Supporting information

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SI Methods

Based on the confounding interpretation of the Meier et al. (1) estimates, a simulation model was built using Mathematica (v6) to generate simulated data samples of similar size. A total of 875 participants were drawn from three socioeconomic status (SES) levels (175 high and low, 525 midlevel). Each participant was characterized by an SES level, a long-run adult IQ, a randomly drawn "childhood environmental influence," and a randomly drawn cannabis exposure. All draws were from distributions that differed by SES.

Adult IQ is here thought of as an equilibrium IQ-value determined by genetic factors and permanent effects of early environment. Adult IQ was drawn from a normal distribution with an overall mean of 100 and a mean conditional on SES of 107.5 (high SES), 100 (mid SES), and 92.5 (low SES). This distribution gives a correlation of about 0.38, between parental SES and adult IQ, comparable to empirical estimates, which are around 0.33 (2).

Childhood IQ is a weighted sum of an individual's adult ("long-run") IQ and a "forced environment" component that compresses IQ differences, based on the assumption that schooling raises the "baseline" cognitive demands faced by low-SES groups. The environmental component is drawn from a normal distribution with SD of 20 and a mean that varied by SES from 103 (high SES) to 100 (mid SES) and 97 (low SES). In line with the differing heritability of childhood IQ for different SES groups, the long-run IQ counted for 70% of childhood IQ for high-SES, 40% for mid-SES, and 10% for low-SES groups. In Mathematica code:

IQadult[SES_]:=RandomReal[NormalDistribution[107.5–7.5*(SES-1),15]], and

childshare={0.7,0.4,0.1};IQchild[IQadult_, SES_]:=childshare[[SES]]*IQadult+(1-childshare[[SES]])*RandomReal[NormalDistribution[103-3*(SES-1),20]]

Taken together, these assumptions imply that low-SES individuals on average will see their IQs decline by ∼4 IQ points (∼0.25 SD units) from childhood to adulthood.

Cannabis exposure was determined by a set of transition probabilities for progressing from nonuse to use and to dependence once, twice, or three or more times. The transition probabilities were constructed to match three targets. First, the expected number in each cannabis-exposure group should be similar to the actual numbers observed in the actual Dunedin cohort. Second, lower-SES individuals should have a higher risk of progressing to the next cannabis-exposure group at each stage. The odds ratio of ever-dependence (conditional on use) for low-SES participants was set close to 18, which is similar to (but smaller) than the odds ratio found in the Munich study (3). Transition probabilities for the baseline specification and a robustness check are shown in Table S1.

Taken together, these assumptions ensure that the mid- and low-SES individuals represent a larger share of higher cannabis-exposure groups.

The model reproduces the Meier et al. (1) results. To examine the confounding model's sensitivity to the assumptions in the baseline model, a battery of sensitivity checks was performed (Table S2). The results are largely reproduced as long as low-SES individuals are more highly represented in higher cannabis-exposure groups, while also having a negative expected IQ-change on average. In the baseline simulation, the transition probabilities imply that all individuals in the highest cannabis-exposure group come from the low-SES group. The alternative transition probabilities (Table S1) reduce the sorting intensity and produce a 46% share of mid-SES individuals in the highest exposure group. The low-SES group's odds ratio for dependence given use falls from 18 to 3. By combining less-strict sorting with a stronger average IQ-decline for low-SES individuals (6 IQ points, equivalent to 0.4 SD), the confounding effects stay more or less the same.

1. Meier MH, et al. (2012) Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci USA* 109(40):E2657–E2664.
2. Neisser U, et al. (1996) Intelligence: Knowns and unknowns. *Am Psychol* 51(2):77–101.
3. von Sydow K, Lieb R, Pfister H, Höfler M, Wittchen HU (2002) What predicts incident use of cannabis and progression to abuse and dependence? A 4-year prospective examination of risk factors in a community sample of adolescents and young adults. *Drug Alcohol Depend* 68(1):49–64.

Table S1. Probability distribution over cannabis exposure groups by SES

	Baseline specification			Weaker selection specification (used in sensitivity analysis (Table S2)		
Cannabis exposure	High SES (n = 175) (%)	Mid SES (n = 525) (%)	Low SES (n = 175) (%)	High SES (n = 175) (%)	Mid SES (n = 525) (%)	Low SES (n = 175) (%)
No use	55.0 (39.3)*	25.0 (53.5)	10.0 (7.2)	55.0 (39.3)	25.0 (53.5)	10.0 (7.2)
Used, never diagnosed	42.8 (15.7)	66.0 (72.7)	31.5 (11.6)	38.3 (14.1)	60.0 (66.1)	54.0 (19.9)
One diagnosis	2.1 (4.4)	7.7 (47.3)	23.4 (48.3)	6.4 (14.8)	7.5 (51.9)	14.4 (33.3)
Two diagnoses	0.1 (0.6)	1.4 (22.2)	14.0 (77.2)	0.3 (1.7)	3.8 (55.6)	8.6 (42.8)
Three+ diagnoses	0 (0)	0 (0)	21.1 (100)	0 (0)	3.8 (46.4)	13.0 (53.6)
Sum	100	100	100	100	100	100

*Parentheses state the expected SES share of each cannabis-exposure group.

Table S2. Effects in Meier et al., (1) and effects (SDs across 500 runs) in the baseline specification of the simulation model, and in different sensitivity checks

Cannabis use	Meier et al. (1)	Baseline simulation	Weight of environmental influence in low SES childhood IQ*		SES-related IQ difference in childhood environmental component†		Sorting by SES into exposure groups‡		Interaction between sorting by SES and size of childhood environmental boost§
			0	0.7	0	15	Lower	Reversed	
No use	0.05	0.02 (0.06)	0.02 (0.06)	0.03 (0.05)	0.03 (0.06)	−0.02 (0.05)	0.02 (0.05)	−0.10 (0.07)	0.03 (0.05)
Used, never diagnosed	−0.07	−0.02 (0.05)	−0.02 (0.05)	−0.01 (0.04)	−0.03 (0.04)	0.02 (0.04)	−0.04 (0.05)	−0.03 (0.05)	−0.07 (0.05)
One diagnosis	−0.11	−0.12 (0.13)	−0.13 (0.14)	−0.04 (0.08)	−0.21 (0.14)	0.20 (0.14)	−0.06 (0.13)	0.03 (0.08)	−0.12 (0.13)
Two diagnoses	−0.17	−0.22 (0.25)	−0.21 (0.28)	−0.07 (0.11)	−0.35 (0.26)	0.34 (0.26)	−0.12 (0.22)	0.07 (0.13)	−0.18 (0.21)
Three+ diagnoses	−0.38	−0.29 (0.26)	−0.31 (0.29)	−0.10 (0.08)	−0.45 (0.26)	0.48 (0.26)	−0.13 (0.21)	0.09 (0.08)	−0.23 (0.21)
Difference max exposure to min exposure	−0.43	−0.31	−0.33	−0.13	−0.48	0.46	−0.15	0.01	−0.26

Each sensitivity check altered one effect in the baseline specification. Reported SDs based on 500 independent runs per specification. The last column shows how weaker selection effects combined with lower SES-related differences in childhood component of IQ brings results back in line with the baseline simulation.

*0.1 in baseline specification; the share is set at 0.4 for mid SES and 0.7 for high SES.

†Because average IQ differs with 7.5 points (0.5 SD units) between each SES level in adulthood, lower differences in the childhood environmental component will raise low SES IQ in childhood (relative to adulthood) and larger values will lower low SES IQ in childhood. Baseline difference on childhood component is 3 points (0.2 SD units).

‡In the "lower" specification, the odds ratio for dependence given use for low-SES individuals fell from 18 to 3, and the share of the "Three+ diagnoses" group that came from low SES fell from 100% to 54%. The probabilities are given in Table S1.

§Combines the assumptions used in the column labeled "Lower" under "Sorting by SES into exposure groups" and the column labeled "0" under "SES-related IQ difference in childhood environmental component."