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Continuity of Cannabis use and Violent Offending Over the Life Course

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Corresponding Author:	Sagnik Bhattacharyya King's College London, Institute of Psychiatry London, UNITED KINGDOM
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	King's College London, Institute of Psychiatry
Corresponding Author's Secondary Institution:	
First Author:	Tabea Schoeler, MSc.
First Author Secondary Information:	
Order of Authors:	Tabea Schoeler, MSc.
	Delphine Theobald, PhD
	Jean-Baptiste Pingault, PhD
	David Farrington, PhD
	Wesley Jennings, PhD
	Alex Piquero, PhD
	Jeremy Coid, FRCPsych
	Sagnik Bhattacharyya, PhD
Order of Authors Secondary Information:	
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Abstract:	Background Although the association between cannabis use and violence has been reported in the literature, the precise nature of this relationship, especially the directionality of this association is unclear. Method Young males from the Cambridge Study of Delinquent Development (CSDD) (N=411) were followed up between ages 8 and 56 years to prospectively investigate the association between cannabis use and violence. A multi-wave (eight assessments, T1-T8) follow-up design was employed that allowed temporal sequencing of the variables of interest and the analysis of violent outcome measures obtained from two sources, (i) criminal records (violent conviction, VC) and (ii) self-reports (SR-V). A combination of analytic approaches allowing inferences as to the directionality of associations was employed, including multivariate logistic regression analysis, fixed effects analysis and cross-lagged modeling. Results Multivariable logistic regression revealed that compared to never users, continued exposure to cannabis (use at age 18, 32 and 48) was associated with a higher risk of subsequent violent behaviour, as indexed by convictions (OR=7.1[95% CI: 2.19 - 23.59]) or self-reports (OR=8.9[95% CI: 2.37 - 46.21]). This effect persisted after controlling for other putative risk factors for violence. In predicting violence, fixed effects analysis and cross-lagged modeling further indicated that this effect could not be explained by other unobserved time invariant factors. Furthermore, these analyses uncovered bi-directional relationship between cannabis use and violence. Conclusions

	Together, these results provide strong indication that cannabis use predicts subsequent violent offending, suggesting a possible causal effect and provide empirical evidence that may have implications for public policy.

Continuity of Cannabis use and Violent Offending Over the Life Course

*Tabea Schoeler, MSc [1]

*Delphine Theobald, PhD [1, 2]

Jean-Baptiste Pingault, PhD [3]

David P Farrington, PhD [4]

Wesley G Jennings, PhD [5]

Alex R Piquero, PhD [6]

Jeremy W Coid, FRCPsych [7]

and

**Sagnik Bhattacharyya, PhD [1]

[1] Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK.
[2] Department of Psychology, Kingston University, London, UK.
[3] Division of Psychology and Language Science, University College London, UK.
[4] Institute of Criminology, University of Cambridge, UK.
[5] College of Behavioral & Community Sciences, University of South Florida, USA.
[6] School of Economics, Political and Policy Sciences, University of Texas and Dallas, USA.
[7] Forensic Psychiatry Research Unit, Queens Mary's University, UK.

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* These authors contributed equally to this work.
**Corresponding author
Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, De Crespigny Park, London SE5 8AF, UK, Tel +44 207 848 0955, Fax +44 207 848 0976, Email: sagnik.2.bhattacharyya@kcl.ac.uk

Background

Although the association between cannabis use and violence has been reported in the literature, the precise nature of this relationship, especially the directionality of this association is unclear.

Method

Young males from the Cambridge Study of Delinquent Development (CSDD) (N=411) were followed up between ages 8 and 56 years to prospectively investigate the association between cannabis use and violence. A multi-wave (eight assessments, T1-T8) follow-up design was employed that allowed temporal sequencing of the variables of interest and the analysis of violent outcome measures obtained from two sources, (i) criminal records (violent conviction, VC) and (ii) self-reports (SR-V). A combination of analytic approaches allowing inferences as to the directionality of associations was employed, including multivariate logistic regression analysis, fixed effects analysis and cross-lagged modeling.

Results

Multivariable logistic regression revealed that compared to never users, continued exposure to cannabis (use at age 18, 32 and 48) was associated with a higher risk of subsequent violent behaviour, as indexed by convictions (OR=7.1[95% CI: 2.19 - 23.59]) or self-reports (OR=8.9[95% CI: 2.37 - 46.21]). This effect persisted after controlling for other putative risk factors for violence. In predicting violence, fixed effects analysis and cross-lagged modeling further indicated that this effect could not be explained by other unobserved time invariant factors. Furthermore, these analyses uncovered bi-directional relationship between cannabis use and violence.

Conclusions

Together, these results provide strong indication that cannabis use predicts subsequent violent offending, suggesting a possible causal effect and provide empirical evidence that may have implications for public policy

1. Introduction

Cannabis is the most widely used illicit drug in most parts of the world (UNDOC 2010), with onset of use often during the developmentally critical period of adolescence and persisting through early adulthood (Patton et al. 2007). Among the many potential aversive consequences of cannabis use on cognitive, behavioural and mental health outcomes (Bhattacharyya et al. 2012a, Bhattacharyya et al. 2012b, Bhattacharyya et al. 2009, Lindsay et al. 2005, Peters et al. 2014, Schoeler and Bhattacharyya 2013, Schoeler et al. 2015, Schoeler et al. in press), previous research has shown that violent behavior (Johnson et al. 1991, Monshouwer et al. 2006, Nabors 2010, Peters et al. 2014) or delinquency and aggression in adolescence (Chabrol and Saint-Martin 2009, Fergusson et al. 2002, Monshouwer et al. 2006) may result from cannabis use. Pharmacologically, cannabis may cause impairments in response inhibition resulting in behavioural control in vulnerable individuals, that may underlie impulsive, violent behaviour, by altering the normal functioning of its underlying neural substrate, the ventrolateral prefrontal cortex in man (Bhattacharyya et al. 2015, Bhattacharyya et al. 2014). Existing observational evidence in this area, mostly cross-sectional, constrains the possibility of drawing causal inferences. Longitudinal evidence in this regard has been limited as well (Brook et al. 2003, Brook et al. 2014, Friedman et al. 1996, Pedersen and Skardhamar 2010), mainly lacking in serial assessments over time and having relatively short follow-up periods [e.g. no study has followed up beyond 15 years (cf. *Table 1*.)]. Effect of risk factors such as antisocial personality, alcohol or other illicit drug use or family history of criminality (Farrington 2000, Jennings et al. 2012, Theobald and Farrington 2012) have also not always been considered (McNaughton Reyes et al. 2014, Norström and Rossow 2014, White and Hansell 1998). Preliminary evidence suggests a dose-

response relationship between cannabis use and violence/delinquency (Brook et al. 2014, Norström and Rossow 2014, Reingle et al. 2012), though the evidence is limited from similar shortcomings as highlighted above. All (Brook et al. 2003, Brook et al. 2014, Chabrol and Saint-Martin 2009, Fergusson et al. 2002, Friedman et al. 1996, Johnson et al. 1991, Monshouwer et al. 2006, Nabors 2010, Norström and Rossow 2014, Peters et al. 2014, Reingle et al. 2012, Resnick et al. 2004, White and Hansell 1998), but one (Pedersen and Skardhamar 2010) of the studies based on longitudinal general population samples assessing criminal behaviour have relied on self-reports of violence. Self-reports may be susceptible to bias such as testing effects, developmental changes or under-reporting of violent behaviour (Lauritsen 1998, Piquero et al. 2014). The only study that collected data from crime registers did not find that cannabis was a significant predictor (Pedersen and Skardhamar 2010), which may suggest either a true null finding or reflect the problem of underreporting of less serious crimes in record data considering that not all acts of violence need to be criminal in nature (Blumstein 1986, Pepper and Petrie 2003). Underreporting of violence in official records may also arise as a result of failure of the criminal justice system to detect and record all offenders as well as bias in arrest processes. While neither self-report nor official records provide an accurate account of the true rate of crime, they are the methods of choice for obtaining longitudinal data on individual violent careers and it has been suggested that both methods may be employed in concert to overcome some of the limitations of each (Blumstein 1986). Furthermore, less is known regarding the directionality of the association between cannabis use and violence, an issue that deserves careful consideration since reverse causation may explain the association. For instance, impulsiveness/disinhibition or conduct problems evident in childhood have also been linked to subsequent use/ abuse of cannabis (Brook et al. 2013,

Pingault et al. 2013, von Sydow et al. 2002) and other studies in adolescents and young adults have reported a reciprocal relationship between substance use and violence (Scholes-Balog et al. 2013, Xue et al. 2009).

In the present study, we have attempted to address the limitations outlined above by employing multi-wave, prospective assessment of a population-based cohort of all school-aged male children from a defined geographical area in London, and included violence data based on both self-report and criminal records to establish the precise nature of the relationship between cannabis use and violent behaviour. They have been followed up over nearly half a century to assess the effect of exposure to cannabis at different stages of life on violent behaviour, as indexed using two independent measures, recorded violent convictions and self-reports. We examined whether '*continued use*' is the critical determinant that underpins the association between cannabis use and violence after controlling for potential confounding factors such as family history of criminality, childhood antisocial behaviour, mental health history, alcohol and other illicit drug use (Bennett et al. 2008, Farrington 1995, Resnick et al. 2004).

Table 1.

2. Methods

2.1 Study sample

The Cambridge Study in Delinquent Development (CSDD), originally designed by Donald J. West and directed since 1982 by David P. Farrington, is a prospective longitudinal study of the development of offending and antisocial behaviour in a cohort of 411 boys born mostly in 1953 and living in a homogenous, working-class urban area of London (Farrington 1995,

West and Farrington 1973). They represented the complete population of boys who were 8 years old at that time (1961/62) and were attending one of six primary schools in a deprived area in London. Multiple waves (T1- T8) of data collection, which included participant interviews [at ages 8 (T1), 10 (T2), 14 (T3), 16 (T4), 18 (T5), 21 (T6), 32 (T7) and 48 (T8)] complemented information obtained from parents (annually) and teachers (bi-annually) between age 8-15 years. 97% of the sample was white and all were raised in two-parent working class households (Farrington 1995). A detailed description of the methods is included as supplementary material (cf. *sAppendix 1*. Supplementary Material).

2.2 Measures

Violent conviction (VC): Criminal records

Conviction information was obtained for every year from age 10-56 through searches at the central Criminal Record Office in London or from countries where they had emigrated to. VC was defined as conviction for robbery, assault, threatening behaviour, or possessing an offensive weapon. We estimated two separate dependent variables (DV). For cannabis users, only convictions that were committed subsequent to cannabis use were considered:

a. DV1$_{VC}$ [cumulative number of subsequent VCs] was computed by calculating the cumulative mean number/year from age 10-56.
b. DV2$_{VC}$ [risk of subsequent VC] was coded as a dichotomized variable, "yes" if at least one conviction was committed between age 10-56.

Self-reported violence (SR-V)

SR-V was measured based on report of the person's involvement in assaults, fights, and use of a weapon in physical fights and estimated as two DVs as for violent convictions.

a. DV1$_{SR\text{-}V}$ [cumulative number of subsequent SR-V]: SR-V (yes/no) was available at three different time points: T5, T7 and T8, based on information on violence between age ranges 15-18, 27-32 and 43-48 respectively.
b. DV2$_{SR\text{-}V}$ [risk of subsequent SR-V] was a dichotomized variable, coded as "yes" if a subject admitted to violence at T5, T7 or T8.

Cannabis use (Independent variable, IV)

Cannabis use during the preceding five years was assessed at ages 14 (T3), 16 (T4), 18 (T5), 32 (T7), and 48 (T8) years. For the purposes of this investigation, we focused on cannabis use at T5, T7 and T8, as very few individuals had reported cannabis use at T4 or earlier (cf. sAppendix 2., Supplementary Material).

a. IV 1 (Ever cannabis use) was coded as "yes" if a subject was classified as a cannabis user in at least one of the assessments.
b. IV 2 (Continuity of cannabis use) was computed as an ordinal variable based on cannabis use: (1) never cannabis user, (2) cannabis user at 1 time point only (e.g., at T5 only but not T7 or T8), (3) cannabis user at 2 time points (e.g., cannabis use at T5 and T7 but not T8), or (3) cannabis user at all 3 time points.

Covariates

The covariates included in the analysis were chosen based on previous research, reporting a link between violence and antisocial behaviour (Farrington 2000), mental illness (Brennan et al. 2000) and substance use, including alcohol, illicit drugs and nicotine (Bennett et al. 2008, Jennings et al. 2012):

a. Antisocial traits were assessed at age ten based on teacher, peer, or parent ratings[1] using the antisocial personality scale (AP) (Farrington 1991).
b. Alcohol abuse defined as presence of binge drinking (>13 units per evening in the last month yes/no) was assessed at T5, T7, and T8 and a continuous variable was computed based on whether binge-drinking was present or not at the 1-3 time-points assessed (score ranging from 0-3)
c. Other drug use (yes/no) assessed at T7 was coded as "yes" if the person had tried drugs other than cannabis.
d. Cigarette use defined as presence of smoking (> £2 spent on cigarettes per week/ over 20 cigarettes/ day) was assessed at T5 and T7 and T8 and a score (from 0 to 3) was computed based on whether smoking was present or not at the 1-3 time points assessed (scoring from 0 - 3).
e. Diagnosis of mental illness (yes/no) was assessed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) (First et al. 1998) as part of a psychiatric interview at T8. Subjects were classified as those with or without a lifetime diagnosis of a mental disorder by age 48.

Childhood risk factors

Based on previous literature (Theobald and Farrington 2012, West and Farrington 1973), essential childhood risk factors that may independently contribute to both violence and drug use were included in these analyses:

[1] For the present analyses, each variable was dichotomized, as far as possible, into the "worst" quarter of males versus the remainder, with those most at risk coded as 2 and the remainder as 1

a. Social class was coded as "low" if the family breadwinner had an unskilled manual job.
b. Family history (presence of delinquent sibling and/or criminal parent) was measured up to the boy's tenth birthday.

2.3 Analysis

Data was analysed using R (R Core Team 2015) comprising four main statistical approaches:

(1) Kruskal-Wallis test was followed by Bonferroni correction for multiple testing to make comparisons among the four different cannabis trajectory groups (never use vs. use at one, two or three time points) on the average number of total violent convictions committed by age 56/ average number of self-reported violence by age 48.

(2) Univariate logistic regression analysis was employed to estimate the effect of cannabis use and other potential risk factors on violence. Subsequently, we carried out multivariate logistic regression analyses to examine the relationship between cannabis use and violence, while accounting for the covariates retained from the initial bivariate models (all factors with $p \leq 0.10$ were included).

(3) Fixed-effects logistic regression models were fitted in order to extend the ordinary logistic regression by adjusting for time invariant non-observed fixed factors that vary across individuals, such as family background, genetic influences, personality or pre-existing violent traits. In order to minimize the influence of reverse causation we (i) implemented fixed-effects models that used lagged outcome, i.e. examined whether changes in cannabis use were associated with subsequent changes in violence and (ii) tested a competing reverse causation model in which we tested the effect of changes in violence on changes in cannabis use. Alcohol use and cigarette use were included as

time-dynamic covariates in the models (for details see *sAppendix 3*., Supplementary Material).

(4) Finally, structural equation modeling was employed, in which cross-lagged reciprocal causal pathway models were fitted to examine the longitudinal bi-directional paths between cannabis and violence, while controlling for time-dynamic factors including alcohol and cigarette use (assessed at age 18, 32 and 48) and time-invariant factors including antisocial personality measured at age 10. Model goodness of fit was assessed on the basis of a number of fit indices described in *sAppendix 4*. (Supplementary Material).

3. Results

3.1 Follow up characteristics

Out of the 411 boys assessed at baseline, complete multi-wave cannabis and violence data (T1-T8) at follow up 48 years later was available for a total number of N=340 for SR-V and N=339 for VC (for follow up flow chart see *sFigure 1*., Supplementary Material). Missing data on alcohol use (n=1), cigarette use (n=6) and family history of crime (n=2) slightly reduced the number of subjects in the multivariate regression models (cf. *Table 3* below). Comparing subjects without complete data who were not included in the univariate analyses (n=71) to those with complete data (n=340) revealed that there were no significant differences between the two groups in predictor variables and violence, except for self-reported violence at age 18. This was less likely to have been reported (p=.04) in those who subsequently dropped out (cf. *sTable1*, Supplementary Material). Sixteen percent of the sample (n=55/339) had at least one registered violent conviction between age 10-56, while 49% (n=165/340) reported a violent act at least once over follow-up. Thirty-eight percent (n=130/340) of this

sample had used cannabis at least once in their life, of whom a large proportion (39%) had used cannabis in their teens only and then stopped (*Figure 1*), while 20% of those who started it by age 18 reported using it at age 32 and 48.

Figure 1.

The highest proportion of the sample was found to have never been violent and never used cannabis (VC- 56%, SR-V- 37%; *sTable 2*.). Over a fifth reported violent behaviour following cannabis use (SR-V- 22%), while a lower proportion were convicted following cannabis use (VC- 7%). This was substantially higher than the proportion of subjects in whom violence preceded cannabis use but did not continue subsequently (VC- 1.2%, SR-V-0.3%) or those subjects in whom violence preceded and also followed cannabis use (VC- 2.1%, SR-V-1.2%).

3.2 Continued cannabis use and number of violent convictions

Results from the Kruskal-Wallis test indicated that there was a significant effect of cannabis use trajectory on total number of VCs by age 56 (p<0.001) and total number of SR-V by age 48 (p<0.001) (*Figure 2a*. and *Figure 2b*.). Pairwise post-hoc testing showed that continued cannabis use was associated with significantly more violent convictions by age 56 compared to never users or those who used it only at one or two time-points throughout follow up (*Table 2*). There was a similar effect on self-reported violence.

Figure 2a and 2b and Table 2.

3.3 Continued cannabis use and risk of subsequent violence

Univariate logistic regression analysis revealed that those who used cannabis at least once in their life had an increased risk for a subsequent violent conviction (OR=2.58[95% CI 1.41-4.73]) and self-reported violence (OR= 2.35[95% CI 1.50-3.68]), but this effect disappeared when controlled for confounders in multivariate analysis (*sTable 3*.). When cannabis use was categorized, only continued cannabis use (as indexed by use at all three time-points assessed over the follow-up period) remained a significant predictor, implicating a dose-dependent effect (cf. *Table 3*. below). Continued cannabis use, remained the strongest predictor for subsequent VC (OR = 7.08[95% CI 2.19-23.59]) and SR-V (OR = 8.94[95% CI 2.37-46.21]). The only other factor that had a significant effect on both VC and SR-V in the multivariate model was antisocial personality (OR = 3.43[95% CI 1.59 - 7.52] for VC and (OR = 2.15[95% CI 1.19 - 3.91] for SR-V). Family history of crime was only predictive of VC (2.51 [95% CI 1.22 - 5.22] and alcohol (OR=1.65[95% CI 1.21 - 2.27] and nicotine use (OR = 1.40[95% CI 1.10 - 1.79]) was associated with SR-V but not VC.

Table 3.

3.4 Directionality of the association between cannabis and violence

The results from the cross-lagged fixed-effects models suggest that change in cannabis use over time increases the Odds by 1.18[95% CI 1.09-1.28] for subsequent SR-V and by 1.08 [95% CI 1.02-1.14] for subsequent VC (cf. *sTable 5*., Supplementary Material), while controlling for factors that may vary over time, including cigarette and alcohol use. The cross-lagged fixed-effects models testing for reverse directionality showed that self-reported violence was a significant predictor for subsequent changes in cannabis use SR-V (1.06[95%

CI 1.00-1.12]); however, a similar effect was not observed for recorded violent convictions (VC) (1.01[95% CI 0.92-1.12]).

The results from structural equation modeling indicate evidence of statistically significant reciprocal relationships between cannabis use and violence, such that (1) cannabis use predicts subsequent VC (0.205[95% CI 0.026-0.385]) and SR-V (0.190[95% CI 0.065-0.314]) and (2) violence in turn also predicts subsequent cannabis use (0.191[95% CI 0.026-0.356] for VC and 0.215[95% CI 0.065-0.366] for SR-V). The fit indices for the reciprocal directionality models from the structural equation analysis are displayed in *sTable 6*. (Supplementary Material). When exploring the unconstrained path estimates for the different time points, the results indicated that the nature of the association differed depending on the developmental stage: reciprocal associations were present in early adulthood [cannabis use at age 18 as a predictor for subsequent VC (0.240[95%CI 0.001-0.479]) and SR-V (0.153[95%CI -0.024-0.329]); violence at age 18 as a predictor for subsequent cannabis use (0.265[95%CI 0.055-0.476] for VC and 0.324[95%CI 0.118-0.530] for SR-V). Significant effects of cannabis on violence were present in late adulthood for SR-V [cannabis at age 32 as a predictor for subsequent SR-V (0.212[95% CI 0.010-0.414])] but not vice versa [SR-V at 32 not a predictor for cannabis use at 48 (0.083[95%CI -0.100-0.266]). No significant associations (p>0.25) were found in late adulthood using the structural equation modeling (cf. *sFigure2*. and *sTable5*., Supplementary Material).

4. Discussion

In the present study, we set out to examine the nature of the association between cannabis use and violent behaviour and the determinants of that relationship. Using data from half a century follow-up of a prospectively recruited cohort from a defined geographical area, we

find that exposure to cannabis is associated with an increased risk for subsequent criminal/violent activity across the life span from childhood through to middle age, that is independent to and persists even after controlling for other measured putative risk factors and unobserved time-invariant factors of confounding. Furthermore, we show that the adverse effect of cannabis use on subsequent violent behaviour is driven by continued use of the substance, as indexed by use endorsed at multiple time-points. Stronger association between violence and use of cannabis endorsed at several time-points spread over a substantial portion of lifetime suggest a dose-response relationship between cannabis use and violence, consistent with previous literature (Brook et al. 2014, Monshouwer et al. 2006, Reingle et al. 2012). We also establish that this relationship is not only true for self-reports of violent behaviour, as in the previous studies (Brook et al. 2003, Brook et al. 2014, Fergusson et al. 2002, Johnson et al. 1991, McNaughton Reyes et al. 2014, Monshouwer et al. 2006, Nabors 2010, Norström and Rossow 2014, Peters et al. 2014, Reingle et al. 2012, Resnick et al. 2004), but go beyond existing evidence by demonstrating for the first time that continued cannabis use is associated with a 7-fold greater odds for subsequent violent convictions, a robust outcome measure that is not vulnerable to some of the methodological weaknesses of self-reported violence. To put this in perspective, the size of this effect is comparable to the effect of continued nicotine use over similar duration (40 years) on the risk of lung cancer in the UK (OR 8.3 [95% CI 2.3-29.7]) (Crispo et al. 2004).

Together, these results imply a reciprocal relationship between cannabis use and violence, which is consistent with a number of studies that reported such a relationship between substance use and violence in adolescence and emerging adulthood (Scholes-Balog et al. 2013, Xue et al. 2009) as well as studies that suggest a link between

impulsiveness/disinhibition or conduct problems evident in childhood and subsequent use/ abuse of cannabis (Brook et al. 2013, Pingault et al. 2013, von Sydow et al. 2002), alcohol (Caspi et al. 1996) or illicit drugs (Fergusson et al. 2008). Our results tend to suggest that these reciprocal effects are only dominant in early adulthood and violence in later life is not associated with subsequent cannabis use, although cannabis use at later age remained a significant predictor for self-reported violence. However, it is worth noting that this may also reflect lack of adequate power to detect such effects in the present sample, as both outcomes become less common in later life. No association was found for violent conviction at later age, which may indicate that cannabis use is a stronger predictor for less serious violent acts rather than those that may lead to conviction. The results add to previous investigations on reciprocal relationships reporting that cannabis use but not violence remained a consistent predictor over time (Wei et al. 2004). It has also been reported that the strength of association between crime and cannabis varies across different developmental stages in adolescence, with younger users being more affected than older users (Fergusson et al. 2002), again suggesting that a range of associated psychosocial risk factors evident in younger cannabis users may increase its effect on violence. Together, the results of the present study speak to several of the criteria (specificity, temporality, biological gradient and strength) commonly considered to ascertain whether an association is causal in nature (Hill 1965). Although the findings indicate pharmacological effects of cannabis on violence, the relatively long lag between the measurement time points (>12 years in SEM models) do not allow one to draw conclusions regarding acute or non-acute pharmacological effects. Nevertheless, the findings are consistent with independent experimental evidence that a single dose of cannabis can cause impairments in behavioural control, that may underlie impulsive, violent behaviour, by

altering the normal functioning of its underlying neural substrate, the ventrolateral prefrontal cortex in man (Bhattacharyya et al. 2014). These results are not only consistent with previous evidence as highlighted earlier, but also internally consistent, as we show that the relationship exists for two separate but related and complementary outcome measures obtained from independent sources, one based on official records and another on self-report from participants.

By using fixed-effects models and taking into consideration potential confounders in risk prediction models, we have tried to account for both measured and unmeasured time-invariant factors (such as genetic or temperamental traits by considering antisocial personality traits assessed at age ten; parental modeling by considering family history of crime; social class etc.) and factors that change over time (e.g. alcohol binge drinking, cigarette use other illicit drug use). Taking these factors into consideration is crucial as they may potentially confound the association between cannabis use and subsequent violence (Norström and Rossow 2014). It is worth noting that despite the range of putative predictors tested here, continued cannabis use remained the most significant predictor in the ordinary multivariate regression analysis and together with antisocial personality traits was consistently associated with both measures of subsequent violent behaviour. The results further indicate that the effect of continued cannabis use is not confounded by antisocial personality traits present at the age of ten, another important predictor, albeit with an weaker association (with odds of 3.4 for risk of conviction and odds of 2.2 for risk of self-reported violence). This is in line with previous research showing that cannabis remains an independent predictor after controlling for early conduct problems (Pedersen and Skardhamar 2010). Antisocial personality traits appear to be a stronger predictor for conviction than for self-reported violence, consistent with previous

research using data from both self-reports and criminal convictions (Moffitt et al. 2002), perhaps indicating that antisocial traits are more likely to be associated with more severe offences (Farrington 1995).

From a public health point of view, these results are particularly relevant in that they show longitudinal effects of persistent cannabis use on violence. More specifically, they suggest that intervention programs in early adulthood are likely to be most beneficial if they target both cannabis use and violent behaviour in light of their reciprocal relationship, and provide an empirical basis for consideration of the consequences of cannabis use in middle age. It is worth noting a few caveats in interpreting the results of this study. Firstly, we did not investigate the effects of cannabis use parameters such as frequency of use or type of cannabis used, which have been shown to moderate the effects of cannabis on violence (Chabrol and Saint-Martin 2009, Fergusson et al. 2002, Friedman et al. 1996, Monshouwer et al. 2006, Norström and Rossow 2014, Pedersen and Skardhamar 2010, White and Hansell 1998). Hence, it may be argued that self-report data of cannabis use as available in this study are imprecise and do not easily demonstrate a dose-response association given the binary (yes/ no) measure of cannabis exposure used in this analysis. Nevertheless, we were able to detect a strong association with violent outcomes that persisted after controlling for putative risk factors. An imprecise estimation of the predictor variable is only likely to have diluted its effect on the outcome variable. However, this is unlikely to have influenced the direction of the results reported herein as the effect of cannabis use on violent outcomes that we report here is unlikely to have been overestimated. On the contrary, the true effect of cannabis use on violent outcomes is perhaps greater than that we observe here. Furthermore, an intuitive approach to examining dose-response relationship in the context of cannabis use has involved

taking into account frequency / number of cannabis joints smoked (Fergusson et al. 2002). Instead, results presented here show that use of cannabis spread over a longer period of an individual's life has a greater effect on violent outcome than use spread over a shorter duration. Persistent cannabis use as in the present study is likely to indicate more frequent use (Schulenberg et al. 2005, Windle and Wiesner 2004). Our results are therefore consistent with studies showing a dose-response relationship between cannabis use and violence. In this context, it is worth mentioning that self-reported cannabis use and violence from age 18 onwards as reported in this cohort do not reflect lifetime use data but use over the 5-years preceding the follow-up time-point under consideration.

Secondly, the study sample comprised only male subjects, thus not generalizable to females. This aspect of study design was beyond the control of the present investigators, as the cohort was initiated over half a century ago. Nevertheless, given that the association between cannabis use and violence seems to be more prominent in males than females (Friedman et al. 1996, Nabors 2010, Pedersen and Skardhamar 2010), this study addresses the relationship in the segment of the population where perhaps this may be most relevant. Notwithstanding these limitations, the present study substantially extends the current literature in a number of ways. Most previous studies were cross-sectional or prospectively investigated outcome over relatively short follow-up periods (Farrington 2010). In contrast, in the present study we were able to investigate prospectively collected data on cannabis use, violent outcome and confounding factors. We used information from multiple time-points from statutory, and multiple non-statutory sources, over nearly 50 years of longitudinal follow-up in a sample of all young males of a certain age from a defined catchment area. Furthermore, this methodology enabled us to accurately estimate temporal sequencing of the independent and

dependent variables of interest that has not been possible in previous studies. Although we cannot conclude formally regarding the causal effects of cannabis on violence as the present study is observational, our methodology enabled us to accurately estimate temporal sequencing of the independent and dependent variables of interest that has not been possible in previous studies. Methodology as adopted here is considered only second best to evidence from randomized controlled trials in the context of investigation of causal relationships (Murray et al. 2009). Together, the results of the present study provide support for a causal relationship between exposure to cannabis and subsequent violent outcomes across a major part of life-span.

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Contributors

SB, DT and DF designed the study and supervised the analyses, TS and DT carried out the data analysis and wrote the first draft together with SB. All other authors provided data, reviewed the results and contributed to the final draft of the manuscript.

Declaration of interest

None.

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Table 1. Summary of observational studies looking at the effect of cannabis use on violence

Study	N	Age (M)/ Time point	IV: Cannabis predictor	DV: Violence outcome	DV coding	DV tool	Results	Confounders considered
Wei et al. (2004)	503	T1: 11 (M) T2: 12 (M) T3: 13 (M) T4: 14 (M) T5: 15 (M) T6: 16 (M) T7: 17 (M) T8: 18 (M) T9: 19 (M) T10: 20 (M)	IV1: User vs non user (T1) IV2: User vs non user (T2) IV3: User vs non user (T3) IV4: User vs non user (T4) IV5: User vs non user (T5) IV6: User vs non user (T6) IV7: User vs non user (T7) IV8: User vs non user (T8) IV9: User vs non user (T9)	DV1: Violence (T2) DV2: Violence (T3) DV3: Violence (T4) DV4: Violence (T5) DV5: Violence (T6) DV6: Violence (T7) DV7: Violence (T8) DV9: Violence (T9) DV9: Violence (T10)	Risk prediction	SR	IV1 -> DV1 (NS) IV2 -> DV2 (NS) IV3 -> DV3 * IV4 -> DV4 * IV5 -> DV5 * IV6 -> DV6 * IV7 -> DV7 (NS) IV8 -> DV8 * IV9 -> DV9 (NS)	age, gender, alcohol use, other drug use, prior violence, depression, impulsivity/hyperactivity/inattention problems at age 7, family risk factors, ethnicity, academic achievement
Brook et al. (2014)	838	T1: 14 (M) T2: 19 (M) T3: 25 (M) T4: 29 (M)	IV1: Chronic user vs non user (T1-T4) IV2: Moderate user vs non user (T1-T4) IV3: Discontinuer vs non user (T1-T4)	DV1: Use of weapon (T4) DV2: Carrying a weapon (T4) DV3: Stealing (T4)	Risk prediction	SR	IV1 -> DV1 * IV1 -> DV2 * IV1 -> DV3 * IV2 -> DV1 * IV2 -> DV2 (NS) IV2 -> DV3 (NS) IV3 -> DV1* IV3 -> DV2* IV3 -> DV3 (NS)	sex, ethnicity, alcohol abuse, criminal history, peer deviance, education
Reingle et al. (2012)	9421	T1: 15 (M) T2: 16 (M) T3: 21 (M) T4: 26 (M)	IV1: Discontinuer vs non user (T1-T3) IV2: Started user vs non user (T1-T3) IV3: Chronic user vs non user (T1-T3)	DV1: Intimate partner violence (T4)	Risk prediction	SR	IV1 -> DV (NS) IV2 -> DV* IV3 -> DV*,	age, sex, ethnicity, alcohol abuse, peer cannabis use, parental involvement, parental alcohol use, depression
White and Hansell (1998)	1201	T1: 12-18 (R) T2: 15-21 (R) T3: 18-24 (R) T4: 25-31 (R)	IV1: Frequency of cannabis use (T1) IV2: Frequency of cannabis use (T2) IV3: Frequency of cannabis use (T3) IV4: Frequency of cannabis use (T4)	DV1: Assault (T1) DV2: Assault (T2) DV3: Assault (T3) DV4: Assault (T4)	Composite score	SR	IV1 -> DV1* IV1 -> DV2 "" IV2 -> DV2* IV2 -> DV3 (NS) IV3 -> DV3* IV3 -> DV4* IV4 -> DV4*	n/a

McNaughton Reyes et al. (2014)	1920	T1: 13-15 (R) T2: 13.5-15.5 (R) T3: 14-16 (R) T4: 15-17 (R)	IV1: Frequency of cannabis use over time (T1-T4)	DV1: Intimate partner violence over time (T1-T4)	Composite score	SR	In boys: IV1 -> DV1 (NS) In girls: IV1 - > DV1*	sex, ethnicity, parental education
Pedersen and Skardhamar (2010)	1353	T1: 15 (M) T2: 20 (M) T3: 27 (M)	IV1: Ever user before T1 (yes/no) IV2: Experimenter vs non user (T1-T2) IV3: Regular user vs non user (T1-T2)	DV1: Charge for crime (T1-T2) DV2: Charge for crime (T2-T3)	Risk prediction	CR	IV1 -> DV1* IV2 -> DV2 (NS) IV3 -> DV2*	age, sex, alcohol abuse, other drug use, parental involvement, conduct problems, cannabis history, criminal history
Fergusson et al. (2002)	1063	T1: 16 (M) T2: 18 (M) T3: 21 (M)	IV1: Frequency of cannabis use (T1) IV2: Frequency of cannabis use (T2) IV3: Frequency of cannabis use (T3)	DV1: Property/violent crime (T1) DV2: Property/violent crime (T2) DV3: Property/violent crime (T3)	Composite score	SR	IV1 -> DV1* IV2 -> DV2* IV3 -> DV3*	adverse life events, peer deviance, alcohol abuse, age of leaving school, age of leaving home
Norström and Rossow (2014)	2681	T1: 17 (M) T2: 22 (M)	IV1: Increase of cannabis use (T1-T2)	DV1: Increase in delinquency (T1-T2)	Composite score	SR	IV1 -> DV1*	age, sex, alcohol abuse, peer deviance
Resnick et al. (2004)	14738	T1: 12-17 (R) T2: 13-18 (R)	IV1: User vs non user (T1)	DV1: Delinquency (T2)	Composite score	SR	IV1 -> DV1 *	criminal history, emotional distress, alcohol abuse, problems with parents, learning problems, repeated grade
Brook et al. (2003)	2226	T1: 15 (M) T2: 17 (M)	IV1: User vs non user (T1)	DV1: Delinquency (T2)	Risk prediction	SR	IV -> DV *	age, sex, ethnicity, SES
Friedman et al. (1996)	380	T1: 24 (M) T2: 27 (M)	IV1: Frequency of cannabis use (T1)	DV1: Non-violent offences (T2) DV2: Violent offences (T2) DV3: Non-violent convictions (T2) DV4: Violent convictions (T2)	Composite score	SR	In men: IV1-> DV1* IV1-> DV2* IV1-> DV3* IV1-> DV4 (NS) In woman: IV1-> DV1 (NS) IV1-> DV2* IV1-> DV3 (NS)	sex, alcohol abuse, family health, family history, conduct problems

							IV1-> DV4 (NS)	
Johnson et al. (1991)	1539	T1: 14-20 (R)	IV1: User vs non-user (T1)	DV1: Delinquency (T1)	Risk prediction	SR	IV1 -> DV1*	n/a
Monshouwer et al. (2006)	5551	T1: 12-16 (R)	IV1: Discontinuer vs non user (T1) IV2: Light user vs non user (T1) IV3: Regular user vs non uses (T1) IV4: Heavy uses vs non uses (T1)	DV1: Delinquent and aggressive behaviour (T1)	Composite score	SR	IV1-> DV1 (NS) IV2-> DV1* IV3-> DV1* IV4-> DV1*	age, sex, family affluence, social support, alcohol abuse, nicotine use
Chabrol and Saint-Martin (2009)	312	T1: 17 (M)	IV1: User vs no user (T1) IV2: Frequency of use (T1)	DV1: Delinquency (T1)	Composite score	SR	IV1-> DV1 (NS) IV2-> DV1*	sex, age, alcohol abuse, psychopathic traits, borderline traits, depression
Nabors (2010)	1938	T1: 19 (M)	IV1: User vs. non user (T1)	DV1: Intimate partner violence (T1)	Risk prediction	SR	IV1 -> DV1*	sex, ethnicity, university year, parents' level of education, SES, relationship status, alcohol abuse, exposure to interparental violence
Peters et al. (2014)	3598	T1 : 40 (M)	IV1: Cannabis use disorder vs nicotine use disorder (T1)	DV1: Intimate partner violence (T1)	Risk prediction	SR	IV1 -> DV1*	age, sex, ethnicity, education

Note. DV = Dependent Variable, CR= criminal records, IV = Independent Variable, M = Mean, R = Range, SES= socioeconomic status, SR= self-reported violence, T= Time point of assessment.
* = cannabis associated with increased violence ($p < .05$)
NS = cannabis not associated with violence (> p.05)
"" = cannabis associated with reduced violence (p<.05)

Figure 1

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Figure 1. Cannabis trajectories

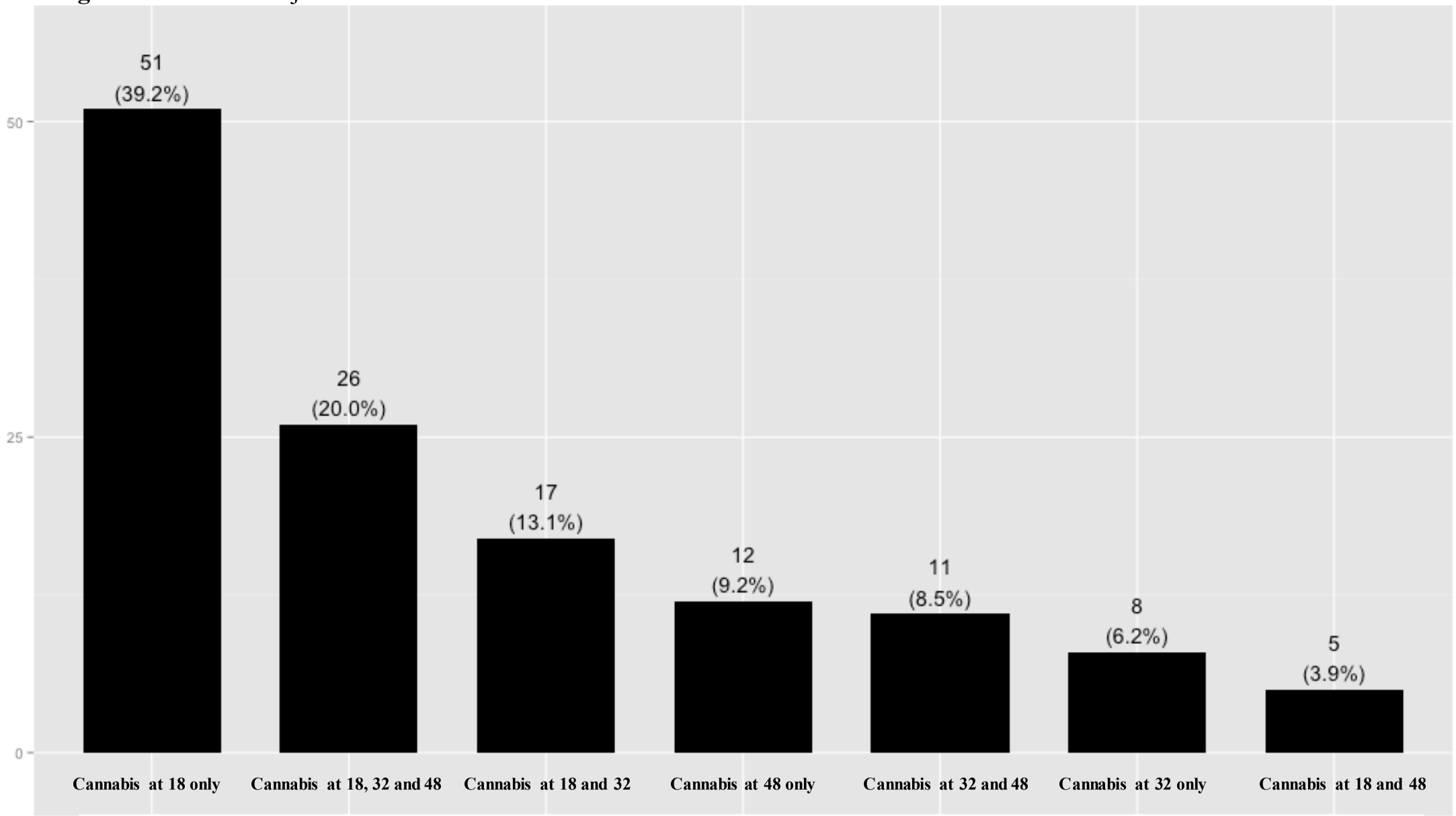
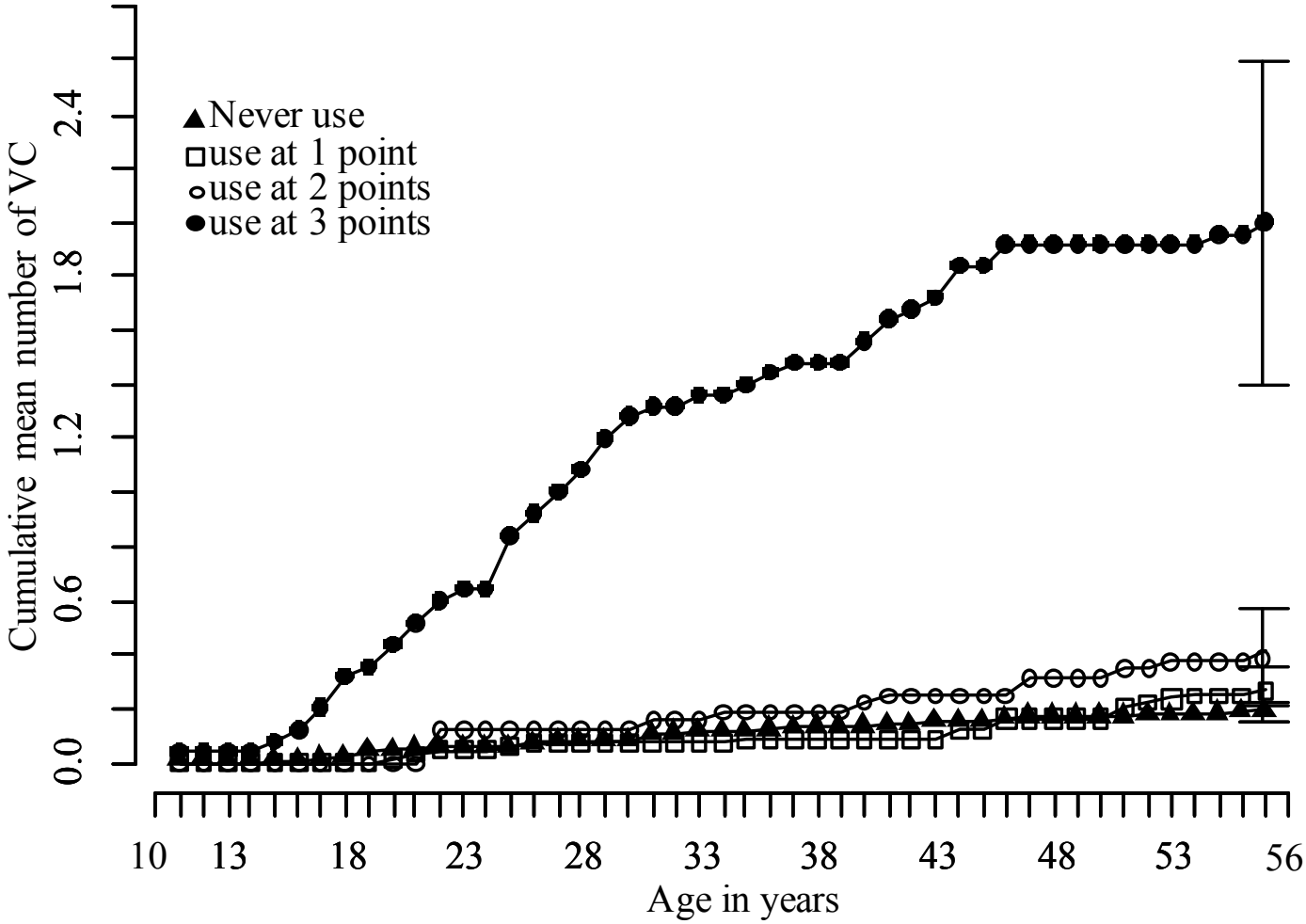


Figure 2a. Violent convictions (VC, cumulative means for N=335) over time per cannabis group



Note. From the total sample, some subjects (n=4) were excluded from the analysis since it was not possible to establish whether the conviction was a preceding event or subsequent to cannabis use.

Figure 2b. Self-reported violence (SR-V, cumulative means for N=340) over time per cannabis group

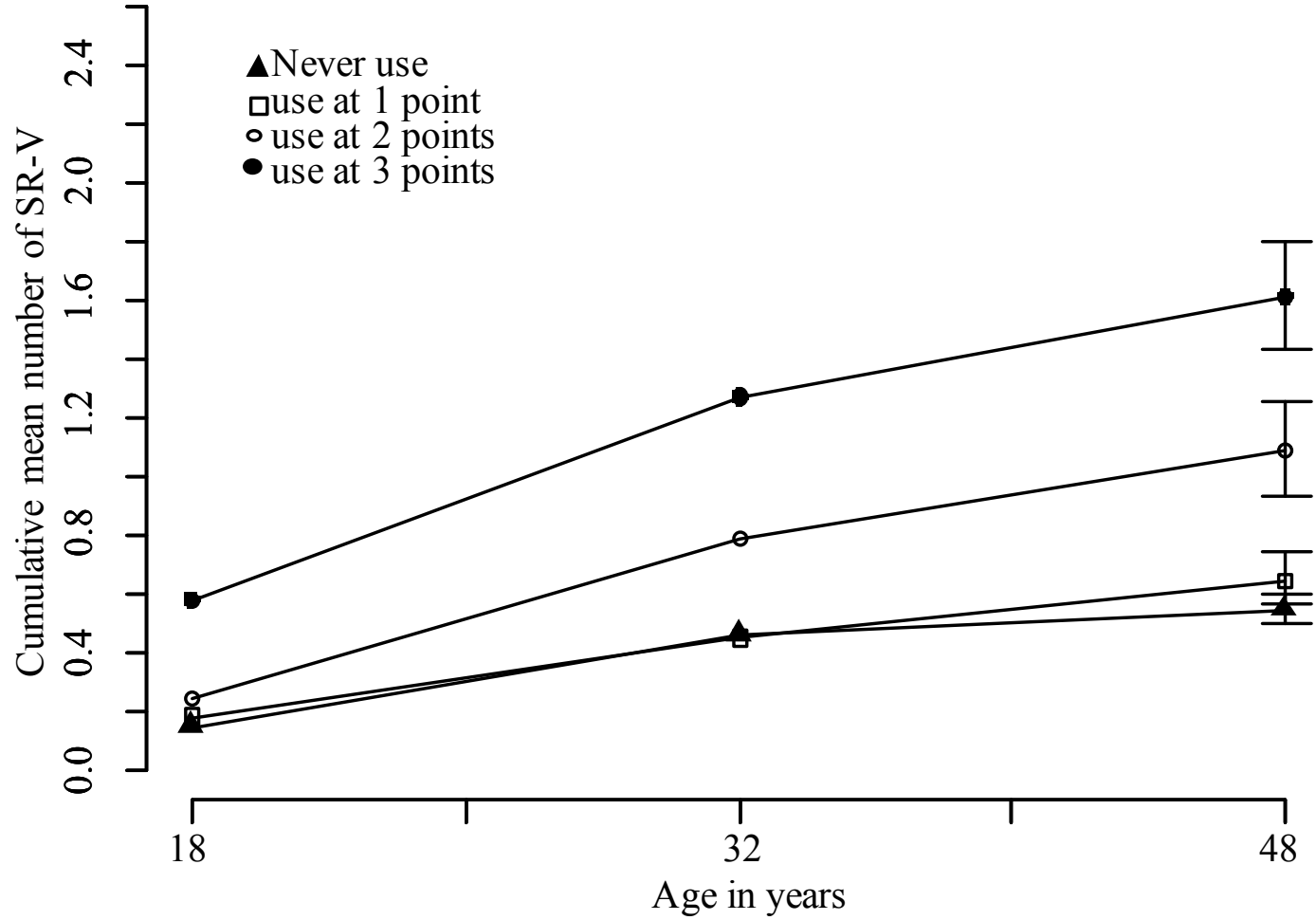


Table 2. Kruskal-Wallis test pairwise comparisons

	Number of VC by age 56		Number of SR-V by age 48	
	Difference	***p* adj.**	**Difference**	***p* adj.**
use at 0 points - use at 1 point	14.69	0.48	14.40	1.00
use at 0 points - use at 2 points	39.00	0.003	57.93	**0.002**
use at 0 points - use at 3 points	78.16	**<0.0001**	104.42	**<0.0001**
use at 1 point - use at 2 points	24.31	0.35	43.54	0.09
use at 1 point - use at 3 points	63.48	**0.0001**	90.03	**<0.0001**
use at 2 points - use at 3 points	39.16	**0.11**	46.49	0.22

Note. SR-V = Self reported violence; VC = Violent conviction
p values adjusted with Bonferroni correction

Table 3. Logistic regression predicting risk of violent conviction (VC) / risk of self-reported violence (SR-V) (following cannabis use)

Univariate Logistic Regression	**Risk of VC (N=335)** [d]			**Risk of SR-V (N=340)**		
	OR	***CI***	***p***	***OR***	***CI***	***p***
Ever cannabis (yes) [a]	2.58	1.41 - 4.73	**0.002**	2.35	1.50 - 3.68	**0.0002**
Cannabis use 1 point [b]	1.14	0.46 - 2.60	0.77	1.43	0.83 - 2.46	0.20
Cannabis use 2 points	2.39	0.87 - 5.96	0.07	2.94	1.38 - 6.60	**0.006**
Cannabis use 3 points	10.88	4.44 - 27.50	**<0.0001**	11.27	3.77 - 48.59	**0.0001**
Antisocial Personality (yes) [a]	3.58	1.90-6.71	**<0.0001**	2.56	1.52-4.41	**0.005**
Family history crime (yes) [a 2]	3.63	1.96-6.81	**<0.0001**	1.88	1.19-3.0	**0.007**
Alcohol use [c 1]	1.84	1.34-2.52	**<0.0001**	2.0	1.52-2.69	**0.0001**
Cigarette use [c 3]	1.67	1.29 – 2.23	**0.0001**	1.69	1.36 – 2.12	**<0.0001**
Other illicit drug use (yes) [a]	4.55	2.00-10.10	**0.0002**	2.99	1.38-7.01	**0.008**
Low social class (yes) [a]	2.99	1.55-5.70	**0.0009**	1.75	1.02-3.04	**0.04**
Mental illness (ever diagnosed) [a 4]	1.61	0.82 - 3.14	0.17	1.13	0.70 - 1.81	0.62
Multivariate Logistic Regression	**Risk of VC (N=327)** [d]			**Risk of SR-V (N=332)**		
	OR	***CI***	***p***	***OR***	***CI***	***p***
Cannabis use 1 point [b]	0.91	0.31 - 2.38	0.85	1.08	0.59 - 1.98	0.80
Cannabis use 2 points	1.91	0.60 - 5.68	0.25	2.26	0.93 - 5.79	0.08
Cannabis use 3 points	7.08	2.19 - 23.59	**0.001**	8.94	2.37 - 46.21	**0.003**
Antisocial Personality (yes) [a]	3.43	1.59 - 7.52	**0.002**	2.15	1.19 - 3.91	**0.01**
Family history crime (yes) [a]	2.51	1.22 - 5.22	**0.01**	1.38	0.82 - 2.33	0.23
Alcohol use [c]	1.34	0.90 - 1.97	0.14	1.65	1.21 - 2.27	**0.002**
Cigarette use [c]	1.36	0.97 - 1.91	0.07	1.40	1.10 - 1.79	**0.007**
Other illicit drug use (yes) [a]	1.88	0.59 - 5.71	0.27	0.79	0.26 - 2.34	0.66
Low social class (yes) [a]	2.05	0.90 - 4.55	0.08	1.35	0.72 - 2.52	0.35

Note. a = Dichotomized variable; b = Ordinal variable (reference group is never cannabis use); c = Continuous variable; d = some subjects (n=4) were excluded since it was not possible to establish whether the conviction was a preceding event or subsequent to cannabis use; SR-V = Self-reported violence; VC = Violent conviction. For some subjects (n=4 for conviction data, n=1 for SR-V) outcome was coded as absence of violence since the violent act only preceded cannabis use (*cf. sTable 2, supplementary material*.)
1 = missing data for n=1; 2 = missing data for n=2; 3 = missing data for n=6, 4 = missing data for n=50

Online Supplementary Material

Continuity of Cannabis use and Violent Offending Over the Life Course

Includes

sAppendix 1. Study sample

The Cambridge Study of Delinquent Development (CSDD), originally designed by Donald J. West and directed since 1982 by David P. Farrington, is a prospective longitudinal study of the development of offending and antisocial behavior in a cohort of 411 boys born mostly in 1953 living in homogenous, working class urban area of South London [a review of major findings may be found in several books (West and Farrington 1977, West and Farrington 1973, West 1982, West 1969, Piquero et al. 2007, Farrington et al. 2013) as well as in several in summary papers (Farrington et al. 2006, Farrington 1995, Farrington and West 1990)]. The men represented the complete population of boys who were 8 years of age at that time (1961/62) and were attending one of six primary schools in a deprived area in South London. There were multiple waves (T1- T8) of data collection which included participants being interviewed in their school [at ages 8 (T1), 10 (T2), and 14 (T3)], in research offices (at ages of 16 (T4), 18 (T5), and 21 (T6)] or in their homes (at ages 32 (T7) and 48 (T8)] by social science graduates. Parents were interviewed (about once per year) and questionnaires were completed by the boys' teachers (about once every two years) between ages 8 and 15 to complement information about troublesome/aggressive behavior in school and difficulties at home. 97% of the sample was white and all were raised in two-parent working class household (Farrington 1995).

sAppendix 2. Measures

Violent conviction: Criminal records

Conviction information was obtained for every follow-up year from age 10 to age 56 through searches at the central Criminal Record Office in London, a central repository containing records of all relatively serious offenses committed in Great Britain or Ireland, as well as minor juvenile offenses committed in the London area. 'Violent conviction' (VC) was defined as conviction for robbery, assault, threatening behavior, or possessing an offensive weapon. In the case of 18 males who had emigrated outside Great Britain and Ireland by age 32, applications were made to search their criminal records in the 8 countries where they had settled, and searches were carried out in five countries. We estimated 2 separate dependent variables (Seillier et al. 2010):

a. $DV1_{VC}$ [cumulative number of (subsequent) VCs]: The variable was computed by calculating the cumulative mean number per year from age 10 to 56. For cannabis users, only convictions that were committed subsequent to cannabis use were counted, excluding those that happened prior to use.
b. $DV2_{VC}$ [risk of (subsequent) VC): This dichotomized dependent variable was coded as "yes" if at least one conviction was committed between age 10 and 56. For cannabis users, only convictions that were committed subsequent to cannabis use were counted.

Self-reported violence

Self-reported violence (SR-V) was measured based on report of the person's involvement in assaults, fights, and use of a weapon in physical fights and also included two DVs as for violent convictions.

a. $DV1_{SR\text{-}V}$ [cumulative number of (subsequent) SR-V]: Data on violence (yes/no) was collected at three different time points, including T5: age 18 (violence between 15 and 18); T7: age 32 (involvement in fights between 27 and 32); and T8: age 48 (involvement in fights between 43 and 48).
b. $DV2_{SR\text{-}V}$ [risk of (subsequent) SR-V]: This dichotomized dependent variable was coded as "yes" if a subject admitted to violence at either T5, T7 or T8. Cannabis use was considered to have preceded SR-V if its use was reported either at the same or a time-point prior to the time-point under consideration for assessment of SR-V.

Cannabis use (Independent variable, IV)

At each face-to-face data collection, i.e. at ages 14 (T3), 16 (T4), 18 (T5), 32 (T7), and 48 (T8) years, the respondents were asked about their use of cannabis during the preceding 5 years.

a. IV 1 (Ever cannabis use): Three dichotomized cannabis variables were computed, including (1) cannabis at T5 or before (yes/no if cannabis has been used at age 18 or before); (2) cannabis at T7 (yes/no if cannabis has been used at least once between the age 27 and 32); and (3) cannabis at T8 (yes/no if cannabis has been used at least once between the age 43 and 48). IV 1 was coded as "yes" if a subject was classified as a cannabis user in at least one of the three variables. No separate cannabis use variables were computed for T3 and T4 as very few individuals (n=2 and n=25 respectively) reported use at these assessment points, which were therefore all considered together while estimating use at the T5 assessment (cannabis at 18 or before).
b. IV 2 (Continuity of cannabis use): An ordinal independent variable was computed based on three cannabis variables, classifying subjects either as (1) never cannabis user, (2) cannabis user at 1 time

point only (e.g., at T5 only but not T7 or T8), (3) cannabis user at 2 time points (e.g., cannabis use at T5 and T7 but not T8), or (3) cannabis user at all 3 time points.

Covariates

a. Antisocial traits were assessed at age 10 based on teachers, peers, or parents ratings[1] using the antisocial personality scale (AP) as described in detail by (Farrington 1991)and included: troublesomeness, conduct problems, difficult to discipline, dishonest, has stolen, gets angry, daring, lacks concentration/restlessness, impulsive, and truants.
b. Alcohol use defined as presence of binge drinking (>13 units per evening in the last month yes/no) was assessed at T5, T7, and T8 and a continuous variable was computed with a score ranging from 0 = never binge drinker at T5, T7 or T8; 1= binge drinker 1 time-point only; 2= binge drinker at 2 time-points; and 3= binge drinker at all 3 time-points.
c. Other drug use (yes/no) was assessed at T7 and was coded as yes if the subjects had tried drugs other than cannabis.

Childhood risk factors

Childhood risk factors that may independently contribute to both violence and drug use were included in this analysis (Farrington et al. 2006, West and Farrington 1973):

a. Social class (socioeconomic status): This variable was dichotomized, with 2 indicating that the family breadwinner (usually the father) had an unskilled manual job. All of the rest were coded as 1.
b. Family history of criminal/delinquent behaviour was measured up to the boy's tenth birthday and referred only to biological relatives, with 2 indicating the presence of delinquent sibling and/or criminal parent. All those without a delinquent sibling and/or parent were coded as 1.

sAppendix 3. Analysis

Data was analysed using *R* (R Core Team 2015) comprising four main statistical approaches:

(1) We used the Kruskal-Wallis Test followed by Bonferroni correction for multiple testing to make comparisons among the different cannabis trajectory groups (never use vs. use at 1 point vs. use at 2 points vs. use at 3 points) on the average number of total convictions committed by age 56/ average number of self-reported violence by age 48. This non-parametric test was chosen as the Shapiro-Wilk Normality Test statistic was highly significant for number of convictions ($p<0.001$) and SR-V ($p<0.001$).
(2) Secondly, univariate logistic regression analysis was employed to estimate the uncontrolled effect of cannabis use and other potential risk factors on violence outcome to identify those variables that are significantly associated with risk of VC/SR-V. The variables were chosen based on previous research (Farrington et al. 2006, Resnick et al. 2004). Subsequently, odds ratios (ORs) were computed using multiple logistic regression analysis to examine the relationship between cannabis use and violence outcome, while accounting for the covariates retained from the initial bivariate models (all factors with $p\leq 0.10$ were included). The violence (yes/no) dichotomization based on conviction data and the self-reported violence served as the dependent variable.
(3) In the third stage, fixed-effects logistic regression models were fitted using the R package lme4 for binary outcome data in order to extend the ordinary logistic regression by adjusting for time-invariant non-observed fixed factors that vary across individuals, such as family background, genetic profile, personality or pre-existing violent traits. This approach allows the estimation of effect of within-person changes over time t for cannabis use [t=C_1(age 18), C_2(age 32), C_3(age 48)] on SR-V[t=V_1(age 18), V_2(age 32), V_3(age 48)] and VC[t=V_1(age 10-18), V_2(age 19-32), V_3(age 32-56)]. In order to minimize any effects that may be at play in the reverse direction (reverse causation, i.e. violence predisposing to cannabis use) we (i) implemented fixed-effects models that used lagged outcome, i.e. examined whether changes in cannabis use (C_1-C_2) were associated with subsequent changes in violence (V_2-V_3) and (ii) tested a competing reverse causation model in which we estimated the effects of changes in violence (V_1-V_2) on changes in cannabis use (C_2-C_3). Alcohol use and cigarette use were included as time-dynamic covariates in the models.

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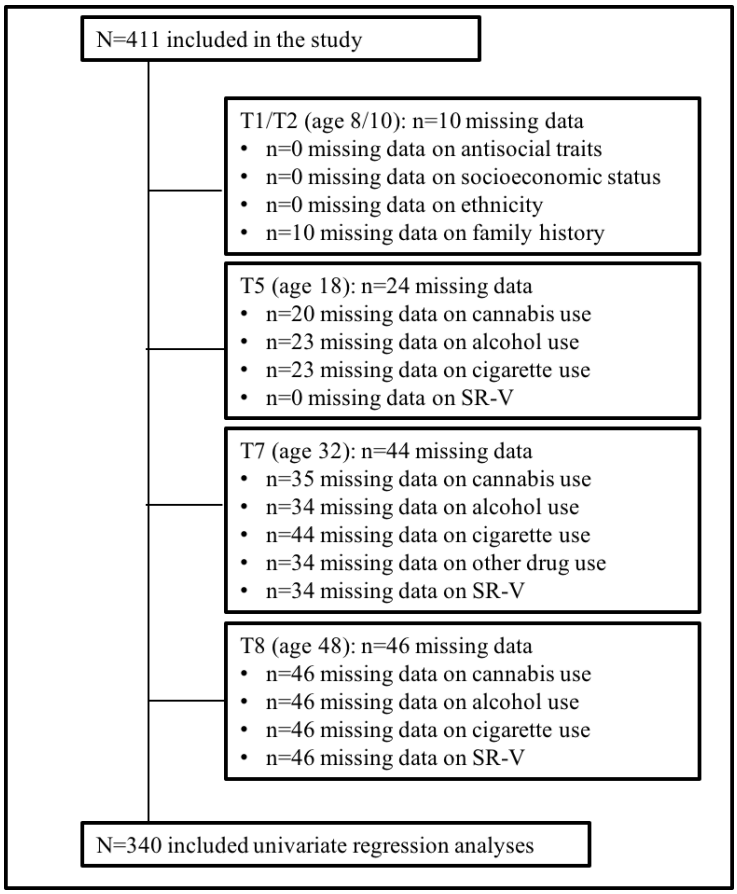
1 For the present analyses, each variable was dichotomized, as far as possible, into the "worst" quarter of males versus the remainder,with those most at risk coded as 2 and the remainder as 1

(4) Cross-lagged structural equation models were estimated using the lavaan package (Rosseel 2012). The cannabis (C_2-C_3) and violence variables (V_2-V_3) were treated as dependent variables, allowing to test for reciprocal changes in the association at different stages of the life span. We tested both an unconstrained model and a model in which the parameters (C_t and V_t) were constrained to be equal across time points. The models were fitted using the robust weighted least squares (WSL) approach. Model goodness of fit was assessed on the basis of a number of fit indices, including the model chi-squared goodness of fit statistic (non-significant or small chi-square value indicates that the model fits the data well), the root mean squared error of approximation (RMSEA, for which values of .05 indicate good fit and values up to .08 represent reasonable errors of approximation) (MacCallum et al. 1996) and the Comparative Fit Index (for which values of .95 are acceptable and of .95 or higher are indicative of good fit (Hu and Bentler 1999). Cross-sectional correlations between violence and cannabis use at were included for t_2 and t_3. All models were fitted while controlling for time dynamic factors including alcohol and cigarette use and time invariant factors including antisocial personality.

sAppendix 4. Supplementary Results

Out of the 411 boys assessed at baseline, complete multi-wave cannabis and violence data (T1-T8) at follow up 48 years later was available for a total number of N=340 for SR-V and N=339 for VC. Comparing subjects that dropped out throughout follow up (n=71) to completers (n=340) in demographic variables and violence data revealed that there were no significant differences between the two groups, expect for self-reported violence at age 18, which was less likely to be reported (p=.04) in those who subsequently dropped out (cf. *sTable1*).

sFigure 1. Flow chart: Follow up assessments



sTable1. Differences in demographics and violence data between completers and drop outs

	Completed n/N (%)	Drop out n/N (%)	*p*
Antisocial Personality (yes)	77/340 (23%)	21/71 (30%)	0.27
Family history crime (yes)	110/338 (33%)	25/63 (40%)	0.34
Low social class (yes)	67/340 (20%)	12/71 (17%)	0.70
Alcohol at 18 (yes)	69/339 (20%)	12/49 (25%)	0.63
Cigarette use at 18 (yes)	94/339 (28%)	10/49 (20%)	0.36
Other illicit drug use (yes)	32/340 (9%)	4/37 (11%)	1.00
Cannabis at 18 (yes)	97/340 (29%)	14/49 (29%)	1.00
VC between age 10 and 56 (yes)	57/339 (17%)	13/71 (18%)	0.90
SR-V at 18 (yes)	72/340 (21%)	7/71 (10%)	**0.04**

Note. *p*= p-value for chi-square test; SR-V = Self-reported violence; VC = Violent conviction

sTable 2. Temporal relationship between cannabis use and violence: Sample distributions in % (n)

	VC data [a]	SR-V data
Never cannabis -> never violence	55.5% (188)	36.8% (125)
Cannabis -> never violence	27.1% (92)	14.4% (49)
Cannabis -> violence	6.5% (22)	22.4% (75)
Violence -> never cannabis	6.5% (22)	25.% (85)
Violence -> cannabis -> violence	2.1% (7)	1.2% (4)
Violence -> Cannabis	1.2% (4)	0.3% (1)

Note. Arrow (->) indicating "followed by". SV-R = Self-reported violence; VC = Violent conviction.
[a] n= 4 could not be classified since it was not possible to establish whether the conviction was a preceding event or subsequent to cannabis use.

sTable 3. Multivariate logistic regression for cannabis use (ever used) in predicting risk of violent conviction (VC) / risk of self-reported violence (SR-V)

Multivariate Logistic Regression	Risk of VC (N=327) [d]			Risk of SR-V (N=332)		
	OR	CI	*p*	OR	CI	*p*
Cannabis use (ever) [a]	1.73	0.81 – 3.68	.155	1.56	0.92 – 2.65	.097
Antisocial Personality (yes) [a]	3.37	1.60 - 7.17	**.001**	2.14	1.20 - 3.88	**.011**
Family history crime (yes) [a 2]	2.50	1.23 - 5.10	**.011**	1.42	0.85 - 2.37	.180
Alcohol use [c 1]	1.33	0.91 - 1.93	.138	1.62	1.20 - 2.21	**.002**
Cigarette use [c 3]	1.41	1.02 - 1.95	**.038**	1.41	1.11 - 1.80	**.005**
Other illicit drug use (yes) [a]	3.60	1.32 - 9.76	**.012**	1.75	0.73 - 4.49	.222
Low social class (yes) [a]	2.03	0.91 - 4.40	.078	1.35	0.73 - 2.50	.339

Note. a = Dichotomized variable; b = Ordinal variable (reference group is never cannabis use); c = Continuous variable; d = some subjects (n=4) were excluded since it was not possible to establish whether the conviction was a preceding event or subsequent to cannabis use; SR-V = Self-reported violence; VC = Violent conviction.

Given the focus of the study, outcome in the uni- and multivariate analysis was defined as violence (yes/no) following cannabis use. As a result, for some subjects (n=4 for conviction data, n=1 for SR-V data) the outcome was coded as absence of violence since the violent act only preceded cannabis use (*cf. sTable 2 above*). The same multivariate analysis was carried out after recoding the outcome for those subjects (from absence of violence to presence of violence), which did not change the main results (cf. *sTable 4.below*).

sTable 4. Multivariate logistic regression predicting risk of violent conviction (VC) / risk of self-reported violence (SR-V)

Multivariate Logistic Regression	**Risk of VC (N=327)** [d]			**Risk of SR-V (N=332)**		
	OR	**CI**	***p***	**OR**	**CI**	***p***
Cannabis use 1 point [b]	1.27	0.48 - 3.15	.622	1.15	0.62 - 2.10	.661
Cannabis use 2 points	2.43	0.81 - 7.04	.105	2.24	0.92 - 5.73	.082
Cannabis use 3 points	5.85	1.81 - 19.26	**.003**	8.92	2.36 - 46.17	**.003**
Antisocial Personality (yes) [a]	3.84	1.81 - 8.32	**.001**	2.11	1.17 - 3.85	**.013**
Family history crime (yes) [a 2]	2.31	1.13 - 4.74	**.022**	1.35	0.80 - 2.28	.255
Alcohol use [c 1]	1.28	0.87 - 1.86	.208	1.66	1.22 - 2.29	**.002**
Cigarette use [c 3]	1.53	1.11 - 2.13	**.010**	1.42	1.12 - 1.82	**.005**
Other illicit drug use (yes) [a]	2.81	0.94 - 8.32	.062	0.78	0.26 - 2.32	.649
Low social class (yes) [a]	1.81	0.79 - 4.01	.148	1.32	0.71 - 2.47	.380

Note. a = Dichotomized variable; b = Ordinal variable (reference group is never cannabis use); c = Continuous variable; d = some subjects (n=4) were excluded since it was not possible to establish whether the conviction was a preceding event or subsequent to cannabis use; SR-V = Self-reported violence; VC = Violent conviction.

sTable 5. Fixed effects cross-lagged logistic regression

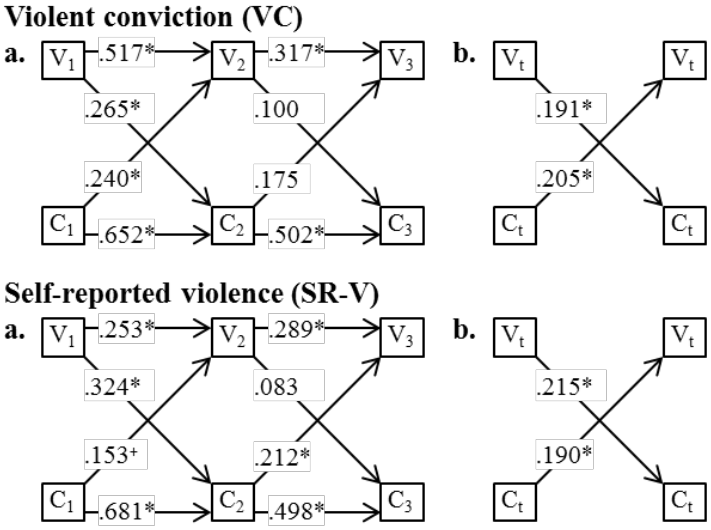
	Univariate		Multivariate		Univariate		Multivariate	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
	Regular causation: Cannabis on SR-V (V_2-V_3)				**Regular causation: Cannabis on VC (V_2-V_3)**			
Cannabis (t_1-t_2)	1.21	(1.12 - 1.31)	1.18	(1.09 - 1.28)	1.10	(1.04 - 1.15)	1.08	(1.02 - 1.14)
Alcohol (t_1-t_2)	1.13	(1.04 - 1.23)	1.10	(1.02 - 1.20)	1.09	(1.03 - 1.15)	1.08	(1.02 - 1.14)
Cigarette (t_1-t_2)	1.10	(1.03 - 1.19)	1.05	(0.98 - 1.14)	1.05	(1.00 - 1.10)	1.02	(0.97 - 1.08)
	Reverse causation SR-V on Cannabis (t_2-t_3)				**Reverse causation VC and Cannabis (t_2-t_3)**			
Violence (t_1-t_2)	1.06	(1.01 - 1.12)	1.06	(1.00 - 1.12)	1.02	(0.93 - 1.12)	1.01	(0.92 - 1.12)
Alcohol (t_1-t_2)	1.03	(0.96 - 1.10)	1.02	(0.95 - 1.08)	1.03	(0.96 - 1.10)	1.02	(0.96 - 1.09)
Cigarette (t_1-t_2)	1.05	(0.99 - 1.11)	1.04	(0.98 - 1.10)	1.05	(0.99 - 1.11)	1.04	(0.98 - 1.11)

Note. N= 672 number of observations; SR-V = Self-reported violence; VC = Violent conviction

[a] Presence of violence (yes/no) per time point t for SR-V[t=V_1(age 18), V_2(age 32), V_3(age 48)] and VC[t=V_1(age 10-18), V_2(age 19-32), V_3(age 32-56)].

[b] t = Presence of cannabis/alcohol/cigarette use (yes/no) at time point t [t=t_1(age 18), t_2(age 32), t_3(age 48)]

sFigure 2. Structural equation: Reciprocal causation model



Note. a. = unconstrained model; b. = C_t and V_t were constrained to be equal across time points; C_t = Cannabis use at time point t [t=C_1(age 18), C_2(age 32), C_3(age 48)]; V_t = Violence at time point t for SR-V[t=V_1(age 18), V_2(age 32), V_3(age 48)] and VC[t=V_1(age 10-18), V_2(age 19-32), V_3(age 32-56)].

* $p \leq 0.05$

$^{+}$ $p \leq 0.10$

sTable 6. Cross-lagged structural equation models [a]

	Model parameter				Goodness-of-Fit Indices				
	Est.	*p*	SE	95% CI	x^2	df	*p*	RMSEA	CFI
Violent conviction (VC) (n=312)									
Reciprocal model (unconstrained)					44.273	29	0.035	0.041	0.964
$C_1 \rightarrow V_2$	0.240	0.049	0.122	0.001-0.479					
$C_2 \rightarrow V_3$	0.175	0.252	0.153	-0.124-0.474					
$V_1 \rightarrow C_2$	0.265	0.014	0.107	0.055-0.476					
$V_2 \rightarrow C_3$	0.100	0.403	0.119	-0.134-0.334					
$C_1 \rightarrow C_2$	0.652	0.000	0.073	0.509-0.794					
$C_2 \rightarrow C_3$	0.502	0.000	0.095	0.315-0.689					
$V_1 \rightarrow V_2$	0.517	0.000	0.119	0.284-0.750					
$V_2 \rightarrow V_3$	0.317	0.027	0.143	0.036-0.597					
$V_2 \leftrightarrow C_2$	0.157	0.226	0.130	-0.097-0.411					
$V_3 \leftrightarrow C_3$	0.065	0.579	0.118	-0.165-0.296					
Reciprocal model (constrained) [b]					45.475	31	0.045	0.039	0.966
$C_t \rightarrow V_t$	0.205	0.025	0.092	0.026-0.385					
$V_t \rightarrow C_t$	0.191	0.023	0.084	0.026-0.356					
Self-reported violence (SR-V) (n=333)									
Reciprocal model (unconstrained)					49.006	29	0.012	0.046	0.959
$C_1 \rightarrow V_2$	0.153	0.090	0.090	-0.024-0.329					
$C_2 \rightarrow V_3$	0.212	0.040	0.103	0.010-0.414					
$V_1 \rightarrow C_2$	0.324	0.002	0.105	0.118-0.530					
$V_2 \rightarrow C_3$	0.083	0.372	0.093	-0.100-0.266					
$C_1 \rightarrow C_2$	0.681	0.000	0.066	0.553-0.809					
$C_2 \rightarrow C_3$	0.498	0.000	0.075	0.350-0.646					
$V_1 \rightarrow V_2$	0.253	0.005	0.090	0.078-0.429					
$V_2 \rightarrow V_3$	0.289	0.007	0.107	0.079-0.499					
$V_2 \leftrightarrow C_2$	0.092	0.405	0.110	-0.124-0.308					
$V_3 \leftrightarrow C_3$	0.023	0.828	0.105	-0.183-0.229					
Reciprocal model (constrained) [b]					52.245	31	0.010	0.045	0.956
$C_t \rightarrow V_t$	0.190	0.003	0.064	0.065-0.314					
$V_t \rightarrow C_t$	0.215	0.005	0.077	0.065-0.366					

Note. C_t = Presence of cannabis use (yes/no) at time point t [t=C_1(age 18), C_2(age 32), C_3(age 48)]; CFI = Comparative Fit Index; RMSEA = root mean squared error of approximation; Presence of violence (yes/no) at time point t for SR-V[t=V_1(age 18), V_2(age 32), V_3(age 48)] and VC[t=V_1(age 10-18), V_2(age 19-32), V_3(age 32-56)].

[a] All models were fitted using the robust weighted least squares (WSL) approach using lavaan (Rosseel 2012).

[b] Model parameters (C_t and V_t) were constrained to be equal across time points. Chi-square difference tests revealed that these constraints did not significantly ($p > 0.05$) worsen the fit of the models.

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