -0.02	.010	-0.10	-0.18, -0.03	.006
	Cannabis Dependence	80.72	80.17	78.93	78.47	76.47	-0.15	-0.22, -0.08	<.001	-0.06	-0.14, 0.01	.106	-0.07	-0.15, 0.00	.064

eTable 3 Continued.

		% or Mean As a Function of Use, Adjusted for Sex ^b					Model 1: Bivariate ^c			Model 2 ^d : + Control for Joint-Years (or Pack-Years)			Model 3 ^e : + Control for Childhood Health and SES		
Age 38 Health ^a	Exposure	Never Used	<5y/ No Dx	5 to <10 y/1Dx	10 to <15 y/2Dx	15+ y/3+ DX	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
C. Systemic Inflammation															
Categorical: % with High C-Reactive Protein (>3 mg/L)	Pack-years	18.41	13.94	33.36	17.66	27.93	1.17	1.04, 1.31	.007	1.16	1.02, 1.32	.023	1.13	0.99, 1.29	.075
	Joint-Years	20.26	19.66	24.95	30.90	22.02	1.09	0.97, 1.23	.145	1.01	0.88, 1.16	.88	1.01	0.88, 1.16	.88
	Cannabis Dependence	20.26	19.60	22.66	29.53	22.96	1.08	0.95, 1.23	.26	0.98	0.85, 1.13	.79	0.99	0.86, 1.14	.84
Continuous: C-Reactive Protein Level (mg/L)	Pack-years	2.32	1.70	3.20	2.05	3.17	0.12	0.05, 0.18	<.001	0.12	0.04, 0.19	.002	0.10	0.03, 0.18	.009
	Joint-Years	2.48	2.33	2.09	4.01	2.28	0.06	-0.01, 0.13	.073	0.00	-0.07, 0.08	.95	0.00	-0.07, 0.08	.96
	Cannabis Dependence	2.48	2.36	2.24	3.24	2.64	0.04	-0.02, 0.11	.21	-0.03	-0.11, 0.05	.46	-0.03	-0.11, 0.05	.50

eTable 3 Continued.

eTable 3 Continued.

eTable 3 Continued.

		% or Mean As a Function of Use, Adjusted for Sex ^b					Model 1: Bivariate ^c			Model 2 ^d : + Control for Joint-Years (or Pack-Years)			Model 3 ^e : + Control for Childhood Health and SES		
Age 38 Health ^a	Exposure	Never Used	<5y/ No Dx	5 to <10 y/1Dx	10 to <15 y/2Dx	15+ y/3+ DX	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
Continuous: HbA1c	Pack-years	5.40	5.33	5.36	5.37	5.53	0.11	0.05, 0.18	<.001	0.15	0.08, 0.23	<.001	0.15	0.07, 0.22	<.001
	Joint-Years	5.48	5.37	5.39	5.43	5.36	0.00	-0.07, 0.06	.94	-0.08	-0.15, -0.01	.037	-0.08	-0.15, -0.01	.030
	Cannabis Dependence	5.48	5.36	5.40	5.45	5.38	-0.03	-0.10, 0.03	.34	-0.13	-0.20, -0.05	.001	-0.13	-0.21, -0.06	<.001
E. Obesity															
Categorical: % with Body Mass Index \geq 30	Pack-years	24.76	23.49	31.16	21.12	22.38	0.98	0.87, 1.10	.69	1.02	0.89, 1.17	.78	0.96	0.84, 1.11	.62
	Joint-Years	31.20	21.98	24.54	22.88	13.70	0.90	0.79, 1.04	.154	0.89	0.76, 1.05	.169	0.90	0.77, 1.05	.166
	Cannabis Dependence	31.23	22.19	20.57	25.64	14.43	0.85	0.74, 0.97	.021	0.82	0.70, 0.95	.010	0.83	0.71, 0.96	.014
Continuous: Body Mass Index (BMI)	Pack-Years	27.50	26.80	27.89	27.30	26.32	-0.06	-0.12, 0.00	.066	-0.02	-0.10, 0.05	.51	-0.06	-0.13, 0.01	.12
	Joint-Years	28.22	26.92	26.26	26.38	25.59	-0.09	-0.15, -0.02	.011	-0.07	-0.15, 0.00	.050	-0.08	-0.15, -0.01	.043
	Cannabis Dependence	28.21	26.82	27.10	26.59	25.75	-0.11	-0.17, -0.04	.002	-0.10	-0.18, -0.03	.009	-0.10	-0.18, -0.02	.011

eTable 3 Continued.

		% or Mean As a Function of Use, Adjusted for Sex ^b					Model 1: Bivariate ^c			Model 2 ^d : + Control for Joint-Years (or Pack-Years)			Model 3 ^e : + Control for Childhood Health and SES		
Age 38 Health ^a	Exposure	Never Used	<5y/ No Dx	5 to <10 y/1Dx	10 to <15 y/2Dx	15+ y/3+ DX	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
F. Self-Reported Health															
Categorical: % with Bad Health (rating of fair or poor)	Pack-years	4.72	3.97	9.88	7.61	12.55	1.51	1.26, 1.82	<.001	1.48	1.17, 1.87	.001	1.42	1.11, 1.81	.005
	Joint-Years	6.34	5.79	11.35	13.04	12.77	1.26	1.06, 1.49	.010	1.04	0.83, 1.30	.75	1.02	0.82, 1.28	.85
	Cannabis Dependence	6.32	5.19	11.31	13.60	13.16	1.28	1.03, 1.58	.023	1.01	0.78, 1.32	.92	1.01	0.78, 1.31	.94
Continuous: Mean Health Rating [±]	Pack-years	3.97	3.96	3.72	3.70	3.43	-0.27	-0.33, -0.21	<.001	-0.26	-0.32, -0.19	<.001	-0.24	-0.31, -0.17	<.001
	Joint-Years	3.86	3.88	3.53	3.46	3.47	-0.15	-0.22, -0.09	<.001	-0.03	-0.10, 0.04	.42	-0.02	-0.09, 0.05	.58
	Cannabis Dependence	3.86	3.91	3.55	3.55	3.27	-0.16	-0.23, -0.10	<.001	-0.03	-0.11, 0.04	.40	-0.03	-0.10, 0.05	.47

Note: COPD=chronic obstructive pulmonary disease. a. Results are presented for categorically-scored (for clinical relevance) and continuously scored (for greater sensitivity to variation) versions of the health measures. b. For presentation of percentages and means, participants were grouped according to pack-years and joint-years between ages 18-38 as follows: never used tobacco daily/never used cannabis, used <5 years, used from 5 to <10 years, used from 10 to <15 years, and used for 15+ years. Participants were grouped according to persistence of cannabis dependence as follows: never used=never used cannabis, no dx=used cannabis at least once between ages 18-38 but never diagnosed, 1 dx= diagnosed once between ages 18-38, 2 dx=diagnosed twice, 3+ dx=diagnosed 3+ times. c. Model 1 controls for sex. d. Model 2 adds controls for joint-years in analyses of pack-years, and adds controls for pack-years in analyses of joint-years and cannabis dependence. e. Model 3 adds controls for childhood health and childhood SES. Statistical analyses tested associations of cumulative pack-years (a continuous variable), cumulative joint-years (a continuous variable), and cannabis dependence (a 5-level ordinal variable) with categorical and continuous outcomes. Relative risks are reported for categorical outcomes. Beta coefficients are reported for continuous outcomes. Continuous variables were standardized for statistical tests. Therefore, relative risks and beta coefficients can be interpreted as the increase in risk of the outcome, given a 1 SD unit increase in pack-years or joint-years. Relative risks greater than 1 and betas with a positive sign indicate poorer health except where noted. [±]Betas with a negative sign indicate poorer health. Statistically significant associations are shown in bold. All analyses control for sex. Analyses of lung function additionally control for height. Tobacco findings were unchanged after controlling for childhood health and SES, with two exceptions: tobacco pack-years was

no longer significantly associated with categorically-scored COPD or high C-reactive protein (although pack-years remained associated with the continuous versions of these measures). Cannabis findings were unchanged after controlling for childhood health and SES, with one exception: cannabis joint-years was now associated with lower BMI.

eTable 4. Associations between tobacco and cannabis use from ages 18 to 38 and lung function at age 38.

Lung Function	Tobacco Pack-Years		Cannabis Joint-Years		Cannabis Dependence	
	β	p	β	p	β	p
FEV ₁	-0.06	.001	-0.02	.43	-0.02	.44
FVC	0.02	.38	0.06	.002	0.05	.013

Note. FEV₁=forced expiratory volume. FVC=forced vital capacity. This table shows the results of regressions predicting FEV₁ and FVC from tobacco pack-years, cannabis joint-years, and cannabis dependence. Estimates are standardized beta coefficients and can be interpreted as the decrease in FEV₁ (and increase in FVC) given a 1 SD increase in pack-years or joint-years. All models control for sex and height. Statistically significant associations are shown in bold.

eTable 5. Associations between persistent regular cannabis use from ages 18 to 38 and age 38 physical health measures.

	Model 1: Bivariate			Model 2: + Control for Pack-Years			Model 3: + Control for Childhood Health and SES		
Age 38 Health ^a	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
A. Periodontal Health									
Categorical: % with 1+ Sites of > 5mm Attachment Loss	1.46	1.35, 1.58	<.001	1.17	1.05, 1.30	.005	1.16	1.05, 1.29	.004
Continuous: Mean Attachment Loss Across Sites (mm)	0.34	0.27, 0.40	<.001	0.11	0.04, 0.17	.002	0.11	0.04, 0.18	.001
B. Lung Function									
Categorical: % with COPD (FEV ₁ /FVC < 70)	1.26	1.02, 1.55	.029	1.13	0.89, 1.44	.31	1.18	0.94, 1.50	.16
Continuous: FEV ₁ /FVC [±]	-0.16	-0.23, -0.09	<.001	-0.08	-0.15, -0.01	.046	-0.09	-0.16, -0.01	.028

eTable 5 Continued.

	Model 1: Bivariate			Model 2: + Control for Pack-Years			Model 3: + Control for Childhood Health and SES		
Age 38 Health ^a	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
C. Systemic Inflammation									
Categorical: % with High C-Reactive Protein (>3 mg/L)	1.09	0.96, 1.24	.18	1.00	0.87, 1.15	.99	1.00	0.87, 1.16	.95
Continuous: C-Reactive Protein Level (mg/L)	0.05	-0.02, 0.12	.16	-0.02	-0.10, 0.06	.62	-0.02	-0.09, 0.06	.68
D. Metabolic Health									
Categorical: % with Metabolic Syndrome	0.99	0.85, 1.16	.91	0.87	0.72, 1.05	.15	0.87	0.73, 1.05	.15
Continuous: Waist (cm)	-0.08	-0.14, -0.02	.010	-0.10	-0.17, -0.03	.007	-0.09	-0.16, -0.02	.009

eTable 5 Continued.

	Model 1: Bivariate			Model 2: + Control for Pack-Years			Model 3: + Control for Childhood Health and SES		
Age 38 Health ^a	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
Continuous: High Density Lipoprotein (HDL) Level [±]	0.04	-0.02, 0.11	.16	0.11	0.03, 0.18	.004	0.11	0.03, 0.18	.005
Continuous: Triglyceride Level (mmol/L)	-0.03	-0.09, 0.03	.39	-0.08	-0.15, -0.02	.017	-0.08	-0.15, -0.01	.018
Continuous: Systolic Blood Pressure (mm Hg)	-0.03	-0.10, 0.03	.29	-0.03	-0.10, 0.04	.40	-0.03	-0.10, 0.04	.42
Continuous: Diastolic Blood Pressure (mm Hg)	-0.04	-0.10, 0.03	.24	-0.06	-0.13, 0.02	.14	-0.05	-0.13, 0.02	.16
Continuous: HbA1c	-0.05	-0.11, 0.02	.17	-0.14	-0.22, -0.07	<.001	-0.14	-0.22, -0.07	<.001

eTable 5 Continued.

	Model 1: Bivariate			Model 2: + Control for Pack-Years			Model 3: + Control for Childhood Health and SES		
Age 38 Health ^a	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
E. Obesity									
Categorical: % with Body Mass Index ≥ 30	0.87	0.75, 0.99	.049	0.85	0.72, 0.99	.044	0.85	0.73, 1.00	.05
Continuous: Body Mass Index (BMI)	-0.11	-0.18, -0.04	.001	-0.11	-0.18, -0.03	.006	-0.10	-0.18, -0.03	.007
F. Self-Reported Health									
Categorical: % with Bad Health (rating of fair or poor)	1.27	1.03, 1.57	.027	1.01	0.77, 1.33	.92	1.02	0.78, 1.32	.91
Continuous: Mean Health Rating [±]	-0.14	-0.21, -0.08	<.001	-0.01	-0.08, 0.07	.83	0.00	-0.08, 0.07	.92

Note: COPD=chronic obstructive pulmonary disease. Persistent regular cannabis use was defined as the number of study waves out of five at which a study member used cannabis for 4 or more days per week (the majority of days in a week). N=265 never used, n=536 used but never regularly, n=50 used regularly at one wave, n=41 used regularly at two waves, n=48 used regularly at 3+ waves. a. Results are presented for categorically-scored (for clinical relevance) and continuously-scored (for greater sensitivity to variation) versions of the health measures. Statistical analyses tested associations of persistent regular cannabis use (a 5-level ordinal variable) with categorical and continuous outcomes.

Relative risks are reported for categorical outcomes. Beta coefficients are reported for continuous outcomes. Relative risks greater than 1 and betas with a positive sign indicate poorer health except where noted. [±]Betas with a negative sign indicate poorer health. Statistically significant associations are shown in bold. All analyses control for sex. Analyses of lung function additionally control for height.

eTable 6. Descriptive summary of findings presented in Table 2 and eTable 3: associations of tobacco and cannabis use from ages 18 to 38 with age 38 physical health measures.

	Tobacco Pack-Years				Cannabis Joint-Years				Persistent Cannabis Dependence			
	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Joint-Years?	Findings Change After Additional Control for Child Health and SES?	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Pack-Years?	Findings Change After Additional Control for Child Health and SES?	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Pack-Years?	Findings Change After Additional Control for Child Health and SES?
Age 38 Health												
A. Periodontal Health	Worse Health	Yes	No	No	Worse Health	Yes	No	No	Worse Health	Yes	No	No
B. Lung Function	Worse Health	Yes	No	Yes. Statistically significant association was apparent only for the continuous version.	Worse Health	No. Statistically significant association was apparent only for the continuous version.	No	No	Worse Health	No. Statistically significant association was apparent only for the continuous version.	Yes. Association was no longer statistically significant.	No
C. Inflammation	Worse Health	Yes	No	Yes. Statistically significant association was apparent only for the continuous version.	None	Yes	No	No	None	Yes	No	No

eTable 6 Continued.

	Tobacco Pack-Years				Cannabis Joint-Years				Persistent Cannabis Dependence			
	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Additional Control for Joint-Years?	Findings Change After Additional Control for Child Health and SES?	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Additional Control for Pack-Years?	Findings Change After Additional Control for Child Health and SES?	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Additional Control for Pack-Years?	Findings Change After Additional Control for Child Health and SES?
Age 38 Health												
D. Metabolic Health												
Metabolic Syndrome	Worse Health	N/A	No	No	None	N/A	No	No	None	N/A	No	No
Waist Circ.	None	N/A	No	No	Better Health	N/A	No	No	Better Health	N/A	No	No
High Density Lipoprotein	Worse Health	N/A	No	No	None	N/A	Yes. Cannabis use was now associated with better health.	No	None	N/A	Yes. Cannabis use was now associated with better health.	No
Triglyc.	Worse Health	N/A	No	No	None	N/A	Yes. Cannabis use was now associated with better health.	No	None	N/A	Yes. Cannabis use was now associated with better health.	No

eTable 6 Continued.

	Tobacco Pack-Years				Cannabis Joint-Years				Persistent Cannabis Dependence			
		Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Joint- Years?	Findings Change After Additional Control for Child Health and SES?		Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Pack- Years?	Findings Change After Additional Control for Child Health and SES?		Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Pack- Years?	Findings Change After Additional Control for Child Health and SES?
Age 38 Health												
Systolic Blood Pressure	None	N/A	No	No	None	N/A	No	No	None	N/A	No	No
Diastolic Blood Pressure	None	N/A	No	No	None	N/A	No	No	None	N/A	Yes. Cannabis use was now associated with better health.	No
HbA1c	Worse Health	N/A	No	No	None	N/A	Yes. Cannabis use was now associated with better health.	No	None	N/A	Yes. Cannabis use was now associated with better health.	No

eTable 6 Continued.

	Tobacco Pack-Years				Cannabis Joint-Years				Persistent Cannabis Dependence			
	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Joint-Years?	Findings Change After Additional Control for Child Health and SES?	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Pack-Years?	Findings Change After Additional Control for Child Health and SES?	Biv. Assoc.	Biv. Assoc. Similar Across Categorical and Continuous Versions of Health Measure?	Findings Change After Control for Pack-Years?	Findings Change After Additional Control for Child Health and SES?
Age 38 Health												
E. Obesity	None	Yes	No	No	Better Health	No. Statistically significant association was apparent only for the continuous version.	Yes. Cannabis use was now not associated with health.	Yes. Cannabis was now associated with better health.	Better Health	Yes	No	No
F. Self-reported Health	Worse Health	Yes	No	No	Worse Health	Yes	Yes. Cannabis use was now not associated with health.	No	Worse Health	Yes	Yes. Cannabis use was now not associated with health.	No

Note. Biv Assoc. = bivariate association. Trigly. = triglycerides. Bivariate associations showed that tobacco pack-years was associated with worse health for eight of the twelve health outcomes (periodontal health, lung function, inflammation, metabolic syndrome, high density lipoprotein, triglycerides, HbA1c, and self-reported health). Associations remained significant for all eight of these health outcomes (when considering either the continuous or the categorical version of the health outcome) after controlling for cannabis joint-years, childhood health, and childhood SES. Bivariate associations showed that cannabis joint-years was associated with worse health for three (periodontal health, lung function, self-reported health) of the twelve health outcomes (when considering either the continuous or the categorical version of the health outcome). Adverse associations remained significant for two (periodontal health, lung function) of those three health outcomes after controlling for tobacco joint-years, childhood health, and childhood SES. Bivariate associations showed that persistent cannabis dependence was associated with worse health for three (periodontal health, lung function, self-reported

health) of the twelve health outcomes (when considering either the continuous or the categorical version of the health outcome). Adverse associations remained significant for one (periodontal health) of those three health outcomes after controlling for tobacco pack-years, childhood health, and childhood SES.

eTable 7. Description of Additional Covariates

Covariate	Description	Association with Cannabis Joint-Years		Association with Persistent Cannabis Dependence	
Teeth Brushing	Study members were asked how often they brushed their teeth at age 38. Responses were “more than once a day,” “once a day,” “not every day,” “less than once a week,” and “never.” Higher scores indicate more frequent brushing.	r=-0.29	p<.001	r=-0.26	p<.001
Teeth Flossing	Study members were asked how often they flossed their teeth at age 38. Responses were “every day,” “sometimes,” “rarely,” and “never.” Higher scores indicate more frequent flossing.	r=-0.13	p<.001	r=-0.15	p<.001
Alcohol Dependence	Past-year alcohol dependence diagnoses were made at age 38 using the Diagnostic Interview Schedule (DIS) following Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria. ²⁰⁻²²	OR=1.48	p<.001	OR=1.83	p<.001
Adult Physical Activity	We measured adulthood physical activity level from data collected during structured interviews with Study members at the age 38 assessment. ²³ Trained interviewers guided study members through reporting the different types of physically demanding activities they engaged in during an average week and an average weekend. Activities were converted to metabolic equivalent (MET) units, with moderate intensity activity given a weight of 4, hard activity given a weight of 6, and very hard activity given a weight of 10. ²⁴ Study members then indicated the number of minutes they spent doing each activity, which we used to calculate MET minutes. We summed weekday and weekend MET minutes to calculate adulthood physical activity levels. Study members were grouped	r=-0.04	p=.28	r=0.00	p=.99

according to United State Department of Health and Human Services Physical Activity Guidelines for Americans (<http://health.gov/paguidelines/guidelines/appendix1.aspx>): 22% of the cohort members were sedentary (they engaged in 0 minutes of moderate or more strenuous activity per week); 18% were non-sedentary, but did not achieve the 500 MET minutes/wk minimum recommended dosage of physical activity; 21% achieved the 500-1000 MET minutes/wk; and 39% were above minimum recommendations (>1000 MET minutes per week).

Fruit and Vegetable Intake

As part of an interview on diet, Study members were asked how many servings of fruit and how many servings of vegetables (excluding juices) they ate daily at age 38. Responses were coded as “less than 1 per day,” “1 per day,” “2 per day,” and “3 or more servings per day.” Responses were summed to create a single scale indexing fruit and vegetable intake. The scale ranged from 0 (less than 1 serving of fruits and vegetables each day) to 6 (3 or more servings of fruit and vegetables per day), with a mean of 3.78 (SD=1.50).

$r=-0.12$

$p<.001$

$r=-0.14$

$p<.001$

Note. r =pearson correlation. OR = odds ratio.

eTable 8. Associations between tobacco and cannabis use from ages 18 to 38 and age-38 periodontal health. Results are presented for models predicting periodontal health from tobacco and cannabis use, with pack-years (or joint-years), childhood health and SES, teeth brushing and flossing, and alcohol dependence entered as simultaneous covariates.

Age 38 Health ^a	Exposure	(RR or β)	95% CI	p
A. Periodontal Health				
Categorical: % with 1+ Sites of >5mm Attachment Loss	Pack-years	1.49	1.33, 1.66	<.001
	Joint-Years	1.09	1.00, 1.19	.05
	Cannabis Dependence	1.11	1.01, 1.24	.046
Continuous: Mean Attachment Loss Across Sites (mm)	Pack-years	0.43	0.36, 0.49	<.001
	Joint-Years	0.10	0.03, 0.16	.004
	Cannabis Dependence	0.08	0.01, 0.15	.029

Note: a. Results are presented for categorically-scored (for clinical relevance) and continuously scored (for greater sensitivity to variation) versions of the health measures. Analyses of pack-years control for joint-years and analyses of joint-years and cannabis dependence control for pack-years. Statistical analyses tested associations of cumulative pack-years (a continuous variable), cumulative joint-years (a continuous variable), and cannabis dependence (a 5-level ordinal variable) with categorical and continuous outcomes. Relative risks are reported for categorical outcomes. Beta coefficients are reported for continuous outcomes. Continuous variables were standardized for statistical tests. Therefore, relative risks and beta coefficients can be interpreted as the increase in risk of the outcome, given a 1 SD unit increase in pack-years or joint-years. Relative risks greater than 1 and betas with a positive sign indicate poorer health. All analyses control for sex.

eTable 9. Within-individual change in lung function from ages 26 to 38: associations between tobacco and cannabis use from ages 26 to 38 and lung function at age 38, controlling for baseline lung function at age 26.

Lung Function		Tobacco Pack-Years		Cannabis Joint-Years		Cannabis Dependence	
		β	p	β	p	β	p
FEV ₁	Bivariate	-0.08	<.001	-0.02	.47	-0.01	.71
	+ Control for Baseline at Age 26	-0.06	<.001	-0.02	.178	-0.04	.030
	+ Control for Joint-Years (or Pack-Years)	-0.06	<.001	0.01	.60	0.00	.91
FVC	Bivariate	0.00	.98	0.04	.019	0.05	.022
	+ Control for Baseline at Age 26	0.00	.84	0.03	.011	0.02	.137
	+ Control for Joint-Years (or Pack-Years)	-0.01	.28	0.03	.006	0.03	.077

Note. FEV₁=forced expiratory volume. FVC=forced vital capacity. This table shows the results of regressions predicting age-38 FEV₁ and FVC from age 26-38 tobacco pack-years, cannabis joint-years, and cannabis dependence. To test within-individual change, we controlled for baseline age-26 lung function. Estimates are standardized betas. All models controlled for sex and height. Statistically significant associations are shown in bold.

eTable 10. Within-individual change in health from ages 26 to 38: associations between tobacco and cannabis use from ages 18 to 38 and age-38 physical health are similar for continuous and categorical health outcomes.

		Model 1: Bivariate			Model 2: + Control for Baseline at Age 26			Model 3 ^b : + Control for Joint- Years (or Pack-Years)		
Age 38 Health ^a	Exposure	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
A. Periodontal Health										
Categorical: % with 1+ Sites of >5mm Attachment Loss	Pack-years	1.62	1.49, 1.75	<.001	1.59	1.47, 1.72	<.001	1.53	1.39, 1.69	<.001
	Joint-Years	1.32	1.23, 1.42	<.001	1.30	1.20, 1.40	<.001	1.08	0.98, 1.18	.110
	Cannabis Dependence	1.57	1.39, 1.77	<.001	1.54	1.37, 1.74	<.001	1.18	1.03, 1.36	.015
Continuous: Mean Attachment Loss Across Sites (mm)	Pack-years	0.50	0.44, 0.56	<.001	0.42	0.36, 0.47	<.001	0.37	0.31, 0.43	<.001
	Joint-Years	0.32	0.25, 0.38	<.001	0.25	0.19, 0.31	<.001	0.10	0.05, 0.16	<.001
	Cannabis Dependence	0.37	0.29, 0.45	<.001	0.30	0.23, 0.38	<.001	0.11	0.04, 0.19	.002

eTable 10 Continued.

Age 38 Health ^a	Exposure	Model 1: Bivariate			Model 2: + Control for Baseline at Age 26			Model 3 ^b : + Control for Joint-Years (or Pack-Years)		
		(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
B. Lung Function										
Categorical: % with COPD (FEV ₁ /FVC < 70)	Pack-years	1.27	1.02, 1.57	.030	1.27	1.05, 1.55	.015	1.33	1.10, 1.62	.004
	Joint-Years	1.13	0.92, 1.39	.24	1.01	0.84, 1.20	.93	0.91	0.78, 1.06	.22
	Cannabis Dependence	1.20	0.92, 1.56	.178	1.18	0.92, 1.53	.199	1.03	0.80, 1.33	.81
Continuous: FEV ₁ /FVC [±]	Pack-years	-0.19	-0.26, -0.12	<.001	-0.14	-0.19, -0.10	<.001	-0.11	-0.16, -0.06	<.001
	Joint-Years	-0.15	-0.21, -0.08	<.001	-0.11	-0.16, -0.07	<.001	-0.07	-0.12, -0.02	.008
	Cannabis Dependence	-0.17	-0.26, -0.09	<.001	-0.14	-0.20, -0.09	<.001	-0.08	-0.15, -0.02	.011

eTable 10 Continued.

		Model 1: Bivariate			Model 2: + Control for Baseline at Age 26			Model 3 ^b : + Control for Joint- Years (or Pack-Years)		
Age 38 Health ^a	Exposure	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
C. Systemic Inflammation										
Categorical: % with High C-Reactive Protein (>3 mg/L)	Pack-years	1.16	1.02, 1.31	.026	1.16	1.03, 1.32	.019	1.11	0.97, 1.28	.135
	Joint-Years	1.14	1.01, 1.29	.038	1.16	1.03, 1.32	.017	1.11	0.97, 1.28	.145
	Cannabis Dependence	1.17	0.97, 1.40	.093	1.21	1.00, 1.46	.050	1.13	0.92, 1.38	.25
Continuous: C-Reactive Protein Level (mg/L)	Pack-years	0.11	0.04, 0.18	.003	0.11	0.04, 0.17	.002	0.09	0.01, 0.16	.021
	Joint-Years	0.08	0.01, 0.16	.026	0.09	0.02, 0.16	.013	0.05	-0.03, 0.13	.199
	Cannabis Dependence	0.02	-0.07, 0.12	.61	0.04	-0.05, 0.13	.38	-0.02	-0.12, 0.07	.62

eTable 10 Continued.

		Model 1: Bivariate			Model 2: + Control for Baseline at Age 26			Model 3 ^b : + Control for Joint- Years (or Pack-Years)		
Age 38 Health ^a	Exposure	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
D. Metabolic Health										
Categorical: % with Metabolic Syndrome	Pack-years	1.18	1.03, 1.36	.020	1.18	1.02, 1.35	.021	1.21	1.04, 1.41	.014
	Joint-Years	1.00	0.86, 1.16	.99	1.01	0.88, 1.17	.88	0.93	0.79, 1.10	.41
	Cannabis Dependence	1.02	0.84, 1.26	.80	1.07	0.88, 1.31	.50	0.98	0.79, 1.21	.84
E. Obesity										
Categorical: % with Body Mass Index ≥ 30	Pack-years	0.96	0.84, 1.09	.49	0.96	0.86, 1.08	.49	1.00	0.89, 1.12	.99
	Joint-Years	0.88	0.76, 1.01	.073	0.91	0.80, 1.05	.21	0.91	0.79, 1.06	.24
	Cannabis Dependence	0.84	0.71, 0.99	.047	0.92	0.79, 1.07	.27	0.93	0.80, 1.09	.37
Continuous: Body Mass Index (BMI)	Pack-Years	-0.07	-0.14, -0.01	.027	0.00	-0.04, 0.04	.91	0.02	-0.03, 0.06	.51
	Joint-Years	-0.09	-0.16, -0.03	.006	-0.02	-0.06, 0.02	.35	-0.03	-0.07, 0.02	.25
	Cannabis Dependence	-0.13	-0.21, -0.04	.004	-0.01	-0.07, 0.04	.60	-0.01	-0.07, 0.04	.59

eTable 10 Continued.

		Model 1: Bivariate			Model 2: + Control for Baseline at Age 26			Model 3 ^b : + Control for Joint- Years (or Pack-Years)		
Age 38 Health ^a	Exposure	(RR or β)	95% CI	p	(RR or β)	95% CI	p	(RR or β)	95% CI	p
F. Self-Reported Health										
Categorical: % with Bad Health (rating of fair or poor)	Pack-years	1.54	1.29, 1.84	<.001	1.37	1.11, 1.70	.004	1.37	1.08, 1.73	.010
	Joint-Years	1.14	0.94, 1.40	.192	1.08	0.87, 1.33	.49	0.96	0.78, 1.19	.72
	Cannabis Dependence	1.26	0.94, 1.69	.118	1.17	0.88, 1.55	.29	1.00	0.73, 1.37	.99
Continuous: Mean Health Rating [±]	Pack-years	-0.27	-0.33, -0.21	<.001	-0.16	-0.22, -0.10	<.001	-0.16	-0.22, -0.10	<.001
	Joint-Years	-0.11	-0.18, -0.05	<.001	-0.06	-0.11, 0.00	.064	0.01	-0.05, 0.07	.77
	Cannabis Dependence	-0.17	-0.26, -0.09	<.001	-0.12	-0.19, -0.04	.002	-0.04	-0.12, 0.04	.34

Note. COPD=chronic obstructive pulmonary disease. a. Results are presented for categorically-scored (for clinical relevance) and continuously scored (for greater sensitivity to variation) versions of the health measures. b. Model 3 adds controls for joint-years in analyses of pack-years, and adds controls for pack-years in analyses of joint-years and cannabis dependence. Statistical analyses tested associations of cumulative pack-years (a continuous variable), cumulative joint-years (a continuous variable), and cannabis dependence (a 5-level ordinal variable) with categorical and continuous outcomes. Relative risks are reported for categorical outcomes. Beta coefficients are reported for continuous outcomes. Continuous variables were standardized for statistical tests. Therefore, relative risks and beta coefficients can be interpreted as the increase in risk of the outcome, given a 1 SD increase in pack-years or joint-years. Relative risks greater than 1 and betas with a positive sign indicate poorer health except where noted. [±]Betas with a negative sign indicate poorer health. Statistically significant associations are shown in bold. All models control for sex. Analyses of lung function additionally control for height.

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