




Psychiatric sequelae of adolescent cannabis use in the 1986 NFBC

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Previously published 1986 NFBC studies addressing this issue

- Miettunen J, Tormanen S, Murray GK, Jones PB, Maki P, Ebeling H, et al. (2008). Association of cannabis use with prodromal symptoms of psychosis in adolescence. *Br J Psychiatry*. 192: 470–1.
- Miettunen, J., Murray, G. K., Jones, P. B., Mäki, P., Ebeling, H., Taanila, A., ... & Veijola, J. (2014). Longitudinal associations between childhood and adulthood externalizing and internalizing psychopathology and adolescent substance use. *Psychological medicine*, 44(8), 1727-1738.
- Mustonen, A., Niemelä, S., Nordström, T., Murray, G. K., Mäki, P., Jääskeläinen, E., & Miettunen, J. (2018). Adolescent cannabis use, baseline prodromal symptoms and the risk of psychosis. *The British Journal of Psychiatry*, 212(4), 227-233.

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The aim of my thesis: the research questions


- Is adolescent cannabis use associated with subsequent...
- ...severe suicide attempts and suicide?
- ...bipolar disorder?
- ...MDD and anxiety disorders? (my supervisor Dr. Antti Mustonen as the 1st author)
- Also planning to write a paper on possible interactions between adolescent cannabis use and different YSR subscales regarding psychiatric outcomes yet to be determined

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Adolescent cannabis, suicide death or severe attempt: the evidence base

- 15 prospective longitudinal studies in all, 8 with significant positive findings
- Very heterogenous in terms of measurement of suicidal behaviors, sample sizes and characteristics, lengths of follow-up and covariates controlled for
- 5/8 of those reporting significant positive finding did not adjust for other substance use
- In the only meta-analysis conducted thus far, Gobbi et al. 2019 included three of these studies and found that cannabis was associated with a 3.46 odds (95 % CI 1.53-7.84) of subsequent suicide attempt.
- Mars et al. 2019 utilized a high-risk subsample of the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort
- At least occasional cannabis use was associated with a 2.61 odds (95 % CI 1.11–6.14) of transitioning from suicidal ideation to suicide attempt and a 2.14 odds (95 % CI 1.04-4.41) of transitioning from non-suicidal self-harm to suicide attempt
- However, the nature of the subsample should be noted as well as the fact that only the effects of sex and socioeconomic position were adjusted for


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Protocol

- 15-16 y/o follow-up, those who consented and answered the question concerning cannabis use, previous attempters excluded (N = 6582)
- Exposure, cannabis use: never, 1-4 times, at least 5 times
- Outcome: pooled variable – suicide attempt def'd as a registered diagnosis implicating severe self harm (a proxy measure) and suicide death
- Potential covariates assessed: sex, family structure, parental education, parental psychiatric diagnosis, adolescent emotional and behavioral problems (YSR total), frequent alcohol intoxications during last year and lifetime illicit drug use
- Covariate selection: Chi Squared ($p < 0.10$), Cox regression modeling

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Strengths & limitations

- 1st prospective longitudinal birth cohort study utilizing comprehensive general population-based data (in contrast to Mars et al. 2019)
- Register-based rather than self report data on outcome measures captures severe attempts – the robustness of the estimate is both a strength and a limitation
- diagnostic codes implying severe intentional self-harm as a proxy measure for a severe suicide attempt requiring medical attention, but ascertaining whether or not an intent to die was tied to each such event recorded during follow up is beyond the scope of the register-based data
- Possibility to control for several potential covariates
- Pooled outcome variable (suicide deaths + attempts) due to power issues

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Adolescent cannabis use and subsequent bipolar disorder, the evidence base

- In all - to our knowledge - only 9 prospective longitudinal studies concerning the association between cannabis use and onset of manic symptoms or bipolar disorder have been published utilizing samples non-bipolar subjects
- 4 longitudinal studies using samples of adolescents or young adults (Duffy et al., Marwaha et al. 2018, Ratheesh et al., Tijssen et al)
- two utilized small high-risk samples and had bipolar disorder as primary outcome
- two studies utilizing general-population based samples had hypomania (Marwaha et al. 2018) and manic symptoms (Tijssen et al. 2010) as their primary outcome measures
- Only one study (Marwaha et al. 2018) utilized a birth cohort sample, the Avon Longitudinal Study of Parents and Children (ALSPAC).

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Study protocol

- Participants who signed the informed consent form, answered questions on cannabis use and had not received a diagnosis of any psychiatric disorder by the age of 16 were included in the present study (N = 6325)
- Predictor: lifetime cannabis use
- Outcome: a registered diagnosis of bipolar disorder
- Potential covariates assessed: sex, family structure, parental education, parental psychiatric diagnosis, adolescent emotional and behavioral problems (YSR total), frequent alcohol intoxications during last year and lifetime illicit drug use, daily smoking
- Selection of covariates and Cox regression modeling essentially as in the Suicide Death or Attempt study

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Study (year)	Sample	Sample size	Follow up (years)	Predictor	Outcome (n, %)	Assessment measure	Point estimate	95 % Confidence intervals	Substance use covariables	
Duffy et al. (2012)	Canada – Ottawa/Halifax: One parent with Type I BD	211	5.2 (mean)	DSM-IV SUD (n =50)	Bipolar disorder (35, 16.58 %)	DSM-IV/ KSADS-PL	aHR 3.40	Not reported	N/A	
Marwaha et al. (2018)	UK-ALSPAC	3370	5	CU at least 2-3 x weekly	Hypomania (243, 7.2 %)	HCL-32	aOR 2.21	1.49-3.28	Other drug/hazardous alcohol use	
Ralheesh et al. (2017)	Australia - High risk clinical sample	52	1	CUD	Bipolar disorder	DSM-IV	unadjOR 1.7	0.7-18.1	N/A	
Tjssen et al. (2010)	Germany/Munich- EDSP	543	8.3	5 + kerta	Mania symptoms	CIDI	aOR 4.26	1.42-12.76	Alcohol use	

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Adolescent cannabis use, MDD and Anxiety disorders (Dr. Mustonen as 1st author)

- A recently published meta-analysis of prospective cohort studies (Gobbi et al., 2019) focused on adolescent cannabis use, depression and anxiety until young adulthood, controlling for baseline symptomology
- With a total sample size of 23,317, the meta-analysis authors reported modest association for adolescent cannabis use and depression (OR=1.37) (7 studies) and a non-significant finding for anxiety disorders (OR=1.18) (3 studies) (Gobbi et al. 2019).
- However, the authors concluded that the results of their meta-analysis need to be confirmed with adequately powered prospective studies.


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Study protocol

- 15-16-year follow up of NFBC 1986; N = 6325; exclusion criteria: psychiatric disorder at baseline, nonresponders to cannabis question
- Exposure: four-class cannabis variable
- Outcome: anxiety disorders (F40-44) and depression (F32.0-F33.9, F34.1, F38.10)
- Potential covariates assessed: sex, family structure, parental education, parental psychiatric diagnosis, frequent alcohol intoxications during last year and lifetime illicit drug use, daily smoking & YSR int/ext assessed separately
- Choice of covariates as in aforementioned studies, Cox-regression modeling

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Strengths

- Long follow up
- Robust outcome measure
- Large sample size: e.g., the 3 studies included in Gobbi's meta-analysis on anxiety disorders had sample sizes of $n < 2000$
- Several covariates controlled for, including substance-use covariates
- General-population-based sample

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