Adolescent cannabis and tobacco use and educational outcomes at age 16: birth cohort study

Alexander I. Stiby¹, Matthew Hickman¹, Marcus R. Munafò², Jon Heron¹, Vikki L. Yip³ & John Macleod¹

School of Social and Community Medicine, University of Bristol, Bristol, Bristol BS8 2PS, UK¹ MRC Integrative Epidemiology Unit, UK Centre for Tobacco Control Studies and School of Experimental Psychology, University of Bristol, Bristol, UK² and Avon Longitudinal Study of Parents and Children, School of Social and Community Medicine, University of Bristol, Bristol, UK³

ABSTRACT

Aims To investigate the relationship between cannabis and tobacco use by age 15 and subsequent educational outcomes. Design Birth cohort study. Setting England. Participants The sample was drawn from the Avon Longitudinal Study of Parents and Children; a core sample of 1155 individuals had complete information on all the variables. Measurements The main exposures were cannabis and tobacco use at age 15 assessed in clinic by computerassisted questionnaire and serum cotinine. The main outcomes were performance in standardized assessments at 16 [Key Stage 4, General Certificate of Secondary Education (GCSE)] in English and mathematics (mean scores), completion of five or more assessments at grade C level or higher and leaving school having achieved no qualifications. Analyses were sequentially adjusted for multiple covariates using a hierarchical approach. Covariates considered were: maternal substance use (ever tobacco or cannabis use, alcohol use above recommended limits); life course socio-economic position (family occupational class, maternal education, family income); child sex; month and year of birth; child educational attainment prior to age 11 (Key Stage 2); child substance use (tobacco, alcohol and cannabis) prior to age 15 and child conduct disorder. Findings In fully adjusted models both cannabis and tobacco use at age 15 were associated with subsequent adverse educational outcomes. In general, the dose-response effect seen was consistent across all educational outcomes assessed. Weekly cannabis use was associated negatively with English GCSE results [grade point difference (GPD), -5.93, 95% confidence interval (CI) = -8.34, -3.53] and with mathematics GCSE results (GPD, -6.91, 95%CI = -9.92, -3.89). Daily tobacco smoking was associated negatively with English GCSE (GPD, -11.90, 95%CI = -13.47, -10.33) and with mathematics GCSE (GPD, -16.72, 95% CI = -18.57, -14.86). The greatest attenuation of these effects was seen on adjustment for other substance use and conduct disorder. Following adjustment, tobacco appeared to have a consistently stronger effect than cannabis. Conclusions Both cannabis and tobacco use in adolescence are associated strongly with subsequent adverse educational outcomes. Given the non-specific patterns of association seen and the attenuation of estimates on adjustment, it is possible that these effects arise through non-causal mechanisms, although a causal explanation cannot be discounted.

Keywords ALSPAC, cannabis use, cotinine, education, English, GCSE, mathematics, school dropout, smoking.

Correspondence to: Alexander I. Stiby, School of Social and Community Medicine, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS8 2BN, UK. E-mail: a.stiby@bristol.ac.uk.

Submitted 4 June 2014; initial review completed 5 August 2014; final version accepted 2 December 2014

INTRODUCTION

Cannabis use, particularly among young people, is still relatively common [1-3]. UK cannabis use has been reportedly declining since its peak, although 2012/13 figures estimate that 30.9% of 16-24 year olds have ever used cannabis and 13.5% have smoked cannabis in the last year [4]. Various adverse psychosocial outcomes have been reported to be associated with cannabis use; however, the causal basis for these associations is often unclear. Lower educational attainment, for example, is associated consistently with higher use of cannabis. Evidence that this association is causal, such that preventing cannabis use among young people would increase their educational attainment, would have important implications for policy. A recent co-twin control study found that cannabis does not cause adverse education outcomes, but both traits are influenced by the same family environmental factors [5]. The available population-based evidence is exclusively observational, reflecting the practical and ethical difficulties inherent in an experimental approach. This situation is common in aetiological epidemiology, and several strategies have been devised to guide causal inference in observational data [6]. These strategies include consideration of evidence for noncausal associations such as those arising through confounding, measurement approaches that reduce the potential for bias and the use of longitudinal data to establish direction of causality. A further, perhaps neglected criterion for causality is specificity of association [7]. In general, non-specific associations are less likely to be causal [8].

In a large population-based prospective observational birth cohort study we investigated the effects of cannabis use by age 15 on subsequent educational outcomes. We examined evidence for confounding by adjusting for multiple possible confounding factors in multivariate models. We used linkage to independent administrative data to ascertain educational outcomes to minimize the risk of measurement bias related to self-report. We also adjusted effect estimates for educational attainment prior to cannabis use to address the issue of reverse causation. Finally, we considered the issue of specificity of association by investigating the effects of tobacco use on the same educational outcomes. We investigated the effects of both biologically verified and self-reported tobacco use, again to consider evidence for possible bias.

METHODS

Data

The core sample of the Avon Longitudinal Study of Parents and Children (ALSPAC) includes 14 541 women who were expecting to deliver infants between 1 April 1991 and 31 December 1992 in the former county of Avon, UK. ALSPAC parents and children have been followed-up regularly since recruitment [9]. Ethical approval for the study was granted by the ALSPAC Law and Ethics Committee and the local research ethics committee. Full details about the ALSPAC study and design are described elsewhere (http://www.bristol.ac.uk/alspac).

Outcome variables

The outcome variables used were standardized compulsory examination results at Key Stage 4, known as General Certificate of Secondary Education (GCSE) results; these were all from the National Pupil Database (NPD) [10]. The variables investigated were: English GCSE results (per cent), Mathematics GCSE results (per cent), did not gain grade C or above in five or more GCSEs and gaining no GCSE passes. GCSE grades in English and Mathematics were converted into a percentage from a letter grade by using the median percentage in each grade category. Grades were available in nine categories and range from A Star' to G and U (ungraded/unclassified), and encompass 10% per grade point category, except U, which corresponds to 20%. We used the outcome not gaining 5 or more GCSE results at grade C because 5 or more GCSEs at grade C is the standard level for entry into post-16 education, therefore not achieving this will probably mean not continuing to college or sixth form. Gaining no GCSE passes would infer dropping out of school at 16 with no qualifications. These were all measured at approximately 16 years of age (the standard age for taking GCSEs and the end of compulsory education in England).

Exposure variables

The exposure variables considered were measured in the clinic using computer-based questionnaires, as follows: cannabis use (never, ever), cannabis use frequency (never, non-weekly, weekly) and a Cannabis Abuse Screening Test (CAST) score of 4 and above (no, yes) [11]. The CAST score is a standard set of questions to measure an individual's use of cannabis. A score of 4 or more was used as a measure of cannabis 'abuse', also known as problematic use (i.e. use which could lead to detrimental health or social consequences) [11].

Self-reported tobacco use (never, less than daily, daily) and tobacco use assessed by measuring serum cotinine biomarker measures were used (Appendix 1). Participants were classified as smoker/non-smoker using the cut-off of 9.5 ng/ml blood [12,13]. As cotinine has a half-life of around 24 hours, this categorization in effect classifies individuals as daily smokers versus non-daily or non-smokers.

Covariates

Covariates were included on the basis of either previous evidence that they were associated with both substance use and educational outcomes or theoretical considerations suggesting that they may confound an association between these. Covariates were grouped into proximate and distal determinants. The distal determinants can have an interrelationship with the more proximate determinants, and therefore need to be ordered in this way for multivariable analysis [14]. Covariate models included measures within broad models; these models were grouped into maternal substance use, demographics, previous educational attainment and child behaviours, such as substance use and conduct disorder (see Appendix S1 for full explanation of the covariate models).

Sample derivation

The starting sample for analysis in the ALSPAC cohort was $14\,062$ singletons and twins; these were born live. The sample's exposure was measured in the clinic; of the $14\,062$ individuals, $9985\,(71\%)$ of these live-born children

were invited to the 'Teen Focus Three' clinic (TF3) at approximately 15.5 years of age [9]; 5190 (52%) of these children attended TF3. Of those who attended the clinic, 5137 (99%) answered questions about cannabis use, 4802 (92.5%) answered the CAST and 4433 (85.4%) answered tobacco use questions. Cotinine was measured in 3350 (64.6%) individuals. GCSE data in the NPD are available only for pupils attending state schools, and not all data items are complete for these individuals. Descriptive

characteristics of the data presented are also included (Table 1a and b).

Analysis

Linear or logistic regression was used as appropriate. Analysis was run on the complete case and imputed data; the results in this study have been extracted from the imputed data in order to increase the power of the findings. All

Table 1 (a) Descriptive characteristics for educational outcomes and substance use exposures using the imputed data set.

Outcome							
		English G	CSE		Mathema	tics GCSE	
Exposure		n	Mean	SE	n	Mean	SE
Cannabis use	Never	3277	71.34	0.24	3198	70.46	0.28
	Ever	1098	68.53	0.42	1066	65.04	0.48
	Total <i>n</i>	4375	70.63	0.20	4264	69.11	0.24
Frequency of cannabis use	Non-smoker	3958	70.77	0.21	3866	69.54	0.26
	Non-weekly smoker	297	71.18	0.75	288	65.71	0.87
	Weekly smoker	120	64.83	1.28	110	62.64	1.49
	Total <i>n</i>	4375	70.63	0.20	4264	69.11	0.24
CAST score of 4 or above	No	3982	71.10	0.21	3876	69.76	0.25
	Yes	105	65.95	1.40	102	60.88	1.53
	Total <i>n</i>	4087	70.97	0.21	3978	69.53	0.25
Smoking status	Non smoker	2996	72.19	0.24	2914	71.63	0.29
	Non-daily smoker	472	69.40	0.59	451	66.08	0.65
	Daily smoker	292	60.29	0.81	293	54.91	0.95
	Total <i>n</i>	3760	70.92	0.22	3658	69.61	0.27
Cotinine-assessed smoking status	No	2572	71.47	0.26	2496	70.71	0.31
	Yes	255	60.75	0.88	251	55.68	1.04
	Total <i>n</i>	2827	70.50	0.25	2747	69.33	0.31

(b) Descriptive characteristics for educational outcomes on substance use exposures using the imputed data set.

		Not gainin	g 5+ C+ grad	e GCSEs	School dro	opout	
Exposure		n (yes)	n (no)	% (yes)	n (yes)	n (no)	% (Yes)
Cannabis use	Never	671	2631	20.32	33	3268	1.00
	Ever	352	782	31.04	31	1102	2.74
	Total n	1023	3413	23.06	64	4370	1.44
Frequency of cannabis use	Non-smoker	893	3105	22.34	47	3950	1.18
	Non-weekly smoker	71	233	23.36	7	297	2.30
	Weekly smoker	59	75	44.03	10	123	7.52
	Total n	1023	3413	23.06	64	4370	1.44
CAST score of 4 or above	No	856	3166	21.28	46	3975	1.14
	Yes	52	64	44.83	10	106	8.62
	Total n	908	3230	21.94	56	4081	1.35
Smoking status	Non-smoker	551	2468	18.25	28	2990	0.93
	Non-daily smoker	116	362	24.27	4	474	0.84
	Daily smoker	196	123	61.44	21	297	6.60
	Total n	863	2953	22.62	53	3761	1.39
Cotinine-assessed smoking status	No	513	2080	19.78	27	2565	1.04
	Yes	155	122	55.96	15	262	5.42
	Total <i>n</i>	668	2202	23.28	42	2827	1.46

CAST = Cannabis Abuse Screening Test; GCSE = General Certificate of State Education; SE = standard error.

© 2014 The Authors. Addiction published by John Wiley & Sons Ltd on behalf of Society for the Study of Addiction.

ate models.
int imputed covarie
se including differe
cent substance us
glish with adolese
sociation of GCSE Eng
Table 2 The ast

		UTILVAT IMDIC		Adjustea 1		∠ naten/me		Adjusted	~	Fully Adj	ISLEA
Exposure		GPD	95% CI	GPD	95% CI	GPD	95% CI	GPD	95% CI	GPD	95% CI
Cannabis use	Never	I	I	I	I	I	I	I	I	I	I
n = 4375	Ever	-2.80	-3.71, -1.90	-2.41	-3.32, -1.50	-2.53	-3.35, -1.70	-2.38	-3.01, -1.76	-0.59	-1.44, 0.28
Cannabis status	None	I	I	I	I	I	I	I	I	I	I
n = 4375	Non-weekly	0.41	-1.15, 1.97	0.61	-0.96, 2.17	-0.21	-1.63, 1.21	-1.37	-2.44, -0.29	0.72	-0.45, 1.90
	Weekly	-5.93	-8.34, -3.53	-5.70	-8.10, -3.30	-4.51	-6.68, -2.34	-4.33	-5.95, -2.70	-2.09	-3.79, -0.40
CAST score 4+	No	I	I	I	I	I	I	I	I	I	I
n = 4087	Yes	-5.15	-7.69, -2.60	-4.86	-7.40, -2.32	-4.16	-6.47, -1.85	-3.24	-4.99, -1.49	-1.35	-3.15, 0.46
Smoking status	None	I	I	I	I	I	I	I	I	I	I
n = 3760	Non-daily	-2.80	-4.06, -1.53	-2.62	-3.88, -1.36	-2.87	-4.02, -1.73	-2.44	-3.30, -1.58	-1.96	-3.01, -0.90
	Daily	-11.90	-13.47, -10.33	-10.79	-12.37, -9.21	-10.04	-11.49, -8.58	-6.49	-7.59, -5.39	-5.84	-7.18, -4.50
Cotinine smoking status	Non-Smoker	I	I	I	I	Ι	I	I	I	I	I
n = 2827	Smoker	-10.72	-12.42, -9.03	-9.77	-11.49, -8.06	-8.42	-9.98, -6.86	-5.15	-6.32, -3.97	-4.37	-5.63, -3.11

models are grouped into proximal and distal determinants. Adjustment 1 model includes binary maternal substance use behaviours (mother smokes, mother binge drinks and mother uses cannabis). Adjustment 2 model included demographics [socio-economic status (SES), maternal education and income] and sex. Adjustment 3 model includes the individuals previous education before substance use is more likely [standard deviation (SD) change for Key Stage 2 English and Mathematics]. The fully adjusted model includes child smoking for the same time as the exposure (child drinking, child weekly cannabis) use for the tobacco smoking exposures and child smoking for the cannabis use exposures are the use to exposures of the tastpart results were P < 0.001. GPD = grade point difference. CAST = Cannabis Abuse Screening Test: CI = confidence interval.

analyses were run on Stata version 12 [15]. Covariates were included on theoretical grounds, and they were tested for their impact on our parameter estimates by using the likelihood ratio test for the non-imputed data and Stata's *testparm* function on the imputed data. The likelihood ratio test compares the fit of the covariate model to the previous model; if there is a difference, then the less restrictive model (the model with more covariates) is said to fit the data better than the more restrictive model [16].

Data completeness

We conducted a complete case analysis, based on 1155 individuals with complete data on self-reported substance use and serum cotinine measured in the tier three clinic. We compared estimates of effects between the imputed and complete case in order to assess any bias that may have been introduced through imputing the sample.

Multiple imputations

To mitigate against loss of power resulting from reduced sample size and investigate possible bias related to missing data, we used multiple imputation of exposures and covariates using the ice function in Stata version 12 using the missing-at-random assumption [15,17]. We imputed non-complete covariates for individuals who had missing data for a covariate and had data on the exposures. The data source on which we are imputing was from selfreported questionnaires. The prediction equation used all other associated covariates in order to impute the missing values. Twenty imputed data sets were created, as recommended by Sterne *et al.* [18]; analysis on this output file used the mim function in Stata.

RESULTS

Assessment of confounding

Maternal substance use, lower social position, poorer educational performance at Key Stage 2 and children's use of other substances were associated positively both with cannabis and tobacco use at age 15 (Table S1) and with poorer educational outcomes at age 16 (Table S2).

We found that previous educational attainment was associated with current educational attainment (Table S2). We also found that previous English assessment prior to age 11 [Key Stage 2] was associated with a CAST score above 4, daily smoking of tobacco and cotinine-assessed smoking status. Previous Mathematics assessment prior to age 11 (Key Stage 2) was associated with cannabis use, CAST score above 4, tobacco use and cotinine-assessed smoking status (Table S1). Therefore, in order to reduce the problem of reverse causation we included previous educational attainment as a covariate in our model. Previous educational attainment is measured at a time-point prior to initiation of these substances; high levels of attenuation within this covariate model would indicate a problem with reverse causation.

Association between cannabis use and educational outcomes

In the univariable analyses, using imputed covariates, cannabis use is associated with lower grade point difference (GPD) in English GCSEs in an approximately dose-response fashion (Table 2). Problematic cannabis use as assessed by CAST is similar to those seen with weekly cannabis use [CAST score: -5.15 GPD, 95% confidence interval (CI) = -7.69, -2.60; weekly cannabis use: -5.93 GPD, 95% CI = -8.34, -3.53]. Adjustment for maternal substance use, social position and prior educational attainment all attenuate these estimates; the greatest attenuation is seen for prior educational attainment and on adjustment for child behaviour. Within these two categories the greatest attenuation is occurring from Key Stage 2 Mathematics and daily smoking in the previous education and child behaviour models, respectively (Table S6). After attenuation there is still evidence of a moderate effect of cannabis on education at age 16.

A similar pattern of association is seen in relation to the effects of cannabis use on attainment in Mathematics at GCSE; however, effects are generally of a greater magnitude (CAST score: -8.88 GPD, 95% CI = -11.98, -5.78) (Table 3). In contrast to attainment in English, the association of cannabis use on attainment in Mathematics remains post-adjustment for maternal substance use, social position and prior educational attainment (CAST score: -3.52 GPD, 95% CI = -5.81, -1.23]. The greatest attenuation is seen in the 'child behaviour' model. Within this model, the greatest attenuation is occurring from the daily tobacco smoking covariate (Table S7).

Similar patterns of association are repeated in relation to the apparent effects of cannabis use on non-completion of five or more GCSEs at grade C or above (table 4) and school dropout (Table 5). In the univariable analysis, weekly cannabis use is associated with higher odds of not achieving 5 or more grade C results at GCSE [odds ratio (OR) = 2.74, 95% CI = 1.93, 3.88] and higher odds of leaving school with no GCSE passes (school dropout) (OR = 6.83, 95% CI = 3.37, 13.85). The greatest attenuation occurs within the 'prior educational attainment' and the 'child behaviour' models. Within these models, the greatest attenuation occurs from the addition of Key Stage 2 Mathematics and being a daily smoker in the education and child behaviour models, respectively.

Association between tobacco use and educational outcomes

In the univariable analyses, using imputed covariates, tobacco use at age 15 was associated with lower GPD in both

le 3 The association of GCSE mathematics with adolescent substance use including different imputed covariate models.
Table

		Univariable		Adjusted 1		Adjusted 2		Adjusted		Fully Adji	ısted
Exposure		GPD	95% CI	GPD	95% CI	GPD	95% CI	GPD	95% CI	GPD	95% CI
Cannabis use	Never	I	I	I	I	I	I	I	I	I	I
n = 4264	Ever	-5.42	-6.52, -4.32	-4.78	-5.88, -3.68	-4.90	-5.92, -3.88	-4.31	-5.10, -3.53	-2.43	-3.53, -1.34
Cannabis status	None	I	I	I	I	I	I	I	I	I	I
n = 4264	Non-weekly	-3.83	-5.73, -1.93	-3.33	-5.23, -1.43	-4.01	-5.76, -2.25	-4.66	-6.01, -3.30	-2.15	-3.64, -0.65
	Weekly	-6.91	-9.92, -3.89	-6.21	-9.22, -3.19	-6.05	-8.82, -3.27	-6.05	-8.18, -3.92	-3.37	-5.59, -1.15
CAST score 4+	No	I	I	I	I	I	I	I	I	I	I
n = 3978	Yes	-8.88	-11.98, -5.78	-8.05	-11.15, -4.95	-7.89	-10.77, -5.01	-6.38	-8.59, -4.16	-3.52	-5.81, -1.23
Smoking status	None	I	I	I	I	I	I	I	I	I	I
n = 3658	Non-daily	-5.55	-7.09, -4.02	-5.28	-6.81, -3.76	-4.62	-6.04, -3.20	-3.61	-4.71, -2.52	-1.78	-3.10, -0.45
	Daily	-16.72	-18.57, -14.86	-15.26	-17.15, -13.38	-13.37	-15.15, -11.59	-9.07	-10.43, -7.71	-6.70	-8.35, -5.05
Cotinine smoking status	Non-smoker	I	I	I	I	I	I	I	I	I	I
n = 2747	Smoker	-15.42	-6.51, -4.32	-13.77	-15.81, -11.72	-11.67	-13.57, -9.77	-7.74	-9.19, -6.29	-6.19	-7.75, -4.62
						,					
The admostion of witcome have u	roe Mothemotice Ce	a anal Cartificata	of State Education (COU	() recults which	man daritrad from madio	nidtin and u	o and opinipariod above	ouninte mode	r need act a	oo puq po	44 no ablived door but the

These models are grouped into proximal and distal determinants. Adjustment 1 model includes binary maternal substance use behaviours (mother smokes, mother binge drinks and mother uses cannabis). Adjustment 2 model includes de-mographics [socio-economic status (SES) maternal education and income] and sex. Adjustment 3 model includes the individuals previous education before substance use is more likely [standard deviation (SD) change for Key Stage 2 English and Mathematics]. The fully adjusted model includes child smoking, child drinking, child drinking, child weekly cannabis use for the tobacco smoking exposures and child smoking for the cannabis use exposures) and conduct disorder. Covariates were imputed to increase *n*. All the *testparm* results were P < 0.001. GPD = grade point difference. CAST = Cannabis Abuse Screening Test: CI = confidence interval.

		Univariab	le	Adjusted	1	Adjusted	5	Adjusted	~	Fully adju	isted
Exposure		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Cannabis use	Ever	I	I	I	I	I	I	I	I	I	I
n = 4436	Never	1.76	1.52, 2.05	1.66	1.42, 1.94	1.79	1.51, 2.12	2.13	1.73, 2.61	1.43	1.06, 1.91
Cannabis status	None	I	I	I	I	I	I	I	I	Ι	I
n = 4436	Non-weekly	1.06	0.80, 1.40	1.01	0.76, 1.34	1.11	0.81, 1.50	1.57	1.08, 2.28	0.92	0.61, 1.38
	Weekly	2.74	1.93, 3.88	2.63	1.84, 3.77	2.57	1.74, 3.80	3.25	2.03, 5.22	1.90	1.16, 3.12
CAST score 4+	No	I	I	I	I	I	I	I	Ι	I	I
n = 3561	Yes	3.01	2.07, 4.37	2.84	1.93, 4.17	2.95	1.93, 4.51	3.40	2.02, 5.72	2.12	1.22, 3.67
Smoking status	None	I	I	I	I	I	I	I	I	Ι	I
n = 3816	Non-daily	1.43	1.14, 1.80	1.39	1.11, 1.76	1.48	1.15, 1.90	1.58	1.16, 2.15	1.22	0.84, 1.78
	Daily	7.14	5.59, 9.11	6.32	4.92, 8.12	6.96	5.27, 9.20	6.72	4.81, 9.39	4.75	3.11, 7.27
Cotinine smoking status	Non-Smoker	I	I	I	I	I	Ι	I	I	Ι	I
n = 2870	Smoker	5.15	3.99, 6.66	4.59	3.53, 5.98	4.36	3.27, 5.80	4.05	2.86, 5.73	3.47	2.36, 5.10
The educational outcome here into proximal and distal detern status (SIS), maternal educatic adjusted model includes child's disordar. Correction taxes immu	was the binary non-comp ninants. Adjustment 1 mo m and income] and sex. A bustance use behaviour.	detion of 5+ Ger del includes bin djustment 3 mc measured at the	neral Certificates of Stat ary maternal substanc del includes the indivi same time as the expo	te Education (G e use behaviou duals previous sure (child drin	CSEs) at grade C or ab rs (mother smokes, mc education before subst king, child weekly can buse Creasarian Tast. O	ove. Four covari other binge drin ance use is mor nabis use for the	ate models have been ks and mother uses ca e likely [standard devi e tobacco smoking exp	used and each b annabis). Adjust ation (SD) chan ossures and child	uilds on the previous r ment 2 model included ge for Key Stage 2 Eng d smoking for the cann	model. These mu d demographics lish and Mathe labis use exposu	dels are grouped [socio-economic matics]. The fully tres) and conduct

664 Alexander I. Stiby et al.

Table 4 The association of non-completion of five or more GCSEs with adolescent substance use including different imputed covariate models.

- lolo	TCIS.
	Ď
. otoinoto	COVALIALE I
bottoo	nanndri
difformet in	n matamn
تصاليطيم	Including
0011	nxc
an hat and an	substatice
مطمامومو	auviescent
dtirr	MILLI
ducent	modom
loodoo	SCIIOUI
5	101
o co cinta con	association
сч Г	THE
ц	n
Tabla	Table

		Univariat	le	Adjusted	1	Adjusted	2	Adjusted	ŝ	Fully Adj	usted
Exposure		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Cannabis use	Ever	I	I	I	I	I	I	I	I	I	I
n = 4434	Never	2.79	1.70, 4.57	2.48	1.49, 4.12	2.55	1.53, 4.24	2.47	1.45, 4.19	2.75	1.18, 6.39
Cannabis status	None	I	I	I	I	I	I	I	I	I	I
n = 4434	Non-weekly	1.98	0.89, 4.42	1.80	0.80, 4.06	1.94	0.86, 4.41	2.48	1.05, 5.84	1.96	0.74, 5.21
	Weekly	6.83	3.37, 13.85	6.24	3.02, 12.92	5.94	2.83, 12.45	5.23	2.33, 11.72	4.44	1.79, 11.00
CAST score 4+	No	I	I	I	I	I	I	I	I	I	I
n = 4137	Yes	8.15	4.00, 16.60	7.19	3.43, 15.08	7.23	3.39, 15.42	5.41	2.40, 12.20	4.40	1.70, 11.38
Smoking status	None	I	I	I	I	I	I	I	I	I	I
n = 3814	Non-daily	0.90	0.31, 2.58	0.86	0.30, 2.48	0.86	0.30, 2.50	0.86	0.29, 2.55	0.73	0.20, 2.66
	Daily	7.55	4.23, 13.47	6.48	3.49, 12.04	6.17	3.29, 11.56	4.78	2.45, 9.35	2.23	1.11, 9.39
Cotinine smoking status	Non-Smoker	I	I	I	I	I	I	I	I	I	I
n = 2869	Smoker	5.44	2.85, 10.36	5.03	2.56, 9.88	4.48	2.26, 8.90	3.27	1.59, 6.70	2.54	1.12, 5.74
The educational outcome here w	vas school drobout. whi	ich was derived	from not gaining any (General Certific	ate of State Education ((GCSE) grades	or receiving only U gra	des (graded as	unclassified): four cova	riate models w	ere used and each

The cuctangent outcome it was shown up out, which was every or new constrained and distribution of the curve of a second second second and distribution of the curve of the c

English (Table 2) and Mathematics GCSE (Table 3). Tobacco use was also associated with lower odds of achieving at least 5 grade C passes at GCSE (Table 4) and greater odds of leaving school with no GCSE passes (school dropout, Table 5). Again, a broadly dose-response pattern was seen, with effects of cotinine-verified tobacco use being similar to those of daily smoking. Apparent effects were generally stronger and of greater magnitude than those of cannabis use. The greatest attenuation of effects was seen on adjustment of 'prior educational attainment' and 'child behaviour' models. In contrast to the effects of cannabis use. the effects of tobacco use on attainment in GCSE Mathematics (-6.70 GPD, 95% CI = -8.35, -5.05) compared to GCSE English (-5.84 GPD, 95% CI = -7.18, -4.50) were very similar in the full model. The greatest attenuation occurs from the addition of weekly cannabis use in the child behaviour model and previous education (Tables S6-S9). After attenuation there is still evidence of a moderate effect of tobacco use on education at age 16.

Influence of imputation

The results presented are based on the imputed data set. We have compared the imputed results with the complete case for the self-report substance use and for the biomarker, cotinine, in order to determine the consistency of the imputed results; there were no major differences (Tables S3–S4, see Appendix 2).

DISCUSSION

Main findings and implications

Cannabis use by young people by age 15 was associated consistently with poorer performance across a range of objective indicators of subsequent educational attainment. This association was attenuated, but remained apparent following adjustment for a wide range of possible confounding factors. Further adjustment for educational attainment prior to cannabis use led to further attenuation. In general, higher cannabis use was associated with lower attainment. Using cannabis was associated with a GCSE score reduction of approximately 5%, which is half a grade. The association was similar in girls compared to boys. In some instances the effects of tobacco seemed stronger and more substantial. Higher tobacco use was generally associated with poorer outcomes, and effects in girls were similar to those in boys. The effects of biologically verified tobacco use were very similar to those of self-reported tobacco use.

Our results are broadly consistent with other evidence suggesting the adverse effect of cannabis use on subsequent educational performance [2,19–23]. Other studies in general have not considered both cannabis and tobacco use by young people and subsequent educational outcomes

in the same cohort; rather, they have reported the effects of cannabis use adjusted for tobacco use. A small number of previous studies have considered the effects of tobacco use on educational attainment, and have reported similar patterns of association to those that we observed [24–27]. The associations for cannabis were found to be non-specific; due to tobacco use by age 15 showing very similar patterns of association with the same educational outcomes.

Associations of biologically verified tobacco use were similar to those of the nearest equivalent self-reported exposure (daily smoking), suggesting that reporting bias had not substantially influenced the latter. Few studies have investigated the specific effect of school-based outcome data with substance use, rather than self-reported education variables [19,20,28]. The heterogeneity between current studies' measures of education and of substance use allows for little statistical comparison between studies.

Previous studies have not attempted to adjust for as comprehensive a range of confounding factors as we included in our multivariable analyses [1,19,28]. Adjustment for these factors considerably attenuated our estimates of effects of cannabis use. Specific adjustment of results from the covariates within each model was also investigated (Tables S6–S9). Adjustment for each covariate individually attenuated estimates to a similar extent. The highest attenuation occurred within the 'prior educational attainment' model and the 'child behaviour' model. The size of the reduction of the association is similar, with a greater than twofold reduction, which in our analyses still provides evidence of a moderate effect of daily tobacco/weekly cannabis use on educational performance. In general, following such adjustment, the association of tobacco use on educational attainment appeared stronger and of greater magnitude than those of cannabis use: the exception to this pattern was in relation to the association on 'school-dropout', wherein the fully adjusted analyses association of cannabis use appeared stronger and of greater magnitude than those of tobacco use.

In the 'child behaviour' model, the largest attenuation occurs from the co-administration of cannabis or tobacco on tobacco or cannabis use, respectively. Demographics appear to attenuate the relationship between substance use exposure and educational attainment in a similar pattern throughout. Consideration of month of birth and maternal education also led to attenuation of the estimates. We observed an association of sex only on frequent cannabis and tobacco use, with the odds of frequently using cannabis being higher for males and the odds of frequently using tobacco being higher for females. There is also an association of sex on education variables, with males having a reduced GCSE English GPD, having higher odds of achieving five or more GCSEs but also having higher odds of being a school dropout. We have attempted to control for reverse causation by including a measure of educational attainment prior to the initiation of cannabis use in our model. We observed an association between previous education and substance use when considered separately (Table S1). This adjustment led to attenuation of the effects of cannabis use suggesting that reverse causation, i.e. prior educational difficulties predisposing to cannabis use, was an issue in our study population. This could be attributed to a third factor, such as clustered behaviours within peer groups.

Strengths and limitations

The strengths of the present study include its general population basis and prospective design and also the availability of extensive prospective measures of relevant covariates, the availability of a biologically verified measure of tobacco use and the availability of objective measures of key dimensions of educational attainment obtained through record linkage. This linkage also allowed us to consider the effects of cannabis use on specific aspects of educational attainment, such as performance in different subjects, in a way that has not been possible in previous studies [28].

The study also has limitations. First, the ALSPAC cohort is subject to loss to follow-up at each stage. Male cohort members and those from lower socio-economic status (SES) groups are also less likely to attend assessment interviews. Therefore, not attending the clinic is the largest contributor to missing data. To an extent, we were able to mitigate this problem and any bias that may have resulted from it through multiple imputations; however, the validity of multiple imputations is based on assumptions that are usually impossible to verify [29]. There may be greater misclassification of cannabis than tobacco. This is because the sensitivity of questions about substance use and other behaviours means that the participant may decide to withhold certain information by not answering the question or not answering it honestly, for fear that it would be passed on to parents or teachers, thereby causing bias. This would therefore underestimate the number of substance users or misclassify users as non-users, in turn causing response bias to the results. The cotinine validates the self-report of tobacco, but there is no equivalent valid biological measure for cannabis. We were unable to measure the effect of peer groups in this study, as delinquent peer groups may have an effect both of substance use and on educational attainment; therefore, there may be unmeasured confounding in our study. Finally, an immunoassay of cotinine has been shown to not be as precise as the gas chromatography-mass spectrometric (GC-MS) quantitative method for cotinine extraction, possibly creating bias in the measurements [30].

Conclusions and policy implications

Given these patterns of association and attenuation, alongside the non-specific nature of the association, our evidence suggests that, rather than being causal, the consistent association between cannabis use by young people and their subsequent poorer educational outcomes is likely to arise through a combination of confounding factors. These factors are related to both the tendency to use psychoactive substances and to perform less well in educational assessments. Alongside this, reverse causation is related to the fact that children who are less successful educationally have a heightened risk of substance use, which could be for several reasons. It is not possible to discount a causal basis for our findings completely, as both cannabis and tobacco use may influence subsequent educational attainment causally through independent mechanisms. Moreover, the question may not have important implications for policy. There are good reasons to prevent both cannabis and tobacco use by young people related to the effects of smoking on cardiorespiratory health and because the former, as it is illegal, exposes young people to risk of criminalization. Our findings, however, which suggest that prevention of cannabis use may improve educational outcomes in young people, particularly the socially disadvantaged, is probably unrealistic. It therefore follows that other interventions are likely to be needed to achieve this important policy objective.

Acknowledgements

We are extremely grateful to all the families who took part in the study, the midwives for their help in recruiting them and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses. The UK Medical Research council and the Wellcome Trust (grant ref: 092731) and the University of Bristol provide core support for ALSPAC. M.H. is a member of the NIHR School of Public Health Research and The Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement (DECIPHer), a UKCRC Public Health Research: Centre of Excellence. Funding from the British Heart Foundation. Cancer Research UK. Economic and Social Research Council (RES-590-28-0005), Medical Research Council, the Welsh Assembly Government and the Wellcome Trust (WT087640MA), under the auspices of the UK Clinical Research Collaboration, is gratefully acknowledged. M.R.M. is a member of the UK Centre for Tobacco Control Studies, a UKCRC Public Health Research: Centre of Excellence. Funding from British Heart Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research Council and the National Institute for Health Research, under the auspices of the UK Clinical Research Collaboration, is gratefully acknowledged. This research was funded in part by the Wellcome Trust (086684). J.H. is supported by the UK Medical Research Council (grants G0800612 and G0802736). This publication is the work of Alexander Stiby, John Macleod, Matthew Hickman, Marcus Munafò and Jon Heron who will serve as guarantors for the contents of this paper. A.I.S. is supported by a Wellcome Trust 4-year PhD studentship in molecular, genetic and lifecourse epidemiology (WT083431MA).

References

- 1. Ashton H. Cannabis or health? *Curr Opin Psychiatry* 2002; **15**: 247–53.
- Hall W., Degenhardt L. Prevalence and correlates of cannabis use in developed and developing countries. *Curr Opin Psychiatry* 2007; 20: 393–7.
- Ashton C. H. Pharmacology and effects of cannabis: a brief review. Br J Psychiatry 2001; 178: 101–6.
- Home Office Statistics. Drug Misuse: Findings from the 2012/13 Crime Survey for England and Wales. Kew, UK: National Archives; July 2013.
- Verweij K. J., Huizink A. C., Agrawal A., Martin N. G., Lynskey M. T. Is the relationship between early-onset cannabis use and educational attainment causal or due to common liability? *Drug Alcohol Depend* 2013; 133: 580–6.
- Lawlor D. A., Macleod J. Investigating causes of disease. In: Ben-Shlomo Y, Brookes S, Hickman M. editors. Epidemiology, Evidence-based Medicine and Public Health Lecture Notes, 6th edn. London: Wiley; 2013.
- Weiss N. S. Can the 'specificity' of an association be rehabilitated as a basis for supporting a causal hypothesis? *Epidemiology* 2002; 13: 6–8.
- Petitti D. Commentary: Hormone replacement therapy and coronary heart disease: four lessons. *Int J Epidemiol* 2004; 33: 461–3.
- Boyd A., Golding J., Macleod J., Lawlor D. A., Fraser A., Henderson J., *et al.* Cohort profile: the 'Children of the 90s'—the index offspring of the Avon Longitudinal Study of Parents and Children. *Int J Epidemiol* 2012; **42**: 112–127.
- 10. The Department for Education. *National Pupil Database*. UK data archive: Colchester, Essex.
- Legleye S., Karila L., Beck F., Reynaud M. Validation of the CAST, a general population Cannabis Abuse Screening Test. *J Subst Use* 2007; 12: 233–42.
- Stiby A. I., Macleod J., Hickman M., Yip V. L., Timpson N. J., Munafo M. R. Association of maternal smoking with child cotinine levels. *Nicotine Tob Res* 2013; 15: 2029–36.
- Jarvis M. J., Primatesta P., Erens B., Feyerabend C., Bryant A. Measuring nicotine intake in population surveys: comparability of saliva cotinine and plasma cotinine estimates. *Nicotine Tob Res* 2003; 5: 349–55.
- Victora C. G., Huttly S. R., Fuchs S. C., Olinto M. T. The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. *Int J Epidemiol* 1997; 26: 224–7.

- 15. Stata Statistical Software: Release 12 [computer program]. College Station, TX: StataCorp; 2011.
- Satorra A., Saris W. E. Power of the likelihood ratio test in covariance structure analysis. *Psychometrika* 1985; 50: 83–90.
- 17. Carlin J. B., Galati J. C., Royston P. A new framework for managing and analyzing multiply imputed data in Stata. *Stata J* 2009; **8**: 49–67.
- Sterne J. A., White I. R., Carlin J.B., Spratt M., Royston P., Kenward M. G. *et al.* Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009; **338**: 157–160.
- Macleod J., Oakes R., Copello A., Crome P. I., Egger P. M., Hickman M. *et al.* Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies. *Lancet* 2004; 363: 1579–88.
- Lynskey M., Hall W. The effects of adolescent cannabis use on educational attainment: a review. *Addiction* 2000; 95: 1621–30.
- 21. Grant J. D., Scherrer J. F., Lynskey M. T., Agrawal A., Duncan A. E., Haber J. R. *et al.* Associations of alcohol, nicotine, cannabis, and drug use/dependence with educational attainment: evidence from cotwin–control analyses. *Alcohol Clin Exp Res* 2012; 36: 1412–20.
- Giovino G.A., Henningfield J. E., Tomar S. L., Escobedo L. G., Slade J. Epidemiology of tobacco use and dependence. *Epidemiol Rev* 1995; 17: 48.
- 23. Bradley B. J., Greene A. C. Do health and education agencies in the United States share responsibility for academic achievement and health? A review of 25 years of evidence about the relationship of adolescents' academic achievement and health behaviors. *J Adolesc Health* 2013; **52**: 523–32.
- Lynskey M. T., Coffey C., Degenhardt L., Carlin J. B., Patton G. A longitudinal study of the effects of adolescent cannabis use on high school completion. *Addiction* 2003; 98: 685–92.
- Bray J. W., Zarkin G. A., Ringwalt C., Qi J. The relationship between marijuana initiation and dropping out of high school. *Health Econ* 2000; 9: 9–18.
- Fergusson D., Lynskey M., Horwood L. J. The short-term consequences of early onset cannabis use. *J Abnorm Child Psychol* 1996; 24: 499–512.
- Ensminger M. E., Lamkin R. P., Jacobson N. School leaving: a longitudinal perspective including neighborhood effects. *Child Dev* 1996; 67: 2400–16.
- Diplock J., Cohen I., Plecas D. A review of the research on the risks and harms associated to the use of marijuana. *J Global Drug Policy Pract* 2009; 3: 22–32.
- Bhaskaran K., Smeeth L. What is the difference between missing completely at random and missing at random? *Int J Epidemiol* 2014; **43**: 1336–9.
- 30. Acosta M. C., Buchhalter A. R., Breland A. B., Hamilton D. C., Eissenberg T. Urine cotinine as an index of smoking status in smokers during 96-hr abstinence: comparison between gas chromatography/mass spectrometry and immunoassay test strips. *Nicotine Tob Res* 2004; 6: 615–20.