STUDY PROTOCOL AND METHODS ADVANCEMENT SUBSTANCE USE

The Monitoring Illicit Substance Use Consortium: A Study Protocol

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Objective: The global impact of substance use, including cannabis, amphetamine, cocaine, ecstasy, hallucinogens, and opioids, is increasing, although the overall prevalence is low. Australia and New Zealand are among the few regions of the world in which use (typically illicit) of these classes of substances remains within the top 10 causes of disease burden. The period of adolescence and young adulthood, during which substance use behaviors accelerate in prevalence, is associated with a particular risk for harm. However, the ability to study each substance class has been limited by their low population prevalence in single population-based cohort studies.

Method: The Monitoring Illicit Substance Use (MISUse) Consortium was established to address this problem by bringing together 4 mature prospective cohort studies across Australia and Zealand: Christchurch Health and Development Study (established 1977; 24 waves; N = 1,265), Australian Temperament Project (established 1983; 16 waves; N = 2,443), Victorian Adolescent Health Cohort Study (established 1992; 11 waves; N = 1,943), and International Youth Development Study (established 2002; 10 waves; N = 2,884).

Conclusion: The MISUse Consortium should enable well-powered studies of the natural history, developmental antecedents, and longer-term consequences of illicit substance use with a focus on identifying modifiable determinants of use that can be targeted in population-level policy and intervention responses.

Plain language summary: Illicit substance use is a leading risk factor for disease burden in Australasia. However, the low prevalence of use limits research efforts. The MISUse Consortium brings together four mature Australasian cohort studies, from adolescence to adulthood, building a harmonized data resource capable of examining the natural history, developmental origins, and consequences of illicit substance use.

Key words: cross-cohort; illicit substance use; prospective

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Global burden of disease estimates[1] suggest that the impact of substance use, including cannabis, amphetamine, cocaine, ecstasy (methylenedioxymethamphetamine), hallucinogens, and opioids, is increasing worldwide. Further, Australasia (including Australia, New Zealand, and neighboring islands in the Pacific Ocean) remains one of the few global regions for which the (primarily illicit) use of these substances is in the 10 leading risk factors for disease burden, and this burden has increased over the past decade.[1] In line with this, in Australia and New Zealand, there is emerging evidence of increases in the population prevalence of substance use,[2,3] although rates remain relatively low. In both Australia and New Zealand, prevention and minimization of harm associated with substance use remain key priorities for public health practice and policy.[4,5] Given the Australian and New Zealand context, the term illicit substance use is used to refer to controlled substances that are typically obtained and used illegally, including cannabis, amphetamines, cocaine, ecstasy, hallucinogens, and opioids. However, it is acknowledged that definitions of legality are not synonymous historically and internationally.

Increasing rates of illicit substance use pose a considerable concern given the extent of potential harm, particularly for adolescents and young adults.[6,7] Illicit substance use behavior accelerates in prevalence across the developmental periods of adolescence and young adulthood.[8] Although terminology and definitions vary, here, adolescence is used to encompass ages 10 to 17 years, and young adulthood is used to encompass ages 18 to 29 years.[9–12]

These are watershed periods in human development, when risk-taking behaviors often peak, occurring across a time when young people are expected to take on adult roles and responsibilities.[10] These periods are characterized by rapid brain development, notably by maturation of limbic and prefrontal cortical systems.[9] Adolescence and young adulthood are also characterized by increasing independence from family and greater influence from peers.[11,12] These and other psychosocial processes create a period of vulnerability for young people that is frequently expressed in risk-taking behaviors, including substance use.

Despite the increases in illicit substance use in adolescence and young adulthood, the population prevalence of use is low for substances other than cannabis. Recent (2019) national Australian estimates of past year use across young people (aged 14-29 years) identify rates of use between 13% and 24% for cannabis, 4% and 10% for ecstasy, 1% and 2% for amphetamines, and 2% and 12% for cocaine.[2] In New Zealand, recent (2021/2022) national estimates across young people (aged 15-34 years) identify past year use between 23% and 28% for cannabis, 8% and 13% for ecstasy, 2% and 3% for amphetamines, 4% and 8% for hallucinogens, and around 2% for both cocaine and opioids.[3] Evidence further suggests a high degree of polysubstance use (ie, the use of more than one substance) among people using illicit substances,[2] imposing additional risk.[13] Notably, the low prevalence of illicit substance use behaviors is further influenced by underreporting related to social desirability bias, particularly for substances that carry a high level of stigma.[14,15]

The low population prevalence of illicit substance use has made it difficult to study the natural history of behaviors, resulting in significant knowledge gaps regarding the etiology of these problem behaviors and their life course consequences at the population level.[16] For example, in several broad, seminal reviews,[17–21] there is a dearth of evidence examining the antecedents and consequences of illicit substances other than cannabis, leading to poorly differentiated conclusions. Additionally, much evidence has been derived from cross-sectional designs, for which the direction of associations is not clear, and from clinical samples (eg, incarcerated and inpatient samples) or substance-using samples, limiting generalizability to the general population. Despite decades of research in illicit substance use, longitudinal, general population studies capable of examining low-prevalence illicit substance use behaviors are needed.

Multiwave, prospective cohort studies are essential for addressing questions about the natural history, antecedents, and consequences of illicit substance use across adolescence and young adulthood. However, individual cohort studies are also generally limited by the low prevalence of illicit substance use behavior, insufficient sample size, and associated lack of statistical power. One approach to maximizing the value of illicit substance use data collected across cohort studies is to employ integrative data analysis,[22] involving the harmonization of variables so that the datasets of 2 or more separate cohorts can be pooled into a single dataset.[23] The single dataset is then analyzed, with control for cohort differences (eg, adjusting for a unique identifier of each cohort). The advantages of integrative data analysis include increased statistical power and more reported cases of low-prevalence behaviors.[22] Although the prevalence will remain low in the integrated dataset (eg, if the prevalence is 5% in each cohort, the base rate will remain 5% in the pooled dataset), the absolute number of participants endorsing the behavior will be higher. Together, this reduces the influence of outliers and allows more stable and complex statistical models to be fitted.

Here, we describe a new Australasian collaboration—the Monitoring Illicit Substance Use (MISUse) Consortium—that brings together 4 of the most mature prospective cohort studies across Australia and New Zealand that include measurements of illicit substance use across adolescence and into adulthood. The cohort studies involved are the following:

- The Christchurch Health and Development Study (CHDS) was established in 1977 in Christchurch, New Zealand, and has followed 1,265 participants from infancy to adulthood across 24 waves of data.[24]
- The Australian Temperament Project (ATP) was established in 1983 in Victoria, Australia, and has followed 2,443 participants from infancy to adulthood across 16 waves of data.[25]
- The Victorian Adolescent Health Cohort Study (VAHCS) was established in 1992 in Victoria, Australia, and has followed 1,943 participants from adolescence to adulthood across 11 waves of data.[26]
- The International Youth Development Study (IYDS), Australian sample, was established in 2002 in Victoria, Australia, and has followed 2,884 participants from childhood to adulthood across 10 waves of data.[27]

With the overall objective to reduce harm, the MISUse Consortium was established to address key knowledge gaps in the natural history, antecedents, and consequences of illicit substance use, including cannabis, amphetamine, cocaine, ecstasy, hallucinogens, and opioids, in the general population. The MISUse Consortium will maximize the value of rare developmental data on illicit substance use through a process of systematically harmonizing data across member cohorts with the aim of building sufficient sample

size to enable well-powered studies of low-prevalence illicit substance use behaviors from experimentation to progression across adolescence and young adulthood. Particular attention will be given to exploring substance use other than cannabis, high-frequency use, and combinations of poly-substance use.

Specifically, the aims of the MISUse Consortium are to examine the following:

1. The natural history of illicit substance use behaviors across adolescence and into adulthood (eg, "What patterns of illicit substance use are most common across both developmental periods and substance types?"), including the exploration of secular trends.
2. The life course antecedents of illicit substance use behaviors (eg, "Do healthy parent/peer relationships in adolescence reduce subsequent opioid use?").
3. The life course consequences of illicit substance use behaviors (eg, "Does frequent amphetamine use in adolescence lead to mental health problems in young adulthood?").

Both antecedents and consequences will be explored across a variety of psychosocial environmental domains in which young people interact.

METHOD

Study Design

A summary of each cohort included in the MISUse Consortium is presented in Table 1. There is considerable overlap across most assessment periods, although cohorts vary in terms of age at the baseline assessment: the CHDS (24 waves; N = 1,265) and ATP (16 waves; N = 2,443) provide opportunities to explore processes extending back to infancy, the IYDS (10 waves; N = 2,884) has the capacity to investigate progressions from middle childhood, and the VAHCS (11 waves; N = 1,943) brings richness of assessment from adolescence. Together, these 4 cohorts provide a total sample size of greater than 8,500 participants and data collection points across adolescence (approximately ages 10-17 years) and young adulthood (approximately ages 18-29 years) critical to the harmonization of low-prevalence illicit substance use.

Some of these cohorts have been successfully brought together in prior consortia. For example, the Cannabis Cohorts Research Consortium brought together data from CHDS, ATP, and VAHCS to study young adult outcomes of adolescent cannabis use.[28] The Cannabis Cohorts Research Consortium included examinations of outcomes such as educational attainment and mental health problems.[29,30] Similarly, data from the ATP and VAHCS cohorts have been used in the Intergenerational Cohort Consortium to examine the extent to which preconception parental life histories, from infancy to parenthood, predict early health and development in the next generation.[31] The Intergenerational Cohort Consortium included exploration of the continuity of substance use from adolescence into parenthood,[32] but with a focus on alcohol, tobacco, and cannabis, not on low-prevalence illicit substance use.

Data Collection and Participant Engagement

Across the 4 cohorts, common methods of data collection have included hard copy questionnaires, web surveys, and telephone and in-person interviews. Data have been collected by a team of trained researchers to ensure standardization of survey methods and measures used across time. Each cohort has comprehensive protocols for engagement processes to maximize participation at each wave and minimize attrition. These protocols include details of sample maintenance procedures, such as regular participant newsletters, use of social media platforms, and procedures for locating lost participants such as electoral roll tracing and linkage to death registries.

Generalizability and Sources of Bias

Participants in the CHDS were recruited to be representative of Christchurch, New Zealand, for which the Canterbury region (in which Christchurch is located) remains generally representative of the broader New Zealand population with only a minor bias toward lower employment and education levels but includes a notably lower proportion of individuals of Māori decent.[33] Similarly, ATP, VAHCS, and IYDS samples were recruited within Victoria, Australia, to be representative of the state. Victoria remains broadly representative of Australia, with a minor bias towards higher employment and education levels but includes a notably lower proportion of individuals with Aboriginal and/or Torres Strait Islander backgrounds.[34] Additionally, Australia and New Zealand share common characteristics, such as being predominantly English speaking and recently colonized by Europeans with similar migrant patterns since the 1950s. While the indigenous populations in both Australia and New Zealand share some similarities in their experience of the downstream effects of colonization, there are important differences in the challenges for Māori and Aboriginal and/or Torres Strait Islander people,[35] for whom experiences are likely to vary over time (cohort effects) and location. Further, there is likely considerable overlap in the exposure to drug markets given that the years during which participants experienced adolescence and young adulthood

TABLE 1 Summary of Cohort Studies Included in the Monitoring Illicit Substance Use (MISUse) Consortium

	Christchurch Health and Development Study		Australian Temperament Study		Victorian Adolescent Health Cohort Study		International Youth Development Study (Australian arm)	
Year established	1977		1983		1992		2002	
Sample, N	1,265		2,443		1,943		2,884	
Number of waves	24		16		11		10	
Sample description	Representative sample of infants (from birth) from Christchurch, New Zealand, and their parents		Representative sample of Victorian infants (aged 4-8 mo) and their parents		Representative sample of mid-secondary school students (aged 14-15 y) in Victoria		Representative sample of primary-secondary school students (aged 11, 13, and 15 y[a])	
Follow-up participation rates	71%-96%		58%-83%[b]		73%-87%		32%-100%[c]	
Waves	Age	Year	Age	Year	Age	Year	Age	Year
Childhood (birth to 9 y)	0, 4 m, 1, 2, 3, 4, 5, 6, 7, 8, 9	1977, 1977, 1978, 1979, 1980, 1981, 1982, 1983, 1984, 1985, 1986	4-8 mo, 1-2, 2-3, 3-4, 5-6, 7-8, 9-10	1983, 1984, 1985, 1986, 1988, 1990, 1992	NA		NA	
Adolescence (10-17 y)	10, 11, 12, 13, 14, 15, 16, 18	1987, 1988, 1989, 1990, 1991, 1992, 1993, 1995	11-12, 12-13, 13-14, 15-16, 17-18	1994, 1995, 1996, 1998, 2000	14.9, 15.5, 15.9, 16.4, 16.8, 17.4	1992, 1993, 1993, 1994, 1994, 1995	11, 12, 13, 14, 15, 16, 17	2002, 2003, 2002/2004, 2003, 2002/2004/2006, 2003/2007, 2008
Young adulthood (18-29 y)	21, 25, 30	1998, 2002, 2007	19-20, 23-24, 27-28	2002, 2006, 2010	20.7, 24.1, 29.1	1998-1999, 2001-2003, 2006-2008	19, 21, 23, 25, 27, 29	2010, 2010/2012, 2010/2012/2014, 2012/2014, 2014, 2018
Adulthood (≥30 y)	35, 40	2012, 2017-2018	31-32	2014	35.1, 42.6	2012-2014, 2019-2021	NA	

Note: *NA = no assessment available.*
[a]*International Youth Development Study recruited using a 2-stage cluster sampling approach in 2002 containing 3 school grades.*
[b]*Based on n = 2023 followed longitudinally.*[54]
[c]*Low percentages reflect follow-ups when not all cohorts were included.*

were similar. For instance, adolescent assessments for the CHDS, ATP, and VAHCS occurred predominately over the 1990s, while these assessments occurred during the early 2000s for the IYDS. However, it is important to consider that the historic nature of these data means that they may not reflect contemporary drug markets.

Despite similarities between the samples, cross-cohort differences, such as those associated with differing samples, sites, and survey content, are acknowledged and will be addressed analytically, where possible. As noted, integrative data analysis involves inclusion of a unique identifier for each cohort to provide estimates of association adjusted for cross-cohort differences and, when including as an interaction term, allows cohort-specific trends to be identified if power permits.[22] Differential risk of bias will also be considered; this could include selection, confounding, measurement, and missing data biases.[36] This is important because pooling data from samples with differential risk of bias may complicate the interpretation of results,[23] such that unique biases could be at play within each cohort, requiring findings to be interpreted with caution.

Source of Support and Management Framework

Each cohort has received nationally competitive research grants since inception, and approval has been obtained from the relevant ethics committee for data collection during the study period. The most recent ethics approvers are the New Zealand Health and Disabilities Ethics Committee for the CHDS, the Australian Institute of Family Studies Human Research Ethics Committee (HREC) for the ATP, the Royal Children's Hospital HREC for VAHCS, and the Deakin University HREC for the IYDS. The MISUse Consortium has been approved by the Royal Children's Hospital (Melbourne) HREC.

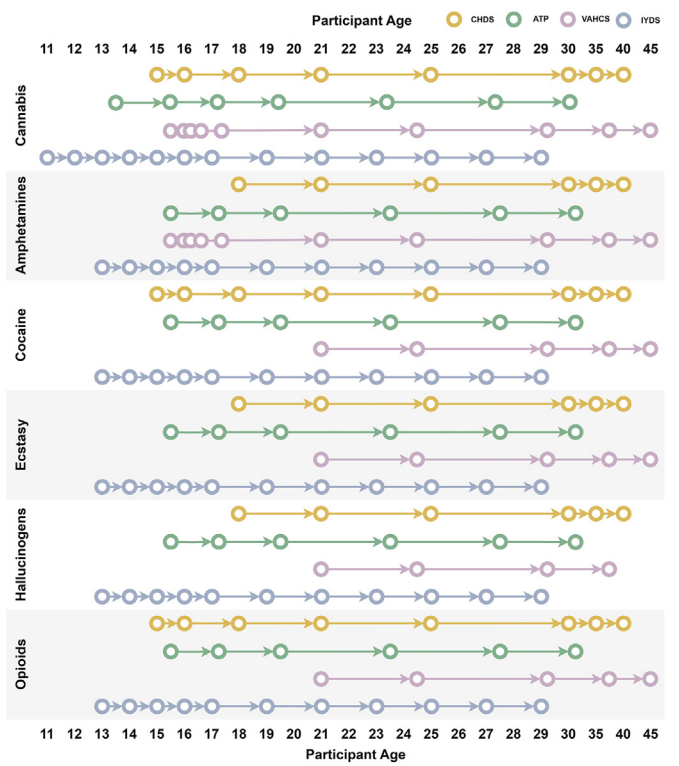
The chief investigators of each cohort lead the design, instrumentation, publications, and grants of their respective cohorts, while the corresponding cohort project management team manages data collection and curation. Chief investigators of each cohort have approved the inclusion of data for the MISUse Consortium. However, each manuscript requires the submission of a formal paper proposal, which must be further approved by the chief investigators and publication managers of each cohort. These formal proposals are completed before analyses and include the specification of clear research questions, which data will be used, and the type of analyses to be conducted (see Downes *et al.*[37]).

Measures

Illicit Substance Use. A range of illicit substances have been assessed in each cohort, primarily including cannabis, amphetamines, cocaine, ecstasy, hallucinogens, and opioids. It is noted that in the majority of years in which these data were primarily collected the use of these substances was illicit. However, changes in legislation across the 2010s and 2020s[38–40] have meant that in recent data collections the use of some substances, including cannabis, psilocybin, and methylenedioxymethamphetamine, may also be medically prescribed for a small portion of participants. Further, data on the illicit use of prescribed substances were not included in the current study as they encompass a wide range of medications with different pharmacological properties and purposes, making meaningful measurement across studies challenging.

A summary of the included types of illicit substances assessed at the various ages for each cohort is presented in Figure 1. Studies included assessments across several ages for most substance types throughout both adolescence (aged 10-17 years) and young adulthood (aged 18-29 years). The CHDS, ATP, and VAHCS additionally include assessments into adulthood (aged ≥30 years).

FIGURE 1 Summary of Monitoring Illicit Substance Use (MISUse) Cohort Study Waves Including Illicit Substance Use Assessments



Note: *Circles indicate ages in which assessment of each illicit substance type was included within each cohort. ATP = Australian Temperament Project; CHDS = Christchurch Health and Development Study; IYDS = International Youth Development Study; VAHCS=Victorian Adolescent Health Cohort Study.*

Across studies, measurement of illicit substance use frequency was mostly consistent. However, there are some differences in illicit substance use frequency measures employed across the cohorts and waves within the same cohort. Primarily, CHDS participants were asked about the number of times used in the past year; ATP respondents were asked about the number of days used in the past month; VAHCS participants were asked about the frequency use in the past year; and IYDS participants were asked about the number of times used in the past year and past 30 days. Therefore, question structure and response options require consideration to ensure alignment across cohorts and waves with respect to frequency of use (eg, monthly, weekly, or daily use). Other metrics, such as quantity and harm (eg, abuse and dependence) are also available; however, assessments are less consistent across the included studies.

To account for variation in assessment time points, data can also be collapsed within developmental periods (eg, adolescence and young adulthood). Using all available data, the prevalence of illicit substance type by cohort and frequency (ie, monthly, weekly, or daily use) across adolescence and young adulthood is presented in Table 2. Broadly, we note expected developmental patterns whereby the prevalence of use generally increases across adolescence into young adulthood: monthly cannabis (adolescence 17%, young adulthood 26%), amphetamine (adolescence 2%, young adulthood 8%), cocaine (adolescence <1%, young adulthood 6%), ecstasy (adolescence 2%, young adulthood 8%), hallucinogens (adolescence 1%, young adulthood 24%), and opioids (adolescence <1%, young adulthood <1%). Considerations warranted for these data with respect to harmonization are discussed subsequently.

Exposures and Outcomes. Numerous exposure and outcome factors have been examined across each cohort and are summarized at the domain level in Table 3, broadly covering mental health/behavior problems, psychological well-being, temperament/personality, family environment, peer/romantic relationships, education and childcare, community involvement, and sociodemographic characteristics. Exposures and outcomes data will also be harmonized as appropriate. The harmonization process may involve approaches such as standardization (eg, *z* scores) or deriving comparable categorical indicators (eg, no risk vs risk) for measures assessing similar domains. More advanced standardization approaches, such as moderated nonlinear factor models,[41] will also be considered. Harmonization across a range of measures has been successful in previous consortia.[28,31]

Statistical Analyses

Data analysis will be conducted in appropriate programs, including (but not limited to) Mplus,[42] R Statistical Software,[43] and Stata.[44] Integrative data analysis, as described previously, will be used to maximize the value of illicit substance use data collected across cohorts. Further, appropriate outcome estimators (eg, linear, logit, negative binomial) will be applied and explored. For analyses, the pooled dataset will primarily be used. However, several sensitivity analyses will be conducted, when relevant, to examine the robustness of modeling assumptions. Given the possibility for potential cohort differences (eg, due to differences in recruitment birth year/location and measurement), models will also be repeated within the individual cohorts, despite the low prevalence of behaviors, to examine effect heterogeneity. Further, models may also be repeated using alternative harmonized variable derivations (eg, varied binary cutoffs, *z*-scored continuous) or study specific raw variables to ascertain the impact of harmonization decisions.

The natural history of illicit substance use behavior (aim 1) will be examined using a combination of descriptive statistics (eg, proportion, mean, median) and growth modeling methods (eg, multilevel mixed-effects regression) to identify trajectories of substance use over time. To examine the antecedents (aim 2) and consequences (aim 3) of illicit substance use, behavior regression models will be estimated. Regression models will be grounded in a causal modeling framework using the target trial approach,[45,46] involving the careful selection of variables for adjustment, as indicators of potential confounding factors.[47] In the context of cross-cohort analyses, several approaches to confounder adjustment, which have been implemented successfully in prior collaborative efforts,[48] may also be implemented, including the development of a null covariate model (ie, covariates not included in a particular cohort have values set to zero), using a reduced set of covariates consistent to all cohorts, and the development of cohort-specific propensity scores using all available covariates.

Although wave-by-wave follow-up participation rates vary both within and across the MISUse Consortium cohort studies, data harmonization procedures (eg, across multiple waves) will likely reduce the impact of missing data at any one wave. Further, several steps will be employed to examine and handle missing data. First levels of missing data across relevant analytic variables will be examined in each cohort. Second participants with incomplete and complete data will be compared to examine potential biases due to missing data. Third, missing data will be handled using appropriate methods such as multiple imputation[49–51] or a full information maximum likelihood approach.[52]

TABLE 2 Preliminary Illicit Substance Prevalence by Cohort, Developmental Period, and Substance Use Frequency

	Monthly				Weekly				Daily			
	Adolescence		Young adulthood		Adolescence		Young adulthood		Adolescence		Young adulthood	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Cannabis												
CHDS	199	(18.84)	355	(34.17)	107	(10.13)	241	(23.20)	95	(9.00)	164	(15.78)
ATP	338	(23.94)	321	(23.26)	117	(8.29)	160	(11.59)	19	(1.35)	40	(2.90)
VAHCS	152	(17.53)	399	(22.83)	95	(10.96)	326	(18.65)	27	(3.11)	189	(10.81)
IYDS	355	(12.36)	699	(26.58)	138	(4.80)	340	(12.93)	23	(0.80)	93	(3.54)
Overall	1,044	(16.82)	1,774	(26.10)	457	(7.36)	1,067	(15.70)	164	(2.64)	486	(7.15)
Amphetamine												
CHDS	9	(0.88)	45	(4.33)	6	(0.59)	18	(1.73)	4	(0.39)	4	(0.38)
ATP	20	(1.71)	107	(7.84)	6	(0.51)	26	(1.91)	0	(0.00)	1	(0.07)
VAHCS	8	(0.93)	86	(5.33)	2	(0.23)	32	(1.98)	1	(0.12)	7	(0.43)
IYDS	65	(2.27)	319	(12.13)	24	(0.84)	130	(4.94)	11	(0.38)	19	(0.72)
Overall	102	(1.72)	557	(8.38)	38	(0.64)	206	(3.10)	16	(0.27)	31	(0.47)
Cocaine												
CHDS	0	(0.00)	21	(2.02)	0	(0.00)	6	(0.58)	0	(0.00)	0	(0.00)
ATP	0	(0.00)	75	(5.43)	0	(0.00)	9	(0.65)	0	(0.00)	0	(0.00)
VAHCS	NA		40	(2.48)	NA		18	(1.11)	NA		5	(0.31)
IYDS	29	(1.01)	261	(9.93)	12	(0.42)	77	(2.93)	8	(0.28)	10	(0.38)
Overall	29	(0.57)	397	(5.96)	12	(0.24)	110	(1.65)	8	(0.16)	15	(0.23)
Ecstasy												
CHDS	NA		15	(1.52)	NA		1	(0.10)	NA		0	(0.00)
ATP	27	(2.30)	113	(8.33)	5	(0.43)	12	(0.88)	0	(0.00)	0	(0.00)
VAHCS	NA		79	(4.61)	NA		29	(1.69)	NA		0	(0.00)
IYDS	69	(2.41)	326	(12.40)	27	(0.94)	105	(3.99)	10	(0.35)	7	(0.27)
Overall	96	(2.38)	533	(7.97)	32	(0.79)	147	(2.20)	10	(0.25)	7	(0.10)
Hallucinogens												
CHDS	NA		2	(0.20)	NA		0	(0.00)	NA		0	(0.00)
ATP	13	(1.11)	89	(6.41)	1	(0.09)	10	(0.72)	0	(0.00)	0	(0.00)
VAHCS	NA		10	(0.62)	NA		2	(0.12)	NA		0	(0.00)
IYDS	47	(1.64)	178	(6.77)	18	(0.63)	49	(1.86)	9	(0.31)	6	(0.23)
Overall	60	(1.49)	279	(4.21)	19	(0.47)	61	(0.92)	9	(0.22)	6	(0.09)
Opioids												
CHDS	3	(0.28)	6	(0.58)	0	(0.00)	4	(0.38)	0	(0.00)	3	(0.29)
ATP	1	(0.09)	17	(1.22)	0	(0.00)	3	(0.22)	0	(0.00)	0	(0.00)
VAHCS	NA		15	(0.86)	NA		12	(0.69)	NA		9	(0.52)
IYDS	20	(0.70)	20	(0.76)	14	(0.49)	11	(0.42)	12	(0.42)	4	(0.15)
Overall	24	(0.47)	58	(0.85)	14	(0.27)	30	(0.44)	12	(0.24)	16	(0.24)

Note: Adolescence is defined as 10-17 y, and young adulthood is defined as 18-29 y. Percentage is based on available data. CHDS also included items assessing both ecstasy and hallucinogens (not reported here). ATP = Australian Temperament Project; CHDS = Christchurch Health and Development Study; IYDS = International Youth Development Study; NA=no assessment available; VAHCS=Victorian Adolescent Health Cohort Study.

Power Analysis. Figure 2 presents an illustration of power for potential analyses examining the antecedents and consequences of illicit substance use, noting though that the data are already collected. Power is determined based on 1,000 simulations ($\alpha = .05$, two-tailed) using a conservative sample size of 6,375 (75% of the total sample size) and iteratively varying both the prevalence of illicit substance use and the effect sizes of interest. For analyses

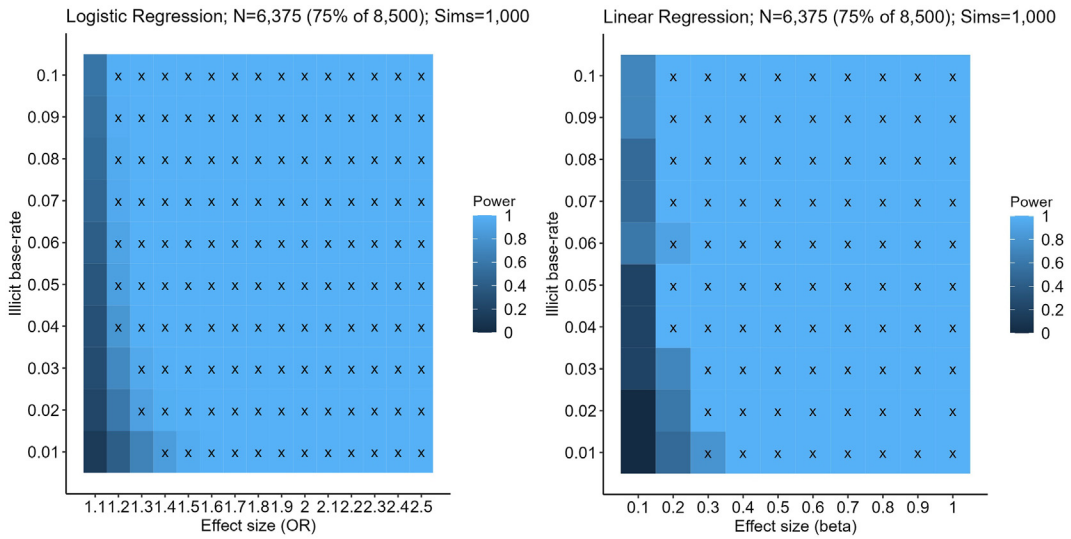
TABLE 3 Domain Level Summary of Data Available in the Monitoring Illicit Substance Use (MISUse) Consortium Cohort Studies

	Christchurch Health and Development Study				Australian Temperament Study				Victorian Adolescent Health Cohort Study				International Youth Development Study (Australian arm)			
	C	AD	YA	A	C	AD	YA	A	C	AD	YA	A	C	AD	YA	A
Physical health																
General health information	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓	✓	
Relational health																
Family relationships	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓	✓	
Peer/romantic relationships	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓	✓	
Emotional health																
Mood and behavior problems	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓	✓	
Psychological well-being			✓	✓		✓	✓	✓		✓	✓	✓		✓	✓	
Temperament and personality		✓		✓	✓	✓	✓	✓		✓	✓	✓		✓		
Social context																
Education, occupation, income level	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓	✓	

Note: *A = adulthood (≥30 y); AD = adolescence (10-17 y); C = childhood (birth to 9 y); YA = young adulthood (18- 29 y).*

examining the antecedents of illicit substance use, power is calculated using logistic regression models assuming an odds ratio (OR) of 1.5 between other variables and the outcome; 80% power is achieved when illicit substance use prevalence is 4% with an OR of 1.2, 2% with an OR of 1.3, and 1% with an OR of 1.4 or greater (Figure 2, left). For analyses examining the consequences of illicit substance use, power is calculated using linear regression models assuming 10% of variance in the outcome accounted for by other variables in the model; 80% power is achieved when illicit substance use prevalence is 4% with a standardized β of .2 and 1% with a β of .3 or greater (Figure 2, right). Thus, the study is appropriately powered to detect effect sizes of interest for a range of illicit substance use prevalence levels, allowing us to examine a variety of illicit substance types.

FIGURE 2 Power Analysis for Logistic Regression (Left) and Linear Regression (Right) Models



Note: *Models are simulated 1,000 times assuming a conservative sample size of around 75% of the available sample (n = 8,500) and iterating through various illicit prevalences (from 1% to 10%) across a range of effect sizes. X indicates models for which power was ≥80%. OR = odds ratio.*

DISCUSSION

Emerging evidence from population surveillance studies suggests that illicit substance use has increased in recent years[2,3] and remains a major contributor to the total burden of disease.[6,7] The developmental period across adolescence and young adulthood is pivotal to the initiation and maintenance of illicit substance use behavior. Although multiwave, prospective, general population cohort studies are ideally positioned to examine illicit substance use across adolescence and young adulthood, low prevalence rates of illicit use within single cohorts has limited etiological research leaving important knowledge gaps critical to informing prevention and early intervention practices and policy. The MISUse Consortium will address important knowledge gaps in the natural history, antecedents, and consequences of illicit substance use by combining multiple samples using integrative data analysis, which will generate more stable analytic models[22] and yield greater confidence in the findings for informing applied evidence-based outcomes.

Illicit Substance Use Across Adolescence and Young Adulthood

Several points of consideration are warranted based on the available prevalence of illicit substance use data in the MISUse Consortium. Although there is variability across studies, generally, the prevalence of past-year substance use in the MISUse Consortium studies is higher than national estimates from corresponding time periods.[2,3] The increased rates of use may reflect the repeated assessments in a particular developmental period, for which endorsement of a behavior could occur at several possible time points, but may also reflect the underreporting identified in national general population surveys.[14] Further, there are some differences in the prevalence of substance types across the included cohort studies, likely reflecting secular and societal differences in substance use choices. Such discrepancies require consideration regarding potential differences in etiological pathways as well as sociocultural and secular influences on substance use choices, such as availability of substance classes at particular times. Further, while not unexpected, examination of some substance type frequency levels is likely to still be underpowered, and impossible in some cases, due to the very low prevalence of behaviors.

Notably, cannabis and amphetamine use are the illicit substances that have been most consistently assessed across studies and developmental periods, with item wording allowing for derivation across a range of frequency levels (ie, monthly, weekly, daily). The consistency of assessment across studies and developmental periods for other substance types was comparable, although separate ecstasy and hallucinogens assessments were fewer, given that the CHDS included only a combined assessment of both before age 30. However, the CHDS did include a retrospective assessment of ecstasy and hallucinogen use separately for young adults aged 26 to 29 years. Across developmental periods, young adulthood has the most consistent assessments across both substance types and frequency levels, for which all studies were able to derive indicators of use at all levels.

Translational Partners

The MISUse Consortium has been purposely designed to link life course research to clinical and public health practice. The inclusion of clinician researchers within the MISUse Consortium team facilitates the translation of population-level research into clinical practice. These experts play a vital role in ensuring the relevance and applicability of research findings to real-world patient care. By actively participating in the consortium, clinician researchers help both to shape research questions that directly address the challenges and needs encountered in clinical settings and to interpret and contextualize research findings from a clinical perspective.

Furthermore, the MISUse Consortium includes partnership with researchers who have a direct impact on public health through government-based initiatives. This partnership aims to facilitate the translation of research findings into the enhancement of government efforts. By engaging with experts in the governmental sphere, the consortium aims to foster effective integration of research outcomes into policy development, decision-making processes, and public health programs. For instance, the MISUse Consortium is critical to informing the markers of substance use, which at a population level can be developmentally monitored.[53] The involvement of these government-focused researchers helps bridge the gap between scientific research and practical implementation at a broader population level.

Consortium Research Collaboration

The MISUse Consortium welcomes further collaboration with other Australasian cohort studies that span similar developmental periods and include similar measures. The inclusion of additional cohorts will further increase capacity to examine nuanced associations and patterns among low-prevalence illicit substance use behaviors. Collaboration with researchers interested in using data from the MISUse Consortium is also welcomed. If interested in collaboration, please contact the corresponding author.

The MISUse Consortium presents an important opportunity to maximize the value of 4 long-running prospective cohort studies across Australia and New Zealand. Despite some variation in the assessments across the cohort studies, the data available in the MISUse Consortium will further understanding of low-prevalence illicit substance use behaviors by exploring the natural history, antecedents, and consequences of use across adolescence and young adulthood, extending to both earlier and later parts of the life course.

CRediT authorship contribution statement

Christopher J. Greenwood: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Primrose Letcher:** Writing – review & editing, Project administration, Investigation, Funding acquisition, Conceptualization. **Esther Laurance:** Writing – review & editing, Project administration, Conceptualization. **Joseph M. Boden:** Writing – review & editing, Project administration, Investigation, Funding acquisition, Data curation, Conceptualization. **James Foulds:** Conceptualization, Data curation, Funding acquisition, Investigation, Project administration, Writing – review & editing. **Elizabeth A. Spry:** Writing – review & editing, Project administration, Investigation, Funding acquisition, Conceptualization. **Jessica A. Kerr:** Writing – review & editing, Project administration, Investigation, Conceptualization. **John W. Toumbourou:** Writing – review & editing, Project administration, Investigation, Funding acquisition, Conceptualization. **Jessica A. Heerde:** Writing – review & editing, Project administration, Investigation, Conceptualization. **Catherine Nolan:** Writing – review & editing, Conceptualization. **Yvonne Bonomo:** Writing – review & editing, Conceptualization. **Delyse M. Hutchinson:** Writing – review & editing, Investigation, Conceptualization. **Tim Slade:** Writing – review & editing, Formal analysis, Conceptualization. **Stephanie R. Aarsman:** Writing – review & editing, Formal analysis, Conceptualization. **Craig A. Olsson:** Writing – review & editing, Supervision, Project administration, Investigation, Funding acquisition, Conceptualization.

This article is part of a special series devoted to the subject of substance use, featuring topics relevant to child and adolescent behavioral health, including genetics, neuroscience, epidemiology, measurement, prevention, and treatment. This special series is edited by Guest Editor Kevin M. Gray, MD, *JAACAP Open* Deputy Editor Kara S. Bagot, MD, *JAACAP* Deputy Editor Mary Fristad, PhD, ABPP, *JAACAP* and *JAACAP Open* Associate Editor Robert R. Althoff, MD, PhD, *JAACAP Open* Editor Manpreet K. Singh, MD, MS, and Editor-in-Chief Douglas K. Novins, MD.

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The research was performed with permission from The Royal Children's Hospital Human Research Ethics Committee.

Consent has been provided for descriptions of specific patient information.

Ethics approvals for the CHDS, ATP, VAHCS, and IYDS do not permit the data to be made publicly available due to limitations of participant consent and concerns regarding potential re-identifiability. For the CHDS, data availability inquiries can be directed to the Principal Scientist of the CHDS: Prof. Joseph M. Boden (joseph.boden@otago.ac.nz). For the ATP, VAHCS, and IYDS, the dataset subset can be made available to a named individual for the purpose of replication of research findings. Requests to access the dataset can be submitted through our institutional data access protocol: https://lifecourse.melbournechildrens.com/data-access/.

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