

What are the effects of methamphetamine use on family and related outcomes at age 40?

Christchurch Health and Development Study (University of Otago Christchurch) – Methamphetamine in New Zealand Research Programme

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What are the effects of methamphetamine use on family and related outcomes at age 40?

The purpose of this report is to examine the effects of casual and regular methamphetamine use on a series of family, financial and psychosocial outcomes at age 40, using data from the Christchurch Health and Development Study database. The reported analyses (below) show the estimates of association between a series of outcomes associated with family structure and function, financial stability, social support and life satisfaction, and methamphetamine use, both before and after adjustment for confounding and contemporaneous covariate factors.

Summary

This report describes a series of analyses using data from the Christchurch Health and Development Study, a cohort of approximately 1000 people born in Christchurch in mid-1977 and followed to age 40 in 2017. The analyses examine the relationship between casual and regular methamphetamine use, and a series of family, economic and social outcomes at age 40 years. A key feature of the analyses is the use of both confounding (prior to the onset of methamphetamine use) and contemporaneous (at the same time as methamphetamine use) covariate factors in the model to test the possible causal role of methamphetamine use in outcomes at midlife.

The distribution of life outcomes at age 40, according to casual and regular (at least weekly) methamphetamine use, shows that methamphetamine users reported generally lower rates of parenthood and partnership, lower home ownership, poorer socioeconomic status and living standards, and lower life satisfaction than those who did not use methamphetamine. The analyses showed that controlling for confounding factors prior to the onset of methamphetamine use explained most of the associations between methamphetamine use and these outcomes. Furthermore, for those outcomes that remained associated with methamphetamine use, control for contemporaneous factors explained these associations in all but one case (having dependent children in the home).

The results of these analyses suggest that there is little evidence that casual or regular methamphetamine use play a causal role in a series of life outcomes at age 40. Therefore, methamphetamine use should be viewed as a risk marker for adverse outcomes in these domains at midlife (instead of their originator). These findings, however, may be due to a relatively low level of statistical power (due to study design, and in particular the timing of outcome measurements), which may have created difficulties in ascertaining the potential causal role of methamphetamine in family, economic and psychosocial functioning at midlife.

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1. Main aim and causality test

In the present investigation, we aimed to examine the potential causal role played by methamphetamine use over the life course in reducing overall quality of life and psychosocial functioning in middle age. In order to ascertain causality in a study using observational data, it is necessary to follow the criteria set out by Bradford Hill in 1965 [1]. Specifically, there are three criteria that allow us to determine whether causality should be inferred using the data available. The first of these is dose/response which tests whether methamphetamine use, or higher levels of methamphetamine use (regular use), is associated with a higher likelihood of relationship and family instability, lower levels of income, home ownership and personal investment, poorer living standards, and lower levels of social support and life satisfaction. The second of these criteria is robustness to control for confounding factors. These factors are variables measured prior to methamphetamine use which are linked to an increase in the likelihood of using methamphetamine (e.g. novelty-seeking at age 16). Robustness in this case means that the association between methamphetamine use and life outcomes at age 40 remains statistically significant after controlling for these factors. The third of the criteria employed in these analyses is specificity, in which, after controlling for factors occurring contemporaneously with both methamphetamine use and life outcomes (e.g. alcohol use disorder between 16 and 40 years of age), the association between methamphetamine use and life outcomes remains statistically significant.

The analyses described in this report are, as was the previous report (Report 3, which focused on criminal offending), concerned with examining the extent to which methamphetamine use over the life course plays a causal role in increasing the risk of adverse life circumstances at age 40. In both the present report and Report 3, the analyses examined this through the statistical control of factors measured in both childhood and adulthood that were associated with increased likelihood of methamphetamine use (as demonstrated in Report 2).

2. Measures

2.1. Methamphetamine use (ages 16-40 years)

At each assessment from age 18 to age 40, cohort members were queried about their use of a range of illicit drugs. One aspect of this questioning concerned methamphetamine. The question stem was worded "Since you turned (age) have you used the following, and how often?". The second part of the question listed a series of substances, with methamphetamine use described as "Methamphetamine, speed, P, ice, etc."¹ Participants were asked about their substance use from the prior to the current study wave.

In the main analyses presented in this report, a methamphetamine use variable with three levels was considered. This variable was sectioned to include a group of participants who reported not using methamphetamine in any of the study waves (reference group), a group of participants who reported casual use of methamphetamine (less than weekly) in at least one of the study waves, and a group of participants who reported using methamphetamine regularly (at least weekly) in at least one of the study waves. Likewise, preliminary analyses including

¹ The reference to "P" and "ice" first appeared in the age 30 (2007) assessment due to their common use as slang terms from that time.

methamphetamine use contrasted values for the *casual methamphetamine use group* and the *regular methamphetamine use group* with values for the *no methamphetamine use group*.

2.2. Life outcome measures (age 40 years)

We used a series of variables representing several different economic, social and family outcomes at age 40, modelling the association between each of these and the individual's history of methamphetamine use from ages 16 to 40. The measures of life outcomes were as follows.

<u>Dependent children</u>. Cohort members were classified as to whether they have had at least one dependent child prior to the age 40 interview.

<u>Marriage/partnership</u>. Marriage/partnership outcomes at age 40 consisted of a classification of whether the cohort member reports being in a marriage or committed partnership.

<u>Home ownership.</u> Those cohort members who reported owning their own home (as opposed to renting their home) will be classified as home owners at age 40.

<u>Net family income.</u> The cohort member's net family income at age 40 was calculated, with amounts in foreign currency being converted to New Zealand dollars using estimates of the Purchasing Power Parities [2] for 2017.

<u>Net investments.</u> Each cohort member's net family investments at age 40 was also calculated, using the same conversion procedure as the income measure.

<u>Socioeconomic status (SES).</u> SES at age 40 was measured using the New Zealand Socioeconomic Index of Occupational Status [3].

<u>Family living standards.</u> Family living standards at age 40 was measured using the Material Wellbeing Index [4], based on the New Zealand Economic Living Standard Index [5], to provide a measure of relative material wellbeing or hardship

<u>Social support.</u> The measure of social support was adapted from the measure used by the Dunedin Multidisciplinary Health and Development Study at the age 32 data collection [6]. This measure assessed the number of people a cohort member reported as being available to help and support them across a variety of situations.

<u>Life satisfaction.</u> Life satisfaction at age 40 was measured using a custom-written questionnaire that asked participants to rate their current satisfaction with eleven areas of their life: work, leisure time, partner relationships, relationships with people of the same sex, relationships with people of the opposite sex, social life, money, independence, daily interactions with others, the future, and life as a whole [7]. Ratings from the 11 items were summed to provide a life satisfaction score.

2.3. Potential confounding factors: Childhood/ adolescent (0-16 years) predictors of methamphetamine use and life outcomes (age 40 years)

We examined the database of the study to determine the variables that would be the most important and useful in examining childhood/ adolescent factors that may confound the association between methamphetamine use and life outcomes at age 40. This was based in previous literature and research within the Christchurch Health and Development Study [8-11]. Variables in five domains were considered as follows.

2.3.1. Measures of family socio-economic and demographic background

Maternal age (at birth). Assessed at the time of the survey child's birth.

<u>Family living standards (0-10 years).</u> At each year, a global assessment of the material living standards of the family was obtained by means of an interviewer rating. These were averaged over the period 0-10 years.

<u>Maternal and paternal education (at birth).</u> Parental education level was assessed at the time of the survey child's birth reflecting the highest level of educational achievement attained, using a three-level scale. These levels were: no secondary school qualifications; at least one secondary school qualification; tertiary qualification.

<u>Family socio-economic status (SES, at birth).</u> Family SES was assessed at the time of the survey child's birth using the Elley-Irving [12] scale of socio-economic status for New Zealand.

<u>Single parenthood (at birth).</u> Family structure was assessed at the time of the survey child's birth.

<u>Averaged family income (0–10 years).</u> At each year, estimates of the family's gross annual income were obtained from parental report and were recoded into decile ² categories.

2.3.2. Measures of family functioning

<u>Parental illicit drug use (11 years)</u>. At age 11, parents were questioned regarding their history of illicit drug use. The cohort member was classified as having a parent history of illicit drug use if one of his/her parents was reported to have a history of illicit drug use.

<u>Parental alcohol problems (15 years).</u> This was assessed at age 15 years via parental report. These reports were used to form a dichotomous measure of whether or not the young person's parents reported experiencing problems with alcohol.

<u>Parental criminality (15 years).</u> At age 15 years, parents were questioned as to whether any parent had a history of criminal offending. The cohort member was classified as having a parent history of criminality if one of his/her parents was reported to have a history of offending.

<u>Changes of parents (0–15 years).</u> At each assessment from birth to 15 years, information was gathered on changes in the cohort member's family situation since the previous assessment. Using this information, an overall measure of family instability was constructed up to age 15, representing the number of changes in parental figures (due to separation, divorce, death, or re-partnering) in the home during the life of the cohort member to age 15.

Parental Bonding (Maternal and Paternal Care and Protection; 16 years). To measure parental bonding, the maternal care and protection scales of the Parental Bonding Instrument (PBI) [13] were administered to the cohort members at the age of 16 years. The young person was asked to rate their mother on the PBI items describing the quality of maternal care and protection throughout their childhood. The care scale measures the extent to which the parents provide support, affection and nurturing with a high score indicating high levels of care. The protection scale measures the extent to which parents exhibit tendencies to over protection or over control with a high score indicating tendencies to over control. The reliabilities of the resulting scale

² Decile categories are obtained by ranking income estimates from highest to lowest, and dividing these into groups representing 10% of the overall distribution. Because income is a highly skewed measure, the decile score serves as the income measure.

scores were assessed using coefficient alpha and found to be good: maternal care α = .89; paternal care α = .91; maternal over protection α = .85; paternal over protection α = .87.

2.3.3. Individual, personality and behavioural factors

Gender (at birth). Recorded at birth.

<u>Child conduct and attention problems, and anxious/withdrawn behaviour (7–9 years).</u> When sample members were aged 7–9 years, information on child behaviour problems was obtained from parental and teacher report using a behaviour questionnaire combining items from the Rutter et al. [14] and Conners [15] parental questionnaires. (α = .97; .93; and .92, respectively).

<u>Neuroticism (14 years)</u>. This was assessed using a short form version of the Neuroticism scale of the Eysenck Personality Inventory [16] at age 14 (α = .80).

<u>Novelty-seeking (16 years)</u>. Novelty-seeking was assessed at age 16 using the novelty-seeking items from the Tridimensional Personality Questionnaire [17] (α = .76).

<u>Childhood IQ (8-9 years).</u> At ages 8 and 9 years, cohort members were assessed using the revised version of the Wechsler Intelligence Scale for Children (WISC-R [18]) modified for New Zealand conditions. At each age, total IQ scores were computed using the method described in the test manual. The reliabilities of these measures assessed by using split half methods ranged from .93 to .95. The IQ measure used in the present analyses was based on an average of the total IQ score at the two ages.

<u>GPA (11-13 years).</u> School performance was assessed via teachers' ratings in each of five areas of the curriculum (reading, handwriting, written expression, spelling, mathematics) using a 5-point scale ranging from very good to very poor. To provide a global measure of the child's educational achievement over the interval from 11-13 years, the teacher ratings were summed across years and curriculum areas and then averaged to provide a teacher rating grade point average for each child.

2.3.4. Abuse exposure

<u>Childhood sexual abuse (0-16 years).</u> At ages 18 and 21 years, sample members were questioned about their experience of sexual abuse during childhood (<16 years) [9]. Questioning spanned an array of abusive experiences from episodes involving non-contact abuse (e.g. indecent exposure) to episodes involving attempted or completed intercourse. A four-level scale was devised reflecting the most extreme form of sexual abuse reported by the young person at either age. The levels were: no sexual abuse; non-contact sexual abuse; sexual abuse involving physical contact but not penetration; penetrative sexual abuse.

<u>Childhood physical abuse (0-16 years).</u> At ages 18 and 21 years, sample members were questioned about their experience of physical punishment during childhood (<16 years) [19]. Questioning spanned an array of experiences with physical punishment and the frequency with which these occurred during childhood. A four-level scale was devised reflecting the most extreme form of physical punishment reported by the young person at either age. These levels were: no physical punishment; occasional physical punishment; regular physical punishment; harsh and abusive physical punishment.

Exposure to parental intimate partner violence (0-16 years). At the age of 18, sample members were questioned concerning their experience of violence between parental figures during their childhood (prior to age 16 years), with questions derived from the Conflict Tactics Scale [CTS:

20]. The items were chosen on the basis that the behaviours could have been readily observed and reported on by the participant, and also to span the potential range of violent behaviour from verbal abuse to physical assault. Separate questioning was conducted for violence initiated by the father against the mother and for violence initiated by the mother against the father, and combined into a single scale score representing overall exposure across both parents.

2.3.5. Adolescent problem behaviour

Information concerning disruptive childhood behaviour was obtained at two assessments taking place when the sample members were aged 15 and 16 years. At each age, sample members were interviewed on a comprehensive mental health interview that examined aspects of mental health and adjustment over the previous 12 months. A parallel interview was also conducted with the child's mother at each assessment stage.

<u>Conduct disorder, oppositional defiant disorder, attention deficit hyperactivity disorder (14-16 years).</u> As part of the assessments at each age, information was obtained on DSM-III-R [21] symptom criteria for disruptive childhood behaviours, including conduct disorder (CD), oppositional defiant disorder (ODD), and attention deficit hyperactivity disorder (ADHD) [22]. For child self-report, the assessment of ODD and ADHD was based on the relevant sections of the Diagnostic Interview Schedule for Children (DISC) [23], whereas CD was assessed using the Self-Report Early Delinquency (SRED) scale [24]. For parental reports, ODD and ADHD were assessed using items from the Revised Behaviour Problems Checklist (RBPC) [25], and CD was assessed using a parent version of the SRED. The combined symptom data thus comprised information on DSM-III-R symptom criteria for two separate 12-month periods (ages 14-15 and 15-16 years) from two sources (parent, self-report).

<u>Alcohol use disorders (15-16 years).</u> At each interview at ages 15 and 16, cohort members were asked a series of questions concerning whether the individual experienced any problems relating to their drinking. This measure was based on the Diagnostic Interview Schedule for Children (DISC) [26], in order to obtain information pertaining to DSM-III-R [21] symptoms of alcohol abuse/alcohol dependence (alcohol use disorder). These data allowed classification of participants as to whether they meet DSM criteria for an alcohol use disorder; during the period following the previous assessment.

Internalizing disorders (14-16 years). Parallel to the assessment of disruptive behaviour disorders, ages 15 and 16 years cohort members and their parents were questioned about symptoms of major depression and anxiety disorders (generalized anxiety disorder; over-anxious disorder; social phobia; simple phobia) occurring in the previous 12 months using the relevant sections of the Diagnostic Interview Schedule for Children [DISC: 23]. These items were used to classify participants according to DSM-III-R [21] symptom criteria for major depression or an anxiety disorder. Participants were classified as having major depression or an anxiety disorder during the period 14-16 years if they met criteria for disorder on the basis of either self or parental report over the period 14-16 years.

<u>Deviant peer affiliation (age 15).</u> At the assessment at age 15, cohort members and their parents were asked to indicate how many of the child's friends were "deviant", defined as smoking cigarettes, drinking alcohol, using illicit drugs, or who committed crimes. The larger of the two answers (child; parent) was used as the measure.

2.4. Potential mediating factors: Contemporaneous variables to methamphetamine use and outcomes in adulthood (ages 16-40 years)

Several potential covariates³, measured contemporaneously with methamphetamine use, will also be employed as factors that potentially mediate the associations between methamphetamine use and outcomes at age 40. Previous CHDS analyses have shown that substance use in adulthood tends to "cluster" particularly in early adulthood, and specifically for illicit drugs in early and later adulthood [27, 28]. In addition, mental health disorders such as depression and anxiety [29, 30], as well as life stress [31] and unemployment [32, 33] have also been shown to be associated with substance use outcomes in analyses of CHDS data. Finally, it is clear that factors such as substance use, life stress and unemployment are associated with psychosocial outcomes in adulthood [32, 33]. The variables considered include:

<u>Alcohol use disorders (16-40 years).</u> At each interview from age 18 years, cohort members were asked a series of questions concerning whether the individual experienced any problems relating to their drinking. This measure was based on the Composite International Diagnostic Interview (CIDI) [34] at ages 18, 21, 25, 30, 35 and 40 years, in order to obtain information pertaining to DSM-IV (age 18 and above) [35] symptoms of alcohol abuse/alcohol dependence (alcohol use disorder). These data allow classification of participants as to whether they meet DSM criteria for an alcohol use disorder at any time during the period 16-40 years.

<u>Major depression (15-40 years)</u>. Cohort members completed the CIDI at ages 18, 21, 25, 30, 35, and 40 years. These data were used to classify individuals as to whether they met DSM-IV criteria for major depression over the intervals 15-18 years, 18-21 years, 21-25 years, 25-30 years, 30-35 years, and 35-40 years. In turn, any participant who met criteria for major depression during at least one assessment period was classified as having major depression during the period 15-40 years.

<u>Other substance use disorders (15-40 years).</u> At ages 18, 21, 25, 30, 35 and 40 years, cohort members were questioned about their substance use behaviours and problems associated with substance use since the previous assessment (tobacco, cannabis), based on the CIDI (items for cigarette smoking were custom written). Using this information cohort members were classified as meeting DSM-IV criteria for nicotine dependence and cannabis dependence over the intervals 15-18 years, 18-21 years, 21-25 years, 25-30 years, 30-35 years, and 35-40 years (for nicotine dependence, the measure refers to current ND at ages 18, 21, 25, 30, 35 and 40 years). These reports were combined over the period 15-40 years to create a single classification of whether participants met criteria for a tobacco or cannabis use disorder at any point during the period 15-40 years.

<u>Unemployment (18-40 years).</u> At each assessment, starting at age 21, cohort members were asked whether they had been unemployed and looking for work for three or more months during any calendar year since the previous assessment (ages 18–21, 21–25, 25–30, 30–35, and 35-40 years). These reports were combined over the period 21-40 years to create an overall classification of unemployment status over the period 18 to 40 years.

<u>Stressful life events other than unemployment (18-40 years).</u> Life events were assessed for each 12-month period during ages 18–40 years using a 30-item inventory based on the Social Readjustment Rating Scale [36] supplemented by custom-written survey items. These items spanned several domains, including, for example, death and illness, relationship problems and

³ In this context, "covariate" refers to contemporaneously-measured covariate factors that may influence the likelihood that an individual uses methamphetamine, and that in turn may influence family, economic and psychosocial outcomes during a particular time period.

difficulties, and crime victimization. All items were scored on a 0 to 4 scale (0 = no event, 1 = not upset or distressed, 2 = a little upset or distressed, 3 = moderately upset or distressed, and 4 = very distressed). Using this information, a measure of exposure to stressful life events was created by summing the scores for each item for each 12-month period, and then summing over each assessment period and across periods, resulting in a total life events distress score for the periods 18-40 years.

3. Preliminary findings

3.1. Association between outcome measures and lifetime methamphetamine use

Based on the criteria set out by Bradford Hill in 1965 to assess causality in an observational study [1], it is important to assess whether methamphetamine use, or higher levels of methamphetamine use, is associated with poorer financial, family and social outcomes in middle adulthood (dose-response criterion).

Table 1 shows the cohort classified according to their highest level of self-reported methamphetamine use (no use, casual use, regular use) and the number of cohort members in each category, aggregated over the period 16 to 40 years. Table 1 shows the percentage (for dichotomous outcomes) or mean score and standard deviation (for scale score measures) for cohort members on each outcome measure at age 40. Table 1 also shows that for all outcomes, those reporting having used methamphetamine casually reported lower rates of family stability, economic stability/success, living standards and poorer psychosocial outcomes than those who did not report using methamphetamine. This pattern was similar for those who reported using methamphetamine regularly, with the percentage/mean scores of those reporting more adverse outcomes being most times substantially larger than of those who reported using the drug casually.

	No methamphetamine use	Casual methamphetamine use	Regular methamphetamine use	
%/Mean (SD)	(n = 742)	(n = 252)	(n = 62)	
Dependent children (%)	76.0	70.5	60.4	
Marriage/partnership (%)	80.3	70.9	67.9	
Home ownership (%)	67.5	56.4	35.9	
Net family income, weekly (Mean, SD)	1,994.35 (1,498.48)	1,937.41 (1,369.30)	1,633.13 (1,798.78)	
Net investments (Mean, SD)	159,125.29 (184,967.80)	166,656.38 (192,730.03)	121,679.06 (166,152.89)	

Table 1: Life outcomes (% reporting/Mean, Standard Deviation) at age 40 classified by highest level of methamphetamine use (ages 16-40)

Socioeconomic status	50.87	49.30	45.02
(Mean, SD)	(17.01)	(15.82)	(16.15)
Family living standards	29.09	29.27	26.11
(Mean, SD)	(6.75)	(5.97)	(9.23)
Social support (Mean, SD)	50.07	50.02	47.23
	(8.38)	(9.48)	(11.74)
Life satisfaction (Mean, SD)	30.58	30.09	28.55
	(5.35)	(5.21)	(5.87)

3.2. Association between childhood/ adolescent predictors of methamphetamine use in adulthood and lifetime methamphetamine use

Based on the criteria set out by Bradford Hill in 1965 to assess causality in an observational study [1], it is important to assess whether the association between methamphetamine use and life outcomes at age 40 remains statistically significant after controlling for factors measured prior to methamphetamine use which are linked to an increase in the likelihood of using methamphetamine (robustness criterion).

Illustrated below are the associations between each of the childhood/adolescent predictors (confounding factors) detailed previously, and lifetime methamphetamine use (ages 16-40). Spearman's *r* was used as the measure of association as lifetime methamphetamine use was a dichotomous variable, and many of the measures reported are also categorical in nature (Spearman's *r* is a non-parametric statistic, which therefore does not require an underlying assumption of a normal distribution of the two variables for which a correlation is being estimated). An important assumption for the evaluation of confounding factors in observational data is that the fixed (time-invariant) confounding factors must be associated with the exposure (in this case, methamphetamine casual use/regular use).

For social research data such as that reported below, a correlation with an absolute value of 0 to 0.09 is considered "weak" in magnitude, 0.10 to 0.19 is considered "moderate", and 0.20 or higher is considered "strong". Significant associations (p-values) are presented in the table below in bold. P-values refer to "probability values", which refer to the likelihood of error in conclusions drawn using the analysed data. Our maximum acceptable likelihood of error is set at 5% as a matter of convention. P-values larger than this are referred to as "non-significant", while p-values smaller than this are referred to as "significant" (and are shown in bold, with significance level noted at the foot of Table 2).

Table 2: Associations between potential confounding factors and lifetimemethamphetamine use

Measure	Casual methamphetamine use	Regular methamphetamine use
Measures of family socio-economic and demographic background		
Maternal age (at birth)	03	07*
Family living standards (0-10 years)	06	05
Maternal education (at birth)	.00	.05
Paternal education (at birth)	06	00
Family socio-economic status (at birth)	00	09**
Single parenthood (at birth)	.02	.03
Averaged family income (0-10 years)	04	02
Measures of family functioning		
Parental illicit drug use (11 years)	.06	.12***
Parental alcohol problems (15 years)	.02	.06
Parental criminality (15 years)	.05	.10***
Changes of parents (15 years)	.07*	.12***
Maternal care (16 years)	04	03
Paternal care (16 years)	09*	08*
Maternal over-protection (16 years)	.07*	.02
Paternal over-protection (16 years)	.10**	.05
Individual, personality and behavioural factors		
Gender (at birth)	14***	06
Child conduct problems (7-9 years)	.09**	.13***
Child attention problems (7-9 years)	.07*	.11**
Anxious/withdrawn behaviour (7-9 years)	09**	.10**
Neuroticism (14 years)	06	07*
Novelty-seeking (16 years)	.22***	.16***
Childhood IQ (8-9 years)	.06	01

GPA (11-13 years)	00	.03
Abuse exposure		
Exposure to childhood sexual abuse (0-16 years)	02	.04
Exposure to childhood physical punishment (0-16 years)	.04	.09**
Exposure to parental IPV (0-16 years)	.03	.04
Adolescent problem behaviour and mental health		
Conduct disorder (14-16 years)	.19***	.16***
Oppositional defiant disorder (14-16 years)	.17***	.12***
Attention deficit hyperactivity disorder (14-16 years)	.11***	.07*
Alcohol use disorder (15-16 years)	.10**	.14***
Major depression (14-16 years)	06	01
Anxiety disorder (14-16 years)	05	.02
Deviant peer affiliation (15 years)	.16***	.15***

* p < .05; ** p < .01; *** p < .001

As can be seen from Table 2, childhood, family functioning and abuse exposure variables were for the most part weakly associated with later methamphetamine use. On the other hand, behaviour problems (externalizing) in childhood and adolescence (and association with deviant peers) were moderately associated with later methamphetamine use. In terms of personality, novelty-seeking was strongly associated with methamphetamine use (and moderately with regular use). The focus of the causal models detailed below will be the statistically significant (p < .05) variables noted above.

It is also worth noting that the profile of potential confounding variables differs with respect to whether a person used methamphetamine casually, or used methamphetamine regularly (at least weekly) at some point. Predictors varied both in their strength of association with the methamphetamine variables, and whether they reached statistical significance. This suggests that models of both "casual use" and "regular use" should employ a common set of potential confounding factors.

3.3. Association between contemporaneous variables, lifetime methamphetamine use and outcomes at age 40

Based on the criteria set out by Bradford Hill in 1965 to assess causality in an observational study [1], it is important to assess whether the association between methamphetamine use and outcomes at age 40 remains statistically significant after controlling for factors occurring contemporaneously with methamphetamine use which are also associated with outcomes measured at midlife (specificity criterion). The associations between contemporaneous predictors, outcomes at age 40, and methamphetamine use are shown in Table 3 below.

Measure	Casual use	Regular use	Alcohol use disorder	Major depression	Nicotine dependence	Cannabis use disorder	Unemployment	Life stress
Casual use			.18***	.07*	.24***	.26***	.18***	.22***
Regular use			.09**	.07*	.13***	.15***	.08*	.10**
Dependent children	04	07*	06	.01	06	07*	14***	.04
Marriage/partnership	09*	06	09*	06	11**	12**	17***	.04
Home ownership	07*	14***	10**	07*	21***	15***	23***	17***
Net family income, weekly	00	12**	11**	11**	22***	17***	29***	11**
Net investments	.02	08*	07*	11**	20***	19***	26***	12**
Socioeconomic status	03	08*	08*	03	28***	15***	15***	06
Family living standards	.01	08*	04	26***	15***	14***	26***	26***
Social support	.02	06	00	09**	14***	10**	19***	04
Life satisfaction	02	08*	11**	13**	11**	13***	22***	15***

 Table 3: Associations between contemporaneous predictors, lifetime methamphetamine use and outcomes at age 40

* p < .05; ** p < .01; *** p < .001

The associations between these factors are displayed because in order to determine if methamphetamine use causes adverse outcomes, it is necessary to first determine whether the contemporaneous variables are associated with both the exposure (methamphetamine use) and outcome measures. As per previous section, Spearman's r and p-values are used to assess the relationship between factors.

As can be seen in the table, the contemporaneous measures are associated with casual and regular methamphetamine use although the magnitude of the association was generally smaller for regular use. For example, life satisfaction was significantly associated with all contemporaneous measures and had moderate to strong effects, suggesting that those individuals who have alcohol use disorder etc reported lower life satisfaction. In addition, each of the contemporaneous measures was significantly associated with one or more of the life outcomes at age 40. Thus, all contemporaneous measures will be considered in the causal models detailed below.

4. Main findings

To model the repeated measures data in order to estimate the associations between casual methamphetamine use/regular methamphetamine use and life outcomes at age 40, logistic regression (for dichotomous outcomes) and ordinary least squares regression (for continuous outcomes) models were fitted.

In the next step of the modelling, the base models were extended, in order to fit logistic and ordinary least squares regression models of the associations between casual methamphetamine use/regular use and life outcomes at age 40, adjusted for the potentially confounding and contemporaneous factors listed in Tables 2 and 3. These models were fitted in steps, as follows.

- In the second model, the potential confounding factors presented in Table 2 (i.e. measures of family socio-economic and demographic background; measures of family functioning; individual, personality and behavioural factors; abuse exposure; and adolescent problem behaviour) were entered in blocks, with forward and backward elimination of variables to identify a stable and parsimonious set of confounding factors.
- The third model extended the second model by including the contemporaneous factors listed in Table 3 (i.e. alcohol use disorder; major depression; nicotine dependence; cannabis use disorder; unemployment; and life stress), with the factors being entered into the models simultaneously, with forward and backward elimination of variables to identify a stable and parsimonious set of covariate factors.

All models were fitted using Stata 16 [37].

4.1. Bivariate models of the association between methamphetamine use and life outcomes at age 40, adjusting for confounding and contemporaneous factors

Table 4 shows the parameter estimates, standard errors of estimate, and probability values for the associations between each life outcome at age 40, and both casual methamphetamine use and regular methamphetamine use. For each outcome, Table 4 presents three models in successive rows: the first row is the unadjusted bivariate association, the second row shows the association adjusted for confounding factors, and the third row shows the association adjusted for both confounding and contemporaneous factors. Model 2 or model 3 is not shown in cases where the previous step of the modelling reduced both methamphetamine variables to statistical non-significance.

For the first model (top row for each outcome), it is clear that for casual methamphetamine use, there were statistically significant associations with marriage/partnership and home ownership at age 40. For regular methamphetamine use, there were statistically significant associations with having a dependent child, marriage/partnership, home ownership, socioeconomic status, family living standards, and life satisfaction at age 40. These results suggest that at the bivariate level, causal methamphetamine use was weakly related to life outcomes at age 40, whereas regular methamphetamine use was associated with significantly poorer outcomes over six of the nine measures, suggesting a pattern of stronger associations.

The second row of each outcome in Table 4 shows the associations between the two levels of methamphetamine use and each outcome, adjusted for the potentially confounding factors shown in Table 2. Table 4 shows that the inclusion of confounding factors in these models reduced the magnitude of these associations (shown by the decreasing unstandardized regression coefficients), in many cases to the point of statistical non-significance. After control for confounding, marriage/partnership and home ownership remained significantly associated with casual use, whereas only three of the six significant associations between regular methamphetamine use and outcomes remained statistically significant (dependent children; home ownership; family living standards).

The third row of each outcome in Table 4 shows the associations between methamphetamine use and each outcome, adjusted for the potentially confounding factors shown in Table 2, and contemporaneous factors shown in Table 3. The final column of Table 4 also reports a test of a direct comparison between the casual use group and the regular use group for the final model. In two cases (homeownership and life satisfaction), the regular use group had significantly different scores from the casual use group. The results of the third models show that after full adjustment, only one outcome (having a dependent child) was associated with regular methamphetamine use, with regular users being significantly less likely to have had a dependent child. In general, this pattern of results, in which the associations between methamphetamine use and life outcomes at age 40 were largely explained by potential confounding and covariate factors, suggests that methamphetamine use at any level played only a minimal causal role (if any) in predicting economic, family and psychosocial outcomes at mid-life in the CHDS cohort.

Table 4: Associations between methamphetamine use (ages 16-40) and life outcomes at age 40, before and after adjustment for confounding and covariate factors.

Outcome	Casual methamphetamine use (reference group = no use)			Regular use (ref	methampl erence gro use)	Test of casual v. regular use	
Dependent children	В	S.E.	р	В	S.E.	р	X ² (df)
Model 1 (unadjusted)	28	.17	.106	73	.30	<.05	
Model 2 (adjusted for confounding factors)	29	.17	.101	73	.30	<.05	
Model 3 (adjusted for confounding factors and time-dynamic covariate factors)	26	.18	.158	70	.33	<.05	X ² (1) = 2.02, p = .16
Marriage/partnership	В	S.E.	р	В	S.E.	р	X ² (df)
Model 1 (unadjusted)	51	.18	<.01	65	.33	<.05	
Model 2 (adjusted for confounding factors)	45	.18	<.05	61	.32	.056	
Model 3 (adjusted for confounding factors and time-dynamic covariate factors)	32	.19	.094	25	.34	.458	X ² (1) = 0.19, p = .67
Home ownership	В	S.E.	р	В	S.E.	р	X ² (df)
Model 1 (unadjusted)	47	.16	<.01	-1.31	.30	<.0001	
Model 2 (adjusted for confounding factors)	39	.17	<.05	-1.11	.31	<.0001	
Model 3 (adjusted for confounding factors and time-dynamic covariate factors)	21	.19	.244	63	.32	.051	X² (1) = 7.04, p < .01
Net family income, weekly	В	S.E.	р	В	S.E.	р	X ² (df)
Model 1 (unadjusted)	-56.95	110.31	.606	-361.22	252.58	.153	

Model 2 (adjusted for confounding factors) †							
Model 3 (adjusted for confounding factors and time-dynamic covariate factors) [†]						-	X² (1) = 1.35, p = .25
Net investments	В	S.E.	р	В	S.E.	р	X ² (df)
Model 1 (unadjusted)	-7531	14915	.614	-37446	23851	.117	
Model 2 (adjusted for confounding factors)							
Model 3 (adjusted for confounding factors and time-dynamic covariate factors) [†]							X ² (1) = 2.98, p = .09
Socioeconomic status							
Model 1 (unadjusted)	-1.56	1.25	.212	-5.84	2.30	<.05	
Model 2 (adjusted for confounding factors)	85	1.17	.468	-2.44	2.12	.252	
Model 3 (adjusted for confounding factors and time-dynamic covariate factors) [†]							X ² (1) = 3.09, p = .08
Family living standards							
Model 1 (unadjusted)	.18	.48	.703	-2.98	1.29	<.05	
Model 2 (adjusted for confounding factors)	.03	.48	.955	-3.16	1.34	<.05	
Model 3 (adjusted for confounding factors and time-dynamic covariate factors)	.00	.56	.960	27	1.24	.827	X² (1) = 5.75, p < .05
Social support							

Model 1 (unadjusted)	05	.71	.940	-2.85	1.64	.082	
Model 2 (adjusted for confounding factors)							
Model 3 (adjusted for confounding factors and time-dynamic covariate factors) [†]							X ² (1) = 2.64, p = .11
Life satisfaction							
Model 1 (unadjusted)	48	.41	.235	-2.02	.83	<.05	
Model 2 (adjusted for confounding factors)	51	.40	.201	-1.62	.83	.051	
Model 3 (adjusted for confounding factors and time-dynamic covariate factors) [†]							X ² (1) = 3.15, p = .08

[†] Models not computed due to non-significance of either methamphetamine variable at the bivariate or adjustment for confounding level.

5. Discussion

There has been consistent evidence that methamphetamine use is associated with family. social and financial problems among people who use the drug regularly [38-42]. Much of the previous research in this area, however, has been limited by the use of selected samples or special populations (such as drug treatment patients), and relies primarily on the use of crosssectional data [43]. The strength of the present study is that it draws on prospective longitudinal data from a representative birth cohort, born in 1977 and followed to age 40, covering the entire life course of the cohort to this point. In addition, the measures of life outcomes at age 40 spanned several domains of functioning at midlife, including family, economic, and individual psychosocial functioning factors, in order to determine whether there was any particular pattern in which methamphetamine could be related to poorer functioning. Finally, the wide range of measures of potential confounding factors, as well as factors that may mediate or "bridge" the associations between methamphetamine use and life outcomes at age 40, allowed us to test whether these associations were likely to be causal. In this particular context, causality can be ascertained through the application of the Bradford Hill criteria for causality in observational studies [1], specifically in terms of the criteria pertaining to dose-response, robustness to control for confounding, and specificity of effect (control for contemporaneous factors).

The data from the CHDS show that, at the bivariate level, it is clear that a history of using methamphetamine, and in particular the regular use of methamphetamine, was associated with poorer family, psychosocial social and economic outcomes when these were assessed at age 40. The dose-response profile in Table 1 shows that those who report using methamphetamine were more likely to also report lower income and investments, were less likely to have a partner or dependent children, reported lower levels of socioeconomic status and living standards, and reported lower levels of social support and life satisfaction. This dose-response profile is one piece of evidence to support a causal conclusion in this analysis.

A second way of testing whether an exposure (in this case, methamphetamine use) and an outcome (in this case, life outcomes at age 40) is causal in nature, is to ensure that the association cannot be accounted for by factors that make the exposure more likely. This is known as confounding. In the present study, confounding was examined by controlling for the influence of factors such as family socio-economic positioning, family functioning, individual factors, abuse exposure, and mental health and behavioural issues in adolescence. The present analyses showed that controlling for confounding reduced the magnitude of the associations between methamphetamine use and life outcomes, and that for casual methamphetamine use, there was relatively little evidence of causality after control for confounding, with only two of the outcomes (marriage/partnership; home ownership) remaining statistically significant. For regular methamphetamine use, three outcomes remained statistically significant after control for confounding (dependent children; home ownership; family living standards), again suggesting that most of the associations between methamphetamine and life outcomes at age 40 could be explained by confounding factors that make methamphetamine use more likely, rather than a direct causal effect of using methamphetamine.

A third means of testing the causal nature of an exposure and outcome is to control for the influence of factors and events that take place at the same time that the exposure and outcome were measured. It is possible, for example, for factors such as life stress or alcohol use disorder to mediate or "bridge" the association between methamphetamine use and adverse life outcomes. If this was the case, the inclusion of such factors would reduce the magnitude of the association between methamphetamine use and life outcomes. This pattern of results was observed, with only a single outcome measure (dependent children) being significantly

associated with regular methamphetamine use after controlling for moderating factors measured at the same time as the measurement of methamphetamine use. This pattern of findings suggests that the use of methamphetamine from late adolescence and into adulthood does not play a strong causal role in adverse family, economic and psychosocial functioning outcomes at age 40. Instead, poorer functioning in these domains is likely to be a consequence of exposure to adverse circumstances earlier in life, as well as the experience of mental health and substance use disorders and stressful life events in adulthood.

One limitation of the present approach is that it is theoretically possible that there is in fact a causal role of methamphetamine use in adverse family, economic and psychosocial functioning outcomes at age 40, but that the study was unable to reliably detect this effect, for several reasons. One reason may be that the number of methamphetamine users, and in particular regular methamphetamine users, was too small for an effect to be reliably detected. A second reason may be that, due to the limitations of the data collected (e.g. economic data were collected at different points over the history of the CHDS), it was not possible to use a repeated measures design, which has shown to increase power to detect an effect using CHDS data [44]. These limitations show the importance of replicating the present findings with other cohorts and in other settings, with one possible example being the use of a multi-cohort design [45] to increase power.

The implications of the present findings are that because there is relatively little evidence of the causal role of methamphetamine in adverse family, economic and psychosocial functioning outcome in midlife, the pattern of bivariate associations between methamphetamine and these outcomes should properly be viewed as a risk marker for later adverse outcomes. On this evidence, a reduction of methamphetamine use across the population is unlikely to have any particular effect on economic and family outcomes, but it is clear that addressing adverse life circumstances earlier in the life course (childhood and adolescence) has the potential to help reduce methamphetamine use.

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