Concept Paper Form

Provisional Paper Title: Long-term Cannabis Use and Midlife Preparedness for Older Age: Results of a Population-Representative Longitudinal Study
Proposing Author: Madeline Meier
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P.I. Sponsor: Terrie Moffitt, Avshalom Caspi   (if the proposing author is a student or colleague of an original PI)
Today's Date: 10/6/2021

Please describe your proposal in 2-3 pages with sufficient detail for helpful review.

Objective of the study:

Cannabis use is associated with poorer functioning in a number of domains that support healthy aging, including cognitive, financial, and interpersonal relationship functioning (Meier, 2021; Castellanos-Ryan et al., 2021).Thus, one hypothesis is that long-term cannabis users will be poorly prepared for the demands of old age. However, few studies have followed cannabis users beyond young adulthood. The present study tests whether long-term cannabis users show accelerated biological aging in midlife and poorer health, financial, and social preparedness for older age.

Data analysis methods:

Analyses will use two complementary approaches: (1) a qualitative approach: comparison of long-term cannabis users with 5 informative subgroups on age-45 biological aging, and health, financial, and social preparedness, and (2) a quantitative approach: tests of dose-response associations between persistence of cannabis dependence from age 18-45 and age-45 outcomes. Tests of dose-response associations will be repeated using persistence of tobacco dependence and persistence of alcohol dependence as exposures, for comparison with persistence of cannabis dependence.

1. Long-term cannabis users will be compared with 5 informative subgroups using t-tests.

Long-term cannabis users: study members who used cannabis weekly or more frequently in the past year at age 45, or were dependent on cannabis at age 45, and also used weekly or more frequently at one or more previous assessment waves.

The 5 comparison groups are defined as:

(i) *Lifelong cannabis non-users*: study members who never used cannabis, never had a diagnosis of any substance-use disorder, and never used tobacco daily.

(ii) *Long-term tobacco users:* study members who smoked tobacco daily at age 45 and also smoked daily at one or more previous waves; were mostly free from cannabis at age 45; and had no history of weekly cannabis use or dependence.

(iii) *Long-term alcohol users*: study members who were weekly drinkers at age 45; had a diagnosis of alcohol dependence at 2+ waves; were mostly free from cannabis at age 45; and had no history of weekly cannabis use or dependence.

(iv) *Midlife recreational cannabis users*: study members used cannabis between 6-51 days per year (i.e., used more than a few times but less than weekly) in midlife (age 32, 38, or 45), and had no history of weekly cannabis use or dependence.

(v) *Cannabis quitters*: study members did not use cannabis at age 45 but previously either diagnosed with cannabis dependence or used regularly (4+ days per week).

2. Dose-response associations will be tested using regression, with age-45 biological aging and aging preparedness outcomes regressed on persistence of cannabis dependence, persistence of tobacco dependence, and persistence of alcohol dependence.

Persistence of cannabis dependence will be defined by grouping study members according to those who (i) never used cannabis, (ii) used but never diagnosed , (iii) diagnosed at one wave, (iv) two waves, (v) three waves, and (vi) 4+ waves.

Persistence of tobacco dependence will be defined by grouping study members according to those who (i) never smoked tobacco, (ii) smoked tobacco daily at one or more assessment waves but were never diagnosed with tobacco dependence, (iii) were diagnosed at one wave, (iv) were diagnosed at two waves, (v) were diagnosed at three waves (n=62), and (vi) were diagnosed at four or more waves.

Persistence of alcohol dependence will be defined by grouping study members according to those who (i) never used alcohol, (ii) drank alcohol at least weekly at one or more assessment waves but were never diagnosed with alcohol dependence, (iii) were diagnosed at one wave, (iiv) were diagnosed at two waves, (v) were diagnosed at three waves, and (vi) were diagnosed at four or more waves.

Variables needed at which ages:

Exposures:
1. Age-45 comparison groups: (i) long-term cannabis users, (ii) non-users of cannabis with no other substance use problems, (iii) long-term tobacco users, (iv) long-term alcohol users, (v) midlife recreational cannabis users, (vi) cannabis quitters.

2. Persistence of cannabis dependence from age 18-45, persistence of tobacco dependence, persistence of alcohol dependence

Outcomes:
1. Composite measures of biological aging and health, financial, and social preparedness from Richmond-Rakerd et al., 2021
2. Individual indicators that make up the composite measures

Covariates:
1. Childhood SES
2. Low childhood self-control
3. Childhood IQ
4. Family history of substance-use problems
5. Persistent alcohol dependence
6. Persistent tobacco dependence
7. Persistent other illicit drug dependence

Significance of the Study (for theory, research methods or clinical practice):

As stated in the grant application, this study has implications for research, prevention, treatment, and policy.

Implications for future research: Positive findings of poor outcomes will attract attention to priority questions warranting further research investment. Conversely, negative findings will help the field identify hypotheses of cannabis harm that are unfruitful so that scientific resources can be directed elsewhere.

Implications for prevention: Knowledge of harms that do or do not characterize long-term users of cannabis will inform substance-abuse preventions. Preventing adolescent cannabis use is a major focus now, but this study can inform whether cessation programs for midlife adults ought to be added to the prevention toolkit. More generally, findings from the Dunedin Study are convincing aging researchers that the first half of the life course has untapped potential for prevention of late-life disease and disability. The proposed work asks if this prevention principle extends to reducing harms from cannabis use in the first half of the life course.

Implications for treatment: Positive findings of poorer aging preparedness will call attention to the need for interventions that aid long-term cannabis users in building the health, financial, and social capital that can fortify and sustain them through later life.

Implications for policy: Cannabis legalization is well underway and findings of harm are unlikely to reverse this trend. What is needed now is information about the likely circumstances of the generation of baby boomer cannabis users who continue to use it today as they enter late life. If our work reveals that their aging preparedness looks inadequate to sustain their health and wellbeing into old age, this will inform service-provision policy and need for additional resources. If the work shows their aging preparedness is not linked to cannabis history, this news will inform policy too.

References

Castellanos-Ryan N, Morin É, Rioux C, London-Nadeau K, Leblond M. Academic, socioeconomic and interpersonal consequences of cannabis use: A narrative review. *Drugs: Education, Prevention and Policy.* 2021.1-19.

Meier, M. H. Cannabis use and psychosocial functioning: evidence from prospective longitudinal studies. *Current Opinion in Psychology.* 2021. 38: 19-24.

Richmond-Rakerd LS, Caspi A, Ambler A, d'Arbeloff T, de Bruine M, Elliott M, Harrington H, Hogan S, Houts RM, Ireland D, Keenan R. Childhood self-control forecasts the pace of midlife aging and preparedness for old age. Proceedings of the National Academy of Sciences. 2021. 118(3).

Data Security Agreement

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☒	I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent)
☒	My project is covered by the Duke ethics committee OR I have /will obtain ethical approval from my home institution.
☒	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: a) encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines) b) password-protected c) configured to lock-out after 15 minutes of inactivity AND d) has an antivirus client installed as well as being patched regularly.
☒	I will not "sync" the data to a mobile device.
☒	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact Moffitt or Caspi.
☒	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
☒	I will not post data online or submit the data file to a journal for them to post. *Some journals are now requesting the data file as part of the manuscript submission process. Study participants have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to Temi or Avshalom for strategies for achieving compliance with data-sharing policies of journals.*
☒	I will delete all data files from my computer after the project is complete. Collaborators and trainees may not take a data file away from the office. This data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses.
☒	I have read the Data Use Guidelines and agree to follow the instructions.

Signature: Madeline H. Meier