HHS Public Access
Author manuscript
Lancet Healthy Longev. Author manuscript; available in PMC 2022 October 11.

Published in final edited form as:
Lancet Healthy Longev. 2022 October ; 3(10): e703–e714. doi:10.1016/S2666-7568(22)00201-X.

Preparedness for healthy ageing and polysubstance use in long-term cannabis users: a population-representative longitudinal study

Madeline H Meier,
Avshalom Caspi,
Antony Ambler,
Ahmad R Hariri,
HonaLee Harrington,
Sean Hogan,
Renate Houts,
Annchen R Knodt,
Sandhya Ramrakha,
Leah S Richmond-Rakerd,
Richie Poulton,
Terrie E Moffitt

Department of Psychology, Arizona State University, Tempe, AZ, USA (M H Meier PhD); Department of Psychology and Neuroscience (Prof A Caspi PhD, Prof A R Hariri PhD, H Harrington BS, R Houts PhD, A R Knodt MS, Prof T E Moffitt PhD) and Department of Psychiatry and Behavioral Sciences (Prof A Caspi, Prof T E Moffitt), Duke University, Durham, NC, USA; Institute of Psychiatry, Psychology, and Neuroscience, King's College London, London, UK (Prof A Caspi, A Ambler MSc, Prof T E Moffitt); Dunedin Multidisciplinary Health and Development Research Unit, Department of Psychology, University of Otago, Dunedin, New Zealand (A Ambler, S Hogan MSc, S Ramrakha PhD, Prof R Poulton PhD); Department of Psychology, University of Michigan, Ann Arbor, MI, USA (L S Richmond-Rakerd PhD)

Correspondence to: Dr Madeline H Meier, Department of Psychology, Arizona State University, Tempe, AZ 85287, USA, Madeline.Meier@asu.edu.

Contributors

We all agree to be accountable for all aspects of the work. MHM and RH accessed and verified the data. MHM contributed to conceptualisation, formal analysis, visualisation, and writing of the original draft. AC contributed to conceptualisation, funding acquisition, methodology, visualisation, and writing, reviewing, and editing. AA contributed to data curation, investigation, project administration, and writing, reviewing, and editing. ARH contributed to funding acquisition, methodology, and writing, reviewing, and editing. HH contributed to data curation, and writing, reviewing, and editing. SH contributed to data curation, investigation, project administration, and writing, reviewing, and editing. RH contributed to formal analysis, verification, and writing, reviewing, and editing. ARK contributed to writing, reviewing, and editing. SR contributed to data curation, methodology, project administration, and writing, reviewing, and editing. LR-R contributed to writing, reviewing, and editing. RP contributed to funding acquisition, data curation, methodology, project administration, and writing, reviewing, and editing. TEM contributed to conceptualisation, funding acquisition, methodology, visualisation, and writing, reviewing, and editing. We were not precluded from accessing data in the study, and we accept responsibility to submit for publication.

Declaration of interests

We declare no competing interests.

See **Online** for appendix

Summary

Background—Cannabis is often characterised as a young person's drug. However, people who began consuming cannabis in the 1970s and 1980s are no longer young and some have consumed it for many years. This study tested the preregistered hypothesis that long-term cannabis users show accelerated biological ageing in midlife and poorer health preparedness, financial preparedness, and social preparedness for old age.

Methods—In this longitudinal study, participants comprised a population-representative cohort of 1037 individuals born in Dunedin, New Zealand, between April, 1972, and March, 1973, and followed to age 45 years. Cannabis, tobacco, and alcohol use and dependence were assessed at ages 18 years, 21 years, 26 years, 32 years, 38 years, and 45 years. Biological ageing and health, financial, and social preparedness for old age were assessed at age 45 years. Long-term cannabis users were compared using independent samples *t* tests with five groups: lifelong cannabis non-users, long-term tobacco users, long-term alcohol users, midlife recreational cannabis users, and cannabis quitters. In addition, regression analyses tested dose–response associations for continuously measured persistence of cannabis dependence from age 18 years to 45 years, with associations adjusted for sex, childhood socioeconomic status, childhood IQ, low childhood self-control, family substance dependence history, and persistence of alcohol, tobacco, and other illicit drug dependence.

Findings—Of 997 cohort members still alive at age 45 years, 938 (94%) were assessed at age 45 years. Long-term cannabis users showed statistically significant accelerated biological ageing and were less equipped to manage a range of later-life health, financial, and social demands than non-users. Standardised mean differences between long-term cannabis users and non-users were large: 0·70 (95% CI 0·46 to 0·94; p<0·0001) for biological ageing, −0·72 (−0·96 to −0·49, p<0·0001) for health preparedness, −1·08 (−1·31 to −0·85; p<0·0001) for financial preparedness, and −0·59 (−0·84 to −0·34, p<0·0001) for social preparedness. Long-term cannabis users did not fare better than long-term tobacco or alcohol users. Tests of dose–response associations suggested that cannabis associations could not be explained by the socioeconomic origins, childhood IQ, childhood self-control, and family substance-dependence history of long-term cannabis users. Statistical adjustment for long-term tobacco, alcohol, and other illicit drug dependence suggested that long-term cannabis users' tendency toward polysubstance dependence accounted for their accelerated biological ageing and poor financial and health preparedness, although not for their poor social preparedness (β −0·10, 95% CI −0·18 to −0·02; p=0·017).

Interpretation—Long-term cannabis users are underprepared for the demands of old age. Although long-term cannabis use appears detrimental, the greatest challenge to healthy ageing is not use of any specific substance, but rather the long-term polysubstance use that characterises many long-term cannabis users. Substance-use interventions should include practical strategies for improving health and building financial and social capital for healthy longevity.

Introduction

Increasingly permissive cannabis policies around the world have spurred questions about the long-term consequences of cannabis use. Accumulating evidence suggests that long-term cannabis use is associated with poorer functioning in several domains.[1,2] Crucially, some of the affected domains, including cognitive, financial, and social functioning, support healthy ageing and longevity,[3–5] suggesting the hypothesis that long-term cannabis users might be poorly prepared for the demands of old age. However, few studies have followed cannabis users beyond young adulthood to evaluate this hypothesis. This scarcity of research represents a significant gap in the literature because the prevalence of cannabis use is increasing rapidly among midlife and older adults,[6,7] many of whom began using cannabis as adolescents.[6] Moreover, over the next decade, the number of older adults in Europe and the USA will swell to an unprecedentedly high proportion of the population,[8,9] which will increase demands on health-care and social welfare systems. Although the evidence for an association between cannabis use and early mortality is mixed,[10–12] cannabis use is associated with excess years lived with disability.[12] Therefore, it is crucial to investigate whether long-term cannabis use is a modifiable risk factor for poorer ageing.

We reported that long-term cannabis users show cognitive deficits that are comparable in size to deficits observed among midlife individuals who go on to develop dementia in later life.[13] This finding is consistent with the notion that long-term cannabis users show reduced midlife cognitive reserves, with cognitive reserves referring to having enough cognitive ability to handle ageing-related decline in brain health without developing dementia.[14] Here, using data from the same population-representative birth cohort followed to midlife, we examined whether long-term cannabis users show accelerated biological ageing in midlife, as well as poorer health, financial, and social preparedness for old age. Preparedness is conceptually similar to cognitive reserves in that a person with better preparedness starts from a healthy point in midlife with ample health, financial, and social reserves to meet ageing-related challenges. We focused on midlife because midlife functioning determines later life trajectories.[15] We also focused on biological ageing and midlife health, financial, and social preparedness for older age because each of these domains is related to health span (appendix pp 1–8). Moreover, evidence from cannabis studies of adolescents and younger adults,[2,16–19] and the few cannabis studies of adults in midlife and older adults (appendix pp 9–12),[20–24] support cannabis use associations with these domains.

To test the hypothesis that long-term cannabis use is associated with accelerated biological ageing in midlife and poorer ageing preparedness in the domains of health, financial, and social functioning, we compared long-term cannabis users with five informative groups: (i) lifelong cannabis non-users, selected to represent the control group used in case-control studies; (ii) long-term tobacco users and (iii) long-term alcohol users, selected to serve as benchmark comparisons for long-term cannabis users, thereby providing important context for addressing the claim that cannabis is safer than alcohol and tobacco and informing the need for policy and treatment efforts targeting cannabis specifically; (iv) midlife recreational cannabis users, selected to represent people who use cannabis infrequently and do not experience cannabis-related problems, because most people who use cannabis use it infrequently and do not experience problems[25] and may not show the same degree of risk for poorer ageing as long-term users; and (v) cannabis quitters, selected to ascertain whether cannabis cessation is associated with better midlife ageing preparedness. In addition to group comparisons, we conducted complementary tests of dose–response associations between persistence of cannabis dependence and midlife functioning, with associations rigorously adjusted for several confounders measured using numerous data waves and sources. Robust dose–response associations would be expected if associations were causal. Findings will inform on the importance of midlife interventions to help long-term cannabis users build the health, financial, and social capital needed to fortify and sustain them through later life.

Methods

Participants

In this population-representative longitudinal study, participants were members of the Dunedin Longitudinal Study, a representative birth cohort (n=1037; 91% of eligible births; 52% male and 48% female) born between April, 1972, and March, 1973, in Dunedin, New Zealand, who were eligible on the basis of residence in the province and who participated in the first assessment at age 3 years. The cohort represents the full range of socioeconomic status in the general population of New Zealand's South Island.[26] As adults, the cohort matched the New Zealand National Health and Nutrition Survey on key health indicators (eg, body-mass index, smoking, physical activity, and physician visits),[26] and the New Zealand Census of citizens the same age on educational attainment.[27] The cohort was primarily White (93%), which matched South Island demographics. Assessments were carried out at birth and ages 3 years, 5 years, 7 years, 9 years, 11 years, 13 years, 15 years, 18 years, 21 years, 26 years, 32 years, and 38 years, and most recently (completed in April, 2019), 45 years. Participants gave written informed consent. Study protocols were approved by the New Zealand Health and Disability Ethics Committee.

Measures

Measures are briefly described here. Descriptions and source information for all measures, including reliability and validity, are provided in the appendix (pp 1–8).

Substance use histories—Analyses used two types of exposures. The first, qualitative measurement, compared long-term cannabis users with five comparison groups. Analyses identified subsets of participants who met criteria for preregistered groups described hereafter. If a participant did not meet the criteria for a group, they were not included in group comparisons. The second, quantitative measurement, assessed the extent of persistence or chronicity of cannabis dependence, and other substance dependence, across the life course. These analyses used the full cohort.

Long-term cannabis users and five comparison groups—At ages 18 years, 21 years, 26 years, 32 years, 38 years, and 45 years, participants were interviewed about their substance use using the Diagnostic Interview Schedule, and past-year substance-use dependencies were assessed following Diagnostic and Statistical Manual of Mental Disorders criteria. This information was used to identify long-term cannabis users and five comparison groups (figure 1; table 1).

Long-term cannabis users (n=86) used cannabis every week or more frequently in the past year at age 45 years, or were dependent on cannabis at age 45 years, and also used cannabis every week or more frequently at one or more previous assessment waves. Of these users, 27

[31%] used cannabis before age 18 years, 77 [89·5%] used regularly (on 4 days or more per week) at one or more waves (mean 3·37 waves, SD=1·36), and 62 [72%] met the Diagnostic and Statistical Manual of Mental Disorders criteria for cannabis dependence (appendix p 1) at one or more waves (one wave [n=23], two waves [n=13], three waves [n=13], four or more waves [n=13]). Cannabis consumption at age 45 years in long-term cannabis users was a median of 300 (IQR 209) days in the past year, with 55 [64%] long-term cannabis users using cannabis on 4 days or more per week.

Lifelong cannabis non-users (comparison group 1; n=202; 82 [41%] male and 120 [59%] female) never used cannabis, never had a diagnosis of any substance-use disorder, and never used tobacco every day.

Long-term tobacco users (comparison group 2; n=75; 30 [40%] male and 45 [60%] female) smoked tobacco every day at age 45 years and also smoked every day at one or more previous waves (mean 5·05 waves [SD=0·99]), were mostly free from cannabis at age 45 years, and had no history of weekly cannabis use or dependence.

Long-term alcohol users (comparison group 3; n=57, 32 [56%] male and 25 [44%] female) drank alcohol every week at age 45 years, had a diagnosis of alcohol dependence at two or more waves (mean 3·49 waves [SD 0·73]), were mostly free from cannabis at age 45 years, and had no history of using cannabis every week or cannabis dependence.

Midlife recreational cannabis users (comparison group 4; n=65; 38 [58%] male and 27 [42%] female) used cannabis between 6 days and 51 days per year (ie, used more than a few times but less than every week) in midlife (at ages 32 years, 38 years, or 45 years), and had no history of using cannabis every week or cannabis dependence.

Cannabis quitters (comparison group 5; n=60; 37 [62%] male and 23 [38%] female) did not use cannabis at age 45 years, but previously either were diagnosed with cannabis dependence or used regularly (for 4 days or more per week).

Persistence or chronicity of substance dependence across the life course— For persistence or chronicity of cannabis dependence across the life course, participants were grouped according to those who never used cannabis (n=262); used cannabis but were never diagnosed with cannabis dependence (n=498); were diagnosed with cannabis dependence at any one wave (n=85); were diagnosed at two waves (n=39); were diagnosed at three waves (n=32); and were diagnosed at four waves or more (n=16).

For persistence or chronicity of tobacco dependence across the life course, with dependence defined by Diagnostic and Statistical Manual of Mental Disorders criteria (appendix pp 1–2), participants comprised those who never smoked tobacco (n=451); smoked tobacco every day at one or more assessment waves but were never diagnosed with tobacco dependence (n=131); and those who were diagnosed with tobacco dependence at any one wave (n=109); two waves (n=91); three waves (n=63); and four or more waves (n=89). For persistence or chronicity of alcohol dependence comprised participants who never used alcohol (n=52), drank alcohol at least every week at one or more assessment waves but were never diagnosed with alcohol dependence (n=533), and those who were diagnosed with alcohol dependence at any one wave (n=181), two waves (n=83), three waves (n=49), and four or more waves (n=32).

Ageing outcomes

At age 45 years, we evaluated four domains indexing preparedness for old age (figure 2).

First, accelerated biological ageing. There were five outcomes for accelerated biological ageing, comprising pace of ageing, brainAGE (the difference between chronological age and estimated age based on multiple MRI-derived measures of structural brain integrity), volume of white matter hyperintensities, gait speed, and facial age. Outcomes were correlated (r_S [absolute values] ranged from 0·09 to 0·33) and were combined to form a composite measure using principal components analysis. We extracted the first component (mean 0 [SD 1]), which accounted for 36% of the variance.[28]

Second, health preparedness. There were three outcomes for health preparedness, comprising practical health knowledge, pessimism toward ageing, and self-predicted life expectancy. Outcomes were correlated (r_S [absolute values] ranged from 0·16 to 0·27) and were combined to form a composite measure using principal components analysis. We extracted the first component (mean 0 [SD 1]), which accounted for 46% of the variance.[28]

Third, financial preparedness. There were four financial preparedness outcomes, comprising practical financial knowledge, financial planfulness, credit scores, and informant-reported financial problems. Outcomes were correlated (r_S [absolute values] ranged from 0·21 to 0·37) and were combined to form a composite measure using principal components analysis. We extracted the first component (mean 0 [SD 1]), which accounted for 47% of the variance.[28]

Finally, social preparedness. There were three social preparedness outcomes, comprising social support, loneliness, and life satisfaction. Outcomes were correlated (rs [absolute values] ranged from 0·48–0·52) and were combined to form a composite measure using principal components analysis. We extracted the first component (mean 0 [SD 1]), which accounted for 66% of the variance.[28]

Covariates

Covariates were selected based on theoretical and documented associations with cannabis use and healthy ageing. Covariates were: sex; childhood socioeconomic origins; childhood IQ; low childhood self-control; family substance dependence history; persistence of tobacco dependence; persistence of alcohol dependence; and persistent other illicit drug dependence.

Statistical analysis

We used independent samples *t* tests to compare long-term cannabis users with the five groups. We used ordinary least-squares regression to test dose–response associations between persistence of cannabis dependence (continuously measured) and measures of biological ageing and ageing preparedness, with associations adjusted as follows: for sex (model 1); sex and childhood socioeconomic status, childhood IQ, low childhood self-control, and family substance dependence history (model 2); and the aforementioned covariates plus persistence of alcohol, tobacco, and other illicit drug dependence (model 3). We conducted parallel dose–response regression analyses for persistence of tobacco and alcohol dependence. We reported E values to assess the robustness of dose–response associations to unmeasured confounding.[29] We reported Spearman correlations between persistence of cannabis dependence and persistence of other substance dependence. All analyses were done using SAS version 9.4. This study was powered (80%) to detect dose–response associations of r=0·10 and to detect effect sizes of d=0·38–0·49 between groups. Analyses were preregistered[30] and checked for reproducibility by an independent data analyst (RH).

Role of the funding source

Funders had no role in study design, in the collection, analysis, and interpretation of data, in the writing of the report, or in the decision to submit the paper for publication.

Results

Of 997 cohort members still alive at age 45 years, 938 (94%) were assessed at age 45. Participants aged 45 years did not differ significantly from other participants, including deceased participants and those still alive who did not take part in the study at that age, on childhood socioeconomic status, childhood IQ, or childhood self-control (appendix pp 13–15). Characteristics of the cohort at age 45 years, long-term cannabis users, and five comparison groups are presented herein (table 1).

Long-term cannabis users fared worse than lifelong cannabis non-users on composite (ie, principal component) measures of biological ageing, health preparedness, financial preparedness, and social preparedness, and on individual measures comprising the composites (table 2). Standardised mean differences between long-term cannabis users and non-users on composite measures were large: biological ageing (0·70 [95% CI 0·46 to 0·94]; p<0·0001), health preparedness (−0·72 [−0·96 to −0·49]; p<0·0001), financial preparedness (−1·08 [−1·31 to −0·85]; p<0·0001), and social preparedness (−0·59 [−0·84 to −0·34]; p<0·0001).

Long-term cannabis users also differed from non-users on the individual measures comprising the composites (table 2). Specifically, compared with cannabis non-users (comparison group 1), long-term cannabis users had significantly greater age-related decline in their bodies, more signs of brain ageing, slower gait speed, older facial age, less health knowledge, shorter self-predicted life expectancy, less financial knowledge, less monetary savings and investments, lower credit scores, more financial problems, less social support, greater loneliness, and less satisfaction with life. Long-term cannabis users also fared worse than midlife recreational cannabis users on most outcomes and fared worse than cannabis quitters in terms of accelerated biological ageing and financial preparedness. Long-term cannabis users fared worse than long-term alcohol users in all domains except social preparedness and fared similarly to long-term tobacco users in all domains (table 2).

Consistent with group comparisons, tests of dose–response associations showed that people who used cannabis more persistently from age 18 years to 45 years fared worse on composite (ie, principal component) measures of biological ageing and health, financial, and social preparedness in midlife than people who used cannabis less persistently or not at all (table 3, model 1). Associations were also observed for the constituent measures comprising the composites (appendix p 16). Associations could not be explained by childhood risks, including low socioeconomic status, low IQ, low self-control, and family substance dependence history (table 3, model 2). After additionally adjusting for persistent tobacco, alcohol, and other illicit drug dependence, people who used cannabis more persistently showed poorer social preparedness in midlife but not accelerated biological ageing or poorer health or financial preparedness (table 3, model 3).

To ascertain which substance, if any, accounted for reduced cannabis associations, dose–response associations were sequentially adjusted for persistent tobacco, alcohol, and other illicit drug dependence (appendix pp 17–18). The combination of adjusting for persistent tobacco, alcohol, and other illicit drug dependence, collectively, resulted in the greatest reduction in associations between persistence of cannabis dependence and each outcome.

People who used tobacco more persistently from age 18 years to 45 years exhibited accelerated biological ageing and poorer health, financial, and social preparedness in midlife compared with people who used tobacco less persistently or not at all (table 4, model 1). Associations could not be explained by childhood risks (table 4, model 2). Moreover, after additionally adjusting for persistent cannabis, alcohol, and other illicit drug dependence, people who used tobacco more persistently still showed poorer functioning in all domains except social preparedness (table 4, model 3).

People who used alcohol more persistently from age 18 years to 45 years exhibited accelerated biological ageing and poorer health, financial, and social preparedness in midlife than people who used alcohol less persistently or not at all (table 5, model 1). Associations could not be explained by childhood risks (table 5, model 2). However, after additionally adjusting for persistent cannabis, tobacco, and other illicit drug dependence, people who used alcohol more persistently only showed poorer social preparedness and not accelerated biological ageing, poorer health preparedness, or poorer financial preparedness (table 5, model 3).

To ascertain the robustness of associations to unmeasured confounding, we computed E values for dose–response associations that were statistically significant after covariate adjustment for family background and childhood characteristics and for persistent dependence on other substances.[31] E values represent how large a relative-risk ratio would need to be between an unmeasured confounder and exposures and outcomes to fully account for observed associations. The E value for the association between persistence of cannabis dependence and social preparedness was 1·42, which represents the risk ratio needed for unmeasured confounders after adjustment for measured confounders. E values for tobacco and alcohol associations were similar (appendix p 19).

People who were persistently dependent on a substance, whether it was cannabis, tobacco, or alcohol, showed accelerated biological ageing and poorer ageing preparedness in midlife than people who were not dependent or who were less persistently dependent. Associations for each substance were reduced after adjusting for persistent dependence on the other substances, which is unsurprising given considerable polysubstance dependence in the population (appendix p 20). People who were persistently dependent on several substances consistently fared the worst in terms of biological ageing and midlife health, financial, and social preparedness (appendix pp 21–25).

Discussion

We followed a representative birth cohort for 45 years, which allowed us to characterise long-term cannabis users' biological ageing and midlife preparedness for old age. By midlife, long-term cannabis users were biologically older than non-users of the same chronological age and were substantially behind age-matched peers in terms of preparing for the health, financial, and social challenges of later life. Standardised mean differences between long-term cannabis users and non-users on composite measures of biological ageing, and health, financial, and social preparedness revealed large effects, ranging from 0·59 (social preparedness) to 1·08 (financial preparedness) SD units. Importantly, these associations could not be explained by childhood risks, including low socioeconomic status, low IQ, low self-control, and family history of substance dependence.

Long-term cannabis users also use tobacco, alcohol, and other illicit drugs,[32] and, in research, as in the real world, disentangling the effects of substances is a challenge. We addressed this in two complementary ways, by comparing long-term cannabis users with long-term tobacco users and long-term alcohol users and by examining dose–response associations for persistent dependence on each substance after accounting for persistent dependence on the other substances. Results across the two approaches suggested that poorer midlife ageing is not specific to long-term cannabis users. The pattern of dose–response associations for each substance (cannabis, tobacco, and alcohol) after accounting for the other substances, other illicit drug dependence, and childhood risks revealed four noteworthy findings. First, persistence of cannabis dependence remained robustly associated with poorer midlife social preparedness, suggesting that poorer social preparedness among long-term cannabis users might be, at least in part, a consequence of long-term cannabis use. Long-term cannabis users were disappointed with life and short of social support, even after accounting for childhood covariates and persistent dependence on other substances. Second, persistence of tobacco dependence remained robustly associated with accelerated biological ageing, poorer health preparedness, and poorer financial preparedness, but not poorer social preparedness, suggesting that long-term tobacco use harms health and finances, consistent with previous research.[33–36] Third, persistence of alcohol dependence was robustly linked with poorer social preparedness, suggesting damaging effects of long-term alcohol use on personal relationships. Fourth, the pattern of findings suggests that it is persistent polysubstance dependence that is associated with the poorest ageing preparedness, highlighting the powerful nature of polysubstance dependence.

This study has limitations. First, observational studies cannot demonstrate causality. Nonetheless, we rigorously addressed confounding in two ways. We incorporated numerous confounding factors identified in the literature, including growing up in socioeconomically deprived circumstances, low childhood IQ, poor childhood self-control, family substance dependence history, and persistent dependence on other substances, using unusually strong measures derived from multiple waves and data sources, and found that cannabis use remained associated with poorer midlife social preparedness. Furthermore, we also computed E values, which suggested that unmeasured confounders would have to show associations with cannabis use and social preparedness on the scale of 1·42 in terms of relative risk, after accounting for measured confounders (childhood socioeconomic status, IQ, and self-control; family substance dependence history and persistent dependence on tobacco, alcohol, and other illicit drugs), to fully explain cannabis associations. Analyses did not adjust for psychopathology, which could confound or mediate cannabis associations. Cannabis associations with psychopathology will be explored in future work. Overall, our findings contribute new knowledge on the social functioning of long-term cannabis users in midlife and suggest the association is larger and more robust than previously reported (appendix pp 9–12). These results could have arisen because we used valid prospective measures to characterise much longer-term cannabis use and used richer measures of social functioning.

Second, cannabis use was based on self-reports. Although biological testing can verify self-reports of cannabis use,[37] limitations include false negatives for lighter (weekly or less) users (who represent the majority of users), short detection windows, and the inability to characterise the intensity and duration of cannabis exposure. Self-reports obtained prospectively across decades are necessary for characterising the intensity and duration of cannabis use over a lifetime, and Dunedin participants were interviewed repeatedly over a lifetime. Moreover, due to the longevity of the Dunedin study, participants have learned to trust the confidentiality guarantee and revealed significantly more cannabis use than a research-naive same-age sample.[38]

Third, participants were followed to age 45 years. Therefore, we could not characterise the functioning in older adulthood of long-term cannabis users. However, previous research has shown that the indicators of poorer midlife functioning that we selected are associated with poorer health span (appendix pp 1–8). Fourth, findings are based on a single cohort from New Zealand. Information about New Zealand and how it compares to other nations is presented in the appendix (p 26). Fifth, the cohort began using cannabis in the 1980–90s. The concentration of delta-9-tetrahydrocannabinol,[39,40] the main psychoactive constituent of cannabis, is much higher in the cannabis available today, suggesting the possibility that associations may be even stronger than shown here. Data are needed in contemporary cohorts. Finally, measurement error and model misspecification could affect our estimates of cannabis associations. For example, if persistent dependence on other (non-cannabis) substances are mediators of cannabis associations, and not confounders, we might have underestimated cannabis associations.

This study has implications for research, prevention, and intervention. First, long-term cannabis users show accelerated biological ageing and poorer midlife health, financial, and social preparedness for later life. Statistical controls to separate the effects of other substance use suggested that other substance use accounts for much, but not all, of the deficits among long-term cannabis users. In reality, however, long-term cannabis users use other substances.[32] It is, therefore, clinically important to recognise that the actual midlife functioning of long-term cannabis users places them behind age-matched peers in terms of preparedness for the demands of old age. Second, holistic midlife interventions are needed to aid long-term cannabis users in building the health, financial, and social capital that can fortify and sustain them through later life. Third, quitting cannabis may help with this goal. Our analyses of cannabis quitters suggested that quitting cannabis might have benefits, which is broadly consistent with research documenting that tobacco users who quit in midlife show greater longevity.[41] Fourth, findings are not specific to long-term cannabis users. Long-term tobacco users and long-term alcohol users showed poorer midlife preparedness for old age. Fifth, the overall pattern of findings suggested that it is persistent polysubstance dependence that is associated with the poorest ageing preparedness. Efforts are needed to provide long-term substance users with practical strategies in midlife for improving their health, financial, and social preparedness for older age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank study founder Phil Silva. The Dunedin Multidisciplinary Health and Development Research Unit at the University of Otago is within the Ngāi Tahu tribal area who we acknowledge as first peoples, tangata whenua (people of this land). Work was supported by National Institute on Aging grants R01AG069939, R01AG049789, AG073207, and R01AG032282, and the UK Medical Research Council grant MR/P005918.

Funding

The National Institute on Aging and the UK Medical Research Council. The Dunedin Research Unit is supported by the New Zealand Health Research Council and the New Zealand Ministry of Business, Innovation and Employment.

Data sharing

The Dunedin Study data are available on request to TEM by qualified scientists. Requests require a concept paper describing the purpose of data access, ethical approval at the applicant’s institution, and provision for secure data access. We offer secure access on the Duke University, Otago University, and King’s College London campuses. All data analysis scripts and results files are available for review.

References

1. Hall W What has research over the past two decades revealed about the adverse health effects of recreational cannabis use? Addiction 2015; 110: 19–35.
2. Meier MH. Cannabis use and psychosocial functioning: Evidence from prospective longitudinal studies. Curr Opin Psychol 2021; 38: 19–24. [PubMed: 32736227]
3. Andersen SL, Du M, Cosentino S, et al. Slower decline in processing speed is associated with familial longevity. Gerontology 2022; 68: 17–29. [PubMed: 33946077]
4. Hajat A, Kaufman JS, Rose KM, Siddiqi A, Thomas JC. Long-term effects of wealth on mortality and self-rated health status. Am J Epidemiol 2011; 173: 192–200. [PubMed: 21059808]
5. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspect Psychol Sci 2015; 10: 227–37. [PubMed: 25910392]

6. Han BH, Sherman S, Mauro PM, Martins SS, Rotenberg J, Palamar JJ. Demographic trends among older cannabis users in the United States, 2006–13. Addiction 2017; 112: 516–25. [PubMed: 27767235]

7. Nigatu YT, Elton-Marshall T, Adlaf EM, Ialomiteanu AR, Mann RE, Hamilton HA. CAMH monitor e-report: substance use, mental health and well-being among Ontario adults, 1977–2019. Toronto, ON: Centre for Addiction and Mental Health. 2020. http://www.camh.ca/camh-monitor (accessed Aug 8, 2022).

8. Vespa J The graying of America: more older adults than kids by 2035. Washington DC: US Census Bureau, 2018.

9. Ageing Europe: statistics on population developments. 2020. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Ageing_Europe_-_statistics_on_population_developments (accessed April 7, 2022).

10. National Academies of Sciences, Engineering, and Medicine. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. Washington, DC: National Academies Press, 2017.

11. Fontanella CA, Steelesmith DL, Brock G, Bridge JA, Campo JV, Fristad MA. Association of cannabis use with self-harm and mortality risk among youths with mood disorders. JAMA Pediatr 2021; 175: 377–84. [PubMed: 33464286]

12. Degenhardt L, Ferrari A, Hall W. The global epidemiology and disease burden of cannabis use and dependence. Handbook of cannabis and related pathologies. London: Elsevier, 2017: 89–100.

13. Meier MH, Caspi A, Knodt AR, et al. Long-term cannabis use and cognitive reserves and hippocampal volume in midlife. Am J Psychiat 2022; 179: 362–74. [PubMed: 35255711]

14. Stern Y Cognitive reserve. Neuropsychologia 2009; 47: 2015–28. [PubMed: 19467352]

15. Lachman ME, Teshale S, Agrigoroaei S. Midlife as a pivotal period in the life course: balancing growth and decline at the crossroads of youth and old age. Int J Behav Develop 2015; 39: 20–31.

16. Reece AS, Norman A, Hulse GK. Cannabis exposure as an interactive cardiovascular risk factor and accelerant of organismal ageing: a longitudinal study. BMJ Open 2016; 6: e011891.

17. Fernandez-Egea E, Scoriels L, Theegala S, et al. Cannabis use is associated with increased CCL11 plasma levels in young healthy volunteers. Progr Neuropsychopharmacol Biol Psychiatr 2013; 46: 25–28.

18. Castellanos-Ryan N, Morin É, Rioux C, London-Nadeau K, Leblond M. Academic, socioeconomic and interpersonal consequences of cannabis use: a narrative review. Drugs 2021; 1: 1–19.

19. Allen JP, Danoff JS, Costello MA, et al. Lifetime marijuana use and epigenetic age acceleration: a 17-year prospective examination. Drug Alcohol Depen 2022; 233: 109363.

20. Green KM, Doherty EE, Ensminger ME. Long-term consequences of adolescent cannabis use: examining intermediary processes. Am J Drug Alcohol Abuse 2017; 43: 567–75. [PubMed: 27929672]

21. Cerdá M, Moffitt TE, Meier MH, et al. Persistent cannabis dependence and alcohol dependence represent risks for midlife economic and social problems: a longitudinal cohort study. Clin Psychol Sci 2016; 4: 1028–46. [PubMed: 28008372]

22. Demir-Dagdas T, Child ST. Religious affiliation, informal participation, and network support associated with substance use: differences across age groups. Health Edu Behav 2019; 46: 656–65.

23. Cobb S, Bazargan M, Smith J, Del Pino HE, Dorrah K, Assari S. Marijuana use among African American older adults in economically challenged areas of south Los Angeles. Brain Sci 2019; 9: 166.

24. Choi NG, DiNitto DM, Marti CN. Older marijuana users: life stressors and perceived social support. Drug Alcohol Depen 2016; 169: 56–63.

25. Leung J, Chan GC, Hides L, Hall WD. What is the prevalence and risk of cannabis use disorders among people who use cannabis? A systematic review and meta-analysis. Addict Behav 2020; 1: 106479.

26. Poulton R, Moffitt TE, Silva PA. The Dunedin Multidisciplinary Health and Development Study: overview of the first 40 years, with an eye to the future. Soc Psychiatry Psychiatr Epidemio 2015;50: 679–693.

27. Richmond-Rakerd LS, D'Souza S, Andersen SH, et al. Clustering of health, crime and social-welfare inequality in 4 million citizens from two nations. Nat Hum Behav 2020; 4: 255–64. [PubMed: 31959926]

28. Richmond-Rakerd LS, Caspi A, Ambler A, et al. Childhood self-control forecasts the pace of midlife aging and preparedness for old age. Proc Nat Acad Sci 2021; 118: 3.

29. E-value calculator. E-value calculator. https://www.evalue-calculator.com/evalue/ (accessed Sept 20, 2022).

30. Duke University. Dunedin & e-risk research projects. https://sites.duke.edu/moffittcaspiprojects/forms/projects_2021/ (accessed Sept 20, 2022).

31. Haneuse S, VanderWeele TJ, Arterburn D. Using the E-value to assess the potential effect of unmeasured confounding in observational studies. JAMA 2019; 321: 602–03. [PubMed: 30676631]

32. Rosen AS, Sodos LM, Hirst RB, Vaughn D, Lorkiewicz SA. Cream of the crop: clinical representativeness of eligible and ineligible cannabis users in research. Subst Use Misuse 2018; 53: 1937–50. [PubMed: 29509060]

33. Mamoshina P, Kochetov K, Cortese F, et al. Blood biochemistry analysis to detect smoking status and quantify accelerated aging in smokers. Sci Rep UK 2019; 9: 1–10.

34. Beach SR, Dogan MV, Lei MK, et al. Methylomic aging as a window onto the influence of lifestyle: tobacco and alcohol use alter the rate of biological aging. J Am Geriatr Soc 2015; 63: 2519–25. [PubMed: 26566992]

35. Grafova IB. Financial strain and smoking. J Fam Econ Issues 2011; 32: 327–40.

36. Peto R, Boreham J, Lopez AD, Thun M, Heath C. Mortality from tobacco in developed countries: Indirect estimation from national vital statistics. Lancet 1992; 339: 1268–78. [PubMed: 1349675]

37. Loflin MJ, Kiluk BD, Huestis MA, et al. The state of clinical outcome assessments for cannabis use disorder clinical trials: a review and research agenda. Drug Alcohol Depen 2020; 2: 107993.

38. Moffitt TE, Caspi A, Taylor A, et al. How common are common mental disorders? Evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment. Psychol Med 2010; 40: 899–909. [PubMed: 19719899]

39. ElSohly MA, Chandra S, Radwan M, Gon C, Church JC. A comprehensive review of cannabis potency in the USA in the last decade. Biol Psychiatr 2021; 6: 603–06.

40. Chandra S, Radwan MM, Majumdar CG, Church JC, Freeman TP, ElSohly MA. New trends in cannabis potency in USA and Europe during the last decade (2008–2017). Eur Arch Psychiatr Clin Neurosci 2019; 269: 5–15.

41. Taylor DH Jr, Hasselblad V, Henley SJ, Thun MJ, Sloan FA. Benefits of smoking cessation for longevity. Am J Public Health 2002; 92: 990–96. [PubMed: 12036794]

Research in context

Evidence before this study

Most cannabis research has focused on adolescent and young adult populations. Little is known about the functioning of midlife and older adult cannabis users, many of whom have much longer histories of use than young cannabis users. This scarcity in research represents a substantial gap in the literature because the prevalence of cannabis use is increasing rapidly among midlife and older adults. Moreover, over the next decade, the number of older adults in Europe and the USA will increase to an unprecedentedly high proportion of the population, which will increase demands on health-care and social welfare systems. Therefore, it is crucial to investigate whether long-term cannabis use is a modifiable risk factor for poorer ageing.

We searched PubMed for studies of associations between cannabis use and the following outcomes assessed in midlife or older adulthood: biological ageing, health literacy, financial literacy, financial functioning, and social support or interpersonal relationship functioning. Search terms were ("cannabis" OR "marijuana") AND ("older adult" OR "middle age" OR "midlife") AND ("[outcome]"), with outcome terms of "biological aging," "accelerated aging," "aging," "health literacy," "health knowledge," "financial literacy," "financial knowledge," "financial," "finances," "social support," "interpersonal relationship," and "social." We selected all studies published by March 31, 2022. There were five studies, only two of which were longitudinal studies. Four of the five studies reported on financial functioning, and three found that cannabis users had poorer financial functioning in midlife or older adulthood compared with non-users. Three of the five studies reported on social relationship functioning, and two found that cannabis users had poorer social relationship functioning in midlife or older adulthood compared with non-users. There were no studies that reported on the pace of biological ageing, health literacy, or financial literacy of cannabis users. The five studies, collectively, had limitations, including reliance on reports of past-year cannabis use, thereby failing to characterise long-term cannabis exposure, and inadequate adjustment for theoretically important covariates, including use of other substances.

Added value of this study

This study contributes new knowledge about the pace of biological ageing in long-term cannabis users and their health, financial, and social preparedness for late life. Long-term cannabis users showed accelerated biological ageing and poorer midlife health, financial, and social preparedness for late life than non-users. The link between long-term cannabis use and poorer social preparedness could not be explained by childhood circumstances (socioeconomic deprivation, low IQ, or low self-control), family history of substance dependence, or use of other drugs.

Implications of all the available evidence

This study suggests that, by midlife, long-term cannabis users are biologically older than non-users of the same chronological age and are substantially behind in terms of preparing for the health, financial, and social challenges of later life. Statistical controls to separate the effects of other substances suggested that the use of other licit and illicit substances accounts for some, but not all, of the deficits observed among long-term cannabis users. In reality, however, most long-term cannabis users do use other substances. It is, therefore, clinically important to recognise the need for interventions that aid long-term cannabis users in building reserves of health, financial, and social capital that can fortify and sustain them through later life.

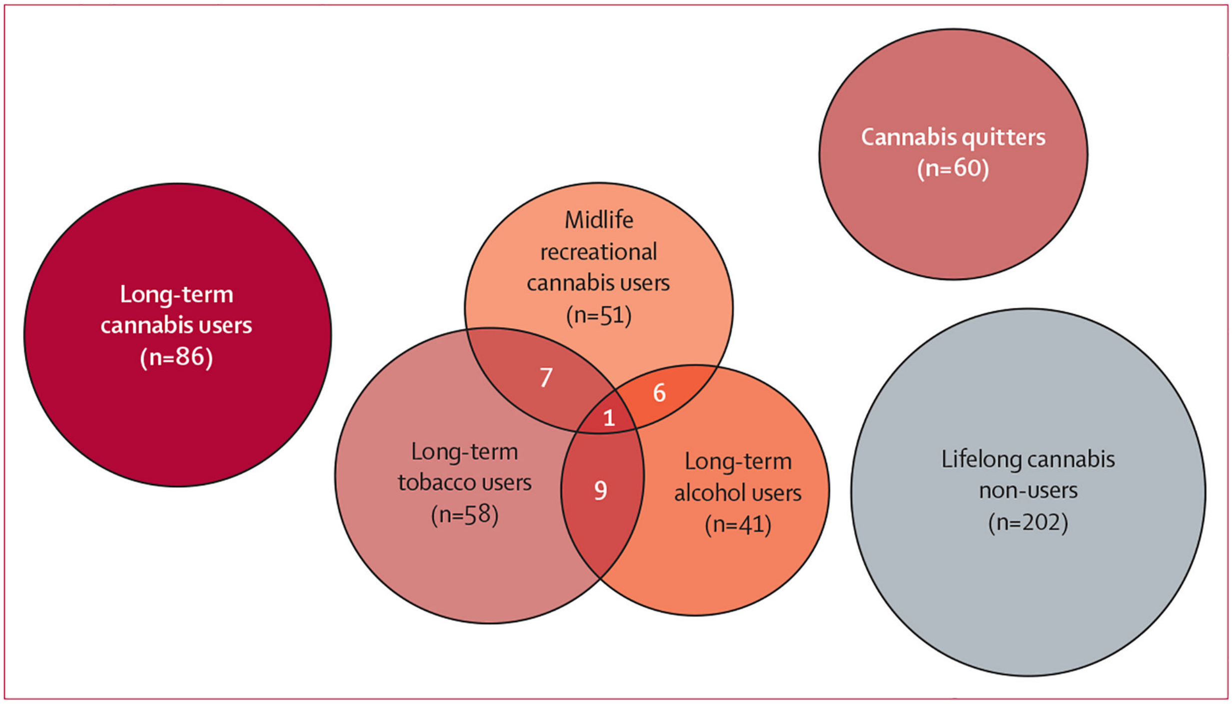

Figure 1: Long-term cannabis users and 5 comparison groups

Long-term cannabis users, n=86. Lifelong cannabis non-users, n=202. Long-term tobacco users, n=75. Long-term alcohol users, n=57. Midlife recreational cannabis users, n=65. Cannabis quitters, n=60. Long-term cannabis users used other substances, including tobacco and alcohol; long-term tobacco and alcohol users were selected to have limited histories of cannabis use.

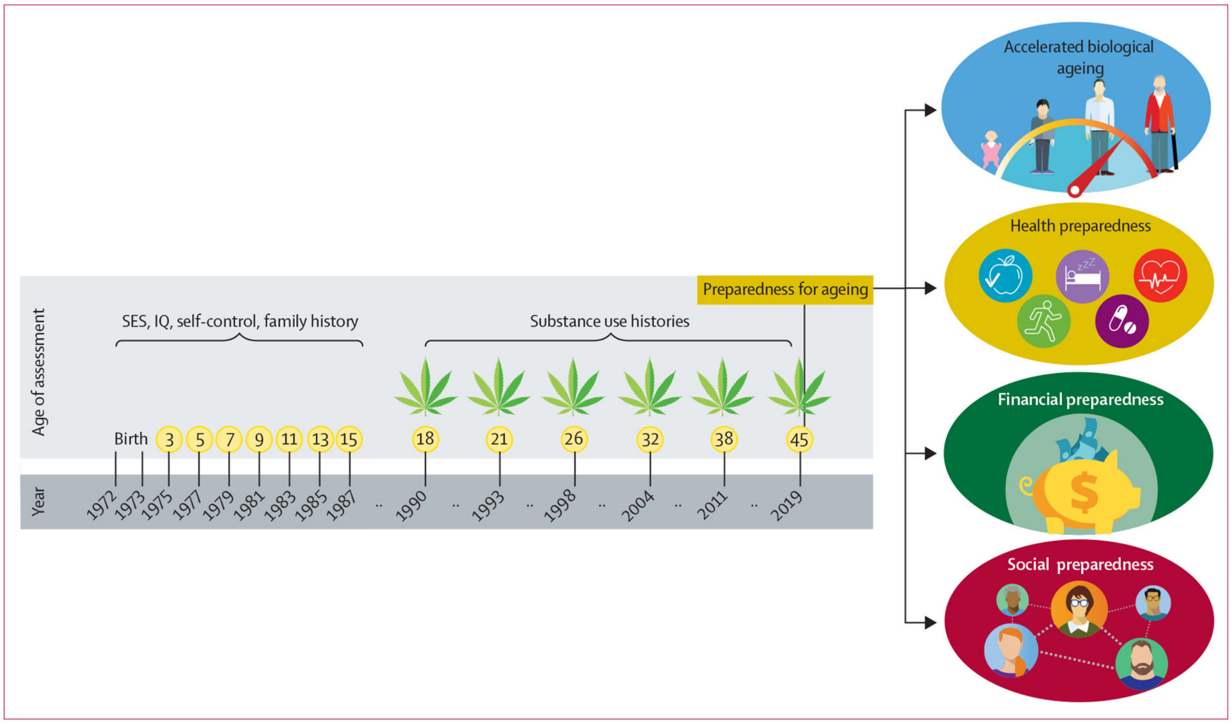

Figure 2: Calendar years and Dunedin Study Cohort members' ages of assessment for substance use exposures, ageing preparedness outcomes, and childhood and family background covariates

SES=socioeconomic status.

Table 1:

Family background, childhood characteristics, and substance use at age 45 years for the full cohort, long-term cannabis users, and five comparison groups

	Full cohort (n=938)	Long-term cannabis users (n=86)	Cannabis non-users (n=202)	Long-term tobacco users (n=75)	Long-term alcohol users (n=57)	Midlife recreational cannabis users (n=65)	Cannabis quitters (n=60)
Sex							
Male	474 (51%)	55 (64%)	82 (41%)	30 (40%)	32 (56%)	38 (58%)	37 (62%)
Female Sex	464 (49%)	31 (36%)	120 (59%)	45 (60%)	25 (44%)	27 (42%)	23 (38%)
Childhood socioeconomic status	3·78 (1·13)	3·42 (1·08)	3·92 (1·17)	3·23 (0·97)	3·80 (1·19)	3·86 (1·24)	3·57 (1·20)
Childhood IQ	101·02 (14·42)	99·33 (13·33)	101·40 (14·35)	93·02 (13·80)	99·27 (12·07)	105·13 (12·65)	97·63 (15·01)
Childhood low self-control	−0·02 (0·96)	0·34 (1·08)	−0·19 (0·88)	0·43 (1·19)	−0·01 (0·92)	−0·06 (1·00)	0·16 (1·06)
Family history of substance dependence	0·15 (0·17)	0·21 (0·21)	0·10 (0·13)	0·20 (0·18)	0·14 (0·15)	0·13 (0·14)	0·19 (0·18)
Substance use at 45 years							
Cannabis frequency*	25·70 (82·90)	257·07 (117·84); 300·00 (156–365)	0 (0); 0·00 (0·00–0·00)	0·11‡ (0·48); 0·00 (0·00–0·00)	0·32§ (1·18); 0·00 (0·00–0·00)	4·88 (8·24); 0·00 (0·00–6·00)	0 (0); 0·00 (0·00–0·00)
Regular cannabis use†	56 (6%)	55 (64%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Daily tobacco use	199 (22%)	54 (63%)	0 (0%)	75 (100%)	10 (18%)	13 (20%)	20 (33%)
Weekly alcohol use	856 (93%)	76 (88%)	184 (91%)	68 (91%)	57 (100%)	62 (95%)	50 (83%)
Cannabis dependence	19 (2%)	19 (22%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tobacco dependence	107 (12%)	38 (45%)	0 (0%)	37 (50%)	6 (11%)	5 (8%)	10 (17%)
Alcohol dependence	104 (11%)	17 (20%)	0 (0%)	7 (9%)	30 (53%)	11 (17%)	10 (17%)
Illicit drug dependence	31 (3%)	13 (15%)	0 (0%)	3 (4%)	1 (2%)	2 (3%)	3 (5%)

Data are n (%), mean (SD), or median (IQR).

*Number of days of cannabis use in past year. Cannabis frequency at age 45 years is skewed, with a range from 0 days to 365 days used. The median for recreational cannabis users was 0 because some midlife recreational users used cannabis in the past year at ages 32 or 38 but not at age 45 years.

†Regular use was defined as using on 4 days or more per week.

‡Only four long-term tobacco users reported cannabis use in the past year, with a maximum use of 3 days.

§Only six long-term alcohol users reported cannabis use in the past year, with a maximum use of 7 days. Some members of the cohort did not meet the criteria for the long-term cannabis user group or any of the comparison groups.

Table 2:

A comparison of long-term cannabis users and five informative subgroups on midlife measures of preparedness for older age

	Long-term cannabis users (n=86)	Comparison group 1: cannabis non-users (n=202)	Comparison group 2: long-term tobacco users (n=75)	Comparison group 3: long-term alcohol users (n=57)	Comparison group 4: midlife recreational cannabis users (n=65)	Comparison group 5: cannabis quitters (n=60)	Difference between long-term cannabis users and comparison groups (p values)				
							Long term *vs* 1	Long term *vs* 2	Long term *vs* 3	Long term *vs* 4	Long term *vs* 5
Biological ageing											
Principal component	0·54 (0·33 to 0·75)	−0·16 (−0·29 to −0·03)	0·67 (0·40 to 0·93)	0·01 (−0·17 to 0·20)	−0·22 (−0·45 to 0·00)	0·19 (−0·07 to 0·46)	<0·0001	0·73	0·0004	<0·0001	0·043
Pace of ageing	0·34 (0·13 to 0·56)	−0·14 (−0·26 to −0·02)	0·37 (0·10 to 0·63)	−0·01 (−0·21 to 0·20)	−0·20 (−0·39 to −0·01)	0·26 (0·00 to 0·52)	<0·0001	0·98	0·025	0·0003	0·65
BrainAGE	0·27 (0·05 to 0·49)	−0·19 (−0·32 to −0·06)	0·48 (0·22 to 0·73)	0·10 (−0·15 to 0·36)	−0·11 (−0·38 to 0·16)	−0·01 (−0·28 to 0·27)	0·0002	0·42	0·32	0·018	0·10
White matter hyperintensities	0·10 (−0·14 to 0·34)	0·06 (−0·08 to 0·19)	0·20 (−0·04 to 0·45)	−0·08 (−0·38 to 0·22)	−0·13 (−0·38 to 0·11)	0·02 (−0·26 to 0·29)	0·80	0·53	0·38	0·17	0·67
Gait speed	−0·18 (−0·37 to 0·00)	0·01 (−0·13 to 0·16)	−0·39 (−0·64 to −0·13)	−0·11 (−0·33 to 0·10)	0·16 (−0·09 to 0·40)	−0·02 (−0·30 to 0·26)	0·041	0·30	0·59	0·019	0·31
Facial age	0·57 (0·35 to 0·79)	−0·15 (−0·28 to −0·02)	0·59 (0·35 to 0·84)	−0·11 (−0·33 to 0·12)	−0·10 (−0·33 to 0·13)	0·24 (−0·04 to 0·53)	<0·0001	0·85	<0·0001	<0·0001	0·069
Health preparedness											
Principal component	−0·55 (−0·78 to −0·32)	0·17 (0·05 to 0·29)	−0·50 (−0·76 to −0·23)	−0·18 (−0·44 to 0·08)	0·04 (−0·18 to 0·26)	−0·31 (−0·58 to −0·04)	<0·0001	0·87	0·045	0·0004	0·17
Health knowledge	−0·39 (−0·59 to −0·18)	0·08 (−0·06 to 0·21)	−0·39 (−0·62 to −0·17)	−0·05 (−0·30 to 0·19)	0·12 (−0·11 to 0·35)	−0·25 (−0·51 to 0·01)	0·0006	0·79	0·050	0·0012	0·41
Ageing pessimism	0·28 (0·04 to 0·53)	0·02 (−0·12 to 0·16)	0·27 (0·01 to 0·52)	0·08 (−0·19 to 0·35)	−0·03 (−0·27 to 0·20)	0·11 (−0·17 to 0·39)	0·088	0·91	0·26	0·067	0·34
Self-predicted life expectancy	−0·39 (−0·65 to −0·14)	0·23 (0·10 to 0·35)	−0·33 (−0·59 to −0·08)	−0·21 (−0·48 to 0·07)	−0·02 (−0·25 to 0·20)	−0·21 (−0·50 to 0·07)	<0·0001	0·97	0·40	0·048	0·37
Financial preparedness											
Principal component	−0·77 (−1·02 to −0·52)	0·31 (0·21 to 0·42)	−0·68 (−0·95 to −0·41)	0·10 (−0·11 to 0·32)	−0·04 (−0·24 to 0·17)	−0·35 (−0·65 to −0·04)	<0·0001	0·54	<0·0001	<0·0001	0·034

	Long-term cannabis users (n=86)	Comparison group 1: cannabis non-users (n=202)	Comparison group 2: long-term tobacco users (n=75)	Comparison group 3: long-term alcohol users (n=57)	Comparison group 4: midlife recreational cannabis users (n=65)	Comparison group 5: cannabis quitters (n=60)	Difference between long-term cannabis users and comparison groups (p values)				
							Long term *vs* 1	Long term *vs* 2	Long term *vs* 3	Long term *vs* 4	Long term *vs* 5
Financial knowledge	−0·44 (−0·65 to −0·23)	0·12 (−0·01 to 0·26)	−0·59 (−0·82 to −0·36)	−0·04 (−0·29 to 0·20)	0·13 (−0·09 to 0·35)	−0·24 (−0·53 to 0·06)	<0·0001	0·74	0·011	0·0002	0·24
Financial planfulness	−0·63 (−0·87 to −0·39)	0·28 (0·16 to 0·39)	−0·33 (−0·57 to −0·08)	0·12 (−0·09 to 0·34)	−0·10 (−0·33 to 0·13)	−0·16 (−0·45 to 0·12)	<0·0001	0·050	<0·0001	0·0018	0·014
Credit scores	−0·59 (−0·87 to −0·30)	0·26 (0·17 to 0·36)	−0·67 (−1·05 to −0·30)	0·17 (−0·08 to 0·43)	−0·07 (−0·28 to 0·15)	−0·39 (−0·75 to −0·04)	<0·0001	0·63	0·0004	0·0067	0·36
Informant-reported financial problems	0·50 (0·19 to 0·81)	−0·21 (−0·32 to −0·09)	0·39 (0·10 to 0·68)	−0·04 (−0·29 to 0·21)	0·05 (−0·20 to 0·30)	0·20 (−0·11 to 0·51)	<0·0001	0·76	0·0096	0·025	0·20
Social preparedness											
Principal component	−0·42 (−0·66 to −0·18)	0·17 (0·04 to 0·30)	−0·32 (−0·59 to −0·04)	−0·28 (−0·56 to −0·01)	−0·08 (−0·36 to 0·20)	−0·47 (−0·77 to −0·17)	<0·0001	0·69	0·48	0·059	0·79
Social support	−0·25 (−0·49 to 0·00)	0·16 (0·05 to 0·28)	−0·16 (−0·43 to 0·10)	−0·19 (−0·47 to 0·08)	0·02 (−0·22 to 0·27)	−0·60 (−0·94 to −0·27)	0·0035	0·98	0·88	0·14	0·069
Loneliness	0·27 (0·03 to 0·50)	−0·06 (−0·20 to 0·08)	0·25 (−0·02 to 0·51)	0·34 (0·03 to 0·64)	0·12 (−0·20 to 0·45)	0·21 (−0·09 to 0·51)	0·0087	0·76	0·79	0·40	0·73
Life satisfaction	−0·47 (−0·69 to −0·24)	0·18 (0·06 to 0·31)	−0·33 (−0·58 to −0·08)	−0·16 (−0·41 to 0·09)	−0·08 (−0·34 to 0·17)	−0·35 (−0·64 to −0·06)	<0·0001	0·63	0·094	0·026	0·56

Data are mean (95% CI) unless otherwise specified. Means represent unadjusted values that were standardised on the full sample (mean =0, SD=1). Statistical tests of group comparisons are adjusted for sex but means are unadjusted.

Table 3:

Dose–response associations between persistence of cannabis dependence from age 18 years to 45 years and midlife measures of preparedness for older age

	Means as a function of persistence of cannabis dependence*						Statistical tests								
	Never used (n=254)	Used but never diagnosed (n=491)	One diagnosis (n=81)	Two diagnoses (n=39)	Three diagnoses (n=31)	Four or more diagnoses (n=15)	Model 1: adjusted for sex			Model 2: + adjustment for childhood SES, childhood IQ, low childhood self-control, and family history of substance dependence†			Model 3: + adjustment for other substance dependence‡		
							β	95% CI	p value	β	95% CI	p value	β	95% CI	p value
Biological ageing	−0·04	−0·11	0·09	0·57	0·72	0·74	0·21	0·14 to 0·28	<0·0001	0·16	0·10 to 0·22	<0·0001	0·03	−0·04 to 0·11	0·37
Health preparedness	0·09	0·13	−0·34	−0·46	−0·91	−0·84	−0·22	−0·29 to −0·16	<0·0001	−0·19	−0·25 to −0·12	<0·0001	−0·08	−0·15 to 0·00	0·051
Financial preparedness	0·20	0·09	−0·37	−0·80	−0·54	−0·96	−0·28	−0·34 to −0·21	<0·0001	−0·23	−0·29 to −0·17	<0·0001	−0·07	−0·14 to 0·00	0·052
Social preparedness	0·13	0·10	−0·37	−0·34	−0·99	−0·49	−0·22	−0·29 to −0·16	<0·0001	−0·19	−0·26 to −0·12	<0·0001	−0·10	−0·18 to −0·02	0·017

SES=socioeconomic status.

*Means represent unadjusted values that were standardised (mean=0, SD=1) on the full sample before analyses.

†Statistical tests were adjusted for sex, childhood SES, childhood IQ, low childhood self-control, and family history of substance dependence.

‡Statistical tests were adjusted for sex, childhood SES, childhood IQ, low childhood self-control, family history of substance dependence, and persistent dependence on other substances.

β coefficients represent standardised estimates.

Table 4:

Dose–response associations between persistence of tobacco dependence from age 18 years to 45 years and midlife measures of preparedness for older age

	Means as a function of persistence of tobacco dependence*						Statistical tests								
	Never used (n=441)	Used but never diagnosed (n=127)	One diagnosis (n=105)	Two diagnoses (n=90)	Three diagnoses (n=61)	Four or more diagnoses (n=87)	Model 1: adjusted for sex			Model 2: + adjustment for childhood SES, childhood IQ, low childhood self-control, and family history of substance dependence†			Model 3: + adjustment for other substance dependence‡		
							β	95% CI	p value	β	95% CI	p value	β	95% CI	p value
Biological ageing	−0·26	−0·21	0·17	0·24	0·59	0·77	0·36	0·30 to 0·42	<0·0001	0·26	0·20 to 0·32	<0·0001	0·24	0·17 to 0·31	<0·0001
Health preparedness	0·20	0·11	0·07	−0·26	−0·52	−0·62	−0·29	−0·35 to −0·22	<0·0001	−0·21	−0·27 to −0·15	<0·0001	−0·15	−0·22 to −0·08	<0·0001
Financial preparedness	0·35	0·07	−0·04	−0·41	−0·79	−0·84	−0·43	−0·49 to −0·37	<0·0001	−0·35	−0·41 to −0·29	<0·0001	−0·31	−0·38 to −0·24	<0·0001
Social preparedness	0·12	0·11	0·14	−0·09	−0·51	−0·48	−0·20	−0·27 to −0·14	<0·0001	−0·16	−0·22 to −0·09	<0·0001	−0·06	−0·14 to 0·02	0·12

SES=socioeconomic status.

* Means represent unadjusted values that were standardised (mean=0, SD=1) on the full sample before analyses.

† Statistical tests were adjusted for sex, childhood SES, childhood IQ, low childhood self-control, and family history of substance dependence.

‡ Statistical tests were adjusted for sex, childhood SES, childhood IQ, low childhood self-control, family history of substance dependence, and persistent dependence on other substances.

β coefficients represent standardised estimates.

Table 5:

Dose–response associations between persistence of alcohol dependence from age 18 years to 45 years and midlife measures of preparedness for older age

	Means as a function of persistence of alcohol dependence*						Statistical tests								
	Never used (n=51)	Used but never diagnosed (n=518)	One diagnosis (n=178)	Two diagnoses (n=83)	Three diagnoses (n=48)	Four or more diagnoses (n=31)	Model 1: adjusted for sex			Model 2: + adjustment for childhood SES, childhood IQ, low childhood self-control, and family history of substance dependence†			Model 3: + adjustment for other substance dependence‡		
							β	95% CI	p value	β	95% CI	p value	β	95% CI	p value
Biological ageing	0·28	−0·10	−0·03	0·11	0·35	0·57	0·14	0·07 to 0·20	<0·0001	0·09	0·02 to 0·15	0·0062	−0·01	−0·08 to 0·05	0·70
Health preparedness	−0·23	0·17	−0·10	−0·11	−0·50	−0·83	−0·18	−0·25 to −0·11	<0·0001	−0·15	−0·21 to −0·08	<0·0001	−0·06	−0·13 to 0·01	0·074
Financial preparedness	−0·14	0·14	−0·10	−0·20	−0·43	−0·39	−0·16	−0·22 to −0·09	<0·0001	−0·11	−0·17 to −0·05	0·0006	0·03	−0·03 to 0·10	0·30
Social preparedness	−0·10	0·16	−0·09	−0·26	−0·44	−0·66	−0·19	−0·26 to −0·13	<0·0001	−0·17	−0·23 to −0·10	<0·0001	−0·10	−0·17 to −0·02	0·010

SES=socioeconomic status.

* Means represent unadjusted values that were standardised (mean=0, SD=1) on the full sample before analyses.

† Statistical tests were adjusted for sex, childhood SES, childhood IQ, low childhood self-control, and family history of substance dependence.

‡ Statistical tests were adjusted for sex, childhood SES, childhood IQ, low childhood self-control, family history of substance dependence, and persistent dependence on other substances.

β coefficients represent standardised estimates.