



Predictors and outcomes of adolescent alcohol and drug use: a scoping review

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Research. Evidence. Action.

Abstract

Background

Adolescence and young adulthood, typically defined as 10-24 years, are pivotal life stages marked by educational advancement, entry into the workforce or further training and formation of lasting relationships. Globally, adolescence is also the peak period during which individuals first engage in alcohol and/or drug consumption. Initiation of substance use during this critical period can disrupt significant life transitions and has been linked to detrimental short- and long-term health as well as social consequences. In 2019, there were 3.2 million young people with substance use disorders in Europe. Substance use during adolescence may co-occur and complicate the trajectory of common mental health disorders that also frequently manifest during this time. This scoping review aims to summarize existing longitudinal research on factors and outcomes related to youth drug and alcohol use. Our objectives were twofold: first, to gain insight and identify research gaps from existing evidence and secondly, to evaluate methodologies commonly used in longitudinal datasets. This work will provide the foundational background for a planned series of longitudinal analyses of the Growing Up in Ireland cohort study.

Methods

This is a scoping review that focuses on longitudinal studies and reviews, conducted in accordance with the PRISMA extension for scoping reviews. A systematic literature search was conducted on PubMed. Further studies were identified through handsearching key reference lists and Google Scholar searches. Studies were eligible for inclusion if they were prospective cohort studies and scoping or systematic reviews, and reported factors predicting, or outcomes associated with youth substance use. Data was extracted into a spreadsheet. Narrative synthesis was completed grouped by outcome reported.

Results

One hundred and twenty-three studies were included in our scoping review, twelve of which were review articles and one hundred and eleven cohort studies based on six-six unique cohorts of young people. Publication dates span 1996 to 2023 but 50% of cohort studies were published in the last seven years. Over 60% of cohort studies originated from North America, 29% from Europe, 7% Australia/New Zealand and 2% from both South America and Asia. Adolescent substance use (ASU) is defined in many different ways ranging from patterns that may represent sporadic or experimental ("ever use") to hazardous patterns of use such as binge drinking or substance use disorders. Factors that are consistently associated with increased risk of ASU include being male, increasing age, externalizing disorders such as conduct disorder, adverse childhood experiences, and peer or parental substance use. Few studies reported wider community or environmental factors but neighborhood availability of drugs was associated with ASU. Regarding outcomes, early initiation and higher frequency of ASU was predictive of later-life substance use patterns. ASU has also been linked with increased risk of education derailment, contact with the justice system and mental health disorders. From a methodological standpoint, most studies (n=78) employed some variation of multivariable regression models to investigate associations. Others used path analysis or structural equation modelling (n=14). Twenty-three studies used latent class methodologies to describe patterns or trajectories of ASU.

Conclusions

The body of longitudinal evidence on ASU is rapidly expanding. However, a number of important research gaps remain, including the influence of social and environmental factors, intermediary mechanisms through which early life exposures influence ASU, factors associated with initiation of illicit drugs other than cannabis, and the relationship between ASU and critical transitions from adolescence to adulthood. Our research group will address these gaps using rich longitudinal data from the Growing Up in Ireland cohort to advance understanding of ASU and generate contemporary evidence that can be used to inform interventions and day-to-day practice.

Background

The health and social harms associated with alcohol and unregulated substance use among young people continue to be significant public health concerns in many jurisdictions. (1,2) In Ireland in 2022, 12,009 people received treatment services for problem drug use and 7,421 for problematic alcohol use.(3,4) A large proportion of people who use drugs (PWUD) first experiment with regulated and unregulated drugs during adolescence and early initiation of substance use is particularly concerning given the neurological, social and educational development that occurs during this period. (5–10) Earlier analyses of the GUI study identify emergence of alcohol use even at age 13 with other drug use also becoming prominent in later waves. (11)

A number of individual, social and structural risk factors for alcohol and unregulated substance use initiation have been identified in previous studies. These include adverse childhood experiences and trauma, familial and peer substance use, psychological vulnerability (e.g., impulse control, sensation seeking) and familial cohesion, among others. (12,13) Other evidence has highlighted the impact of structural risk factors such as community economics and violence, substance use policy and drug availability via licit and illicit markets. (13–16) Based on these findings, theoretical frameworks have been developed that conceptualize substance use risk and harms caused by micro- and macro-environmental determinants. (17) However, the empirical support for these frameworks and the relative contribution of each risk factor has been difficult to quantify as many existing studies are cross-sectional or include limited follow-up to evaluate the impact of substance use trajectories over time. (18) Longitudinal studies with repeated measures of individual, social and contextual risk factors for substance are therefore needed to characterize these associations with more certainty.

The specific harms associated with alcohol and other substance use among youth and young adults have been well-described and include health, social and emotional consequences. (19–21) Among youth alcohol and other substance use has been linked to lower academic performance, engagement in criminal activities, as well as mental health problems and accident-related mortality. (19–23) Earlier initiation of tobacco and substance use is also an established risk factor for polysubstance use, the development of substance use disorders and the incidence of other mental health disorders such as depression. (23–25) After initiating substance use, youth tend to quickly progress to high-risk use behaviors such as bingeing and experience greater drug-related harm than older more established PWUD. (26–29) As a result, identifying youth at-risk for drug-related harm and delaying substance use exposure are primary objectives of prevention programmes among youth and young adults. (13,23)

Given the harm associated with youth alcohol and unregulated substance use and the need to characterize patterns of substance use vulnerability, this review aims to collate the published evidence on the risk and protective factors, and outcomes of adolescent substance use patterns and trajectories. This review will establish the foundational context for a planned series of longitudinal analyses of the Growing Up in Ireland (GUI) cohort study. (30)

Methods

Study design and research questions

This is a scoping review of longitudinal studies on youth drug and alcohol use and impact which is reported as per the PRISMA extension for scoping reviews (PRISMA-ScR). (31)

The agreed review questions were:

- 1. What are the factors associated with patterns of drug and alcohol use in young people?
- 2. What outcomes are associated with youth substance use?
- 3. What methods and analytical approaches are used in other longitudinal datasets investigating adolescent substance use?

Search strategy

An initial search was performed to identify appropriate keywords. General search themes and keywords were agreed through consensus discussion between the research team. The search strategy was formulated using the Population, Exposure, Outcome (PEO) framework. Search terms were linked using appropriate Boolean operators. A systematic search was conducted of the PubMed database from inception to 2023. Additional studies of relevance were identified through citation searching and the web search engine Google Scholar.

Population	(((adolescent [Abstract] OR teenager[Abstract] OR teen[Abstract] OR youth[Abstract] OR school-going children[Abstract] OR youngster[Abstract] OR pediatric[Abstract])))
Exposure	AND (drug[Abstract] OR narcotic[Abstract] OR opioid[Abstract] OR psychoactive substance[Abstract] OR amphetamine[Abstract] OR cannabis[Abstract] OR ecstasy[Abstract] OR heroin[Abstract] OR cocaine[Abstract] OR hallucinogen*[Abstract] OR depressant[Abstract] OR stimulant[Abstract] OR marijuana[Abstract] OR illicit drug[Abstract] OR tranquilizers[Abstract] OR sedatives[Abstract] OR LSD[Abstract] OR Fentanyl[Abstract] OR illegal drug[Abstract] OR street drug[Abstract] OR club drug[Abstract] OR recreational drug[Abstract] OR substance*[Abstract] OR alcohol[Abstract])
Outcome	AND (abuse[Abstract] OR addiction[Abstract] OR dependence[Abstract] OR habituation[Abstract] OR overdose[Abstract] OR misuse[Abstract] OR overuse[Abstract] OR use[Abstract])

Figure 1: Search strategy

Inclusion and exclusion criteria

Studies were included if they;

- Reported factors associated with alcohol and/or drug use in children, adolescents, or young adults.
- Reported outcomes associated with youth drug and/or alcohol use
- Study design: prospective cohort studies or systematic/scoping reviews

Studies were excluded if they;

- Did not report factors affecting the use of drugs in adolescence and young adulthood, or the impact of drug use on trajectory.
- Had a small sample size, $n \leq 250$
- Rodent studies
- Neuroimaging and/or bio-specimen sampling
- Non-industrialised countries with a view to identifying studies using longitudinal datasets with similar characteristics to GUI.
- Study design: cross-sectional, ecological, interventional, commentary, editorial, conference abstracts, retrospective cohort studies, non-systematic/scoping reviews.

Eligibility screening

All references identified by the PubMed search were imported to an Endnote library where duplicates were removed.

Following screening for duplicates, studies were screened using pre-defined inclusion and exclusion criteria. Screening took place in two phases; first involved review of title and/or abstracts, and second was a review of full text articles.

Data extraction

Data extracted included: title, author, publication year, study design, sample size, study

population characteristics, study aim, methods, results, outcomes measured, risk factors, protective factors, neutral factors and later life outcomes.

Data was initially extracted to an Excel using a pre-specified data extraction template by one researcher. This was subsequently reviewed and updated by a second member of the research team.

Narrative synthesis

A narrative synthesis of the evidence was completed grouped by study type and outcome assessed.

Results

Description of included studies

One hundred and twenty-three studies were included in our scoping review, twelve of which were review articles and one hundred and eleven were cohort studies. Publication dates span 1996 to 2023. The search process and results are presented in the PRISMA flow diagram (Figure 2).

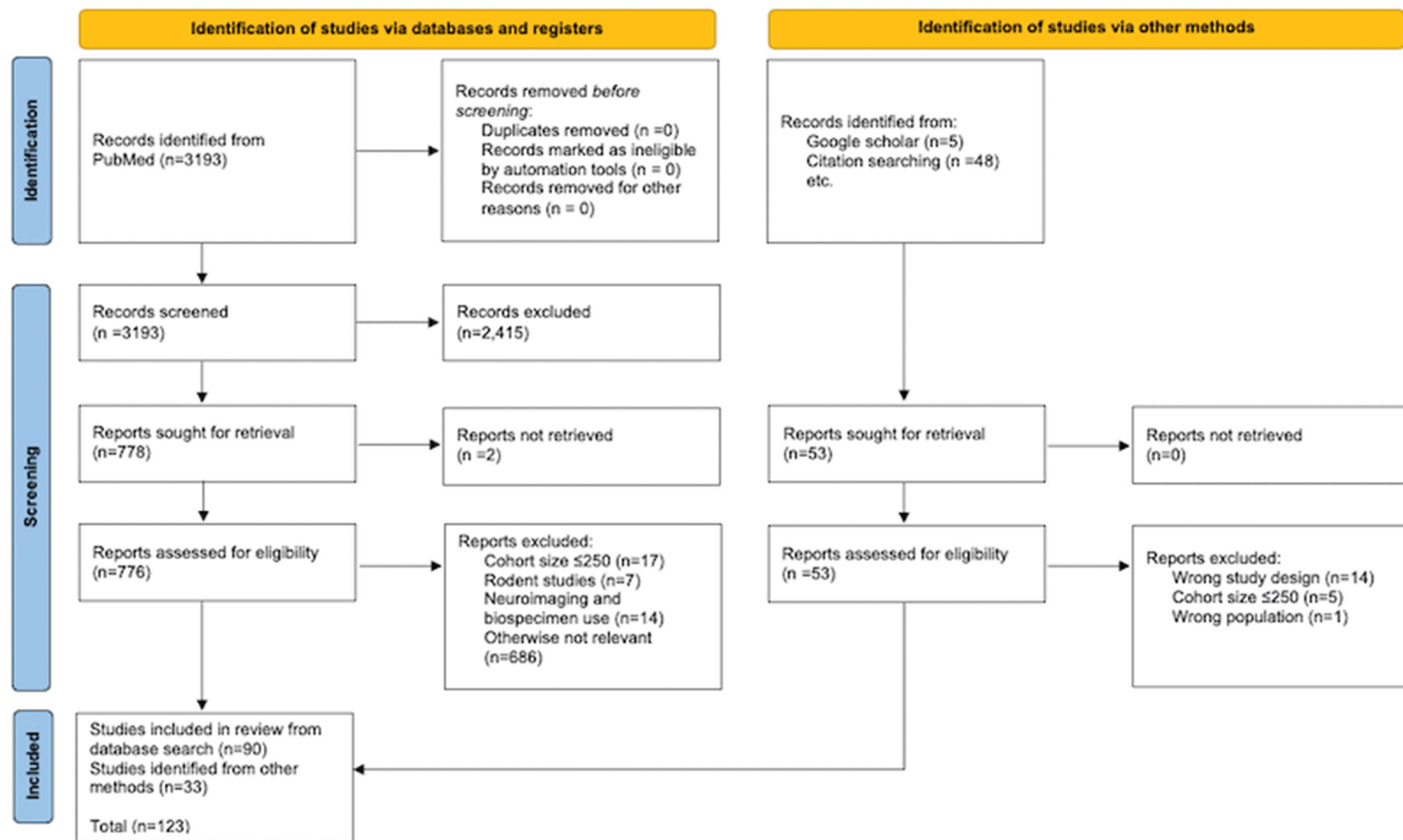


Figure 2: PRISMA flow diagram

Reviews

Overview

The twelve reviews were systematic (n=11) and scoping reviews (n=1). Seven focused on predictors of youth substance use. (32–39) Three reported outcomes of youth substance use. (23,40,41) Two reported on latent classes of substance use amongst young people. (42,43)

The majority of identified reviews (n=7) include a mixture of observational study design (cross-sectional, cohort, case-control). (32,34,36–38,41–43) Four report only on cohort studies. (23,33,39,40)

Predictors of adolescent substance use

A broad mixture of individual and familial factors associated with youth substance use were reported in the seven identified reviews:

Individual risk factors reported were adverse childhood experiences, previous substance use, risky sexual behaviours. (32,34–39) There is some evidence for a positive association between anxiety in childhood and adolescent and subsequent alcohol use disorder but findings are inconsistent. (39)

Familial risk factors included parental use of drugs and/or alcohol, family history of crime, parent-child relationships, parental marital status and parental education level. (33,36,37)

None of the reviews identified reported on community or environmental predictive factors, and there was much more focus on factors that increase risk relative to protective factors.

Outcomes of adolescent substance use

The three reviews reporting outcomes of adolescent substance use considered alcohol, cannabis and methamphetamine use respectively. (23,40,41)

McCambridge concludes that there is consistent evidence that higher alcohol consumption in adolescence (age 15-19) continues into adulthood (age ≥20) and this is associated with alcohol problems including dependence. (40)

In a meta-analysis by Gobbi *et al*, adolescent (18 years and younger) cannabis users were reported to have a 37% increase in the odds of developing depression relative to non-users (pooled OR: 1.37 (95% CI 1.16-1.62, I²=0%), a 50% increase in the odds of suicidal ideation (1.50 (1.11-2.03, 0%)), and 346% increase in the odds of suicidal attempt (3.46 (1.53-7.84, 61.3%)). (23)

Lastly, Marshall reports consistent associations between methamphetamine use and several mental health outcomes including depression, suicidal ideation and psychosis. Suicide and overdose appear to be significant sources of morbidity and mortality amongst young methamphetamine users. However, there was equivocal evidence for risk of HIV and other STDs and only weak evidence for association with dental diseases. (41)

Latent classes of substance use in young people

Reviews by Tomczyk *et al* and de Jonge *et al* focused on adolescents (aged 10-19) and young adults (aged 18-25), respectively. Both reported that similar latent class structures are identified in most studies: “low-level engagers”, “light alcohol and tobacco use”, “heavy alcohol and tobacco use class” and “heavy-use/polysubstance use”. (42,43)

Young adult membership of “heavy-use or polysubstance use” classes is predicted consistently by male gender, white race, peer substance use, depressive symptoms and parental drinking across studies. (43)

Whereas adolescent polysubstance use classes were predicted by higher age, higher parental and peer substance use and poor academic performance. (42)

Both de Jonge and Tomczyk highlighted important methodological points:

- Firstly most studies only reported a single polysubstance use latent class, therefore anyone who used substances aside from alcohol and marijuana were a member of this class, regardless of their risk of substance use disorders (SUDs), or other harmful outcomes. De Jonge asserts that this is suboptimal, as this approach does not distinguish between young adults who are at risk for developing harmful substance use and those who are not and consequently limits opportunities to develop targeted prevention strategies. (43)
- Ten out of twenty studies included multiple alcohol related measured indicators which could violate LCA assumptions of local independence and might make it less likely to distinguish different classes for other substance use even though such classes could exist. (42,43)
- All studies used 'type of drug' and 'frequency or pattern of use' as indicators to model classes. However, there are other characteristics that also impact the risk for SUDs such as the social setting in which the drugs are used and personal characteristics like SES. Including more diverse indicators could increase insight into the characteristics of young adults who are at risk of developing or maintaining SUDs. (43)

Table 1: Characteristics of reviews

Reference	N of studies by study design	Review aim	Evidence synthesis	Conclusion/Results
Predictors of Adolescent Substance Use				
De la Pena-Arteaga 2021	9 cohort 4 cross-sectional	Assess the relationship between childhood physical and sexual abuse and adolescent cannabis use	Systematic review & weighted means meta-analysis on studies that reported odds ratios & confidence intervals	Weighted mean effect (based on 4 studies): OR 1.39 (95% CI 1.12-1.66) for the relationship between child physical abuse & adolescent cannabis use. Weighted mean effect (based on 6 studies): OR 1.29 (95% CI 1.08-1.49 for the relationship between child sexual abuse & adolescent cannabis use.
Rossow 2016	99 cohort	Assess relationship between parental drinking and adverse outcomes	Scoping review with narrative synthesis	Large literature identified but with many limitations restricting ability to draw causal conclusions. However parental drinking was found to be statistically significantly associated with a child harm (alcohol use or related problems, other substance use, other outcomes) in almost 2 of every 3 published associations.
Rahin 2015	6 papers Did not specify designs	Assess the association between shame and substance use in young people	Systematic review with narrative synthesis	Vulnerability to shame appears to be associated with increased drug and alcohol use in young people.
Russel 2008	9 cross-sectional 3 case-control	Evaluate risk factors for methamphetamine (MA) use	Systematic review	Studies heterogenous which precluded pooling results for most risk factors: Pooled results presented below: When compared to low-risk youth, factors associated with MA use: hx heroin/opiate use (OR=29.3, 95% CI 9.8-87.8), family history of drug use (OR=4.7, 95% CI=2.8-7.9), risky sexual behavior (OR=2.79, 95%CI 2.25-3.46). In high-risk

				youth, factors associated with MA: family history of crime (OR 2, 95% CI 1.2-3.3), family history drug use (OR 4.7, 95%CI 2.8-7.9), family history of alcohol abuse (OR=3.2, 95% CI 1.8-5.6), and psych treatment (OR=6.8, 95% CI 3.6-12.9)
Hughes 2017	26 cross-sectional 11 cohort	Assess the effect of multiple adverse childhood experiences on health	Systematic review & meta-analysis using random effects model	Individuals with at least four ACEs were at increased risk of all health outcomes compared with individuals with no ACEs. Associations were weak or modest for physical inactivity, overweight or obesity, and diabetes (ORs of less than two); moderate for smoking, heavy alcohol use, poor self-rated health, cancer, heart disease, and respiratory disease (ORs of two to three), strong for sexual risk taking, mental ill health, and problematic alcohol use (ORs > three to six), and strongest for problematic drug use and interpersonal and self-directed violence (ORs > seven) . We identified considerable heterogeneity (I ² of >75%) between estimates for almost half of the outcomes.
Adan 2017	27 cross-sectional 5 cohort	Identify personality traits related to binge drinking	Systematic review: narrative synthesis	The main characteristics of personality related to the practice of BD, regardless of the theoretical model used, are high Impulsivity and high Sensation seeking, as well as Anxiety sensitivity, Neuroticism (Hopelessness), Extraversion and low Conscientiousness.
Dyer 2019	51 cohort (3 used in meta-analysis)	Assess associations of child and adolescent anxiety with later alcohol use and disorders	Systematic review: narrative synthesis & meta-analysis	Narrative synthesis: some evidence for a positive association between anxiety and later alcohol use disorders. Associations of anxiety with later drinking frequency/quantity and binge drinking were inconsistent. Type and developmental period of anxiety, follow-up duration, sample size and confounders considered did not appear to explain the discrepant findings. The meta-analysis also showed no clear evidence of a relationship between generalized anxiety disorder and later AUD (OR = 0.94, 95% CI = 0.47–1.87).
Outcomes of Adolescent Substance Use				
McCambridge 2011	54 cohort	Evaluate Adult Consequences of Late Adolescent Alcohol Consumption:	Systematic review: narrative synthesis	Consistent evidence that higher alcohol consumption in late adolescence continues into adulthood and is also associated with alcohol problems including dependence; Although a number of studies suggest links to adult physical and mental health and social consequences, existing evidence is of insufficient quality to warrant causal inferences at this stage.
Gobbi 2019	35 cohort	Assess association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood	Systematic review: narrative synthesis & random effects meta-analysis	Risk of depression, anxiety & suicidality in young adulthood (18-32 years) paralleled by academic unpreparedness, delinquency and poorer academic performance in some studies. Pooled OR of developing depression for cannabis users relative to non-users was 1.37 (95% CI 1.16-1.62, I ² =0%). OR for anxiety: 1.18 (0.84-1.67, I ² =42%). OR for suicidal ideation: 1.50 (1.11-2.03, 0%), and for suicidal attempt was 3.46 (1.53-7.84, 61.3%). Estimated population attributable risk of depression= 7.2%.

Marshall 2010	5 prospective cohort 4 retrospective reviews 34 cross-sectional 6 case control	Health outcomes associated with methamphetamine use among young people	Systematic review: narrative synthesis	Consistent associations between MA use and several mental health outcomes including depression, suicidal ideation and psychosis. Suicide and overdose appear to be significant sources of morbidity and mortality amongst young MA users. Equivocal evidence for risk of HIV and other STDs. Only weak evidence for association with dental diseases.
Methodological				
Tomczyk 2015	9 cohort 14 cross-sectional	Latent classes of polysubstance use among adolescents	Systematic review: narrative synthesis	Usually, 3-4 latent classes identified included= "no use" "low use", "alcohol only" "polysubstance use". Polysubstance use classes were unanimously predicted by higher age, higher parental and peer substance use, poor academic performance, other predictors were highly heterogeneous.
DeJonge 2022	20 studies (did not specify designs)	Latent classes of substance use in young adults	Systematic review: narrative synthesis	14 studies identified "low-level engagers", "light alcohol and tobacco use", "heavy alcohol and tobacco use" and "heavy use / polysubstance use" classes. 4 studies differentiated within the "heavy/polysubstance" class and found "traditional clubdrugs", "hallucinogens", and "wide-range illicit drugs" classes. Male gender and white race predicted membership of the "heavy-use/polysubstance use classes consistently across studies. Other predictors of polysubstance use that were consistent across studies were peer substance use, depressive symptoms, parental drinking and participating in an honor society.

Cohort Studies

Overview

One hundred and eleven cohort studies were included in our review. A large proportion were conducted in North America (n= 67). The remainder were from Europe (n=32), Australia and New Zealand (n=8), South America (n=2), and Asia (n=2). There were no studies identified from the Republic of Ireland (ROI).

The majority of the cohort studies utilised general population samples (n=89), while the remainder (n=22) specifically sampled young people with characteristics that may increase risk of substance use. Characteristics included previous substance use or mental health problems, a family history of alcoholism or drug use, adverse childhood experiences, low socioeconomic status, living in a high-crime neighbourhood, homelessness or contact with the justice system.

Factors associated with adolescent substance use

Eight-three longitudinal studies reported on factors associated with the initiation and pattern of alcohol and/or drug use during adolescence. (12,44–124) For the purposes of this review, we will report risk, protective and neutral factors. We further divide these into individual, family, social and environmental factors. (Table 2)

Individual factors

Male gender and advancing age among adolescents consistently exhibit connections with early initiation and increased frequency of substance use during adolescence. Externalising disorders, such as conduct disorder, are reliably associated with increased risk for early initiation of substance use. (89,90,99,110) Hopfer *et al* reported elevated risk (adjusted hazard ratios (aHR)) for initiation of ten different substances amongst those with conduct disorder compared to those without at age 15: alcohol (aHR: 1.99, 95%CI: 1.69-2.36), tobacco (2.10, 1.75-2.53), marijuana (2.76, 2.29-3.34), cocaine (9.38, 5.91-14.87), amphetamines (4.07, 2.96-5.61), club drugs (8.24, 4.89-13.89), sedatives (10.60, 5.65-19.91), opiates (3.73, 2.53-5.51), inhalants (4.73, 2.17-10.32), hallucinogens (6.26, 4.20-9.31). The analysis was replicated at the ages of 18 and 21 and with each iteration, a diminishing gap emerged between individuals with and without conduct disorder. (99) The evidence is less consistent for internalizing disorders, such as depression and anxiety.

Family factors

Adverse childhood experiences (ACEs) or traumas, such as neglect, emotional abuse, exposure to violence or parental incarceration, have been reported to have direct and indirect influence on risk of adolescent substance use. (56,59,69,75,93,94,125,126) Scheidell illustrated a dose-response relationship between the quantity of traumas experienced, and drug utilization. Adolescents who had experienced 4+ traumas had 6.43 the odds of marijuana use, and 9.86 the odds of cocaine use compared to those with no history of traumas. Similar association were demonstrated with drug use in emerging adulthood and adulthood but the strength of the relationship was attenuated relative to that during adolescence. (93)

Social factors

Peer substance use or deviance consistently emerges as a strong predictor of youth substance use. (45,73) Dubowitz reported that those with friends who use drugs had 4.76 times the odds of marijuana use relative to those with friends who are not using drugs. (94) Conversely, having friends who disapproved of alcohol or drug

use was protective. There are inconsistent results for relationships with the school environment and sports participation. (46,82,123)

Environmental factors

Delva demonstrated an association between negative neighborhood characteristics such as visible drinking or drug use on the streets. (74) Casswell reports that those in high alcohol consumption trajectories across adolescence had easy access to licensed premises. (101)

Table 2: Factors associated with adolescent substance use

Risk	Protective	Neutral	Inconsistent evidence
Individual			
<u>Demographic</u>	<u>Demographic</u>	Self-awareness	Academic ability
Male	Female sex	Cognitive empathy	Ethnicity
Increasing age	Black/African-American	Future expectations	Neuroticism
White ethnicity/race	Obesity		Anxiety
LGBT	<u>Mental health/behavioural</u>		Depression
Normal weight	Social/emotional competencies		Sexual abuse
Polygenic risk scores	Social awareness		Physical abuse
<u>Mental health/behavioural</u>	Empathy		
Externalising disorder (e.g. conduct disorder, ADHD)	Agreeableness		
Deviance/anti-social/criminal/delinquency	Conscientiousness		
Poor social skills or awareness	Objects to substance use		
Sensation seeking or risk taking or impulsivity	Recognizes substance use harmful for health		
Maladaptive coping	Optimism		
Lower self-control			
Dysregulated			
<u>Substance use</u>			
Age of initiation			
Frequency of use			
Past substance use			
Favourable attitudes towards alcohol			
Family			
Lower parental support	Caregiver connectedness	Perpetrator of maltreatment identity	Parental supervision
Parent-adolescent conflict	Larger household	Neglectful parenting style	High parental involvement
Poor relationship with parents	Higher quality of parental relationship	Discipline or attachment	Parental permissive norms e.g. provision of alcohol
Sibling substance use	Authoritative parenting style		SES/poverty
	Greater father involvement		Parental education

Siblings in gangs	Family fun together	Caregiver punitive behaviour	Living with two biological parents
Living alone	Parents who read with the child		Two/single parents household
Homelessness			
<u>Adverse childhood experiences</u>			
Exposure to violence			
Stress			
Emotional abuse			
Neglect			
Parental incarceration			
Parental divorce/separation			
Domestic violence			
Poor parental mental health			
Parental substance use			
Social			
Peer substance use	Peer disapproval of substance use	School staff trained in alcohol prevention	Peer popularity/ acceptance
Bullying	Less friends who drink	Peer grades	School bonds/engagement
Anti-social peers e.g. in gangs	Engagement in activities and relationships outside the family	Friends parents drinking	Religious engagement
Larger social network			Participation in sports
Environmental			
Neighbourhood levels of drug availability		Noxious neighbourhood characteristics	Urban/rural home location
Living in neighbourhood with more deviant youth		Area level SES	Neighbourhood crime
Ease of access to licensed premises		Community violence	
Liking for alcohol advertising			
Negative neighbourhood activities(e.g. drinking or drug-taking, robbery, arrests, fighting)			

Measures representing adolescent substance use

The definition of adolescent substance use varied considerably across different studies. Some focused on any use of substances, or the age at which drugs or alcohol were first initiated. Others examined the frequency of use over different time frames, including the past week, month, six months or year. Additional investigations characterized risky, hazardous or problematic substance use in diverse ways such as consumption before school or work, identifying harmful drinking through the AUDIT score, instances of binge or heavy episodic drinking, experiences of drunkenness or the diagnosis of substance use disorder (primarily employing DSM-IV criteria). Furthermore, the measures employed to quantify adolescent substance use were applied in wide range of methodologies within predictive modelling. Some studies employed a single outcome measure, while others amalgamated multiple substance use indicators into composite scores or latent classes to define their outcome. We detail these different outcome measures, how they were modelled and the different types of models used in Table 3.

Table 3: Outcome measures representing Adolescent Substance Use in cohort studies

Ref	Age (years)	Wave s	Outcome(s)	Timeframe	Outcome in models	Analysis
Lee 2022	12 to 18	4	Cigarette Alcohol Alcohol binges Marijuana use	In past 30 days	Each substance in separate models	Two-level hierarchical linear modelling
Adjei 2022	9 months to 14	6	Alcohol or drug experimentation	Use ever by age of 14	Alcohol & drugs in separate models	1)Group-based multi-trajectory cluster model (adversity) 2)Logistic regression
Ruiz 2021	9/17 to 10/18	2	Beer, wine, strong alcohol, tobacco, cannabis, other drugs	In past 6 months	Each substance use pattern in separate model	1)Latent transition analysis (substance use patterns) 2)Multinomial logistic regression
Yoon 2021	Recruited at 4 but drug Qs 12-18	4	Number of substances used incl. alcohol cigarette, marijuana and other drugs use	In past year.	Different substances combined within 1 model	Latent growth Poisson model (unconditional and conditional)
LaSpada 2021	14/16 to 21	2	Marijuana, cocaine, crack, ecstasy, hallucinogens, steroids, inhalants, pasta base, tranquilizers, stimulants, sedatives/barbiturates, analgesics	Use ever	1) Incident illicit substance use Vs never user (NU) 2)incident marijuana Vs NU 3)Cont. marijuana Vs NU 4)Discontinued marijuana Vs NU	Multinomial & binary logistic regression

Hopfer 2013	14/15 to 20	2	Tobacco, alcohol, marijuana, cocaine, amphetamines, sedative, inhalants, hallucinogens, opiates and club drugs)	Ever use, age of initiation	Time to onset of first substance use (all substances together) and also time to onset of each substance	Cox regression
Gau 2007	12 to 15	3	SUD (alcohol or nicotine or betel nut or illicit drugs)	Age at onset of SUD	All SUDs considered together	Cox regression
Houtepen 2020	Birth to 22 years	Uncle ar	I)) Harmful drinking (>16 AUDIT) II)) Problematic cannabis use (6 item screening test) III) Use of cocaine, amphetamines, inhalants, sedatives, hallucinogens, opioids	In past 12/12	Separate models for each substance use outcome	Binary logistic & linear regressions
Dubowitz 2019	4/6 to 18 years	7	Tobacco, alcohol, marijuana, cocaine, heroin, amphetamines, ecstasy, inhalants, hallucinogens, prescription medications	Frequency of use since age 18 & until a year ago	Models ran separately for each substance	1)Latent class analysis (LCA, neglect patterns) 2)Regression
Dubowitz 2019	Birth-18	9	Marijuana use recorded at 12. 14, 16,18	Ever in past year Frequency of use	Single substance	Logistic regression
Salcin 2019	16 to 18	2	Cannabis consumption	Scale: never, only once, 2-3 times, >3 times	Single substance	Logistic regression
Lamont 2014	12/13 to 17/18	5	Alcohol, tobacco, and other drugs (ATOD)	Frequency of use in past month & risky use	Patterns of ATOD created with LCA	1)LCA (ATOD use patterns) 2)Multinomial logistic regression
Shin 2012	13/18- 15/20	2	Alcohol, cannabis, cocaine, opioids and hallucinogens	Past year use	Combined 5 substances (= past year use of 5 illicit substances over 2 years)	Mover-stayer latent transition model
Maldonado- Molina 2010	15 to 16	2	Alcohol, cigarettes and cannabis	Ever use	Each substance in different models	Latent transition analysis
Scheider 2018	13 to 17	4	Alcohol use (consumption of >=1 full drink)	Past year	Single substance	Cross-lagged panel models
Gearhardt 2018	3/8 to 21/23	7	Alcohol problems, Drug problems Nicotine dependence:	Unclear? Number of problems at wave 7	Substance outcomes in different models	1)Latent class growth analysis (BMI trajectories) 2)Regression

McLaughlin 2015	11 to 20/21	7	Alcohol problems (AUDIT)	Assessed at ages 15, 16/17 and 20/21	Single substance use outcome	Unclear
Zapolski 2018	11/12 to 17/18	3	Alcohol (at least 1 drink) smoked cigarettes, smokeless tobacco, marijuana, other drugs	Frequency of use in last 30 days	Frequency measure based on the composite score of 6 substance use items	Structural equation modelling (SEM)
Yoon 2017	12 to 18	Unclear	Tobacco Alcohol (at least one drink) Marijuana use	How many days in past month	Substance use specified as latent var using log- transformed frequency of alcohol, tobacco & marijuana	SEM
Li 2018	15-28	Unclear	Heavy episodic drinking (≥ 5 drinks in 24 hours)	Frequency in last 12 months	Single substance	1)Generalised linear mixed model with log link and Poisson distribution. 2)Hierarchical Poisson regression model.
Scheidell 2019	11/12 to 24/32	3	Marijuana and cocaine use	Ever use Use in past year Initiation of use	Cocaine and marijuana in different models	Logistic regression
Ramos- Olazagasti 2017	10/13 – 13/16	3	Early initiation of alcohol (by 14)	Full drink ever	Single substance use outcome	Cox regression
Jackson 2016	10/15 to 13/18	6	Initiation of alcohol in early adolescence	Full drink ever	Single substance use outcome	Cox regression
Savage 2017	12 to 20s	Unclear	Alcohol, cigarettes	Ever use, frequency of use	Latent var combining alcohol & cigarette use	1)Latent growth curve analyses (trajectories of substance use) 2)Linear regression
Skinner 2016	18 months/ 6 to 31/41	Unclear	Substance misuse (Mediated by adolescent alcohol use and depression)	Simple screening instrument for substance abuse	Adult substance misuse incorporated into latent variable with mental health problems	1)LCA (substance misuse + mental health) 2)SEM
Evans Polce 2015	16 to 20	4	I)Cigarette use II)Binge drinking III Marijuana use	I)& III) Past 30 days	Substance trajectories presented separately	Intercept-only logistic time varying effect models

				II) > 1/month in last year		
Chen 2010	12 to 34	4	I) Alcohol use II) Binge drinking III) Marijuana use	I) & II) Frequency in past 12/12 III) Frequency in past 30 days	Substance outcomes in different models	Multilevel hierarchical regression modelling
Berge 2016	12/13 to 14/15	2	I) Drunkenness II) Onset of illicit drugs	I) ever happened II) ever use	Drunkenness and illicit drugs in separate models	Logistic regression
Windle 2019	17 to 33	3	Cigarette Alcohol Marijuana Heavy drinking episodes	Frequency over last 6 months	Substance use outcomes in different models	Longitudinal mixed model with a random intercept
Martino 2008	13 to 19	6	i) Heavy alcohol use (3-5 drinks in 24 hours) ii) Marijuana use	I) Frequency in last month II) Ever, frequency in past year and over last month	Substance use outcomes in different models	Latent growth curve analysis (trajectories of alcohol & marijuana)
Karamanos 2022	3 to 17	6	Marijuana, cocaine, LSD, ecstasy, speed/amphetamines, semeron, ketamine, mephedrone, psychoactive substances	Ever tried (assessed at age 14 and 17)	Grouped together as "drug use at age 14" and "drug use at age 17"	Logistic regression
Mehanovic 2020	12/14 to 12/15	2	Any illicit drug use	Past 30 days	Single substance use outcome	1) Multilevel logistic regression 2) Mediation models
Dubowitz 2016	4/6 to 18	Unclear	Marijuana use at 12, 14, 16 & 18	Ever use Level of use	Single substance use outcome	Multinomial logistic regression
Hilt 2015	14 to 16	2	Alcohol	Ever used, Frequency in past month	Single substance use outcome	Hierarchical multiple regression
Ennet 2016	11/13 to 13/15	5	Alcohol misuse scale constructed from: >5 drinks in a row, got drunk, got into a fight because of drinking	In past three months	Single substance use outcome	1) Latent profile analysis (of alcohol socialisation measures) 2) Growth curve model (of alcohol misuse scores)
Wills 1996	12 to 15	Unclear	Cigarette, alcohol and marijuana use	"Typical frequency"	Combined frequency score to represent substance use	Clustering analysis

Arpawong 2015	16 to 19	Unclear	I)Cigarettes, alcohol, getting drunk, marijuana =“social drugs” II)cocaine, hallucinogens, stimulants, inhalants, ecstasy, pain killers, tranquilizers, other hard drugs = “hard drug) III) Binge drinking IV) Substance abuse (DSM-IV)	I to III=Frequency in last 30 days IV = in past year	Four outcomes in separate models	Multilevel linear regression
Meyers 2014	12 to 22	Unclear	I)Alcohol initiation (age 12) II) Intoxication frequency (age 14 & 17) III)Alcohol dependence criteria (age 22) (DSM-IV)	I)ever use II) per month III) not specified	Combined into 1 outcome variable: “alcohol use behaviours”	Hierarchical linear regression
Samek 2014	Unclear to 22	Unclear	Nicotine, alcohol and other drug dependence (DSM-IV)	Meeting DSM-IV criteria at age 22	3 incorporated into a latent outcome var for externalising behaviours (also with risky sex, antisocial behaviour)	SEM
Hicks 2014	11 to 17	Unclear	I) alcohol, nicotine, and marijuana abuse and dependence. II)alcohol III)quantity of alcohol IV) nicotine V) marijuana use	I)ever II)past 12 months III) avg per occasion, max in 24 hours IV)per day V)lifetime	10 indicators combined into composite of adol. substance use and abuse and used as single outcome variable	Path analysis
Kendler 2014	All born 1970-1985 in Sweden	NA: registry study	Drug abuse identified in registries by ICD codes	ever	Single substance use outcome	1)Cox regression 2)Aalen linear hazards model
Delva 2014	12/17 to 14/19	2	Marijuana use	In past year	Single substance use outcome	Ordinal logistic regression
Mills 2014	Pregnancy to 14	5	I)cigarettes II)any alcohol use III) heavy drinking	I) past week II)Ever drank. Frequency in past week/month/year. III) >=5 drinks in 1 session, >=3 at least monthly	Four outcomes in separate models	Logistic regression
Wright 2013	7/16 to 11/22	3	Frequency of alcohol use and marijuana use	Number of days in past year that consumed	Alcohol and marijuana use in separate models	Fixed effect Poisson models in

						Hierarchical Linear modelling
Tompsett 2013	13/18 to 19/25	6	Alcohol abuse symptom, drug abuse symptoms	Not clear Potentially at the time of assessment	Two outcomes in separate models	Hierarchical linear modelling
Hicks 2013	11 to 17	3	Composite of adolescent substance use and abuse was calculated using 10 measures of alcohol, nicotine, marijuana use and symptoms of abuse/dependence	Ever/lifetime Past 12 month Quantities within 24 hrs	1 outcome so 1 model	1)Linear mixed models 2)Path analysis models
Shakya 2012	12/18 to 13/19	2	Binge drinking, Smoked Drunk, Used marijuana	In last year (Y/N)	Separate regression analyses for each outcome	Logistic regression
Marmorstein 2012	11/20 to 14/23	2	Nicotine, alcohol use or cannabis dependence (DSM IV criteria)	If fulfilled DSM criteria at either assessment	3 outcomes in 3 separate models	Logistic regression with generalized estimating equations (GEE)
Shin 2012	12/18 to 24/32	4	Heavy episodic drinking (HED)	Past year frequency	1 substance use outcome	Two-level growth curve modelling (HED trajectories)
Hicks 2012	11 to 17	2	I)Nicotine: frequency, quantity, dependence/abuse (DSM) II)Alcohol: quantity, dependence/abuse (DSM) III)illicit drug : number of types tried, number of lifetime marijuana uses, abuse & dependence symptoms (DSM)	I)days per month, average per day, ever II) per occasion, max per 24 hours & ever III) ever, lifetime, ever	9 measures used to calculate a substance abuse composite and used as single outcome	Standard biometric models
Traube 2012	11 to 14	3	i)Alcohol, tobacco ("social drugs") ii)Sniffed glue, gasoline. Marijuana, cocaine, crack, heroin, pain killers, tranquilizers, stimulants, sedatives ("hard drugs")	In last 30 days (Y/N) for each substance	Social drugs and hard drugs evaluated in 2 different models	Logistic regression
Mundt 2011	12/16 to 13/17	2	Alcohol initiation	Ever drank alcohol when not with parents or other family	1 substance outcome considered	Multi-level modelling using GEE
Ayer 2011	13/15 to 18/21	2	Alcohol use	W1: ever used W2: frequency quantity	1 substance outcome considered	1)Latent profile analysis (personality) 2)Linear mixed models

Corliss 2010	12 to 23	3	i)Marijuana ii)"Illicit drugs": ecstasy, cocaine, heroin, amphetamines, LSD/mushrooms (psilocybin) iii)Prescription drugs w/o prescription	Past year use (Y/N)	3 outcomes in separate models	Multivariable GEE repeated measures modified Poisson regression
Botticello 2009	12/17 – 13/18	2	Alcohol misuse: number of days of use, number of days consuming 5/more drinks, days of drunkenness	In past year	1 substance outcome considered	Multilevel multinomial logistic regression
Shin 2009	12 to 21	3	Binge drinking	In past year	1 substance outcome considered	Logistic regression
King 2008	13 to 25	5	Young adult drug dependence (DSM II-R diagnoses) of 8 different classes of drugs	Lifetime	DD considered as single outcome	1)Logistic regression 2)Path analyses
Merline 2008	18-35	4	i)Current alcohol use frequency ii)Heavy alcohol use (5/more drinks in a row) frequency iii)Alcohol use disorder (DSM-IV)	i)In past 30 day ii)In last 2 weeks iii)In past 5 year	3 outcomes in separate models	SEM
Buckner 2008	16-30	4	Alcohol abuse, alcohol dependence, cannabis abuse, cannabis dependence	Lifetime history assessed at T4	4 outcomes in separate models	1)Hierarchical logistic regression 2)Cox regression
Pardini 2007	13 to 25	Uncle ar	Alcohol use disorders (score representing total number of abuse and dependence symptoms)	Lifetime	1 substance outcome considered	Multivariable logistic regression
Sylvestere 2022	20 to 33	3	Combustible cigarettes, e- cigarettes, alcohol, binge drinking, cannabis	Any use Weekly use Daily use	Each outcome modelled separately	Modified Poisson regression
Lui 2023	0/4 to 19	Uncle ar	i)Alcohol & ii) cannabis use at frequency at ages 15-18 (and high school completion by age 19)	i) past 12 month ii) past month	Alcohol and cannabis treated as separate variables (investigated as both outcomes and mediators for high school completion)	Multilevel path models

Casswell 2002	18 to 26	3	i) Frequency of alcohol ii) Quantity of alcohol consumed per occasion	Yearly	in separate models	1)Random coefficients model 2)Latent class mixture modelling (drinking trajectories) 3)Logistic regression
Enstad 2007	1 to 14	6	Early onset of intoxication (EOI), early onset of drunkenness (EOD)	EOI=ever EOD=in last 12 months	EOI relative to abstinent, EOD relative to abstinent, EOI relative to EOD	Multinomial logistic regression
Taylor 2017	13 to 21	7	i)Patterns of cannabis use ii)Problematic substance use behaviours at age 21 (>16 on AUDIT, fagerstrom test, any use of illicit drugs	i) frequency of use ii)in previous 2 months.	Different models	1)Longitudinal LCA (cannabis trajectories) 2)Multinomial logistic regression
Martinez-Loredo 2018	13 to 16	3	I) alcohol, tobacco and cannabis use, II)intoxication episodes, III))presence of problem drinking	(I) and (III) past year (II) past month	combined into latent var	1)Latent class mixed modelling (polydrug trajectories) 2) Mixed multivariate analysis of covariance (MANCOVA)
Rougeaux	11 to 14	6	Health risk behaviours: I)alcohol, II)binge drinking, III)cigarettes IV)e-cigarettes V)illegal drugs VI)antisocial behaviour VII)sexual contact	I)full drink ever II) V) VI) ever III) & IV) tried at least once	separate models	Binary and multinomial logistic regression
Rawana 2011	12 to 23	7	Frequency of alcohol use & heavy drinking i.e. drunkenness	past year	separate models	Multilevel modeling
Lansford 2022	16 to 34	3	Substance use in established adulthood: AUDIT, Cannabis Use Disorders Identification Test Revised and Drug Abuse Screening Test	past 6/12	Separate models	Path analyses
Peterson 2018	11 to 17	9	Trajectories of alcohol consumption frequency	Across adolescence	Single substance	1)Group based trajectory modelling (drinking trajectories) 2)SEM 3)Growth curve analyses

MacLeod 2008	0 to 19	Unclear	Smoking tobacco Drinking alcohol	In 6/12 preceding assessment at age 10	Modelled separately and together	Logistic regression
Johnson 2019	12/26 to 30	3 or more	Cannabis use trajectory membership	Frequency in last 12/12	Single substance	Mixed effect logistic and linear regression
Picoito 2021	13/14 to 14	2 or more	Adolescent substance use and antisocial behaviours in latent classes: I) polysubstance use & ASB, II) alcohol & tobacco III) alcohol and physical fighting	use ever in lifetime	Combined into latent classes	1) Growth mixture modelling (emotional and behavioral symptoms aged 3-14) 2) LCA (patterns of substance use and antisocial behaviors at 14)
Lopez Vergara 2016	12 to ?	6	Any alcohol use, escalation in alcohol use		Single substance	Two-part random-effects model
Lee 2017	14 to 18	5	Alcohol and tobacco use trajectories	Frequency in last 30 days		Semiparametric
Maggs 2007	Birth to 42	6	Weekly drinking quantity at age 16, 23 and 33 and lifetime incidence of harmful drinking by age 42	weekly, lifetime		Hierarchical multiple and logistic regression
Guo 2001	10 to 21	4	Alcohol abuse and dependence	Those who met criteria in last 12 months at age 21		Logistic regression
Williams 2017	13/14 to 19/20	6	Regularity of cigarette smoking, alcohol drinking and cannabis use from early to late adolescence	ever, last 12 months	model 1: onset of substance use model 2: persistence in later adolescence (age 18-20)	Multinomial logistic regression
Manhica 2020	5 to ?	NA register study	Drug use disorder (DUD) & Drug crime conviction (DCC)	from 19 until diagnosis of DUD or DCC	different models	1) Group based trajectory analysis (poverty trajectories) 2) Cox regression
Nelson 2015	12 to 24	8	Trajectories of alcohol marijuana and tobacco use, substance use problems		substances separately, looked for overlap also	1) Group-based trajectory modelling approach
Maggs 2015	Birth to 11	2	Alcohol use: drinking, feeling drunk, having 5+ drinks	In last year of primary school	single substance outcome	Logistic regression

Hines 2023	Birth to 24	9	Patterns of cannabis use frequency and onset in adolescence		one substance	1)Longitudinal LCA (cannabis use frequency at multiple timepoints) 2)Multinomial logistic regression
Peck 2008	12 to 28	4	Heavy alcohol use & General alcohol use	At 21	single substance but different dimensions in different models stratified by gender	regression
Lewinsohn 1999	14/18 to 24	3	Substance use disorder (alcohol, cannabis, hard drug, multiple (vs single))	Between T2 and T3 meeting DSM criteria	Each SUD in different model adjusted for parental education & history of psychopathology	Logistic regression
DeBeck 2013	14/26 to 21/33	Unclear	Regularly injecting drugs		One outcome	Logistic regression

Outcomes associated with adolescent substance use

Twenty-eight cohort studies were identified that reported later-life outcomes associated with adolescent substance use. Broadly, outcomes reported were: substance use related, (44,98,100,127–141) social effects such as employment, education or contact with the justice system, (100,127–134,142–147) and lastly physical or mental health outcomes. (129–132,134,139,146,148–150) Some studies reported multiple outcomes. (127–134,139,146) As with studies reporting predictors of substance use, modelling approaches were varied. Characteristics of these studies are detailed in Table 4.

Substance use outcomes

All identified studies reported that adolescent substance use was a significant predictor of later life substance use patterns.

Regarding alcohol: Stephenson reported that young adult alcohol misuse was predicted by higher adolescent substance use, externalizing problems, time with friends, peer deviance, sports involvement, sleeping difficulties, parental discipline, positive alcohol expectancies and difficulty of life events. Protective factors were higher adolescent internalizing problems, parent–child relationship quality and time with parents. (135) Findings from Kim and Irons were consistent: each found that early initiation of alcohol (before age 13-14) was predictive of later-life alcohol problems. (127,136) Lee reported that chronicity of adolescent binge drinking and peer influences were predictive of persistent patterns of alcohol abuse amongst young adults. (44) (Table 3).

McCabe *et al* reports on successive cohorts of students followed up between 1976 and 2018 in the Monitoring the Future study. This showed that adolescents with the highest SUD symptom severity had increased odds of prescription drug use (aOR 1.55 (95% CI 1.11-2.16), prescription drug misuse (1.97 (1.39-2.80)) and SUDs symptoms (2.62(2.00-3.43)) in adulthood relative to adolescents with no symptoms of SUD at age 18. (137) Fothergill found that adolescent males who had used drugs or alcohol were significantly more likely to experience substance use problems in adulthood but this association was not present for females. (138)

Green, Trim and Higgins all used latent class methodologies: Green identified four latent classes of youth alcohol and marijuana use. All in the adolescent substance use classes had higher rates of adult substance dependence relative to non-users. (128–130) Rioux noted that early adolescent delinquency and deviant peers

was indirectly associated with drug abuse symptoms at age 28 via age of cannabis onset and drug use frequency at age 17. (98)

Social outcomes

Social outcomes included education, employment, “life success” and contact with the justice system.

With regard to education: Kelly reports that Australian adolescents who are polydrug users or consume alcohol are less likely to complete school than adolescents who do not use drugs or alcohol. (151) Green reports a link between alcohol consumption amongst English students and lack of educational progression, but identified that downstream factors associated with drinking, such as truancy and school suspension contribute to negative educational outcomes. (145) Similarly, O’Neill found that adolescents who drank alcohol (relative to minimal users) were significantly more likely to be NEET in the future relative to minimal alcohol users. Parental monitoring and good teacher-student relationships were protective against alcohol use. (142)

El Haddad *et al* reported that cannabis use at least weekly amongst French students was associated with increased odds of unemployment (OR 1.72(1.16-2.57)) as was alcohol dependence (OR 1.65 (1.16-2.34)) and multiple substance use (OR 2.44(1.44-4.12)). Education was a protective factor. (147) Interestingly, Najman found that adolescent use of cannabis or amphetamines did not adversely impact life success (a composite measure including employment) at 30 years however concurrent drug use did. (144)

Contact with the justice systems is consistently predicted by patterns of heavy or prolonged substance use such as binge drinking, daily cannabis use or polydrug use. (128,130,131,133)

Health outcomes

There were ten studies that reported health outcomes associated with substance use during adolescence.

The majority focus on mental health outcomes such as psychosis, depression or anxiety and self-harm. As with justice system contact, heavier patterns of substance use predict greater risk of negative mental health outcomes. (130,134)

Noorbakhsh and Meier each investigated cognitive outcomes. (139,149) Noorbakhsh reported on neurocognitive functioning amongst North Americans and concluded that early initiation of cannabis potentially results in more working memory deficits in female users than males. (149) Meier reported on neuropsychological decline. While adolescent cannabis users with dependence at age 18 had lower Intelligence Quotient (IQ) at ages 5, 12 and 18, there was no significant evidence that they showed greater IQ decline from age 12-18 relative to non-dependent adolescents. (139) (Table 6)

Pascale reported weak direct effects between adolescent alcohol misuse and early midlife physical health (self-reported somatic symptoms) and life satisfaction but there was stronger evidence for indirect effects whereby young adult and early midlife alcohol problems serially mediated the relationship between adolescent alcohol misuse and early midlife somatic symptoms. (148)

Roy investigated mortality rates and factors increasing the risk of death amongst a cohort of street youth in Montreal. Drug injection in the last six months (adjusted hazard ratio (aHR) 2.7 (95%CI: 1.2-6.2)) and daily alcohol use in last month (3.2 (1.3-7.7)) were independent predictors of mortality. (28)

Table 4: Studies reporting later-life outcomes associated with youth substance use (n=29)

Reference	Age	Study population	Exposure(s)	Outcome(s)	Analysis
Substance use outcomes only					
Stephenson 2020	12/14 to 20/26	N=3402 Twins	<u>Risk</u> : Adolescent substance use, positive alcohol expectancies, higher academic performance, externalising problems, peer deviance, sports involvement, sleeping difficulties <u>Protective</u> : internalizing problems, parental relationship quality, spending time with parents	Alcohol misuse	1) Split-half exploratory factor analysis & confirmatory factor analysis 2) Linear mixed model
Kim 2017	13 to 15	N=1833 Students	<u>Risk</u> : Early initiation and frequent alcohol, antisocial peers & siblings, <u>Protective</u> : school protection <u>Neutral</u> : family influence	Heavy drinking, alcohol harm	Multiple-group SEM
McCabe 2022	18 to 35/50	N=5317 Students	<u>Risk</u> : Adolescent SUD symptom severity (alcohol, cannabis or other drug use disorders (DSM))	Use of prescription drugs, prescription drug misuse, SUD symptoms in adulthood	Logistic regression using GEE
McCauley Ohannessian 2015	15/19 to 26	N=225 Children of parents with SUD relative to those without	<u>Risk</u> : Age of onset of regular drinking, <u>Neutral</u> : Age of onset of tobacco and marijuana use	Alcoholism, drinking to get drunk	Multivariate analysis of variance (MANOVA)
Fothergill 2006	6 to 32	N=1242 Community	<u>Risk</u> : adolescent substance use, low SES, first grade underachievement, low parental supervision, First grade aggression <u>Protective</u> : Educational attainment, shyness, <u>Moderating</u> : Gender (males 26% more likely than females to report abuse/dependence)	Substance use problems	1) Latent construct for drug & alcohol problems 2) SEM
Lee 2011	10 to 21/33	N=808 Students in schools in high-crime areas	<u>Risk</u> : Chronicity of adolescent binge drinking, antisocial peers	Alcohol abuse disorder persistence	1) Growth mixture models 2) Multinomial logistic regression
Meier 2018	3 to 38	N=1037 Community	<u>Risk</u> : frequent substance use in childhood, family SUDs, child psychopathology (conduct disorder, depression), early exposure to substances, sex & SES	Persistent substance dependence	1) Summed risk factors to create index 2) Evaluated predictive accuracy using AUC, sensitivity,

					specificity, PPV & NPV
Rioux 2018	6 to 28	N=1038	<u>Risk</u> : Early cannabis use onset (13-17), early adolescent delinquency <u>Mediators</u> : Cannabis, alcohol & other drug frequency at age 17	Drug (any) abuse symptoms	1)Logistic regressions 2)Path models
Enstad 2019	14/16 to 18/25	N=1115	<u>Risk</u> : Early onset of drinking, early onset of excessive drinking, male, hyperactivity <u>Neutral</u> : Conduct problems, early sexual intercourse, friend substance use, age, maternal education, family alcohol & drug use.	Hazardous drinking (AUDIT score>8)	1)Modified Poisson regression 2)Logistic regression (robustness check)
Englund 2008	Birth to 28	N=178 Low-income	<u>Risk</u> : higher alcohol consumption (age 16), maternal alcohol consumption, externalising behaviour (age 9), higher academic achievement	Quantity of alcohol per occasion, alcohol use disorders	Multinomial logistic regression
Swift 2008	14 to 24	N=1520 School	<u>Risk</u> : adolescent cannabis and tobacco use, mental health problems	Problematic cannabis use (24)	Logistic regression
<i>Social outcomes only</i>					
El Haddad 2022	18/30 to 21/33	N=1427 Students who had not worked previously	<u>Risk</u> : High frequency of cannabis use, depression, alcohol dependence <u>Protective</u> : Education <u>Neutral</u> : frequency of tobacco and alcohol use, area deprivation, living place	Employment at 3 year follow up	GEE
O'Neill 2015	11/12 to 20/21	N=4500 Students	<u>Risk</u> : School disengagement (11-15), "late onsetters", "steady increasers"	NEET	1)Latent class growth analysis (alcohol use) 2)Regression
Kelly 2014	10 to 16	N=2287 Students	<u>Risk</u> : mid adolescent polydrug use, adolescent alcohol consumption, peer drug use, academic failure <u>Protective</u> : no drug use <u>Neutral</u> : low school connectedness	High school non-completion	1)LCA (substance use) 2)Logistic regression
Najman 2022	21 to 30	N=2350 Population	<u>Risk</u> : cannabis or amphetamine use at 30, cannabis use disorder by 21, cannabis & amphetamine co-use, adolescent behaviour problems <u>Neutral</u> : early age of onset of cannabis or amphetamine use (not significant when adjusted for drug use at 30 year mark)	Life success: composite measure of income, education, home ownership, intimate relationships, life satisfaction & happiness)	Binary or multinomial logistic regression
Green 2010	14 to 17	N=10000 Students	<u>Risk for I</u> : drinking alcohol, truancy, suspension from school (alcohol risk factor for other factors) <u>2015</u>	I) NEET II) GCSE score	1)Multilevel framework 2)Regression modelling

<i>Health outcomes only</i>					
Pascale 2022	16 to 34	N=2733 Twins	<u>Risk</u> Adolescent alcohol misuse: weak direct, and indirect via young adult and early midlife alcohol problems.	Physical health, life satisfaction	Serial multiple mediational models
Noorbakhsh 2019	12/13 to 16/17	N=3826 Students	<u>Risk for I)</u> cannabis use <u>Moderator:</u> Gender (females seemed to experience a stronger effect)	Neurocognitive functioning: I) spatial working memory, II) delayed recall memory, III) perceptual reasoning & IV) inhibitory control	Multilevel linear models
Roy 2004	14 to 25	N= 1013 Street youth	<u>Risk:</u> daily alcohol use in the last month, homelessness in the last 6 months, drug injection in the last 6 months	Mortality	Cox regression
<i>Multiple outcomes</i>					
Lui 2023	5 to 19	N=5521 General	<u>Risk for I) and II):</u> Early childhood adversity (0-4), early cannabis onset (14), greater behavioral problems, alcohol & cannabis use frequency (15-18) <u>Protective for II:</u> low academics	<u>Social</u> I) High school non- completion <u>Substance</u> II) Alcohol & cannabis use frequency at 15-18	Multilevel path analysis
Irons 2015	11 to 24	N=1512 High-risk	<u>Risk for I) to III):</u> alcohol exposure &/or intoxication by age of 14 <u>Neutral for IV) to V):</u> alcohol exposure &/or intoxication by age of 14	<u>Substance</u> I) Use & abuse of alcohol <u>Social</u> II) Antisocial behaviour III) Dependent stressful life events IV) Social functioning V) Independent adult functioning	Logistic regression
Green 2016	8-12 to 25	N=678 Urban	<u>Risk for I to III):</u> "High dual use" and "moderate alcohol increasing marijuana" classes <u>Protective for I to III):</u> "non-use" or "moderate alcohol classes" <u>Neutral for IV to V):</u> alcohol and marijuana use classes	<u>Substance</u> I) Adult substance dependence <u>Social</u> II) High school graduation III) Criminal justice records IV) Income V) Employment	1) Latent profile analysis patterns of alcohol & marijuana use) 2) Examined differences in outcomes by latent class membership
Trim 2015	16 to 22	N=536 High-risk	<u>Risk for I to III):</u> "dual chronic" <u>Protective for I to III):</u> "resolved" <u>Neutral for IV):</u> all classes Latent classes: dual chronic, increasing. ADU/persistent ASB, persistent. ADU/adolescent ASB, decreasing drugs/persistent .ASB and resolved	<u>Substance</u> I) Substance dependence <u>Health</u> II) Antisocial personality disorder III) Negative psychosocial outcomes <u>Social</u>	1) Latent class growth analyses (antisocial behavior + substance use) 2) Multinomial logistic regression

				IV) Role attainment	
Higgins 2021	11/12 to 20/21	N=2039 General	<u>Risk</u> : Polydrug use class at higher risk for all negative outcomes relative to "alcohol", "alcohol+tobacco", "alcohol+tobacco+cannabis"	<u>Substance</u> I) Excessive drinking, drug or cannabis abuse <u>Social</u> II) NEET III) Justice, IV) Offending <u>Health</u> V) Psychosis, self-harm, depression, medication, services	1) LCA (substance use patterns) 2) Linear & logistic regressions
Copeland 2022	9 to 30	N=1420 General	All definitions of early cannabis use were associated with multiple adult outcomes in models that adjusted for sex and race/ethnicity. Daily, continued-over-time cannabis use beginning on adolescence was most problematic for a range of adult outcomes	<u>Substance</u> I) SUD <u>Health</u> II) Anxiety/depressive disorder III) health <u>Social</u> IV) risky/illegal behaviors V) wealth VI) social function 7) "derailments": dropping out of high school, felony charge, social isolation, severe health problems	Logistic, Poisson and linear regressions
Meier 2018	5 to 18	N=1989 Twins	<u>Risk for I</u>): low IQ <u>Neutral for II</u>): cannabis use	<u>Substance</u> 1) Cannabis use & dependence <u>Health</u> II) Neuropsychological (IQ) decline (between 12-18)	Linear regression
Shanahan 2021	7 to 20	N=1482 Schools	Frequent teenage cannabis use was more consistently associated with age 20 functional outcomes compared to frequent teenage nicotine or alcohol use. Strongest associations with subsequent substance use	<u>Substance</u> I) problematic substance use <u>Health</u> II) psychotic symptoms III) internalizing symptoms <u>Social</u> IV) Aggression, V) delinquency, VI) financial difficulties/debt, VII) social exclusion VIII) general well-being, IX) NEET	Linear or logistic regressions

Goodrum 2020	12 to 17	N=3604 General	<u>Risk for I:</u> adolescent risk behavior including substance use <u>Risk for II:</u> violence exposure <u>Protective for I) & II):</u> High family cohesion	<u>Social</u> I)Violence exposure (wave 2) <u>Health</u> II)PTSD and depression (wave 3)	SEM
Hill 2000	10 to 21	N=808 High-risk	<u>Risk for I & II:</u> binge drinking <u>Protective for I & II:</u> non bingers	I)Negative outcomes: Depression, criminality, alcohol use or dependence, and drug abuse or dependence at age 21. II) Positive outcomes: academic attainment, involvement in productive activity, involvement in prosocial activities, and parental bonding at age 21.	1)semiparametric group based modelling (binge drinking trajectories) 2)Logistic regression
Boden 2019	Birth to 35	N=1065 General	<u>Risk for all outcomes:</u> Membership of trajectories with higher levels of use	<u>Substance</u> I)SUDs <u>Health</u> II)) Mental health disorders: <u>Social</u> III) Socio-economic: education, SES; weekly income; savings & investments; home ownership; on welfare unemployed 4)Social: family situation, intimate partner physical violence; & arrest/conviction	1.Latent class modelling (cannabis use trajectories) 2.Multinomial and linear regressions

Discussion

Summary of evidence

This review examined one-hundred and eleven prospective cohort studies based on sixty-six unique cohorts of young people, and twelve systematic or scoping reviews that reported on the predictors of, and outcomes associated with ASU.

There is consistent evidence that adolescence is the peak period during which substance use first occurs. Alcohol is the most commonly used substance among European adolescents, with 79% of school students (aged 15 to 16) describing use of alcohol at least once in their lifetime, and 47% in the last month. (152) 41% and 40% report use of cigarettes or e-cigarettes use respectively at least once in their life. Lifetime prevalence use of cannabis was 16%, with 5% reporting use of illicit drugs other than cannabis. (152) Notably, substance use rapidly escalates during early adolescence, with 33% trying alcohol, 6.7% experiencing intoxication, 18% experimenting with cigarettes, 2.9% becoming daily smokers, and 2.4 % trying illicit drugs at age 13 or younger. (152)

Most substance use peaks in late adolescence and early adulthood however a proportion do not follow the usual trajectory. (155) Clear differences are noted between substances for the risk of continued use, cessation, or progression to problematic or dependent use. For instance, most who are exposed to cannabis do not become regular or dependent users but there is a minority who develop persisting heavy cannabis use into mid-adulthood. (134) On the contrary, amongst a cohort of street youth who initiated drug injecting, 63% became regular injectors within a month. (154)

A wide range of factors are associated with adolescent substance use with strongest effects reported for history of conduct disorder, prior substance use, peer or parental substance use and adverse childhood experiences. There is consistent evidence that early and/or heavy substance use during adolescence is a risk factor for continued problematic substance use during adulthood. It has also been associated with disruption of education, reduced chance of employment, and negative health outcomes.

Limitations of the evidence

Adolescent substance use (ASU) is defined in numerous different ways in the published literature ranging from “ever use” to hazardous patterns of use such as heavy episodic drinking to SUDs. This makes drawing direct comparisons across studies challenging and likely contributes to inconsistent results.

There has been limited exploration of the role of the wider community (beyond family and peers) and environmental factors associated with adolescent substance use. Only four papers, originating from the US, South America and New Zealand, reported on environmental factors aside from area-level deprivation and living in an urban or rural location. (74,101,116,126) It is well accepted that the determinants of health arise from factors at individual, social and community networks, living and working conditions, general socio-economic, cultural and environmental levels. (155) Further exploration of the determinants of adolescent substance use taking into account all layers of influence are warranted. Consideration could be given to use of alternative data sources to provide indicators of drug availability in communities, such as instances of drug seizures or arrests.

The literature is dominated by papers focusing on alcohol and cannabis. (156) Adolescent use of other illicit drugs such as cocaine, heroin or stimulants are frequently grouped into composite measures of “hard drugs” or “polysubstance users” limiting ability to disentangle the predictors and harms associated with different substances. For instance, only three studies in our review investigated the influence of neglect, conduct disorder and ACEs on cocaine initiation and use, using data collected in the US eleven to fifteen years ago.

(93,99,124) Many risk and protective factors, and outcomes associated with adolescent use of specific illicit drugs other than cannabis remain unexplored.

Far more emphasis has been placed on investigating predictors of substance use, relative to outcomes associated with adolescent substance use. Delineating outcomes associated with ASU including risks of acute intoxication, short term effects of regular heavy use, disruption of social transitions to adulthood, entrenching sustained, heavy or dependent substance use that affects health in adulthood and intergenerational risks is important to guide harm reduction and treatment efforts. (1,157)

Lastly, although most studies adjusted for potential confounders, the variables adjusted for vary substantially between studies. This makes it challenging to delineate possible causal relationships due to potential unmeasured confounding.

Strengths and limitations of the review

The inclusion of prospective cohort studies serves to reduce concerns about recall bias and reverse causation. This review is limited by the fact that only one database was searched however search comprehensiveness was improved through citation searches and use of web search engines. Assessing the quality of included studies was beyond the scope of this review.

Conclusions

Evidence regarding adolescent substance use has rapidly expanded in recent years. However, a number of important research gaps remain. Firstly, there is a preponderance of studies focusing on individual and family risk factors with less attention given to upstream and protective factors thus far. Further exploration of the social and environmental determinants of ASU in a European context is warranted to guide development and implementation of targeted interventions in the most appropriate settings. Secondly, substance use patterns are rapidly changing. A particularly striking trend is the escalating prevalence of cocaine use amongst the Irish population. (158) Longitudinal exploration of factors specifically associated with cocaine initiation in general adolescent cohorts are limited as historically the prevalence of cocaine use was low during adolescence. Leveraging the timeliness of GUI data, we will investigate the factors associated with cocaine initiation and frequency of use, to provide evidence that can be used to interrupt and reverse this trend. While there is consistent evidence that early life exposures, such as parental substance use, are associated with ASU, there is less understanding of the pathways through which these effects are realized. In our analyses we will clarify causal direct and indirect pathways, thereby identifying a range of targets for interventions. Lastly, there has been comparatively less focus on the longitudinal social and health outcomes linked to ASU, relative to predictors of ASU, including its potential to disrupt critical transitions between adolescence and adulthood. We will harness the extensive GUI data which includes a wide range of important measures of progression to inform potential interventions impacting on progression or recovery and harm reduction. Our analyses of GUI will advance understanding of ASU and generate contemporary evidence that can be used to inform policy interventions and day-to-day practice. This literature review also examined analytical approaches in this literature. This, alongside the pattern of data collection within specific waves of GUI will guide the analytical approaches used in this work.

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