Trajectories of alcohol-related harm among young people

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ABSTRACT

In many high-income countries such as Australia, alcohol use has declined in young people since the early 2000s but there is conflicting evidence around reductions in alcohol-related harm. A key issue around quantifying alcohol-related harm is that different data sources can show vastly different patterns due to varying sample characteristics or methods of measurement. The studies comprising this thesis aimed to address these gaps by using a variety of data sources to examine: 1) trends in self-reported harms across age, period, and birth cohort using national surveys (n=121,281); 2) developmental patterns of blackouts, a very common harm, and predictors of high-risk patterns in a recent birth cohort (n=1,821); 3) developmental transitions between different types of alcohol-related harm and predictor of high-risk patterns in a recent birth cohort (n=1,828); and 4) risk factors for experiencing clinical alcohol-related harm for the first time at a younger age and compare rates of subsequent harm by age at first experience of clinical harm in a linked cohort (n=10,300).

Several notable findings were identified. National data indicate that alcohol-related risky behaviours are much less common in recent birth cohorts, though they continue to be most prevalent in young people. Males generally had twice the prevalence of risky behaviours compared to females, but with reduced effect among more recent birth cohorts. Longitudinal cohort data indicated that escalating experience of harms, particularly blackouts and psychosocial harms (e.g., getting into fights) increased risk of early adulthood alcohol use disorder symptoms. Females were at higher risk of experiencing physiological harms such as blackouts earlier in life compared to males. Finally, analyses of linked hospital service data indicated that females were at higher risk of accessing hospital services for an alcohol-related problem for the first time at a younger age. Younger people were more

likely to have subsequent injury-related ED presentations but less likely to be hospitalised. Past year hospital service access rates in this cohort were much higher than the same-aged general population.

This thesis highlights important developments in young peoples' experience of alcohol-related harm. The identification of a closing male-female gap in harms and of female status as a risk factor for early harm warrants future research and shifts to the approach of harm reduction and prevention among young people.

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ABBREVIATIONS

AIC	Akaike Information Criterion
APC	age period cohort
APDC	Admitted Patient Data Collection
APSALS	Australian Parental Supply of Alcohol Longitudinal Study
ARR	adjusted rate ratio
AIRR	adjusted incidence rate ratio
AUD	alcohol use disorder
BAC	blood alcohol content
BIC	Bayesian Information Criterion
CI	confidence interval
ED	emergency department
EDDC	Emergency Department Data Collection
DACS	Data-linkage Alcohol Cohort Study
DALY	disability-adjusted life years
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, fourth edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, fifth edition
HED	heavy episodic drinking
ICD-9	International Classification of Diseases, ninth edition
ICD-10-AM	International Classification of Diseases, tenth edition Australian modification

IRR	incidence rate ratio
NDSHS	National Drug Strategy Household Survey
NSW	New South Wales
OR	odds ratio
PR	prevalence ratio
RECORD	REporting of studies Conducted using Observational Routinely-collected Data
RR	rate ratio
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
WHO	World Health Organisation

LIST OF PUBLICATIONS INCLUDED IN THIS THESIS

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alcohol consumption and harms: A prospective cohort study. Drug Alcohol Depend. 2022;237:109533. Available from: https://doi.org/10.1016/j.drugalcdep.2022.109533

LIST OF PRESENTATIONS DURING CANDIDATURE

1. **Yuen WS**. Trajectories of adolescent alcohol consumption: A prospective cohort study. Presented at the National Drug and Alcohol Research Symposium, Sydney, 2019.
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5. **Yuen WS.** Transitions Across Physiological and Psychosocial Alcohol-related Harms in Adolescence. Presented at the National Drug and Alcohol Research Symposium, Sydney, 2020.
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7. **Yuen WS.** Trajectories of alcohol-induced blackouts in adolescence: Early risk factors and alcohol use disorder outcomes in early adulthood. Presented online at the National Drug and Alcohol Research Centre HDR Showcase, 2020.
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11. **Yuen WS.** Patterns of Alcohol-related Harm: Findings from a national survey, longitudinal cohort, and hospital records. Presented as part of the University of Tasmania School of Psychology seminar series, Hobart, 2022.
12. **Yuen WS.** Gen Z: Drinking less, but what about alcohol-related harms? Presented online as part of the National Drug and Alcohol Research Centre Webinar Series, 2022.

1. CHAPTER 1: INTRODUCTION

This chapter examines the published research on alcohol consumption and associated harms in people aged 12-24 years (hereafter referred to as 'young people' or 'youth'). In the first section, I present an overview of the current prevalence of alcohol consumption in youth and the impacts of alcohol on young peoples' development. In the second section, I discuss the different conceptualisations of alcohol-related harm and the various harms that young people typically experience. In the third section, I summarise the recent trends in young peoples' alcohol consumption and related harms. In the fourth section, I examine what is currently known about the development of alcohol-related harms in young people. In the fifth section, I discuss different ways of measuring alcohol-related harm in addition to the advantages and disadvantages of each method. Finally, I present a summary of the current gaps in knowledge regarding alcohol-related harm among young people and propose a program of research to address these gaps.

1.1. Alcohol consumption in young people

1.1.1. Prevalence of alcohol consumption

Due to its legality in many countries, alcohol is one of the most commonly consumed psychoactive substances in the world (1, 2). In 2016, 43% of the global population reported having consumed alcohol in the past 12 months (3). Notably, this includes people who are younger than the legal age of alcohol purchase and/or drinking in their respective countries (typically 18-21 years; 4). Indeed, global surveys report that people in countries where alcohol consumption is the norm tend to initiate alcohol consumption between 16 and 19 years of age (1, 5). In Australia, where the legal age of alcohol purchase and drinking at a licensed venue is 18 years, 17% of secondary school students aged 12 years reported that

they had consumed alcohol in the past year, increasing to 55% for students aged 15 years and 76% for students aged 17 years in 2017 (6). Evidently, alcohol remains accessible to young people who are underage, with adolescents reporting that they are supplied alcohol by parents, peers, family members, or other adults (6).

One common pattern of alcohol consumption observed among young people is heavy episodic drinking (HED; 3). This is defined by the WHO as the consumption of at least 60g of alcohol on at least one occasion per month, and is known to increase risk of acute harms such as injury (7), in addition to chronic harms such as alcohol use disorders (AUD; 8). Globally, the prevalence of HED amongst people who drink alcohol is 45.7% in people aged 15-19 years and 48.5% in people aged 20-24 years, which is in contrast to 39.5% of the total population aged 15 years and older (3). In 2017, 31% of Australian students aged 12-17 years who consumed alcohol drank five or more standard drinks (i.e., ≥ 50g of alcohol; 6, 9). Risky drinking typically peaks for Australians aged 18-24 years, with a higher proportion (41%) exceeding the single-occasion risk guideline compared to any other adult age group for both men and women (10).

1.1.2. The impact of alcohol consumption on adolescent development

Adolescence and young adulthood is an important period of neurodevelopment (11, 12) that is vulnerable to developmental disruption from heavy alcohol exposure (13, 14). For instance, a neuroimaging study of alcohol-naïve adolescents aged 14 to 19 years found that those who subsequently initiated alcohol consumption within 24 months had impaired neurodevelopment across brain regions associated with executive processes such as inhibitory control and memory compared to those who remained abstinent (15). A similar study of young people aged 12 to 21 years who had never used alcohol found that those

who subsequently initiated alcohol showed delayed development of white matter, particularly in those who engaged in heavy drinking (16). Another study found that people aged 16 to 20 years who engaged in heavy drinking (defined as > 100 lifetime episodes of alcohol consumption) had impairments in white matter tracts, the tissues responsible for communication between brain regions (17). These imaging results are reflected in studies of cognitive performance which show that adolescents who drink more show poorer performance on working memory, perceptual reasoning, and inhibitory control tasks in adolescence and early adulthood (18-20). Though the majority of studies described here considered some baseline characteristics that may influence brain development (e.g., socioeconomic status, externalising symptoms), other contributing factors such as diet and family history of substance use problems were not taken into account (15-18, 20). In sum, alcohol consumption in adolescence may have substantial negative impacts on brain development. Examination of how alcohol impacts young people as they age from adolescence to adulthood is therefore crucial in order to prevent further harm.

Summary of Section 1.1. Alcohol consumption in young people

- Alcohol consumption is prevalent amongst people who are underage.
- Young people are more likely to engage in heavy episodic drinking than older adults.
- Alcohol consumption in adolescence and early adulthood may be associated with deficits in brain development.

1.2. Alcohol-related harms in young people

1.2.1. Health and socioeconomic burden of alcohol consumption

An analysis of the global burden of alcohol consumption found that any alcohol consumption is a risk to health, with the likelihood of health loss increasing at higher consumption levels (21). The impacts of alcohol consumption result in a substantial economic burden, with societal costs due to alcohol consumption accounting for over 1% of gross national product across high- and middle-income countries (22). In Australia, the estimated societal and economic cost of alcohol in 2018 was over AUD$66.9 billion, which was more than ten times the revenue generated by alcohol taxation in the same year (AUD$6.5 billion; 23). Many of these costs were attributable to health-related expenses, which included direct costs to the health system (8%) and costs due to disability and years of life lost as a result of morbidity (31%) or premature mortality (39%; 23).

Globally, alcohol consumption is the single greatest contributor to years of life lost due to disease or premature mortality among young people aged 15 to 24 years ('disability-adjusted life years' [DALY]; 21, 24). This is also the case in Australia, where alcohol consumption was the leading risk factor for death and disease among young people in 2018 (27% of DALYs in people aged 15-24 years are attributable to alcohol; 25). Though there are at least 60 chronic diseases that have been linked to long-term heavy alcohol consumption (e.g., liver disease; 26, 27), young people are primarily impacted by conditions resulting from acute alcohol exposure with the exception of AUD. Indeed, among Australians aged 15 to 24 years, alcohol-attributable years of life lost due to disability are predominantly AUDs but most alcohol-attributable deaths are due to suicide, self-inflicted injuries, and road traffic injuries (25).

1.2.2. Defining alcohol-related harms in the context of this thesis

The term 'alcohol-related harms' in the context of this thesis refers to a wide variety of negative consequences of alcohol consumption that are not limited to the health conditions discussed in the previous section. Whilst alcohol-related harms such as AUDs and injuries constitute more severe, high impact harms with direct links to death and disability, these are uncommon among the general population. Among young people, harms that are more prevalent include negative physiological consequences with short-term impact to the individual such as hangovers and blackouts (28-30). As alcohol consumption typically occurs in a social context, there are also negative consequences of alcohol consumption outside of physical health, ranging from social conflicts on a night out to causing extensive relationship and/or work problems.

In this thesis, harms that predominantly impact the individual's physical functioning are referred to as 'physiological alcohol-related harms' (e.g., hangovers). Harms that impact the individual on a psychological and/or interpersonal level are referred to as 'psychosocial alcohol-related harms' (e.g., damaging relationships). Harms that accrue due to prolonged risky levels of alcohol consumption are known as 'chronic alcohol-related harms' (e.g., liver disease), whereas harms occurring during or in close temporal proximity to the period of intoxication are referred to as 'acute alcohol-related harms' (e.g., falls). Acute alcohol-related harms are often the result of alcohol-related risky behaviours, which are activities undertaken while under the influence of alcohol that increase risk of harm (e.g., operating a motor vehicle). Whilst these behaviours do not always lead to harm, assessment of risky behaviours can nonetheless provide a way of estimating potential harms associated with alcohol use.

1.2.3. Alcohol-related harms experienced by young people

This thesis focuses on alcohol-related harms that young people typically experience, including harms of varying degrees of severity. Though alcohol-related harm is not a definitive outcome of alcohol consumption, harms are still a relatively common experience among young people who use alcohol. According to survey studies, over a third of young people who drink report experiencing some form of alcohol-related harm in the past 12 months (28-31). Among adolescents and young adults, physiological harms tend to be more common than psychosocial harms (28-30). This is to be expected given that most physiological harms captured in these surveys are a consequence of high blood alcohol concentration (BAC; e.g., hangovers and vomiting) resulting from heavy drinking sessions, which is a common pattern amongst young people (3, 10). On the other hand, psychosocial harms are dependent on many factors other than high BAC, such as the individual's personality, the people they drink with, and quality of existing relationships. Psychosocial harms are also highly variable, with consequences that can arise from a single instance of drinking (e.g., doing something embarrassing while drunk) or from repeated patterns of heavy drinking (e.g., damaging relationships due to prolonged problematic behaviour).

Despite not requiring medical attention in most cases, these psychosocial and common physiological harms are nonetheless adverse consequences of alcohol consumption. These harms can also be indicators of more severe harms such as AUD (32). Two of the eleven criteria of AUD are directly related to problems with social networks, family, and/or work (according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [DSM-5]; 32). Other DSM-5 criteria for AUD include physiological experiences that are common amongst young people, including being sick or having memory loss (32).

Of the alcohol-related harms experienced by young people that do require medical attention, many harms such as falls tend to only be partially attributable to alcohol consumption (with the exception of alcohol poisoning). However, there is abundant evidence to show that alcohol consumption is associated with increased likelihood of acute harm (33). One global study of ED admissions spanning 18 countries found that consumption of one standard drink doubled the risk of subsequent injury and a dose-response relationship was found with injury risk increasing with the number of drinks consumed (up to ~30 drinks; 34). This is particularly concerning given that young people have the highest prevalence of HED compared to any other age group globally (aged 20-24 years; 3) and in Australia (aged 18-24 years; 10). Indeed, traumatic injuries such as those resulting from motor-vehicle accidents, interpersonal violence, and self-harm have constituted the majority of alcohol-related deaths globally in people aged 15-24 years since 1990 (35).

The following sections concentrate on overviewing literature first around some forms of acute alcohol-related harm experienced by young people, followed by chronic alcohol-related harm.

1.2.4. Acute alcohol-related harms

As there are a myriad of acute alcohol-related harms experienced by young people, this section will focus on some specific acute harms that have lasting impacts on the individual. First, I provide an overview of an alcohol-related harm that is commonly experienced by young people, alcohol-induced blackouts. As discussed in the following section, blackouts are distinct from other common harms as they have predictive utility for further, more severe harm (36-39). This will be followed by an overview of the two most common acute

causes of alcohol-related DALYs in young people; namely, motor-vehicle accidents and self-harm.

1.2.4.1. Blackouts

Loss of memory during a drinking session, i.e., an alcohol-related blackout, is one of the most common alcohol-related harms among young people. Indeed, surveys of young people who use alcohol show that the prevalence of blackouts is 30-50%, typically being third most common behind hangovers and nausea (29, 30, 40). As the periods of anterograde amnesia experienced during blackouts are the result of alcohol interfering with the formation of long-term memories, blackouts are an acute harm that have potential lasting implications on an individual's neurological health (41). This distinguishes blackouts from other common physiological harms such as hangovers and nausea, which tend to only have short-term impacts.

Though the risk of experiencing blackouts increases with increasing and rapid build-up of BAC, high BACs may only partially account for blackouts as there is also evidence to suggest that some individuals are more vulnerable based on neurobiological (42) and genetic (43) factors. That is, regardless of the absolute quantity of alcohol consumed, the occurrence of a blackout is indicative of significant cognitive impairment due to intoxication. Notably, alcohol-related blackouts are a predictor of future harms such as injury, sexual assault, and AUDs (36-39). These associations between blackouts and later harm persist even after adjusting for factors such as alcohol consumption and trait sensation seeking (36-39), which suggests that blackouts predict future harm over and above the effects of heavy alcohol consumption and/or personality. Thus, the experience of blackouts may serve as a useful proxy for harmful levels of alcohol consumption that takes into account individual

differences in tolerance. Given the high prevalence of blackouts (29, 40), they may play an important role in risk assessment for early intervention among non-clinical populations of young people.

1.2.4.2. Self-harm and suicide

Deliberate self-harm is a serious global public health problem for young people. Worldwide, around 1 in 6 adolescents aged 12 to 18 years have engaged in self-harm in their lifetime (44). Although most self-harming behaviour in adolescence tends to cease without intervention by early adulthood (45), deliberate self-harm and repeated self-harm are some of the strongest predictors for future suicide (46-48). Indeed, self-harm has been the second leading cause of death in young people worldwide since as early as 1990 (24) and from 2018 to 2020, suicide was the most common cause of death in young Australians (49, 50).

Alcohol consumption has been well-established as a major risk factor for self-harm and suicide (45, 51-55). It is thought that the disinhibiting properties of alcohol in vulnerable individuals leads to increased impulsivity and impaired judgement, which reduces barriers to self-harm and suicide (56). Any alcohol consumption, heavy use in particular, has been associated with increased risk of deliberate self-harm in countries such as Australia (45, 51), Norway (53, 55), and the U.S. (51). Notably, a cross-sectional study on schools across Australia and Europe found that repeated alcohol intoxication in mid-adolescence was associated with deliberate self-harm after controlling for potential confounders such as gender, depression, impulsivity, and psychosocial problems (54). This is supported by longitudinal studies, which find that heavy drinking is associated with increased likelihood of future self-harm (45, 53, 57). Given the role of alcohol in self-harm, efforts to reduce consumption often also have the benefit of reducing rates of suicide. Policies including

higher legal age of purchase and consumption, lower outlet density, and increased alcohol taxation have been found to reduce suicide mortality (for a review, see 58). However, much of this policy research has been focused on the U.S. and as such may not be applicable globally as characteristics associated with suicide rates, such as rates of firearm ownership and accessibility (59), are substantially different in the U.S. compared to other countries (60).

1.2.4.3. Motor vehicle accidents

Alcohol consumption impairs the motor and cognitive functions required for operating a motor vehicle (61) and increases risk of motor-vehicle injuries (62). In the U.S. and Australia, alcohol-impaired drivers are involved in approximately 30% of all road fatalities (63, 64). From 2017 to 2018, alcohol-attributable motor-vehicle accidents resulted in around 200 fatalities and 48,770 injuries (23). Not only does alcohol consumption result in substantial healthcare burden due to premature mortality and injury, but there are a myriad of other societal costs such as permanent disability and property damage (AUD$2.4 billion in 2017-2018; 23). There is no evidence to suggest that there are safe levels of alcohol consumption when motor vehicles are involved. Even levels of BAC that are lower than the legal limits in most countries have been associated with increased risk of fatal road injuries (65, 66), with a clear dose-response relationship between road injury risk and number of drinks consumed (62).

Irrespective of alcohol consumption, many studies have found that young drivers are at greater risk of injury compared to older drivers due to inexperience and factors associated with adolescence such as lack of sleep, increased risk-taking behaviour, underdeveloped frontal-executive function and control, and limited psychomotor skills (67, 68). Despite

increasing restrictions on the age at which driving licenses are available and the number of hours required for young drivers to become fully licensed, road injuries are the leading cause of death in young people worldwide (24). In Australia, 18.7% of deaths in young people between 2018 and 2020 were caused by road accidents, which is the highest prevalence of any age group in the country (50). Concerningly, drivers aged 25 years and under in countries such as Australia and the U.S. represent the largest proportion of alcohol-impaired drivers who are involved in a crash resulting in a fatality or serious injury (64, 69). Considering that young drivers are already at elevated risk of injury, these factors highlight the substantial dangers unique to this age group.

1.2.5. Chronic alcohol-related harms

Among young people, the largest burden attributable to alcohol consumption is due to AUDs, constituting over half of all alcohol-attributable DALYs in people aged 15 to 24 years in Australia (25). Other chronic conditions attributable to alcohol consumption, such as liver cancer and liver disease, typically emerge after many years of sustained heavy alcohol consumption (70, 71). Indeed, these other chronic harms have minimal contribution to alcohol-attributable DALYs until later in life (i.e., after age 45 years; 25). Therefore, discussion of chronic alcohol-related harms among young people will focus on AUDs only.

1.2.5.1. Alcohol use disorders

Characterised by recurring alcohol problems such as compulsive alcohol consumption, symptoms of alcohol withdrawal, and troubles with relationships and work, AUDs are the single greatest contributor to years of life lost due to disability in young people (24, 25). The most common ages of onset for alcohol consumption (16-19 years; 5) coincides with a period of vulnerability for age of onset associated with increased risk of developing AUDs

(72). Indeed, most people with AUD tend to be first diagnosed prior to age 25 years (73). Young people with AUDs are much more likely than young people from the general population to engage in HED (74), which is a cause for concern given the strong positive associations between the number of drinks consumed and risk of injury (to be discussed in the following sections). Indeed, people with AUDs have increased rates of all-cause and cause-specific mortality, with heightened risk of gastrointestinal and traumatic deaths compared to the general population (75). Additionally, a meta-analysis by Roerecke and Rehm (76) showed that, of all adults with AUDs, those below the age of 30 had a substantially higher risk of mortality compared to older age groups. Traumatic injuries and deaths notwithstanding, AUDs in young people have also been associated with other lifelong adverse outcomes such as comorbidity with major depressive disorder (77) and eating disorders (78). In an Australian study by Mewton, Teesson (74), young people with AUDs were twice as likely to report comorbid anxiety disorders and 15 times more likely to report having other drug use disorders compared to young adults without an AUD diagnosis.

Not only are young people with AUDs at higher risk of further harm compared to older age groups, but AUDs are also fairly prevalent among young people. In Australia, 11.1% of young people met 12-month AUD diagnosis criteria in 2007 (74), with similar rates in the United States (U.S.; 26.7% in 2012-13; 79) and New Zealand (7.1% alcohol abuse, 3.0% alcohol dependence in 2003-04; 80). In each of these three countries, young people also had the highest prevalence of AUDs compared to older age groups ('young people' classified as 18-29 years for U.S., 16-24 years for Australia and New Zealand, see 74, 79, 80). However, it is possible that the prevalence of AUDs are overestimated among young people due to heavy drinking patterns emerging in adolescence that typically do not persist past early adulthood (81).

Though incidences of AUD often resolve without treatment in young people as their alcohol consumption declines after the early 20s (73), around 1 in 3 young people who 'recover' are re-diagnosed with AUD before age 30 years (73). Very few young people who have been diagnosed with an AUD seek treatment. In Australia, 11.3% of young people diagnosed with 12-month AUD accessed mental health services in the previous 12 months (74) and less than 8% of adults with 12-month AUD in the U.S. had ever sought treatment (79). A study comparing people with AUD who do and do not seek treatment found that people in the non-treatment-seeker group were significantly younger than those in the treatment-seeker group (82). In sum, young people are disproportionately affected by AUDs which confer increased risk of co-morbidities and mortality, yet only a small proportion seek treatment.

Summary of Section 1.2. Alcohol-related harms in young people

- Alcohol is the leading risk factor for death and disease in young people worldwide.
- Harms resulting from alcohol consumption can take many different forms.
- Young people commonly experience acute harms, typically resulting from single occasion heavy drinking.
- Blackouts are a common acute harm among young people that may have long-term impacts.
- Self-harm and motor vehicle accidents are the two most common acute harms that contribute to alcohol-related death and disability in young people.
- AUDs are by far the most common chronic alcohol-related harm in young people.
- AUDs are the single greatest contributor to alcohol-related death and disability in young people.

1.3. Recent changes in young peoples' alcohol behaviours

1.3.1. Trends in alcohol consumption

Promisingly, some regions have observed decreases in young peoples' alcohol consumption since the early 2000s. Between 2002 and 2010, weekly adolescent alcohol consumption declined in 20 high-income counties across Europe and North America (83, 84). Among young people who are male, a demographic that often shows high-risk drinking patterns (3), alcohol consumption has been declining at a greater rate than young people who are female in Europe and North America (85, 86). In Australia, the proportion of people aged 14 to 19 years who had not consumed alcohol in the past 12 months increased from 25% in 2001 to 56% in 2019 (10). Given that Australia, Europe, and North America have the highest percentage of people aged 15-24 years who currently use alcohol and engage in HED, and also the highest percentage of total deaths attributable to alcohol in this age group (3), these trends may be a particularly positive public health development.

To clarify these trends in alcohol consumption, studies have utilised age, period, cohort (APC) analyses. APC analyses enable the examination of how each component of age, period, and cohort influences changes over time whilst adjusting for the other components. The age component examines changes associated with aging (e.g., accumulation of experiences with alcohol consumption), the period component examines changes that affect the population over time (e.g., introduction of alcohol policies), and the cohort component examines changes occurring between people in born in different years (e.g., generational differences in attitude towards alcohol). APC studies comparing rates of alcohol consumption among different birth cohorts in Australia, the United Kingdom, Sweden, Russia, and the U.S. have reported that more recent cohorts of young people have

lower prevalence of alcohol consumption and lower levels of alcohol consumption (87-91). As these findings take into account period and age effects, we can thus be fairly confident that these changes in young peoples' alcohol consumption are due to differences among birth cohorts rather than the aforementioned differences over time and life stage.

These trends have generated increased interest in the potential reasons for the decline in youth alcohol consumption. A 2019 systematic review reported that the explanation with the most robust evidence was changes in parental practices such as reduced parental supply of alcohol and increased parental monitoring (84). Other proposed explanations with supporting evidence include changes in attitudes towards school (females only; 92) and increasing normalisation of non-drinking among young people (93). Though this suggests that there are widespread shifts in attitudes toward alcohol consumption among both young people and their parents, it is unclear whether these changes in drinking behaviour at the population level have resulted in changes in the experience of alcohol-related harms among young people.

1.3.2. Trends in alcohol-related harm

Given the recent reduction in consumption, it seems reasonable to expect that the harms attributable to alcohol consumption experienced by young people will have also reduced. There is some Australian evidence indicating that some risky behaviours may have declined over time in concert with alcohol consumption levels (94). Though this study measured risk behaviours (e.g., driving while intoxicated) rather than harms specifically (e.g., being injured in a motor vehicle accident), these behaviours often precede acute harms and as such are a useful proxy for quantifying harm.

Indeed, alcohol-attributable hospitalisation rates across Australia between 2010 and 2017

decreased among people aged 15 to 34 years but this finding was not observed for older adults (95). Though males in the 15-to-34-year age group have much higher rates of alcohol-attributable hospitalisation, they appear to be driving the overall decline in this age group as they showed steeper decreases in alcohol-attributable hospitalisation rates compared to same-aged females (95). These trends in alcohol-attributable hospitalisation rates are similar in New South Wales (NSW), Australia, where people aged 15 to 34 years have declined between 2010 and 2020 but older people show slightly increasing rates (96). Again in agreement with national Australian data, these trends among young people appear to be driven by larger decreases in alcohol-attributable hospitalisation rates in males than females (96).

These trends in harm are not consistent, however, as other evidence suggests that the proportion of young people experiencing harms attributable to alcohol consumption may have recently increased or remained stable (97, 98). For instance, youth hospital admissions in Sweden due to alcohol-related diagnoses increased between 2000 and 2010 (99), which is in contrast to alcohol consumption decreasing across most Swedish youth in the same period (97). In Victoria, Australia, a similar divergence was found where rates of alcohol-related emergency department (ED) and ambulance attendances increased substantially between 2000 and 2008 (98) even though alcohol consumption in Australian youth has been declining since the early 2000s (6). More recent data from Victoria shows that the rate of alcohol-related ambulance attendances among people aged up to 24 years have increased between 2011 and 2020, and alcohol-related hospital admissions have been relatively stable (100).

Importantly, the studies discussed in the previous paragraph are broadly comparing trends

between young people born in different birth cohorts but have not adjusted for effects that are a result of aging nor effects that are a result of population-level changes over time. Thus, it remains unclear whether trends in young peoples' experience of alcohol-related harms have followed the same trends as identified by APC studies on alcohol consumption.

If harms have indeed remained stable or are increasing, a potential explanation is that the trends in consumption have been polarised across low-risk and high-risk drinkers. That is, the trends in drinking for the much smaller group of youth who drink at levels that place them at high-risk harm are obscured by the much larger group of youth who are at low risk of experiencing harm when looking at per-capita consumption. For instance, whilst overall youth alcohol consumption and bingeing decreased over time in Sweden, youth who were in the top 10% of alcohol consumers increased consumption and heavy episodic drinking between 2000 and 2010 (97). A more recent analysis showed similar trends, with most Swedish youth showing declines in consumption but the heaviest consuming youth had stable drinking patterns between 2000 and 2014 (101). This bifurcation of alcohol consumption trends observed by Hallgren, Leifman (97) and Zeebari, Lundin (101) support the polarisation explanation for the potential increase in harm. Thus, it may be that alcohol-related harms are not declining with declining consumption because young people who drink at risky levels, who are a relatively small proportion of all young people who drink, are maintaining their alcohol consumption levels. On the other hand, there have been recent studies that have reported collective declines in young peoples' alcohol consumption across Sweden (102) and England (103) between the 2000s and 2010s.

In sum, there is conflicting evidence regarding whether recent declines in consumption have resulted in a decline of comparable magnitude in young people experiencing alcohol-related

harms. One hypothesis for the lack of consistent trends between alcohol consumption and harm in young people is that a high-risk subgroup of young people is driving sustained harms despite changes in population-level alcohol consumption. Identifying which groups of young people are experiencing alcohol-related harms and how these harms typically develop can aid in our understanding of how to improve the health of young people.

Summary of Section 1.3. Recent changes in young peoples' alcohol behaviours

- Young people in high-income counties across Europe, North America, and Oceania have been drinking less alcohol since the early 2000s.
- Age, period, cohort analyses confirm that these trends are due to declines with more recent cohorts, particularly in people born during and after the 1990s.
- Trends in alcohol-related harm vary, with no clear declines.
- There are a lack of age, period, cohort studies examining changes in harm.
- There may be a subset of young people who diverge from the new norm by continuing to drink at risky levels and experiencing alcohol-related harm.

1.4. Adolescent trajectories of alcohol consumption and harms

Whilst examination of population-level trends is useful in understanding the broad state of alcohol consumption and harms, they provide limited information regarding the identification of high-risk individuals. Examining how young peoples' experience of alcohol consumption and harms changes over time at an individual level allows us to distinguish between young people who have transient patterns of heavy drinking and harm and young people who have escalating and/or persistent experiences of heavy drinking and harm. Longitudinal data allows us to identify distinct developmental patterns of alcohol consumption and related harms, as well as examine factors associated with particularly risky trajectories. This can be addressed through group-based longitudinal trajectory analyses. Group-based growth analyses model changes in measured variables over time and identifies clusters of individuals who follow similar progressions, i.e., trajectories. To understand variations in young peoples' experience of alcohol-related harms, this section will first summarise the different developmental trajectories of alcohol consumption that have been identified in previous research. Subsequently, this section will examine what is known regarding trajectories of alcohol-related harms and whether there is evidence identifying particular risk factors for experiencing persistent alcohol-related harm in adolescence.

1.4.1. Trajectories of alcohol consumption

From the typical point of alcohol initiation in mid-adolescence, people tend to increase in their quantity and frequency of alcohol consumption until a lifetime peak in their mid to late twenties (1, 104). While recognising that the normative developmental pattern of alcohol consumption is useful in informing population-level strategies, this approach does not capture more nuanced patterns of drinking. As with any behaviour, there is substantial

variation amongst individuals. The age at which people first start drinking alcohol differs widely and may be a marker for different health outcomes, with cohort studies reporting that those who initiate alcohol consumption before age 12 years have greater risk of binge drinking (105) and alcohol dependence (106) in late adolescence. Additionally, longitudinal studies aimed at identifying distinct developmental trajectories of drinking typically find broad groups of young people who escalate alcohol consumption to varying degrees after initiation (e.g., 107, 108-111). Common patterns reported by these studies include abstaining/low alcohol consumption, escalating alcohol consumption with late adolescence onset (i.e., ≥ 16 years of age), and escalating alcohol consumption with early adolescence onset (i.e., ≤ 15 years of age; 107, 109, 110, 111). Importantly, adolescents with early onset and escalating alcohol consumption patterns tend to have higher risk of adverse health outcomes in early adulthood such as symptoms of AUD (107, 108), HED, injuries (110), and illicit substance use (112).

1.4.2. Trajectories of alcohol-related harm

As acute alcohol-related harms are at a lifetime peak during early adulthood (3), attempts to study the experience of alcohol-related harms in young people have mainly focused on factors that predict alcohol-related harms in early adulthood (e.g. 113, 114-116). However, alcohol-related harms are experienced by adolescents as young as 10 years of age (117) and initial signs of AUDs can be identified in adolescents as young as 14 years of age (118, 119). In line with the evidence on heterogenous adolescent alcohol consumption trajectories, there are likely similar substantial variations in young peoples' experience of alcohol-related harm.

Whilst experience of alcohol-related harm can deter further risky drinking (120), this is not

the case for all young people. Whereas young people who experience more positive alcohol consequences (e.g., facilitating social interactions) perceive these consequences as being more pleasant, young people who experience more negative consequences (i.e., harm) do not necessarily perceive these consequences as being more negative (121). Indeed, some young people do not perceive certain alcohol-related harms as being 'negative' at all (e.g., hangovers, blackouts; 122, 123). Though these studies on young peoples' perception of alcohol-related consequences typically use college student samples, one study reported that people aged 14 to 15 years who experienced alcohol-related harms in the past 30 days were willing to experience the same harms in the future (e.g., vomiting, regretted sexual situations; 124). Thus, previous experience of harm does not necessarily serve as an incentive to avoid further harm by reducing alcohol consumption (125), which may explain why a proportion of young people experience repeated alcohol-related harm (126).

1.4.2.1. Trajectories of common alcohol-related harm

To date, studies of alcohol-related harm trajectories in non-clinical populations of young people have typically focused on one specific harm such as blackouts (e.g., 127, 128, 129). Similar to the trajectories of alcohol consumption discussed in Section 1.4.1, common trajectories of blackouts include no blackouts, escalating blackouts, and consistent frequent blackouts (127-129). These studies also identified risk factors for frequent blackouts such as female sex and peer substance use (127-129). However, the participant samples were of older adolescents and young adults who have already been exposed to alcohol, meaning developmental patterns earlier in life, particularly at the time of alcohol consumption initiation, are unknown.

Studies that examine developmental patterns of a range of harms in non-clinical populations

are comparatively rare. One study examined trajectories of a wider range of alcohol-related harms in conjunction with HED from age 16 years until age 28 years (130). Harms trajectories in Betts, Alati (130) consisted of: 1) early experience of harm followed by decline after age 20 years; 2) increasing harm until age 20 years; and 3) minimal harm (130). Importantly, these harms patterns were not parallel with HED patterns (e.g., HED was stable when harms declined in one trajectory), meaning that developmental trajectories of harm are distinct to that of HED. However, Betts, Alati (130) did not examine the predictors of different harms trajectories and thus it is unknown whether there are certain sociodemographic and family factors in early adolescence that differentiate those who experience harms throughout adolescence from those who experience harms during late adolescence only. Betts, Alati (130) also used a count of harms in their model, meaning that different forms of harm were treated equally. One study that did distinguish between types of harm found that college students were more likely to shift from not experiencing harm to the experience of physical and/or multiple types of harm (e.g., social, academic) if they moved from on-campus to off-campus residence (131). As experience of multiple types of harm is reflective of AUD symptomatology (32), these transitional patterns are likely to have some utility in identifying young people at risk of alcohol problems. However, it is currently unknown whether similar patterns of transitioning can be observed in adolescence and whether there are early risk factors for certain patterns.

1.4.2.2. Trajectories of severe acute alcohol-related harm

Young people who access health services such as hospitals and EDs for alcohol-related reasons represent a subgroup of young people who experience alcohol-related harm. Examining data from these young people can aid in identifying risk factors for trajectories of

severe harm. For instance, one study of hospital data in Western Australia reported that 21% of young people aged 12 to 24 years with an alcohol-related hospitalisation were readmitted for an alcohol-related reason (132). Despite being only a fifth of the sample, these young people who experienced repeat harm accounted for nearly half of the alcohol-related hospitalisations in the study (132). These readmissions were more likely among males, people who identify as Aboriginal, and people with prior illicit drug hospitalisation or prior mental health contact (132). A similar study of people aged 12 to 18 years in England found that each subsequent readmission tended to involve a longer stay and shorter duration between readmissions (133), suggesting increasing severity of problems. In contrast to Sims, Pereira (132) however, Hoy (133) found that readmissions were less likely among males, though this may be due to differences in cultural context and the sampling timeframe (2003 to 2004 in Hoy (2017) versus 1992 to 2017 in Sims et al. (2022)). These studies show that there are some young people who repeatedly experience alcohol-related harms requiring hospitalisation and have characteristics that differentiate them from the majority for whom these severe harms are a one-time experience.

Whilst some studies have examined whether age at first experience of alcohol-related hospitalisation affects the likelihood of any subsequent readmission and/or total number of readmissions and found no association (133, 134), is unclear whether the characteristics of these readmissions differ by age. It is possible that people who have their first alcohol-related hospitalisation at a younger age are, for instance, more likely to experience readmissions that are alcohol-specific.

Though it is important to identify whether age is associated with readmissions, age alone as a risk factor presents limited information for policy and public health interventions. Studies

of alcohol-related hospitalisations in young people have found that younger adolescents are more likely to be female but older adolescents and young adults are more likely to be male (117, 135). However, other differences by age, such as in socioeconomic status, have not been examined and it is unclear in the aforementioned studies whether these young people have had prior alcohol-related hospitalisations. Therefore, in addition to examining age-specific differences in types of readmissions, we should also identify whether there are age-specific differences in young peoples' sociodemographic and clinical characteristics at their first alcohol-related hospitalisation.

Summary of Section 1.4. Adolescent trajectories of alcohol consumption and harms

- Young people show variations in how they initiate and escalate alcohol consumption as they age.
- Young people who start drinking earlier in life and rapidly escalate their alcohol consumption are more likely to have adverse health outcomes in early adulthood.
- There is a lack of research examining patterns of escalation in experience of alcohol-related harm, particularly across different types of harm.
- Most young people who experience hospitalisation for alcohol-related harm only do so once.
- There is a need to identify the characteristics of young people who experience repeated hospitalisations for alcohol problems.
- It is unclear whether young people who experience alcohol-related hospitalisations in adolescence differ in sociodemographic and clinical characteristics and readmissions from those whose first experience was in early adulthood.

1.5. Measuring alcohol-related harm

Given that there are many forms of alcohol-related harm, there are consequently many ways of quantifying alcohol-related harm among individuals. Young peoples' experience of harm can also be examined as patterns observed over time (i.e., comparing changes between cohorts of young people; Section 1.3) or patterns observed with age (i.e., developmental trajectories within a cohort; Section 1.4), which often necessitates different methods of measurement. This section will discuss some common methods of measuring harm, including their utility in examining different patterns and populations, and their advantages and disadvantages.

1.5.1. Self-reported surveys

Self-report surveys are commonly used to measure alcohol-related harms among young people (28-31). This method of measuring harm allows researchers to examine a wide range of harms, including less severe harms that do not require medical attention and/or social harms (as detailed in Section 1.2.3). People who experience severe harms but do not or do not have the means to seek medical attention or other help for their problems can also be captured in survey samples. Indeed, survey participant samples can be very broad, such as nation-wide household surveys (e.g., 10), or focused on certain demographic groups such as secondary school students (e.g., 6), university students (e.g., 136), or high-risk youth (127).

Surveys are typically conducted in one of three forms: cross-sectional, repeated cross-sectional, or longitudinal. Cross-sectional surveys capture the experience of harms of a sample recruited at a particular point in time, with repeated cross-sectional surveys enabling the examination of changes across the population over time. An example of this is the Australian National Drug Strategy Household Survey (NDSHS; 10), which is a population

survey examining alcohol and other substance use behaviours that has been conducted across Australia once every three years since 1985. Repeated cross-sectional surveys typically also allow researchers to compare trends across age groups, time periods, and birth cohorts (i.e., APC analyses; see 87, 90). However, as respondents are recruited at each instance of a cross-sectional survey, they do not capture changes at an individual level. This is done using longitudinal surveys, which consist of the same sample surveyed multiple times at periodic intervals. An example of this is the Australian Parental Supply of Alcohol Longitudinal Study (APSALS; 137), which recruited participants from Grade 7 classes in 2010-2011 and surveyed the same participants annually. Longitudinal surveys can be used to show how people change as they age, including the identification of high-risk developmental patterns of behaviour and potential risk factors for later adverse health outcomes (e.g., 107, 111, 138, 139).

There are several downsides to surveys that should be carefully considered in the context of measuring alcohol-related harm. While trends in survey data have been shown to provide consistent estimations of alcohol consumption trends when compared with sales and per-capita alcohol consumption data (140, 141), the overall level of alcohol measured is typically much lower than the amount sold (142). This raises questions about the exclusion of heavy drinkers, issues with response validity and recall bias that may also affect how surveys measure alcohol-related harms. Since any alcohol-related harms are reported of the respondents' own volition, they are subject to social desirability characteristics (143). That is, harms that are seen as less socially acceptable or have legal repercussions (e.g., driving while intoxicated) are likely to be underreported. There may also be variations within the sample that are a result of the timing of the response, with studies reporting that the time of year can bias estimates of alcohol consumption (e.g., higher levels of past-year alcohol

consumption reported in responses collected during hotter months; 144, 145). Given that surveys often ask respondents to retrospectively recall their past experiences, this also increases the potential for underreporting as heavy alcohol consumption impairs memory (41). Finally, there are also downsides to self-reported surveys as a result of sampling. For instance, some broad population surveys do not capture certain disadvantaged groups such as people who are homeless (146). Participation in survey research is also often not mandatory, so any results are biased towards people who choose to respond. Notably, people who are male, younger, and/or have lower levels of education are less likely to respond to public health surveys (147, 148), which is a cause for concern given that these demographics tend to have high levels of alcohol consumption (10).

1.5.2. Administrative records from health and other government services

Health and other government services routinely collect personal data for clinical and administrative purposes; for instance, hospitals have records of a patient's demographic information and reasons for admission for the purposes of providing appropriate treatments. These records, although not collected for the purposes of research, can provide important information for governments and researchers to generate evidence that has external validity. For instance, administrative data can be used to describe trends in the rate of deaths and hospitalisations that are attributable to alcohol consumption (95). Administrative data can also be used to evaluate policies, for example, comparing rates of assault before and after the introduction of restrictions to liquor trading hours (149).

Whereas information about the number of records has limited value in research outside of examining trends, being able to examine an individual's records across a variety of health and other government services provides much more utility in terms of identifying correlates

of chronic disease and mortality. For example, a recent study identified people who were hospitalised for alcohol-related problems and examined subsequent hospital records, finding that these people were far more likely than the general population to be readmitted for alcohol-related reasons and to also die from alcohol-related causes (150). This can be achieved through record linkage, which is the process of joining information about a single person using multiple instances or sources of data (151). Not only does linked administrative data allow researchers to leverage existing health and other government service records, but there is also no additional burden required of the people who access these services to participate in the research.

One major disadvantage to the use of administrative data is that only people who access these services are captured, meaning that people who choose not to or are unable to access these services are not included. Additionally, as the name suggests, these data are created for administrative rather than research purposes. Thus, only information that is relevant to the healthcare service being provided is collected. In hospital and other health data, alcohol-related presentations are often underreported for various reasons including lack of routine assessment of alcohol involvement by health professionals, the prioritisation of other health conditions over alcohol, and lack of scope to identify alcohol in diagnosis fields (152). Indeed, cases where alcohol is not the primary reason for requiring medical attention are often not recorded as being alcohol-related due to issues with commonly used coding instruments such as the International Classification of Diseases (153). Administrative data are also subject to availability, which can result in datasets that are biased towards services that agree to provide the data (e.g., if ED records are only available from public hospitals; 154).

Summary of Section 1.5. Measuring alcohol-related harm

- There are many ways of quantifying alcohol-related harm in individuals.
- Different methods of measurement are used for different purposes, such as repeated cross-sectional surveys for comparing cohorts and longitudinal surveys for examining changes that occur with age.
- Surveys of alcohol-related harm can be targeted towards very broad or specific populations and answer specific questions but are liable to self-report and sampling biases.
- Administrative records from health services can capture people who experience severe alcohol-related harms, and any information is recorded by health professionals, but the data are not intended for research purposes and the involvement of alcohol is often underreported.

1.6. Thesis structure and research questions

Despite clear reductions in alcohol consumption among young people in recent years (10, 83, 84), there have been mixed trends regarding alcohol-related harm and alcohol consumption remains the leading risk factor for death and disability among young people (GBD 2016 Alcohol Collaborators, 2018; Mokdad et al., 2016). There is a need to first clarify the magnitude of changes in the prevalence of alcohol-related harms as well as whether these changes have been primarily driven by the natural course of aging, population-level shifts, or socio-cultural differences between birth cohorts. Identifying the characteristics of those who are experiencing alcohol-related harms and high-risk developmental patterns of harm can aid in our understanding of how to reduce the prevailing health burden of alcohol among young people from recent birth cohorts who are driving declines in alcohol consumption (i.e., people born during or after the 1990s). Using a variety of methods and data sources to address these gaps in knowledge will provide more robust evidence regarding the trends and trajectories of alcohol-related harm in young people. The proposed program of research seeks to address these gaps in the literature by answering the following five questions:

1. Are self-reported harms among young people less prevalent in recent birth cohorts, in line with previous findings on declining alcohol consumption?
2. What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving declines in alcohol consumption?
3. In recent birth cohorts, are there early adolescent factors that predict high-risk developmental patterns of harm?

4. Are there risk factors for experiencing clinical alcohol-related harm for the first time at a younger age in recent birth cohorts?
5. Does experiencing clinical alcohol-related harm for the first time at a younger age predict greater subsequent harm in recent birth cohorts?

1.6.1. Overview of chapters

Chapter 2 (Study 1) addresses research question 1: '*Are self-reported harms among young people are less prevalent in recent birth cohorts, in line with previous findings on declining alcohol consumption?'* and research question 2: '*What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving declines in alcohol consumption?'* This study examines age, period, and cohort effects on the prevalence of alcohol-related risky behaviour among the Australian population of people who drink using repeated cross-sectional household survey data. As there are no national data available on alcohol-related harm, this study uses risky behaviours, which include driving while intoxicated, as a proxy measure for alcohol-related harm.

Chapters 3 and 4 (Studies 2 and 3) addresses research question 2: '*What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving declines in alcohol consumption?'* and research question 3: *'In recent birth cohorts, are there early adolescent factors that predict high-risk developmental patterns of harm?'* Study 2 uses latent class trajectory analyses to identify developmental patterns of alcohol-related blackouts, including early adolescent risk factors and adulthood AUD outcomes, in a longitudinal cohort of young people in Australia. Study 3 uses latent transition analyses in the same cohort to identify developmental patterns of transitioning between different types of alcohol-related harm, also including the identification of early adolescent risk factors and

adulthood AUD outcomes.

Chapter 5 (Study 4) addresses research question 4: '*Are there risk factors for experiencing clinical alcohol-related harm for the first time at a younger age in recent birth cohorts?'* and research question 5: *'Does experiencing clinical alcohol-related harm for the first time at a younger age predict greater subsequent harm in recent birth cohorts?'.* This study examines whether the age at which a young person first experiences an alcohol-related hospital admission or ED presentation can be predicted by sociodemographic factors, and whether younger people were more likely to have subsequent readmissions in a retrospective linked data cohort of young people in NSW, Australia.

Finally, Chapter 6 discusses the study findings in the context of existing literature and provides a conclusion for the thesis.

1.7. References for Chapter 1

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2. CHAPTER 2: AGE, PERIOD, AND COHORT EFFECTS ON ALCOHOL-RELATED RISKY BEHAVIOURS IN AUSTRALIA FROM 2001 TO 2016

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This study has been accepted for publication by Addiction. The text, tables, and figures do not differ from the submitted version other than the addition of section numbers and editing of table and figure heading numbers for consistency within this thesis.

2.1. Copyright Statement

I declare that this publication occurred during my candidature as a direct result of my research towards this thesis and, to the best of my knowledge, does not breach copyright regulations nor intellectual property rights.

Yuen, W. S., Peacock, A., Man, N., Callinan, S., Slade, T., Farrell, M., Mattick, R. P., & Livingston, M. (2022). Age, period, and cohort effects on alcohol-related risky behaviours in Australia from 2001 to 2016. Addiction. *In Press.*

2.2. Preamble

In the first chapter of this thesis, a summary of the evidence regarding young peoples' use of alcohol and experience of alcohol-related harm was presented. Alcohol consumption has declined among young people but not older adults between the 2000s and 2010s (1-3). However, trends regarding young peoples' experience of alcohol-related harm appear to be mixed (4-7). There is a need to clarify recent trends in alcohol-related harm, particularly whether there have been declines among young people who are driving declines in alcohol consumption.

This chapter aims to address research question 1: '*Are self-reported harms among young people less prevalent in recent birth cohorts, in line with previous findings on declining alcohol consumption?'* and research question 2: '*What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving declines in alcohol consumption?*'. Though the research questions pertained to alcohol-related harm, there is currently no national Australian data that captures harm other than hospitalisations. As we wished to examine trends in any alcohol-related harm (i.e., not only restricted to harms requiring hospitalisation), we examined alcohol-related risky behaviour as an analogue to estimates of harm. We use repeated cross-sectional household survey data to examine the effects of age, period, and birth cohort on the prevalence of alcohol-related risky behaviour from 2001 to 2016 among people who drink alcohol and reside in Australia.

2.3. Abstract

Aims: To examine age, period, and birth cohort trends in the prevalence of any alcohol-related risky behaviour, and to compare these trends between men and women.

Design and Setting: Age, period, cohort analysis of repeated cross-sectional survey data from the Australian National Drug Strategy Household Survey from 2001 to 2016.

Participants: 121,281 people aged 14 to 80 years who reported consuming alcohol in the past 12 months.

Measurements: Any risky behaviour undertaken while under the influence of alcohol in the past 12 months (e.g., operating a motor vehicle); male or female.

Findings: Controlling for age and cohort, cubic spline models showed that any alcohol-related risky behaviour declined with time across participants who consumed alcohol (2016 vs 2007 Rate Ratio [RR] = 0.80; 95% confidence interval [CI] = 0.76-0.84). Risky behaviour peaked in the 1954 birth cohort (1954 vs 1971 RR = 1.42; 95% CI = 1.30-1.55), then steadily declined with more recent birth cohorts (2002 vs 1971 RR = 0.32; 95% CI = 0.27-0.39). Risky behaviour peaked at age 21 years, followed by steady decline and stabilisation at around age 70 years. Males were overall twice as likely as females to report alcohol-related risky behaviour (RR = 2.10; 95% CI = 1.84-2.39), but this effect was smaller in cohorts born after 1980 (1980 PRR = 2.09 [95% CI = 1.81-2.43]; 2002 PRR = 1.31 [95% CI = 1.03-1.68]).

Conclusions: Alcohol-related risky behaviour in Australia has declined generally since 2001, with rates for recent cohorts having the sharpest decline. Risky behaviour remains most prevalent in young adults and the male-female gap in risky behaviour is closing for more recent birth cohorts. These trends are consistent with alcohol consumption trends observed in Australia and worldwide.

Keywords: alcohol, risky behaviour, alcohol-related harm, trends, age period cohort

2.4. Introduction

Alcohol is the seventh leading risk factor for death and disability worldwide, and the leading risk factor for people aged 15-49 years (8). Whilst the prevalence of alcohol consumption and binge drinking across Europe, North America, and Oceania appears to have increased since the early 2000s in people aged 50 years or older (2, 9, 10), this has not been the case across all age groups and birth cohorts. Indeed, many of these high-income countries have seen declines in alcohol consumption among younger people (1, 11-13). In Australia, the number of people aged 14 to 17 years who abstained from alcohol increased from 39% in 2007 to 73% in 2019 (2).

Examining the effects of age, period, and birth cohort (APC) on alcohol use and related behaviours can aid in our understanding of how changes are influenced by factors across the life-course. 'Age' refers to differences due to stages of life (e.g., increased drinking from adolescence to early adulthood), 'period' refers to differences due to changes that affect the population (e.g., alcohol policy implementation), and 'cohort' refers to differences due to socio-cultural norms (e.g., changes in attitudes toward heavy drinking) (14). APC models attempt to disentangle these related effects APC modelling has been extensively used to demonstrate that cohorts born after the 1980s are drinking less alcohol than earlier birth cohorts in countries such as the United Kingdom (15), United States (16), Sweden (17), and Finland (18). Similarly in Australia, data from 1995 to 2013 shows that cohorts born in the 1990s had lower rates of any drinking and lower volumes of alcohol consumption compared to earlier cohorts (12). Importantly, these cohort effects exist after adjusting for the effects of aging and time period.

Similarly, trends in harm resulting from alcohol-related risky behaviour do not necessarily

occur in a collective manner. Indeed, nationwide data from England and the United States shows that overall alcohol-related hospitalisations increased between the early 2000s to the mid-2010s, but hospitalisations among adolescents decreased (19, 20). In Australia, alcohol-attributable hospitalisation rates also appear to have increased between 2010 and 2017, but rates by age group show decreases among people aged 15 to 34 years (4). However, recent data from Victoria, Australia shows that the rate of alcohol-related ambulance attendances among people aged up to 24 years have increased and alcohol-related hospital admissions were relatively stable between 2011 and 2020 (7). Though these studies and sources of data show differences between birth cohorts, they do not adjust for age and period effects. Thus, it remains unclear whether trends in risky behaviours have followed the same trends as identified by APC models of alcohol consumption.

Another recently observed phenomenon that may have substantial impacts on public health is the closing of the gap between males and females in alcohol use. Whilst alcohol use has historically been more prevalent amongst men, rates of alcohol consumption and risky drinking among men and women have been converging since the early 2000s across high-income countries (21-23). This male-female convergence is, however, not homogenous across the population. Indeed, a 2016 meta-analysis reported that global male-female ratios of the prevalence of alcohol use, risky drinking, and alcohol-related harms had decreased by more than half when comparing cohorts born in the early 1900s versus the late 1900s (21). In Australia, the convergence in risky drinking has only been observed in 50-69-year-olds (24). A review of studies in the United States found that the male-female convergence in adolescent and young adult populations appears to be largely driven by males decreasing consumption at a greater rate than females (25). In contrast, the convergence in adults aged 30 years and older tends to be driven by increases in drinking amongst women (25). If these

recent changes in alcohol use result in similar changes to risky behaviours and harms, gender-specific strategies to reduce alcohol-related harm may need to be updated.

We aimed to examine overall trends in any risky behaviour associated with alcohol consumption and to decompose the effects of age groups, time periods, and birth cohorts to test whether: 1) there has been an overall decline in the prevalence of any alcohol-related risky behaviour across the Australian population of current drinkers; 2) whether there are declines in the prevalence of any alcohol-related risky behaviour with more recent birth cohorts and/or younger ages; and 3) whether these birth cohort and age trends vary between males and females.

2.5. Methods

2.5.1. Data sources and sample

We used data from the Australian National Drug Strategy Household Survey (NDSHS), which is a national survey using multi-stage stratified random household sampling that has been conducted every three years since 1985. Given changes in survey methodology and content over time (26), we limited our analyses to six waves of survey data (2001-2016). Although 2019 data were available, changes to the positioning and response options of the variable capturing risky behaviours following alcohol use resulted in a break in the time series (26), with the proportion of people reporting risky behaviours declining by half for most behaviours. Therefore, we excluded the 2019 wave of data. Survey response rates from 2001 to 2016 were similar, ranging from the highest at 51% in 2016 to the lowest at 46% in 2004. People aged 14 to 29 years are typically underrepresented whereas people aged 60 years and above are typically overrepresented in the NDSHS (27-32). To address imbalances due to sampling, the NDSHS data includes weights that consider geographical stratification,

household size, age, and sex according to Australian Bureau of Statistics population estimates (27-32). As alcohol-related risky behaviours are contingent on alcohol consumption, analyses were limited to respondents aged 14 to 80 years who reported consuming alcohol within the past 12 months at the time of survey completion ('current drinkers'; n = 121,281).

2.5.2. Measures

2.5.2.1. Outcome

To quantify alcohol-related risky behaviours, we used a single set of items: 'In the last 12 months, did you undertake the following activities while under the influence of or affected by alcohol?' Respondents can select yes or no for ten possible activities (e.g., drove a motor vehicle; see Table 1 for full list). Due to the relatively low prevalence of risky behaviours, we created a variable for any activities undertaken while under the influence of alcohol (yes/no).

2.5.2.2. Predictors

Age in years, birth year, and survey year were included as continuous integer variables for primary analyses. As the NDSHS does not record birthdates, birth year was calculated by subtracting age from the survey year. Age and birth year were also categorised into 10-year groups (except for the 75-80 age group and the 1995-2002 cohort group) for the purposes of plotting descriptive trends. For examination of male-female effects, we used one item: 'Are you male or female?' (this item varied in 2016: 'What is your sex?' with 'Male', 'Female' and 'Other' response options).

2.5.3. Analyses

Our analyses were not pre-registered and should thus be considered exploratory. All analyses were conducted in Stata version 16 (33) using complete-case data and reporting is consistent with STROBE guidelines (Appendix A1). To describe the sample, the proportion of male, female, and all respondents who reported each and any alcohol-related risky behaviour were estimated for each survey period, weighted by NDSHS sampling weights. For all subsequent analyses, a weighted sample using NDSHS sampling weights was created with counts of respondents who reported any alcohol-related risky behaviour for each combination of age, period, and cohort.

2.5.3.1. APC modelling

Our primary analysis examined the effects of age, period, and cohort on the prevalence of any alcohol-related risk behaviour among current drinkers in an APC modelling framework. As the APC components are linearly dependent (e.g., period – age = cohort), there exists an 'identification problem' where modelling each of these effects results in the exclusion of one component due to overparameterization. To address this, model constraints need to be applied. We used Rutherford's 'apcfit' Stata package implementation of Carstensen's approach, where APC effects are analysed using restricted cubic spline functions in a Poisson regression model with log(number of respondents) as the offset (34, 35). As age is a major risk factor in many types of alcohol-related risk behaviours, linear temporal changes ('drifts') are attributed to either the cohort or the period functions. Thus, the age function is presented as:

1) Age-period-cohort (AP-C), i.e., cross-sectional age-specific rates adjusting for cohort effects, where drift is included in the period function. This age function shows how drinkers of different ages in a particular year differ. The period function is set to zero

for the year 2007, the median wave of data. Period effects are presented as prevalence ratios (PR) with respect to 2007, and the cohort function represents residuals in relation to estimates for age and period effects.

2) Age-cohort-period (AC-P), i.e., longitudinal age-specific rates adjusting for period effects, where drift is included in the cohort function. This age function shows how drinkers in a particular birth cohort change as they become older. The cohort function is set to zero for the median birth cohort of 1971. Cohort effects are presented as PR with respect to the 1971 cohort, and the period function represents residuals in relation to estimates for age and cohort effects.

We first examined descriptive plots for the prevalence of any alcohol-related risk behaviour by age for different survey periods and prevalence by period for different age groups. If these plots both show parallel patterns, an age-period (AP) model is supported as this indicates that age-specific rates are proportional between periods (35, 36). Similarly, we examined descriptive plots for prevalence by age for different cohorts and prevalence by cohort for different age groups to determine if an age-cohort (AC) model was supported (35, 36).

After confirming support for AP and AC models, AP, AC, and full APC models were fitted using different numbers of equally spaced internal knots and compared using Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and deviance statistics, where deviance is calculated from log-likelihood (LL) as $-2\times(LL_{nested} - LL_{full})$ of the fitted models. Details of the model selection process are provided in Appendix A2.1.

This model comparison also serves as a sensitivity test to examine whether the APC effects are robust against changes to model complexity. Another sensitivity analysis is presented for

the primary APC model using an unweighted sample.

2.5.3.2. Male-female APC interaction modelling

To examine male-female effects, we fitted interaction models with a reduced number of splines and calculated time-dependent PR as demonstrated in Rutherford, Lambert, and Thompson (2010) (34; see Appendix A2.2 for model selection details). With females as the reference, PRs equal to 1.0 indicate no detectable differences between male and female prevalence, whereas PRs greater than 1.0 indicate that males have higher prevalence compared to females and lower prevalence for PRs less than 1.0. Since the identifiability problem is reintroduced due to the interaction term, one of the APC terms needs to be excluded. As the convergence in male and female alcohol consumption appears to largely be dependent on age and cohort rather than period (24, 25), we fitted models for:

1) Age interaction adjusting for birth cohort, where the period effect is assumed to be similar between males and females, and;
2) Cohort interaction adjusting for age, where the period effect is similarly assumed to be comparable across males and females.

To confirm that the period effect did not substantially differ between males and females, separate male and female APC models were estimated and the period effect was compared.

2.6. Results

2.6.1. Sample descriptives

As shown in Table 1, the proportion of respondents reporting any risk behaviour was relatively low (16.0-23.9%), with 'driving while under the influence of alcohol' being the most common behaviour (9.9-15.5%) across the sample. There were higher proportions of

males reporting any and each risk behaviour at each timepoint compared to females.

Table 1. Activities undertaken while under the influence of alcohol 2001-2016 as a percentage of respondents who consumed alcohol in the past 12 months**.**

	2001			2004			2007			2010			2013			2016		
Activity	**Males**	**Females**	**All**	**Males**	**Females**	**All**	**Males**	**Females**	**All**	**Males**	**Females**	**All**	**Males**	**Females**	**All**	**Males**	**Females**	**All**
Went to work	7.5	2.8	5.2	7.6	2.5	5.0	6.9	2.5	4.7	6.8	3.1	5.0	5.9	2.3	4.2	4.8	2.7	3.8
Went swimming	8.5	3.9	6.3	8.2	4.0	6.1	8.2	4.0	6.1	9.1	5.4	7.3	10.0	4.7	7.4	8.2	4.8	6.5
Operated a boat	2.2	0.3	1.3	2.4	0.3	1.3	2.0	0.2	1.1	1.7	0.3	1.0	1.7	0.2	1.0	1.5	0.2	0.9
Drove a motor vehicle	20.9	9.8	15.5	21.2	10.1	15.7	18.5	9.7	14.2	17.1	8.7	13.0	16.2	7.8	12.1	13.0	6.6	9.9
Operated hazardous machinery	1.3	0.1	0.7	1.5	0.0	0.8	1.7	0.1	0.9	1.1	0.1	0.6	1.2	0.1	0.7	0.9	0.1	0.5
Created a public disturbance	4.8	2.3	3.6	4.6	2.2	3.4	5.0	2.0	3.5	4.2	2.1	3.2	3.4	1.2	2.3	1.6	1.0	1.3
Caused damage to property	3.2	1.1	2.2	2.9	0.9	1.9	3.1	0.8	2.0	2.6	1.1	1.9	1.8	0.7	1.2	1.1	0.3	0.7
Stole money, goods, or property	1.0	0.5	0.7	0.8	0.2	0.5	0.8	0.3	0.6	0.6	0.3	0.5	0.6	0.3	0.4	0.4	0.2	0.3
Verbally abused someone	9.7	5.4	7.6	9.0	5.2	7.1	8.7	4.9	6.8	7.1	4.3	5.7	5.2	2.7	3.9	3.5	1.9	2.7
Physically abused someone	2.1	0.7	1.4	1.7	0.7	1.2	1.9	0.6	1.3	1.5	0.6	1.1	1.0	0.4	0.7	0.5	0.3	0.4
Any risky behaviour	30.8	16.7	23.9	30.5	16.7	23.7	28.1	15.8	22.1	26.5	15.8	21.3	25.0	13.0	19.1	20.6	11.3	16.0

Note: Percentages are weighted using sampling weights from the National Drug Strategy Household Survey that take into account geographical stratification, household size, age, and sex.

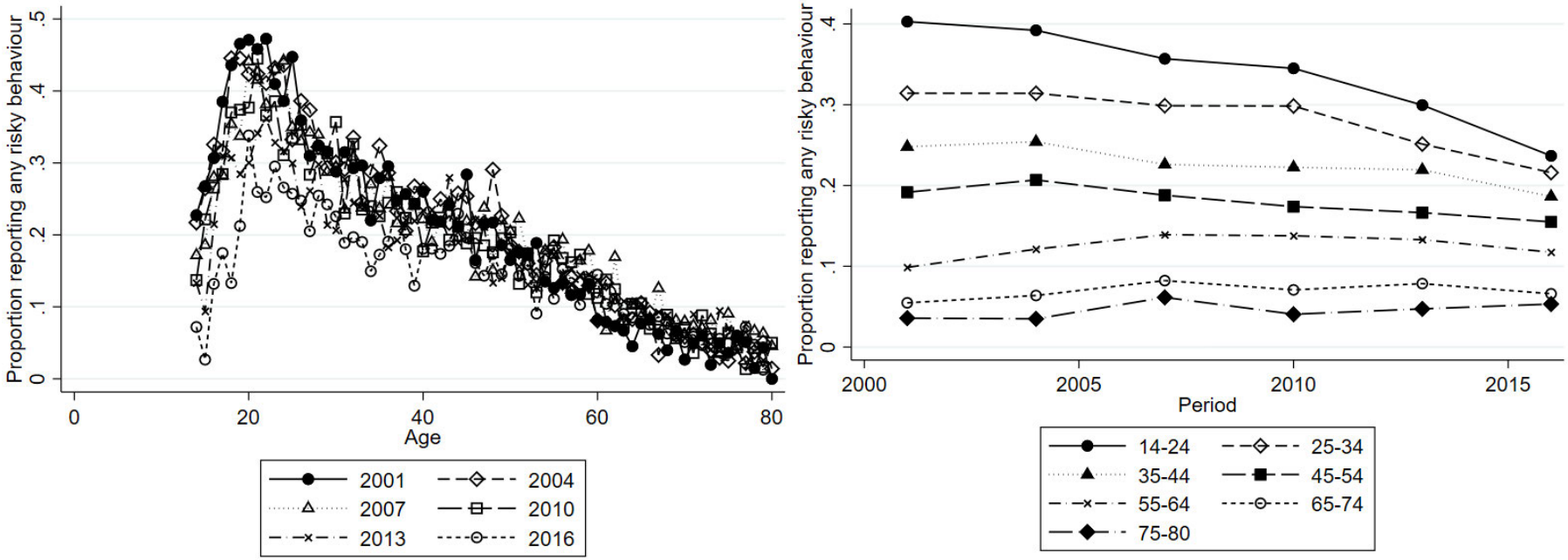

Figure 1. Prevalence of reporting any alcohol-related risky behaviour in the National Drug Strategy Household Survey (NDSHS) to examine age-period effect.

Note. Prevalence by age for each period shown on left panel, prevalence by period for each age group shown on right panel.

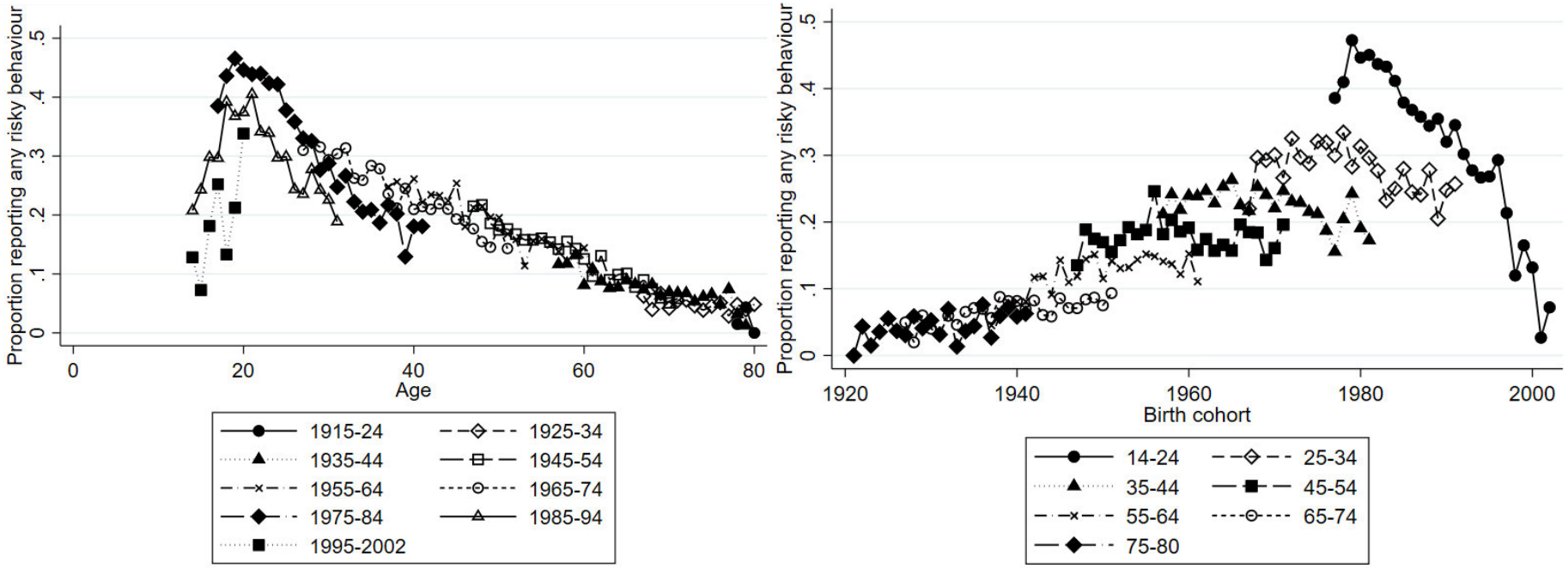

Figure 2. Prevalence of reporting any alcohol-related risky behaviour in the National Drug Strategy Household Survey (NDSHS) to examine age-cohort effect.

Note. Prevalence by age for each birth cohort shown on left panel, prevalence by cohort for each age group shown on right panel.

2.6.2. Support for age-period-cohort modelling

The age-period curves in each of the panels in Figure 1 show evidence of age-period effects, with parallel lines in each panel. Similarly, age-cohort curves in Figure 2 are mostly parallel except for the 14-24 age group on the righthand panel. These effects appear to be non-linear, showing support for an APC model.

2.6.3. Age-period-cohort models

To describe the non-linear effects in our primary APC models, we used four equally spaced internal knots of age and nine equally spaced internal knots for each of age and cohort (see Appendix A2.1 for model selection details). Table 2 shows the fit statistics for this model, with the full APC model having improved fit over the AP and AC models (see Appendix A3 for fit statistics using other combinations of internal knots). The AC model had better fit than the AP model, indicating that cohort had a more pronounced effect than period. Fitted values for the AP-C and AC-P functions are shown in Figure 3. Both the cross-sectional (AP-C; Figure 3 top) and longitudinal (AC-P; Figure 3 bottom) age trends showed that the prevalence of any alcohol-related risky behaviour peaked at age 21 years and then declined with age. Cohort functions showed sharper decline than period functions, indicating that there was a larger cohort effect than a period effect. The prevalence of respondents reporting any risky behaviour peaked in the early 2000s and declined with time (2016 vs 2007 RR = 0.80 [95% CI = 0.76-0.84]). The prevalence of respondents reporting any risky behaviour increased from the earliest birth cohort of 1921, peaked at the 1954 birth cohort (1954 vs 1971 RR = 1.42 [95% CI = 1.30-1.55]) then declined in more recent birth cohorts (2002 vs 1971 RR = 0.32 [95% CI = 0.27-0.39]).

Sensitivity analyses using different combinations of internal knots for age and cohort, as

well as using an unweighted sample showed similar trends for each APC component (Appendix A4 and A5).

Table 2. Fit statistics for age, period, and cohort model.

Model	AIC	BIC	Log-likelihood	d.f.	Deviance	p
APC	6.799	-1795.811	-1334.82	375		
AC	6.858	-1788.334	-1350.54	379	31.4431	< 0.001
AP	7.129	-1699.770	-1409.8	384	149.96434	< 0.001

Note. Using 4 equally spaced internal knots for period and 9 equally spaced internal knots for each of period and cohort. APC = age-period-cohort; AP = age-period; AC = age-cohort; AIC = Akaike Information Criterion, smaller values indicate better model fit; BIC = Bayesian Information Criterion, smaller values indicate better model fit; d.f. = degrees of freedom.

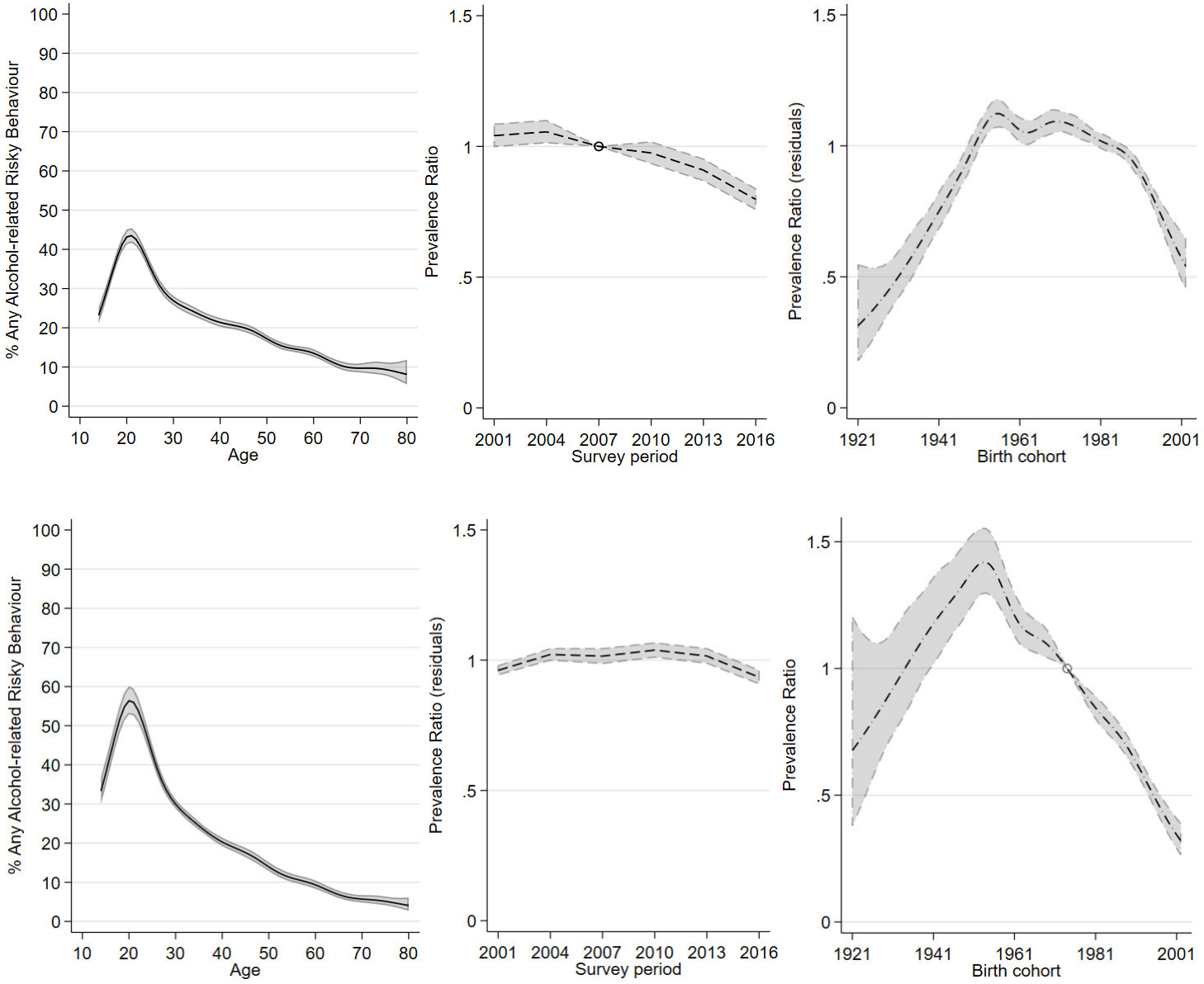
% Any Alcohol-related Risky Behaviour
Age
Prevalence Ratio
Survey period
Prevalence Ratio (residuals)
Birth cohort
% Any Alcohol-related Risky Behaviour
Age
Prevalence Ratio (residuals)
Survey period
Prevalence Ratio
Birth cohort

Figure 3. Estimated effects with 95% confidence intervals from the APC model using age-period-cohort (AP-C) and age-cohort-period (AC-P) functions for any risky behaviour with 4 internal knots for period and 9 internal knots for age and birth cohort.

Note. Top panels show AP-C, bottom panels show AC-P. Cross-sectional age effects for the reference period of 2007 are shown on the top left (solid line) as a percentage. Period effects are shown on the top centre (dashed line) as a rate ratio. Residuals for the cohort effect are shown in the top right (dash-dot line). Longitudinal age effects for the reference birth cohort of 1971 are shown on the bottom left (solid line) as a percentage. Cohort effects are shown in the bottom right (dash-dot line) as a rate ratio. Residuals for the period effect are shown on the bottom centre (dashed line).

2.6.4. Male-female interaction models

For each of the age and cohort components, three equally spaced internal knots were used to describe non-linear effects in the reduced-spline male-female interaction models (see Appendix A2.2 for model selection details and Appendix A6 for fit statistics). Figure 4 shows the estimated time-dependent prevalence rate ratios (PRR) for males versus females for the age effect and cohort effect. An overall age interaction effect was present, with males being approximately twice as likely as females to report any alcohol-related risky behaviour (PRR = 2.10 [95% CI = 1.84-2.39]). The interaction effect size increased with age (i.e., the male-female gap widened with age), with divergence starting at age 16 years (PRR = 1.19 [95% CI = 1.04-1.35]) and peaking at age 69 years (PRR = 2.76 [95% CI = 2.02-3.77]). The cohort interaction effect decreased from the oldest birth cohort (1921 PRR = 3.82 [95% CI = 1.68-8.72] to the youngest birth cohort (2002 PRR = 1.31 [95% CI = 1.03-1.68]), although the male-female gap remained. The cohort interaction effect was relatively stable from the 1950 cohort (PRR = 2.16 [95% CI = 1.89-2.46]) to the 1980 cohort (PRR = 2.09 [95% CI = 1.81-2.43]). However, estimates for the earliest birth cohorts were less precise due to low cell sizes.

Separate APC models for males and females using four knots for period and three knots for each of age and cohort showed considerable overlap in the period effect (Figure 5, top centre), which supported the assumption that the period effect does not differ substantially between males and females and thus exclusion of the period component was unlikely to have impacted estimates in the interaction model. Separate male and female cohort effects (Figure 5, bottom right) suggest that there have been steeper declines among recent cohorts of males than females.

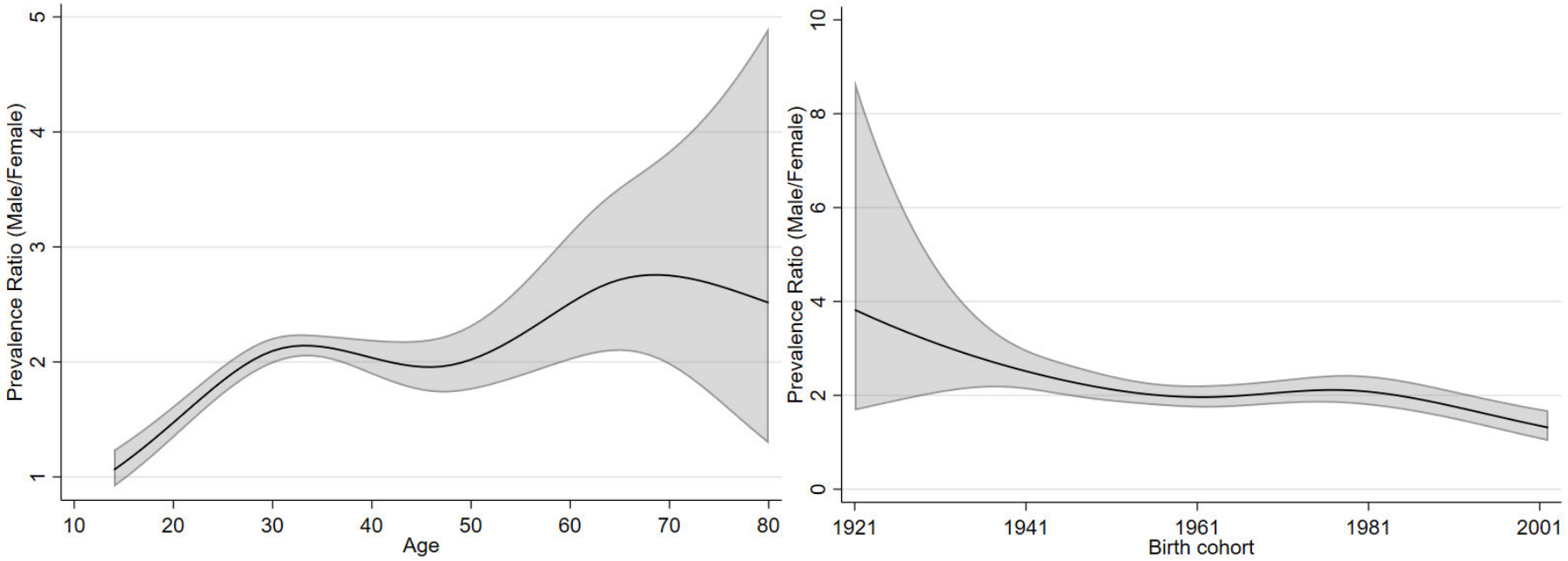

Figure 4. Estimated time-dependent prevalence rate ratios with 95% confidence intervals for males with females as the reference.

Note. Age effects adjusting for cohort effects are shown on the left panel. Cohort effects adjusting for age effects are shown on the right panel. PRR = Prevalence Rate Ratio.

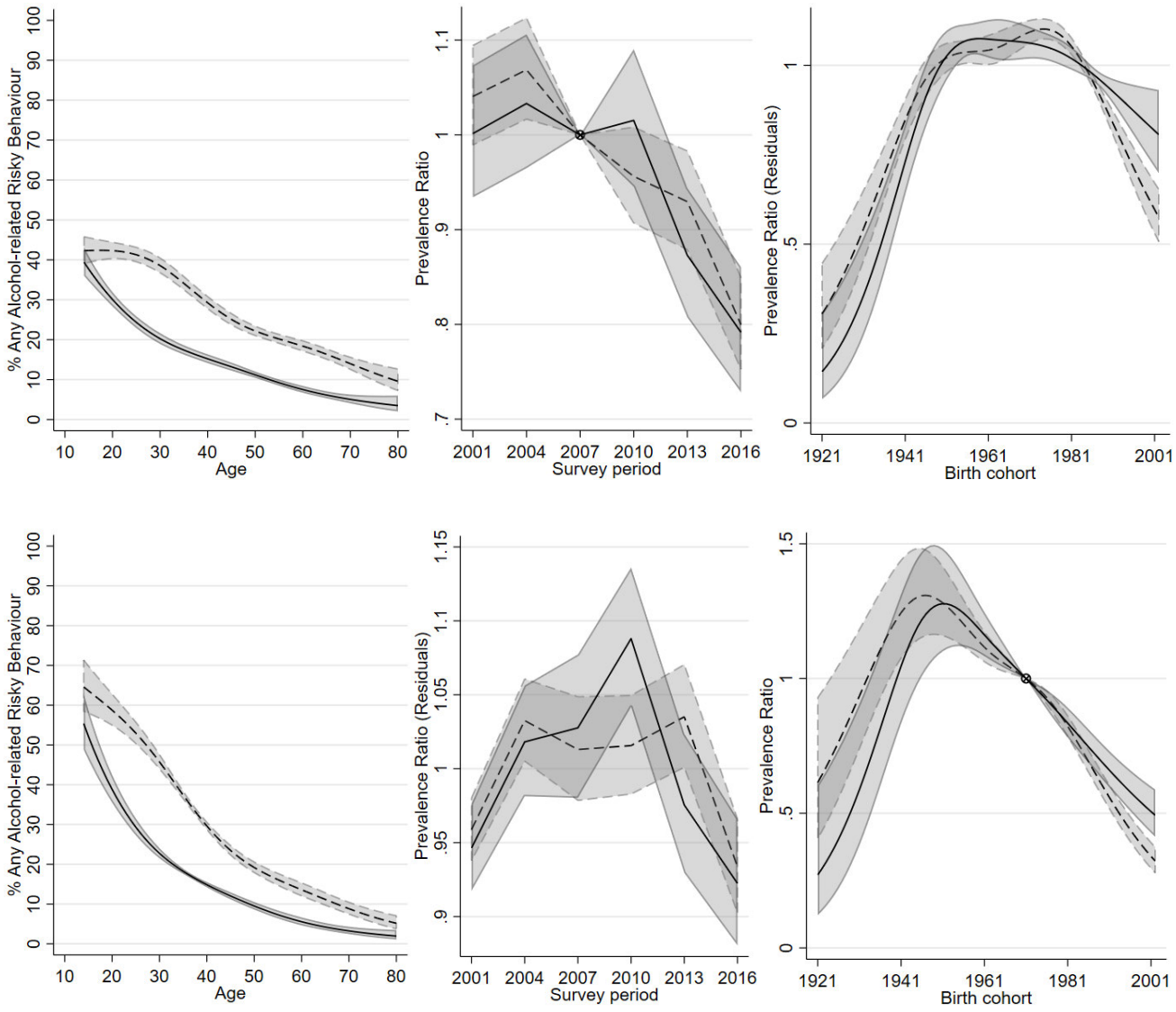

Figure 5. Estimated effects with 95% confidence intervals from separate male (dashed lines) and female (solid lines) APC models using age-period-cohort (AP-C) and age-cohort-period (AC-P) functions for any risky behaviour with 4 internal knots for period and 3 internal knots for age and birth cohort.

Note. Top panels show AP-C, bottom panels show AC-P. Cross-sectional AP-C age effects for the reference period of 2007 are shown on the top left as a percentage. AP-C period effects are shown on the top centre as a prevalence ratio. Residuals for the AP-C cohort effect are shown in the top right. Longitudinal AC-P age effects for the reference birth cohort of 1971 are shown on the bottom left as a percentage. AC-P cohort effects are shown in the bottom right as a prevalence ratio. Residuals for the AC-P period effect are shown on the bottom centre.

2.7. Discussion

Using national survey data, we found steady declines in the prevalence of any alcohol-related risk behaviour among current drinkers in Australia between 2001 and 2016. Our use of APC methods has shown that recent cohorts reported markedly lower rates of any risky behaviour at a given age than earlier birth cohorts. The prevalence of these self-reported risk behaviours peaked in early adulthood, then decreased with age and stabilised at around age 70 years. Overall, males were twice as likely to report alcohol-related risk behaviours compared to females, although this difference was smaller in younger people and in more recent birth cohorts. Recent birth cohorts of males appear to have steeper declines in any risky behaviour compared to females.

A previous study using NDSHS data reported that the relationship between alcohol consumption levels and risky behaviours has remained consistent from 2001 to 2016, with greater alcohol consumption being associated with more risky behaviour (37). Our APC model supports this finding, showing population-level decreases in any risky behaviour in addition to cohort and age-specific effects during this period of declining alcohol consumption (2). Commensurate with recent reductions in alcohol use among people born during or after the 1990s (1, 11-13), we find that risky behaviour was least common amongst more recent birth cohorts. Importantly, this cohort effect exists independent of the increases in abstention for recent cohorts as we exclude non-drinkers in our APC models. However, these decreases in prevalence of self-reported risky behaviour should be interpreted with caution as they do not necessarily translate to reductions in harm. Existing Australian data examining trends in alcohol-attributable hospitalisation rates show overall increases in alcohol-attributable hospitalisation rates with variations by age group (2, 4, 38),

but there has yet to be a study statistically comparing trends in Australian alcohol-related hospitalisation rates in an APC framework. Thus, the reductions in alcohol-related risky behaviour we have identified in our study may result in similar reductions in alcohol-related harm, but this applies mainly to the young people in more recent birth cohorts who showed the sharpest decline in risky behaviours.

Despite these apparent reductions in alcohol-related risky behaviour among recent birth cohorts, young people were still more likely to report risky behaviour compared to older adults. Both the cross-sectional (APC) and longitudinal (ACP) models in our study showed peaks in early adulthood for the age effect. This is likely due to increased propensity for risk-taking in late adolescence and early adulthood (39) combined with risky drinking patterns that are common in this age group (2). Indeed, whilst the proportion of Australian adults aged 18 to 24 years exceeding the single occasion risk guidelines (> 4 standard drinks on one occasion) (40) decreased from 54% in 2007 to 41% in 2019, they remained the age group most likely to drink at these levels (2). Given that young adults are more likely to experience alcohol-related injuries and other acute harms compared to any other age group (2), alcohol-related risky behaviour at this age remains a serious public health issue. Promisingly, reductions in adolescent drinking observed in recent birth cohorts appear to continue as they age into adulthood (41), which should lead to reduced risky behaviour (37) and lower risk of future harm (42, 43).

Reflective of the closing male-female gap in alcohol use (21), the male-female ratio in any alcohol-related risky behaviour also appears to be converging in more recent birth cohorts. Separate male and female APC models suggest that both sexes show declines in risky behaviour with more recent birth cohorts, but this decline has been steeper among males.

Indeed, recent Australian evidence suggests that the narrowing gap in drinking is being driven by greater decreases in male alcohol use (41). A study of young adults in the United States reported that heavy drinking has increased in more recent birth cohorts of females but not males (44). Similarly, an APC study of data from the United Kingdom showed that in recent birth cohorts, male drinkers have been drinking less but female drinkers have been drinking more (15). As these differences are between cohorts, they are likely due to social changes such as shifts in the perception of drinking as an activity that is predominantly masculine to being widely accepted and encouraged among females (45, 46). Since this has been a recent phenomenon, studies on the efficacy of population-level alcohol policy have thus far rarely compared effects on males versus females (47). One study in 2021 did, however, find that alcohol pricing policies in England were more effective at reducing alcohol use and alcohol-attributable hospitalisations in males compared to females (48). Overall, it appears that there is a need to rethink strategies aimed at reducing alcohol-related harm to include approaches that are as effective for females as they are for males.

Our findings should be considered in the context of some important limitations. The NDSHS sample does not include people who are homeless or reside in non-private (e.g., hotels) or institutional settings (e.g., rehabilitation centres), which can lead to an underestimates of alcohol-related risky behaviours as these populations tend to consume more alcohol than the general population (49). All risky behaviours in our data were self-reported, which may have resulted in underestimations of prevalence due to issues with memory resulting from heavy drinking. There may have also been underreporting due social desirability biases (50, 51), particularly as most activities in the risky behaviour measure have legal repercussions. Additionally, the NDSHS does not include questions regarding the frequency of these risky behaviours and nor did our analyses include the number of different risky behaviours

reported. Thus, we cannot comment on risk severity as we did not distinguish between people who engage in many risky behaviours versus people who have engaged in risky behaviours on rare occasions. Due to the relatively short period of data analysed (16 years), the period effect should be interpreted with caution, particularly when making comparisons to the cohort and age effects. The short period of analysis also means that each birth cohort is only observed for 16 years, and life course patterns are then estimated based on age distributions across the sample. Longer study periods will provide more robust results. As the NDSHS is conducted once every three years, this means that there is no information regarding risky behaviours in the intervening years. Methodological differences between the six NDSHS survey waves may have also biased trends over time. The 2016 wave was the first to introduce an online option for the survey, whereas previous waves were either paper or phone based. Online respondents differed significantly on a range of demographics such as education level (26), however, the impact of this on our study is likely to be minimal as no differences were found between paper and online respondents in terms of drinking status and lifetime risky drinking, and only small differences were observed for single occasion risk (26). Future research examining trends in alcohol-related harms would benefit from supplementing survey data with more objective records of harm such as those from healthcare services and offending databases (52).

2.7.1. Conclusion

To our knowledge, this is the first study to examine age-period-cohort trends in alcohol-related risky behaviour. We found that the prevalence of any alcohol-related risky behaviour declined across the population between 2001 and 2016, which appears to be primarily driven by more recent birth cohorts. However, young people were still more likely to report

risky behaviour than older adults. Overall, males were more likely to report alcohol-related risky behaviour compared to females, but we found evidence of a closing male-female gap in more recent birth cohorts. Our findings highlight the continued need to address alcohol use and harms, particularly in high-risk populations such as young people.

2.8. Declarations of competing interest

AP has received investigator-initiated untied educational grants from Mundipharma and Seqirus for post-marketing surveillance of pharmaceutical opioids. MF has received untied educational grants from the Australian Government Department of Health. These grant parties had no role in the study design, conduct, and reporting. All other authors have no conflicts of interest to declare.

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2.10. Acknowledgements

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3. CHAPTER 3: TRAJECTORIES OF ALCOHOL-INDUCED BLACKOUTS IN ADOLESCENCE: EARLY RISK FACTORS AND ALCOHOL USE DISORDER OUTCOMES IN EARLY ADULTHOOD

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3.1. Copyright Statement

I declare that this publication occurred during my candidature as a direct result of my research towards this thesis and, to the best of my knowledge, does not breach copyright regulations nor intellectual property rights.

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3.2. Preamble

In Chapter 2, we examined the effects of age, period, and birth cohort on the prevalence of alcohol-related risky behaviour from 2001 to 2016 in Australia among people aged 14 to 80 years who consumed alcohol. Using repeated cross-sectional data from a national household survey, we found that the prevalence of any risky behaviour declined with time. Although the prevalence of any risky behaviour has steadily declined with more recent birth cohorts, young people in recent generations still showed higher prevalence of risky behaviour compared to older adults. Indeed, the prevalence of any risky behaviour increased as young people age into adulthood, peaked at age 21 years, then steadily declined with age. Males were overall twice as likely to report any risky behaviour compared to females, although this difference was smaller among younger people and among recent birth cohorts.

Though Chapter 2 provided an overview of the current state of alcohol-related harm in the population, we are unable to examine how harms typically develop within individuals nor identify whether there are risk factors for certain patterns of harms development using repeated cross-sectional data. Our understanding of alcohol-related harm among recent cohorts of young people would be strengthened with longitudinal data.

This chapter aims to address research question 2: '*What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving declines in alcohol consumption?'* and research question 3: *'In recent birth cohorts, are there early adolescent factors that predict high-risk developmental patterns of harm?'*. We examine developmental trajectories of a specific type of alcohol-related harm, blackouts, using a longitudinal cohort of young people. We chose to focus on blackouts as a starting point since blackouts are

known to be relatively common amongst young people who drink (1, 2). Additionally, unlike other common harms such as hangovers, blackouts have previously been found to be a strong predictor of other future harm such as injury and (3-6). We identify common developmental trajectories of blackouts from age 14 to age 19 years, trajectories that are associated with AUD at age 20 years, and factors at age 13 years that predict these high-risk trajectories.

3.3. Abstract

Background and aims: Experience of alcohol-induced memory blackouts in adolescence may be an important risk factor for later harms. This longitudinal study: i) modelled trajectories of alcohol-related blackouts throughout adolescence; ii) explored early-adolescent predictors of blackout trajectories; and iii) examined the association between blackout trajectories and alcohol use disorder (AUD) symptoms.

Methods: Data from six annual surveys of a longitudinal cohort of Australian adolescents (n=1821; M_{age}=13.9 years until M_{age}=18.8 years) were used to model latent class growth trajectories of self-reported blackouts, adjusting for alcohol consumption frequency and typical quantity. Regression models were used to determine whether parent, child, and peer factors at baseline (M_{age}=12.9) predicted profiles of blackout trajectory membership and whether blackout trajectories predicted meeting criteria for self-reported DSM-5 AUD in early adulthood (M_{age}=19.8).

Findings: We identified a three-class solution: *delayed alcohol initiation, rare blackouts* (n=701; 38.5%); *early initiation, rare blackouts* (n=869; 47.7%); and *early initiation, increasing blackouts* (n=251; 13.8%). Female sex was associated with increased risk of *early initiation, increasing blackouts* relative to *delayed initiation, rare blackouts* (RRR: 3.90; 99.5% CI: 1.96, 7.76) and relative to *early initiation, rare blackouts* (RRR: 2.89; 99.5% CI: 1.42, 5.87). *Early initiation, rare blackouts* (OR: 1.96; 99.5% CI: 1.17, 3.29) and *early initiation, increasing blackouts* (OR: 4.93; 99.5% CI: 2.32, 10.48) were each associated with increased odds of meeting criteria for AUD in early adulthood relative to *delayed initiation, rare blackouts*. *Early initiation, increasing blackouts* was associated with increased odds of meeting criteria for AUD in early adulthood relative to *early initiation, rare blackouts* (OR: 2.51; 99.5% CI: 1.18, 5.38).

Conclusions: Sex predicts adolescent alcohol-related blackout trajectories independent of alcohol consumption levels and age of initiation. These trajectories are in turn predictive of clinically significant alcohol-related harms, suggesting that blackouts may be important early intervention targets in reducing risk of subsequent AUDs.

Keywords: blackouts, anterograde amnesia, alcohol drinking, adolescent, longitudinal studies, alcohol use disorder

3.4. Background

One of the most commonly reported negative consequences of alcohol use in youth is alcohol-induced memory blackouts (1, 2), caused by the interference of alcohol with neural function involved in the formation of long-term memories. Characterised by periods of anterograde amnesia whilst intoxicated (7), a person experiencing a blackout can engage in behaviours such as talking, walking, and driving, but are unable to later recall these actions. This phenomenon is thus entirely distinct from the loss of consciousness following very heavy drinking. Depending on the amount of alcohol consumed and the speed of consumption, blackouts can range from fragmentary, characterised by partial retrieval of events (facilitated by cues such as someone else recounting the event), to en bloc, involving complete and permanent memory loss of events that occurred while intoxicated (8). The occurrence of a blackout is indicative of significant acute cognitive impairment due to rapid intoxication, with the risk of experiencing blackouts increasing with the rate of increase in blood alcohol concentration (7).

Whilst it has been established that levels of alcohol consumption increase steeply from initiation in adolescence to early adulthood (9), it is unclear how the experience of alcohol-induced blackouts changes over time, and whether different patterns of experiencing blackouts are associated with differential risk of experiencing other alcohol-related harms. Blackouts in early adulthood have been associated with increased odds of future alcohol-related injury, sexual assault, and other harms after adjusting for factors such as alcohol use and trait sensation seeking (3, 4, 6). Studer, Gmel (5) found that blackouts at age 20 were associated with symptoms of alcohol dependence five years later, after controlling for alcohol use and other risk factors for alcohol dependence. Thus, blackouts may serve as a

useful proxy for harmful levels of alcohol consumption involving both individual differences in tolerance and speed of alcohol consumption.

Current attempts to examine the risk and protective factors for experiencing an alcohol-induced blackout have focused on people aged 18 years and older, and predominantly comprised cross-sectional studies (10). Whilst alcohol consumption and associated harms peak in early adulthood, one study using data from a longitudinal cohort representative of the British population reported that almost 30% of adolescents aged 15 years who had ever consumed at least one full serve of alcohol had experienced a blackout in the past year (11). Distinct trajectories of escalating blackouts have previously been identified through longitudinal research, with some consistent risk factors for frequent blackouts including female sex, other substance use, and peer influences (11-14). These studies examined cohorts of young people who have already initiated alcohol use (11, 13), and/or have been identified due to their problematic alcohol use (12, 14). It is currently unknown how the experience of blackouts may escalate differentially among adolescents from the time of drinking onset, and whether any such trajectories have subsequent consequences. Additionally, previous studies have not taken into account parenting and other familial factors shown to be associated with binge drinking in adolescence, such as parental supply of alcohol and alcohol-specific household rules (15-17). An examination of how child, parent, and family factors influence developmental trajectories of alcohol-induced blackouts, and whether these trajectories are associated with risk of experiencing clinically relevant harms, can aid in identifying high-risk individuals for targeted early intervention.

The aims of this study were to identify the typical trajectories of alcohol-induced blackouts in a longitudinal cohort of young Australians. Specifically, this study examined: i) trajectories

of self-reported alcohol-induced blackouts from age 13 to 19 years, whilst adjusting for frequency and typical quantity of alcohol consumption; ii) sociodemographic factors at age 12 that predict the trajectory of alcohol-induced blackouts; and iii) associations between blackout trajectory and meeting Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV; 18) criteria for alcohol abuse, alcohol dependence, and Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5; 19) criteria for alcohol use disorder (AUD) based on self-reported symptoms at age 20 years.

3.5. Methods

3.5.1. Participants and procedure

This study used the Australian Parental Supply of Alcohol Longitudinal Study (APSALS; registered at ClinicalTrials.gov: NCT02280551) cohort of 1927 young people. Participants and one parent or guardian were recruited via an opt-in process in 2010 and 2011 from Grade 7 classes in Australian private/independent (49%), Catholic (12%), and government (39%) schools. Distribution of sex, household composition, racial background, and parental education in the cohort was comparable to the Australian population, although families with higher socioeconomic status were somewhat over-represented. For more details about the recruitment methods and cohort profile, see Aiken, Wadolowski (20). Online or paper hardcopy surveys were sent to participants each year. Parents were also surveyed until the 6th annual wave of data collection. To minimise reporting bias, surveys were sent separately to each adolescent and parent. APSALS was approved by the University of New South Wales Research Ethics Committee and ratified by the universities of Tasmania, Newcastle, and Queensland, and Curtin University.

Analyses for this study used eight annual waves of data collection (Wave 1 to Wave 8; 2010-

11 to 2017-18; mean ages 12.9 years and 19.8 years, respectively), including data collected from parents at Wave 1. Of the 1927 adolescents recruited into the study, 73.4% (n=1415) completed the Wave 8 survey (see Appendix B1 for flowchart of cohort retention). Participants who had completed at least three annual surveys were included in the current analyses (n=1821). Reporting is in accordance with Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines (see Appendix B2 for checklist).

3.5.2. Measures

3.5.2.1. Alcohol consumption.

Self-reported alcohol consumption frequency and typical quantity in each wave were measured using two items, each with eight possible responses: “In the last 12 months, how often have you had an alcoholic drink of any kind?” (never, less than once/month, once/month, 2-3 days/month, 1-2 days/week, 3-4 days/week, 5-6 days/week, every day) and “In the last 12 months, on a day you have an alcoholic drink, how many standard drinks do you usually have?” (none, a sip, 1-2 drinks, 3-4 drinks, 5-6 drinks, 7-10 drinks, 11-12 drinks, 13 or more drinks), where a standard drink is defined as 10g of alcohol (21).

3.5.2.2. Blackouts.

The alcohol-induced blackout measure consisted of a single item adapted from the School Health and Alcohol Harm Reduction Project (SHAHRP; 22): “In the last 12 months, how many times have you been unable to remember what had happened while you had been drinking?” with six possible responses (never, once, twice, 3-4 times, 5-11 times, 12+ times). This item was recoded to consider whether participants had consumed any alcohol within the last 12 months (i.e. the original “never” category was separated into “did not drink” and “drank but never had a blackout”).

3.5.2.3. Alcohol dependence, alcohol abuse, and alcohol use disorder.

The alcohol abuse measure consisted of 4 items adapted from the Diagnostic Interview Schedule for Children Version IV (DISC-IV; 23) which corresponded to DSM-IV symptoms of alcohol abuse. The alcohol dependence measure consisted of 7 items, likewise adapted from the DISC-IV and corresponding to DSM-IV symptoms of alcohol dependence. The measure for AUD consisted of 11 items corresponding to DSM-5 symptoms of AUD. Three binary variables were coded for: i) meeting DSM-IV criteria for alcohol abuse (at least one of the four symptoms and have never met criteria for alcohol dependence); ii) meeting DSM-IV criteria for alcohol dependence (at least three of the seven symptoms); and iii) meeting DSM-5 criteria for AUD (at least two of the eleven symptoms).

3.5.2.4. Wave 1 characteristics.

Wave 1 predictors of alcohol-induced blackout trajectories were identified from a literature search (see Appendix B3 for review of literature and details of measures used); these included: *child variables* (sex, externalising), *peer variables* (peer disapproval of tobacco/alcohol use, peer tobacco/alcohol use), *parent variables* (highest level of education, alcohol-specific rules, parental monitoring), and *family variables* (socioeconomic status, one/two parent household, alcohol accessibility at home without parental knowledge, family history of alcohol problems, family conflict).

3.5.3. Statistical analysis

These analyses were not pre-registered and as such, results should be considered exploratory.

3.5.3.1. Latent class growth analyses.

Latent class growth analyses (1-4 classes) were performed using Mplus version 8 (24). This form of latent growth curve modelling identifies 'classes' or clusters of individuals where variance and covariance estimates in the growth factors of observed variables within each class are assumed to be zero (25) to identify meaningful homogenous subgroups that display similar patterns of growth. One set of growth parameters were specified within each class based on the number of blackouts (did not drink, drank but no blackouts, once, twice, 3-4 times, 5-11 times, 12+ times) experienced within each 12-month period from Wave 2 to Wave 7, adjusting for zero-standardised 12-month frequency multiplied by typical quantity of alcohol consumption. Akaike's Information Criterion (AIC) and sample-size adjusted Bayesian Information Criterion (ssaBIC) were used to assess model fit, where lower values indicated better fit. The Lo-Mendell-Rubin adjusted log-likelihood ratio test (LMR-ALRT; 26) statistic was used to compare fit of a *k* class model with a *k*-1 class model, where $p < 0.05$ indicated that the *k*-1 class model should be rejected for the *k* class model. Average class classification probability was used as an index of classification quality, where values approaching 1 (range 0.0-1.0) indicated better differentiation of individuals between classes. Class composition of models was examined alongside fit statistics to determine the most parsimonious and theoretically meaningful class structure.

3.5.3.2. Accounting for latent class classification uncertainty.

As latent classes cannot be assigned to individuals with certainty, the modified three-step Bolck-Croon-Hagenaars estimation method (BCH; 27, 28, 29) was used to account for classification uncertainty in subsequent analyses: 1) a latent class growth model is estimated; 2) an expanded data file with one record for each latent class for each individual

is created, with weights assigned to each record calculated from the inverse of a matrix containing the classification probabilities for most likely latent class membership by latent class (30); and 3) associations between latent class membership and other variables are estimated as a multiple group model using the BCH weighting variable.

3.5.3.3. Regression analyses.

Logistic regression analyses were performed using Stata version 16 (31), weighted by the BCH variable. Multivariate multinomial logistic regression analyses were used to predict trajectory class membership using Wave 1 characteristics as a predictor (presented as relative risk ratios [RRR] with 99.5% confidence intervals [CIs]). Adjusted binary logistic regression analyses were used to predict whether participants met DSM-IV criteria for alcohol dependence and alcohol abuse, in addition to DSM-5 criteria for AUD, at Wave 8 using class membership as a predictor (presented as odds ratios [OR] with 99.5% CIs). All Wave 1 characteristics described above were included in adjusted regression analyses as covariates.

3.5.3.4. Missing data.

A summary of missing data can be found in Appendix B4. To reduce any potential bias introduced by missingness in the data, primary analyses were conducted on multiply imputed data. The data were imputed using Mplus version 8 (24) using an unrestricted H1 model (32) as recommended by Asparouhov and Muthén (30). Based on the percentage of missing information, we used M = 20 imputations (33). Latent class growth analyses were then conducted on each imputed dataset. The resulting datasets containing BCH weights from each run were manually combined and imported into Stata as a multiply imputed dataset for regression analyses. Sensitivity analyses using complete-case data can be found

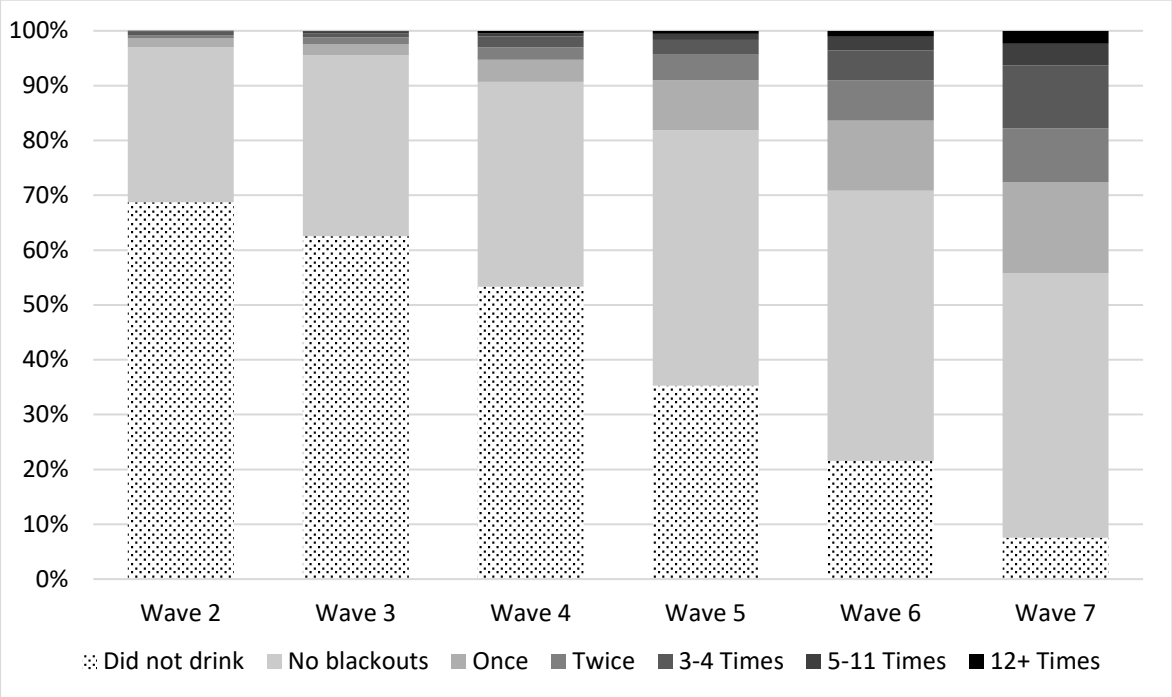
in Appendix B5 to B11.

3.6. Results

3.6.1. Number of blackouts

Figure 6 shows the distribution of the number of 12-month alcohol-related blackouts from Wave 2 to Wave 7. In Wave 2, nearly 10% of adolescents who had consumed alcohol in the past 12 months reported experiencing at least one blackout. By Wave 7, over 47% of young people who had consumed alcohol had experienced at least one blackout. Of the young people who had experienced a blackout in Wave 7, around 14% had experienced five or more blackouts.

Figure 6. Proportion of sample that reported self-reported blackouts in the past 12 months by follow-up wave.

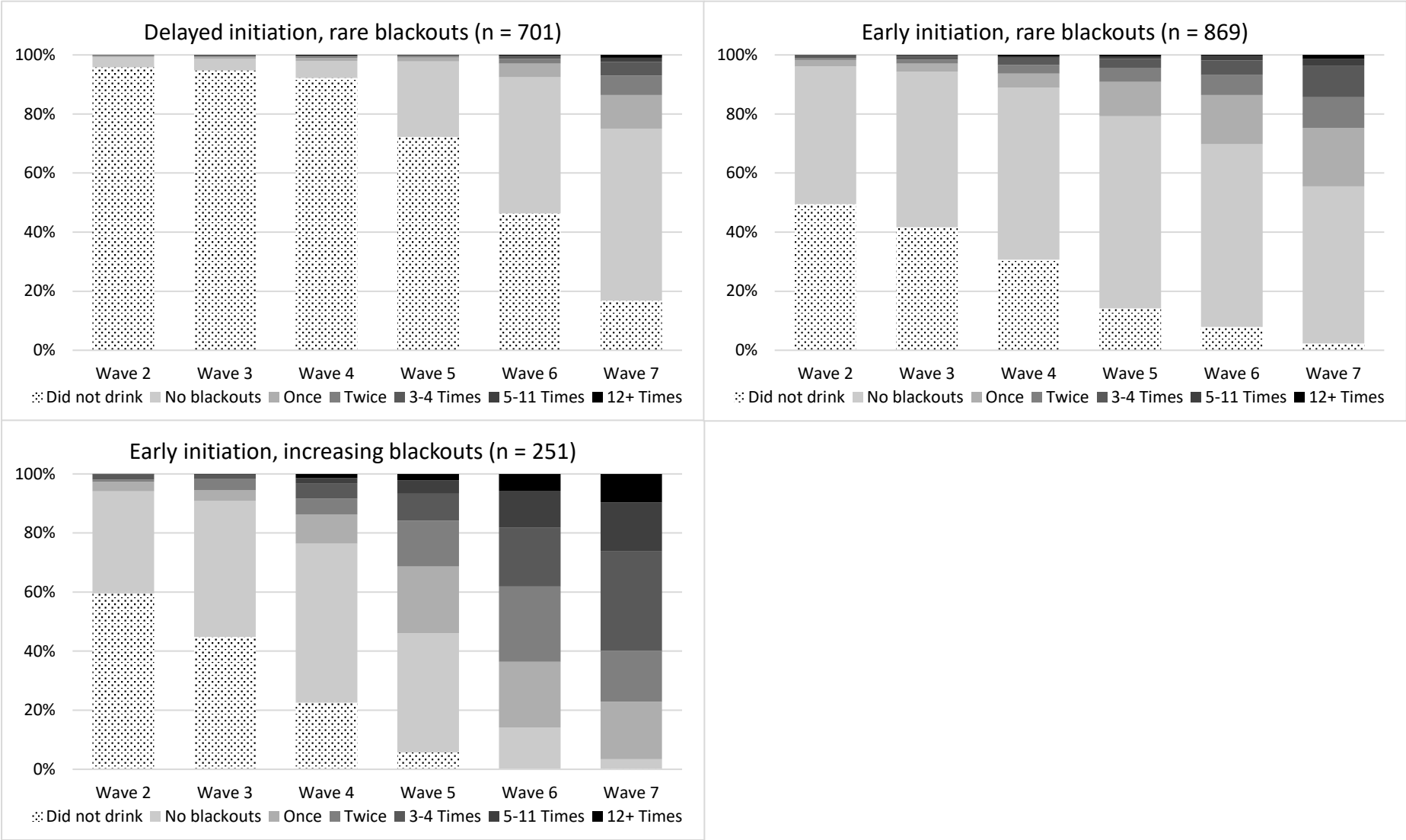


3.6.2. Trajectories of blackouts

Fit statistics for the 1- to 4-class latent class growth models are shown in Appendix B12.

Although the 4-class model had the smallest ssaBIC, the LMR-ALRT did not indicate improved model fit over the 3-class solution and the model contained a class with less than 10% of the full sample. Examination of the average latent class probabilities matrix showed that the classes were reasonably distinct, with average classification probabilities of 0.830 for Class 1, 0.765 for Class 2, and 0.749 for Class 3 (see Appendix B13). Class composition supported selection of the 3-class model as each class was of substantive size and showed distinct trajectories of blackouts. Probabilities of endorsing each category of the blackouts variable for each class are summarised in Figure 7. Class 1 was labelled as the *delayed initiation, rare blackouts* class (n=701; 38.5%), where the majority did not initiate alcohol use until age 17-18 years and less than 30% of the class members had ever experienced a blackout by age 18-19 years. Class 2 was labelled as the *early initiation, rare blackouts* class (n=869; 47.7%) where the majority had initiated alcohol use by age 14-15 years, with less than 50% ever experiencing a blackout by age 18-19 years. Class 3 was labelled the *early initiation, increasing blackouts* class (n=251; 13.8%) where the majority had initiated alcohol use by age 14-15 years, with around 97% having experienced a blackout by age 18-19 years. Latent class growth models using complete-case data similarly supported the 3-class solution, with similar average latent class probabilities and class profiles (Appendix B5 to B7).

Figure 7. Proportion endorsing different numbers of blackouts in each class, 3-class solution.



3.6.3. Predictors of blackout trajectory

Results of the multivariate multinomial logistic regression models are presented in Table 3 (see Appendix B8 and B14 for bivariate models). Wave 1 factors associated with increased risk of *early initiation, increasing blackouts* relative to *delayed initiation, rare blackouts* were: female sex (RRR: 3.90; 99.5% CI: 1.96, 7.76), having more peers who use substances (RRR: 1.37; 99.5% CI: 1.07, 1.77), and greater accessibility to alcohol at home (RRR: 1.12; 99.5% CI: 1.01, 1.25). Having more peers who use substances (RRR: 1.34; 99.5% CI: 1.06, 1.70) and greater accessibility to alcohol at home (RRR: 1.08; 99.5% CI: 1.01, 1.15) were each associated with increased risk of *early initiation, rare blackouts* relative to *delayed initiation, rare blackouts*. Female sex (RRR: 2.89; 99.5% CI: 1.42, 5.87) was the only Wave 1 factor associated with *early initiation, increasing blackouts* relative to *early initiation, rare blackouts*. Multivariate multinomial logistic regression models using complete-case data showed a similar pattern of results (Appendix B9).

Table 3. Multivariate multinomial logistic regression predicting latent class membership using baseline characteristics.

	Reference: Delayed initiation, rare blackouts				Reference: Early initiation, rare blackouts	
	Early initiation, rare blackouts		Early initiation, increasing blackouts		Early initiation, increasing blackouts	
	RRR	99.5% CI	RRR	99.5% CI	RRR	99.5% CI
Female sex	1.35	(0.82, 2.22)	3.90	(1.96, 7.76)	2.89	(1.42, 5.87)
Child externalising	1.02	(0.99, 1.04)	1.00	(0.97, 1.04)	0.99	(0.96, 1.02)
Peer disapproval of substance use	1.04	(0.91, 1.19)	0.98	(0.81, 1.17)	0.94	(0.78, 1.12)
Peer substance use	1.34	(1.06, 1.70)	1.37	(1.07, 1.77)	1.02	(0.91, 1.15)
Parent education (Reference: High school or less)						
Diploma	1.00	(0.56, 1.79)	1.20	(0.51, 2.8)	1.20	(0.52, 2.76)
University	0.97	(0.53, 1.76)	1.40	(0.63, 3.14)	1.45	(0.63, 3.34)
Alcohol specific household rules	0.82	(0.47, 1.40)	0.84	(0.49, 1.44)	1.03	(0.85, 1.25)
Parental monitoring	0.94	(0.85, 1.04)	0.93	(0.82, 1.05)	0.98	(0.89, 1.10)
Socio-economic status	0.95	(0.86, 1.04)	1.00	(0.86, 1.16)	1.06	(0.92, 1.21)
Single parent household	1.73	(0.87, 3.43)	1.40	(0.58, 3.38)	0.81	(0.35, 1.88)
Accessibility of alcohol at home	1.08	(1.01, 1.15)	1.12	(1.01, 1.25)	1.04	(0.94, 1.16)
Family history of alcohol problems	1.02	(0.63, 1.65)	0.98	(0.52, 1.85)	0.96	(0.50, 1.85)
Family conflict	1.18	(0.89, 1.57)	1.16	(0.81, 1.68)	0.98	(0.70, 1.37)

3.6.4. Blackout trajectory as predictor of meeting criteria for DSM-IV alcohol abuse and dependence, and DSM-5 AUD based on self-reported symptoms

Results of the adjusted logistic regression models are presented in Table 4 (unadjusted models are presented in Appendix B10). *Early initiation, rare blackouts* (OR: 1.96; 99.5% CI: 1.17, 3.29) and *early initiation, increasing blackouts* (OR: 4.93; 99.5% CI: 2.32, 10.48) were both associated with increased odds of meeting self-reported DSM-5 criteria for AUD at Wave 8 relative to *delayed initiation, rare blackouts*. *Early initiation, increasing blackouts* (OR: 2.51; 99.5% CI: 1.18, 5.38) was also associated with meeting self-reported DSM-5 criteria for AUD at Wave 8 relative to *early initiation, rare blackouts*. *Early initiation, increasing blackouts* was associated with meeting self-reported DSM-IV criteria for alcohol

dependence at Wave 8 relative to *delayed initiation, rare blackouts* (OR: 3.07; 99.5% CI: 1.46, 6.48). Blackout trajectory was not associated with DSM-IV criteria for alcohol abuse. Adjusted logistic regression models using complete-case data showed that these results remained robust (Appendix B11).

Table 4. Adjusted logistic regression predicting meeting criteria for DSM-IV alcohol dependence and abuse, and DSM-5 AUD by latent class.

	Dependence		Abuse		AUD	
Class	OR	99.5% CI	OR	99.5% CI	OR	99.5% CI
Reference: Delayed initiation, rare blackouts						
Early initiation, rare blackouts	1.58	(0.82, 3.04)	0.98	(0.15, 44.52)	1.96	(1.17, 3.29)
Early initiation, increasing blackouts	3.07	(1.46, 6.48)	0.38	(0.03, 5.70)	4.93	(2.32, 10.48)
Reference: Early initiation, rare blackouts						
Early initiation, increasing blackouts	1.95	(1.00, 3.80)	0.39	(0.02, 6.87)	2.51	(1.18, 5.38)

Note. Analyses adjust for all Wave 1 covariates.

3.7. Discussion

Over eight annual waves of survey data on 1821 young people assessed from age 12 years to age 19 years, we identified three distinct classes of alcohol-related blackout trajectories after adjustment for drinking frequency and quantity, in addition to early-adolescent predictors of blackout trajectory and associated adulthood outcomes. The three classes identified consisted of: 1) *delayed initiation, rare blackouts*; 2) *early initiation, rare blackouts*; and 3) *early initiation, increasing blackouts*.

Consistent with a recent study which found that blackouts predicted later alcohol dependence (5), our findings indicate that escalation of blackouts in adolescence is associated with three times the odds of meeting DSM-IV criteria for alcohol dependence. Our study also adds the novel finding that early alcohol initiation, in conjunction with

increasing blackouts, is associated with alcohol dependence; this was not the case for alcohol initiation alone. We found no difference in meeting DSM-IV criteria for alcohol abuse between the three classes, with neither blackouts nor age of initiation being associated with meeting DSM-IV criteria for alcohol abuse in early adulthood. This is unsurprising given that the symptoms of DSM-IV alcohol abuse pertain to social and work conflicts arising from alcohol use, as opposed to DSM-IV alcohol dependence which includes symptoms that more closely relate to blackouts (e.g., drinking more than intended, drinking more due to increased tolerance, spending more time drinking). Additionally, we found that early initiation and increasing blackouts each independently contributed to increased risk of meeting self-reported DSM-5 criteria for AUD, with the joint effect having the largest effect size of nearly five times the odds of meeting criteria for AUD. Escalating blackouts in adolescence are an important indicator of clinically-relevant alcohol problems, and should be considered as part of a risk factor assessment by clinicians. Prevention and intervention strategies targeting alcohol-induced blackouts may reduce the risk of future alcohol problems and also reduce injury and associated healthcare costs (3, 34).

Among the young people in our sample who rarely experienced blackouts, no sex differences were found between the delayed and early initiation classes, indicating that sex was associated with experience of blackouts, but not with age of initiation alone. Females had nearly three times the risk of males in experiencing increasing blackouts, which increased to nearly four times the risk when earlier age of initiation was considered. Studies have established that young adult females are at increased risk of experiencing blackouts compared to males after adjusting for levels of consumption (6, 35), an effect which is likely due to differences in metabolism and body composition (36). Our finding that female sex is associated with increased risk of increasing blackouts supplements those of Schuckit, Smith

(11) and Schuckit, Smith (14), with an additional novel finding that sex is associated with blackout trajectory independent of alcohol consumption levels and age of alcohol initiation. That is, adolescent females had increased risk of experiencing increasing blackouts compared to adolescent males at equivalent levels of consumption, but females were not more likely than males to start drinking at an earlier age. Although young people tend to understand the behavioural risk factors for alcohol-related blackouts, such as rapid consumption of alcohol, they have limited understanding of biological risk factors such as sex (37). As such, schools should consider educating students and caregivers about the biological risk factors for blackouts, in addition to blackouts themselves being a risk factor for future harm.

Young adolescents residing in households where alcohol was easier to access without parental knowledge had around 1.1 times the risk of early initiation to alcohol relative to delayed initiation, regardless of blackouts. Thus, accessibility of alcohol at home was weakly associated with the timing of alcohol initiation, but not necessarily blackouts. Having more peers who used substances at age 12-years was associated with over 1.3 times the risk of early alcohol initiation relative to delayed initiation, regardless of blackouts. Our results suggest that peer substance use at age 12-years was only associated with the timing of alcohol use initiation, not with blackout experiences. This is consistent with previous longitudinal research regarding self-selection of alcohol-using peers in adolescents who drink (38), albeit with a small effect size. Contrary to other studies on blackout trajectories (11, 13), we found no evidence to suggest that peer substance use was linked to increasing blackouts as the peer effect was only present between the delayed and early initiation groups. A notable difference between our study and the aforementioned is that the blackout trajectories identified in our study adjusted for same-year alcohol consumption,

whereas the trajectories reported by Merrill, Treloar (13) and Schuckit, Smith (11) were unadjusted. It is possible that the presence of substance-using peers drove increases in alcohol consumption (38) and thus blackouts increased due to escalation in drinking levels. Future research examining blackouts should note that analyses that do not adjust for alcohol consumption may instead be capturing patterns of heavy drinking rather than blackouts.

3.7.1. Strengths and limitations

To our knowledge, this is the first study to examine alcohol-related blackout trajectories from pre-exposure in early adolescence to early adulthood, whilst also adjusting for frequency and typical quantity of alcohol use. The blackout trajectory classes we identified are comparable to that of previous studies on older adolescents (11) and young adults (13, 14), where increasing blackout and moderate/low blackout groups have also been identified. Our study builds on this prior work by including age of alcohol initiation into the models, given its established association with later alcohol use and disorder (39, 40). Notably, this study identified two distinct blackout trajectories (i.e., rare and increasing) in adolescents who initiated alcohol in early adolescence, suggesting that increasing blackouts are not necessarily linked to age of initiation. Additional strengths include a large sample size (1821 young people), high retention rate over 8 years (73.4%), repeated 12-month follow-up assessments, and consideration of child, parent, and peer covariates associated with adolescent alcohol use.

There are several limitations to note. Entropy for the chosen 3-class model was 0.586, which may indicate poor delineation of latent classes. However, the classes were theoretically meaningful and classification probabilities ranged from 0.749 to 0.830, meaning that classes

were reasonably distinguished and comparable to the blackouts trajectory model chosen by a similar study (11). Our results may not be generalisable at the population level as participants were recruited using an opt-in process rather than randomly sampling from the population. Although our cohort does have similar levels of alcohol use and demographic profile to Australian population, families with low socioeconomic status are somewhat underrepresented due to a lower proportion of government schools participating (20). Additionally, as alcohol consumption is often underestimated at higher levels of consumption (41), and given that blackouts are characterised by memory loss (7), our retrospective measures of alcohol use and blackouts may have resulted in underestimation of these variables. The extent to which other substance use may have also contributed to alcohol-related blackouts is also unclear, as we did not explicitly ask participants about other substance use in the context of blackouts. Finally, the measure we used for blackouts does not distinguish between en bloc and fragmentary blackouts. Given that en bloc blackouts are more commonly associated with poly-substance use and are perceived more negatively than fragmentary blackouts (8, 42), we suggest that future studies measure both types of blackouts.

3.7.2. Conclusion

This longitudinal study shows that there are heterogenous patterns of experiencing alcohol-related blackouts across adolescence. Caregivers and educators of adolescents should note that females are particularly at risk of experiencing increasing blackouts which, in turn, places them at increased risk of alcohol-related harms in early adulthood. Although not part of a formal diagnosis of AUD, clinicians may wish to consider the experience of blackouts in adolescents as a risk factor for future clinical problems related to alcohol use independent

of alcohol consumption frequency, typical quantity, and age of initiation.

3.8. Declarations of competing interest

RB has received untied educational grants from Mundipharma and Indivior for studies relating to pharmaceutical opioids. MF has received untied educational grants from the Australian Government Department of Health, in addition to Mundipharma, Indivior, and Seqirus for post-marketing surveillance of pharmaceutical opioids. AP has received untied educational grants from Mundipharma and Seqirus for post-marketing surveillance of pharmaceutical opioids. These agencies had no role in study design, conduct and reporting, and funding was not for work reported here. All other authors have no conflicts of interest to declare.

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4. CHAPTER 4: EXPERIENCE OF PHYSIOLOGICAL AND PSYCHOSOCIAL ALCOHOL-RELATED HARMS ACROSS ADOLESCENCE AND ITS ASSOCIATION WITH ALCOHOL USE DISORDER IN EARLY ADULTHOOD: A PROSPECTIVE COHORT STUDY

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4.1. Copyright Statement

I declare that this publication occurred during my candidature as a direct result of my research towards this thesis and, to the best of my knowledge, does not breach copyright regulations nor intellectual property rights.

Yuen, W. S., Bruno, R., Chan, G., McCambridge, J., Slade, T., Clare, P. J., Aiken, A., Kypri, K., Hutchinson, D., McBride, N., Boland, V., Upton, E., Farrell, M., Mattick, R. P., & Peacock, A. (2021). The experience of physiological and psychosocial alcohol-related harms across adolescence and its association with alcohol use disorder in early adulthood: A prospective cohort study. Alcoholism: Clinical and Experimental Research, 45(12), 2518–2527. https://doi.org/10.1111/acer.14726

4.2. Preamble

In Chapter 3, we identified three developmental patterns of alcohol-related blackouts from age 14 to age 18 years in a longitudinal cohort of young people. These were: delayed alcohol initiation, rare blackouts (38.5%); early initiation, rare blackouts (47.7%); and early initiation, escalating blackouts (13.8%). Young people who experienced escalating blackouts were 2.5 to 4.9 times more likely to have AUD symptoms at age 20 compared to young people who rarely experienced blackouts. Female adolescents were 2.9 to 3.9 times more likely than male adolescents to experience escalating blackouts, but not more or less likely to initiate alcohol earlier compared to male adolescents. Young people with peers at age 13 who used alcohol or tobacco were 1.3 times more likely to initiate alcohol earlier but were not more or less likely to experience escalating blackouts.

Chapter 3 focused on trajectories of one specific alcohol-related harm which is common among young people. However, there are many other types of alcohol-related harm that can be experienced by young people (1-3). These harms range from those that only impact the individual (e.g., hangovers), to those that impact the individual as well as others around them (e.g., getting into fights). Broader examination of trajectories that involve multiple types of harm is necessary to further understand how harms develop in young people, particularly whether there are higher risk developmental patterns characterised by specific groupings of harms.

Similar to Chapter 3, this chapter also aims to address research question 2: '*What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving declines in alcohol consumption?*' and research question 3: *'In recent birth cohorts, are there early adolescent factors that predict high-risk developmental patterns of harm?*'. We

examine patterns of transitioning between different types of alcohol-related harm at ages 15, 17, and 19 years using the same longitudinal cohort of young people as the previous chapter. Transition patterns that are associated with AUD at age 20 years and factors at age 13 years that predict these high-risk transition patterns are also identified.

4.3. Abstract

Background: Different forms of alcohol-related harm (e.g., hangovers vs fighting) may confer differential risk of clinically-relevant alcohol problems. We examine: i) patterns of transition in experiencing alcohol-related harms across adolescence; ii) whether factors in early adolescence predict transition patterns; and iii) whether transition patterns predict later alcohol use disorder (AUD) symptoms.

Methods: We used a longitudinal Australian cohort (n=1828) to model latent class transition patterns of alcohol-related harms across three timepoints (M_{age}=13.9, 16.8, 18.8 years). Regression models assessed whether child, peer, and parent factors in early adolescence (M_{age}=12.9) predicted harms transition patterns and whether these patterns predicted AUD symptoms in early adulthood (M_{age}=19.8).

Results: Five transition patterns comprised most of the cohort (n≈1609, 88.0%): i) *minimal harms* (n≈381, 20.8%); ii) *late physiological harms* (n≈702, 38.4%); iii) *early physiological harms* (n≈226, 12.4%); iv) *late all harms* (n≈131, 7.2%); and v) *gradual all harms* (n≈169, 9.2%). With *late physiological harms* as the reference, females had increased risk of experiencing *early physiological harms* (Relative risk [RR]: 2.15; 99.5% CI: 1.19, 3.90). *Late all harms* (RR: 1.71; CI: 1.19, 2.47) and *gradual all harms* (RR: 1.84; CI: 1.37, 2.47) were each associated with increased odds of meeting criteria for AUD, even when patterns of alcohol consumption are considered.

Conclusions: Adolescents display heterogenous transition patterns across physiological and psychosocial alcohol-related harms. Females are at greater risk of experiencing early physiological harms. Experience of both physiological and psychosocial harms in late adolescence is an important and potentially modifiable precursor to clinically-relevant

alcohol problems in early adulthood.

Key words: alcohol, adolescence, transitions, alcohol-related harm, alcohol use disorder

4.4. Introduction

Alcohol use is the leading global risk factor for death and disability in young people aged 15–24 years (4, 5). Two in five young Australians drink at levels that increase risk of acute harm (e.g., alcohol poisoning) and one in five drink at levels that increase risk of long-term harm (6). Given that adolescents who engage in risky drinking tend to continue this behaviour in adulthood (7-9), early interventions addressing alcohol harms at this stage of life are important in preventing alcohol-related premature deaths and chronic conditions.

Negative consequences resulting from alcohol consumption, or "alcohol-related harms", include consequences ranging from feeling sick to having a fight. These alcohol-related harms are experienced by adolescents as young as 13 years of age and are common among late adolescent and early adulthood drinkers (2, 10, 11). Efforts to examine the risk and protective factors for alcohol-related harms have typically focused on harms in early adulthood (12, 13). Whilst alcohol-related harms peak during this period, cross-sectional approaches do not capture the developmental course of these harms and provide little information regarding early indicators of high-risk patterns of harm.

To date, there has been limited research examining trajectories of alcohol-related harms. Betts, Alati (14) found heterogenous patterns of experiencing harms from late adolescence to adulthood in an Australian population cohort, identifying one group characterised by early-onset of harms increasing until adulthood, and another group characterised by a lack of harm despite rapid escalation in binge drinking. As patterns in alcohol use do not necessarily translate to patterns of alcohol-related harm, this highlights the need to examine patterns of harm as an indicator of health risk separate to alcohol use. However, it remains unknown whether there are sociodemographic and/or family factors that

differentiate those young people who experience harms throughout adolescence from those who experience harms in late adolescence only. Considering the rapid escalation of health risk attributable to alcohol use between 10 to 24 years (5), it is important to identify adolescents who are most at risk of consistently experiencing harms which may endure in adulthood.

Given that alcohol consumption in adolescence and young adulthood typically occurs in a social context, acute alcohol-related harms commonly carry social significance; that is, some harms impact only the individual's physiology whereas others have interpersonal and broader societal impacts (15, 16). Despite evidence that alcohol-related harms cluster into multiple factors (17, 18), many quantitative studies that examine alcohol-related harms aggregate factors (e.g., by summing the number of harms instead of separating by category; 12, 13, 19, 20). Prince, Read (21) reported that young adults with alcohol use disorder (AUD) experienced increasing alcohol-related consequences (e.g., passing out, interpersonal problems) each year in the five years prior, whereas those who did not have AUD showed stable levels of these consequences. Whether AUD outcomes vary between young people who only experience the physiological effects of alcohol, and those who experience a broader range of harms, remains unclear. Close examination of how different patterns of alcohol-related harms develop across adolescence, may be usefully accompanied by investigations of predictors of escalating harms, and consequences in early adulthood.

We aimed to examine: i) patterns of transition across social dimensions of alcohol-related harm in adolescence; ii) whether factors in early adolescence predict transition patterns; and iii) whether transition patterns predict AUD symptoms in early adulthood.

4.5. Materials and Methods

4.5.1. Participants and procedure

We used data from the Australian Parental Supply of Alcohol Longitudinal Study (APSALS; registered at ClinicalTrials.gov: NCT02280551) cohort, comprising 1,927 young people. Participants and one parent or guardian were recruited to complete annual online or hardcopy surveys via an opt-in process in 2010 and 2011 from Grade 7 classes in Australian private independent (49%), Catholic (12%), and government (39%) schools across New South Wales, Tasmania, and Western Australia. Signed consent was obtained from participating families. To minimise reporting bias, surveys were sent separately to each adolescent and parent. The sociodemographic distribution was comparable to the Australian population, although families with higher levels of education and employment were over-represented (see 22 for more details about the cohort). APSALS was approved by the University of New South Wales Research Ethics Committee and ratified by the universities of Tasmania, Newcastle, and Queensland, and Curtin University. We used five waves of data collection (Wave 1 [2010-11], Wave 3 [2012-13], Wave 5 [2014-15], Wave 7 [2016-17], Wave 8 [2017-18]; mean ages 12.9, 14.8, 16.9, 18.8, 19.8 years respectively; see Appendix C1 for details of cohort retention), including data collected from parents at Wave 1. Participants who had completed at least three annual surveys were included in the current analyses (n=1,828; 45.6% female). All findings are reported in accordance with STROBE guidelines (Appendix C2).

4.5.2. Measures

4.5.2.1. Alcohol-related harms.

We used an alcohol-related harms measure consisting of 13 items that was adapted from a 17-item scale developed by the School Health and Alcohol Harm Reduction Project

(Appendix C3; 23). These items had six possible responses (12+ times, 5-11 times, 3-4 times, twice, once, never), which we recoded as binary variables (at least once, never). We excluded three items that were not consequences incurred because of the respondent's consumption of alcohol (planning to get drunk; experiencing verbal abuse; experiencing sexual harassment), and one item not applicable to participants not attending school or post-school age (getting into trouble with teachers).

4.5.2.1. Alcohol abuse, alcohol dependence, and alcohol use disorder (AUD).

To measure alcohol abuse, we used 4 items adapted from the Diagnostic Interview Schedule for Children Version IV (DISC-IV; 24), corresponding to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV; 25) symptoms of alcohol abuse. To measure alcohol dependence, we used 7 items, likewise adapted from the DISC-IV and corresponding to the DSM-IV symptoms of alcohol dependence. To measure AUD, we used 11 items corresponding to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5; 26) symptoms of AUD. Details of these items can be found in Appendix C4. We coded a 3-level categorical variable for DSM-IV symptoms: i) does not meet criteria; ii) meets DSM-IV criteria for alcohol abuse (at least one of four symptoms and have never met criteria for alcohol dependence); and iii) meets DSM-IV criteria for alcohol dependence (at least three of seven symptoms). We coded a binary variable for meeting DSM-5 criteria for AUD (at least two of eleven symptoms).

4.5.2.1. Wave 1 characteristics.

We selected potential Wave 1 predictors of transitions in alcohol-related harms from a literature search (Appendix C5), consisting of: *child variables* (sex, externalising), *peer variables* (peer tobacco/alcohol use, peer disapproval of tobacco/alcohol use), and

parent/family variables (alcohol accessibly at home without parental knowledge, alcohol-specific rules, monitoring of child activities, socioeconomic status, one/two parent family, family history of alcohol problems, family conflict).

4.5.3. Statistical Analysis

We pre-registered the analyses on the Open Science Framework (https://osf.io/4ph6y/).

4.5.3.1. Latent transition analysis.

We used latent transition analysis (LTA) to identify patterns of transitioning across different categories of alcohol-related harm. As a preliminary step towards building the LTA model, we used latent class analysis (LCA) in Mplus version 8.3 (27) to determine the number of latent statuses at each timepoint (28). An underlying grouping variable, latent class, was inferred from the 13-binary alcohol-related harms indicator variables. The subsequent LTA model extended the LCA longitudinally, capturing changes in latent statuses (i.e., latent class membership) over time, including the probability of transitioning from one latent status to another. As the latent transition classes consist of all combinations of the latent statuses at each timepoint, we chose three timepoints for the LTA to minimise the number of possible transition classes whilst capturing change across key periods of adolescence. We used data from Waves 3, 5, and 7 to fit independent latent class models using LCA and to fit the final LTA model in Mplus version 8.3 (27). We selected these timepoints as Wave 3 (M_{age} = 14.8 years) captured most participants prior to the median age of onset for alcohol use (29), Wave 5 (M_{age} = 16.9 years) was the first wave where > 50% of the cohort have initiated alcohol use, and Wave 7 (M_{age} = 18.8 years) was the first wave that occurs after the cohort has reached legal age of purchase in Australia. For the LCA models, we assessed model fit with the sample-size adjusted Bayesian Information Criterion (ssaBIC), where lower values

indicated better fit. Additionally, the Lo-Mendell-Rubin adjusted log-likelihood ratio test (LMR-aLRT; 30) statistic was used to compare fit of a *k* class model with a *k*-1 class model, where $p < 0.05$ indicated that the *k*-1 class model should be rejected for the *k* class model.

4.5.3.1. Regression analysis.

Using Stata version 16 (31), we conducted regression analyses to examine the predictors and outcomes associated with transition class membership. The procedure used to account for latent transition class classification uncertainty can be found in Appendix C6. We used multinomial logistic regression models to examine whether child, parent, and peer factors at Wave 1 (M_{age} = 12.9 years) predicted patterns of transitioning, presented as relative risk ratios (RR). For the early adulthood outcomes, we used multinomial logistic regression models to examine whether patterns of transitioning predicted meeting criteria for DSM-IV alcohol abuse or DSM-IV alcohol dependence at Wave 8 (M_{age} = 19.8 years), presented as RR. Additionally, we used Poisson models with a robust error variance to examine whether patterns of transitioning predicted meeting DSM-5 criteria for alcohol use disorder (AUD) at Wave 8, presented as RR (32). To align with recommendations to improve research reproducibility (33), 99.5% confidence intervals (CI) are presented for regression models. Effect sizes where the CI includes the null value of 1.00 have not been interpreted. The latent transition model, including Wave 1 predictors and distal outcomes, is presented in Appendix C7.

4.5.3.2. Missing data.

As this is a longitudinal study, some participants had missing data from partial completion or failing to complete follow-up waves (summarised in Appendix C8). To reduce potential bias introduced by missingness, we imputed the data using an unrestricted H1 model (34) with

Mplus version 8.3 (27). Based on the percentage of missing information, we used M = 20 imputations (35). We then conducted LCAs on each imputed dataset and repeated this process for the latent transition model once the number of classes was confirmed from the LCA. We combined and imported the resulting datasets containing weights (see Appendix C7) from each run of the LTA into Stata as a multiply imputed dataset for regression analyses.

4.5.3.3. Post-hoc hierarchical logistic regression.

Whilst not outlined in the pre-published analytic plan (https://osf.io/4ph6y/), an additional post-hoc analysis was undertaken given similarities between the current harms transition patterns and alcohol consumption trajectory classes previously modelled in the same cohort (36) and research suggesting that alcohol-related harms are highly related to heavy alcohol use (37-39). Thus, analyses examining alcohol-related harms as a predictor of later AUD without considering levels of alcohol use may not be meaningful. Nested logistic and multiple logistic regression models were conducted to examine: i) whether the current harms transition classes contribute a substantial amount of variance to the AUD outcome over parallel latent class growth trajectories of alcohol use frequency and typical quantity (Waves 2 to 6 as previously modelled in Yuen, Chan (36)); and ii) whether the overall results of the AUD outcome model remain the same after adding the aforementioned alcohol use trajectories. Most likely class membership from the alcohol use latent class model was first entered into the logistic and multiple logistic regression models, followed by alcohol-related harm latent transition class. To match the approach used for planned outcome analyses, all models adjusted for Wave 1 predictors. McFadden's pseudo R^2 (40) was calculated for each imputation and averaged. Likelihood ratio tests determined whether the latent transition

classes of alcohol-related harm contributed a significant amount of variance to the AUD outcomes over latent class growth trajectories of alcohol use frequency and typical quantity in the cohort.

4.6. Results

4.6.1. Sample characteristics

Table 5 shows the frequencies of the alcohol-related harms experienced at least once in a 12-month period at Wave 3, 5 and 7. In Wave 3, 88% of respondents had not experienced any alcohol-related harms. At Wave 5, this decreased to 61%, and by Wave 7 only 18% had not experienced any alcohol-related harms within 12 months. At Wave 8, around 1% of the sample met DSM-IV criteria for alcohol abuse, whereas 44% met DSM-IV criteria for alcohol dependence and 44% met DSM-5 criteria for AUD.

Table 5. Frequency of alcohol-related harms experienced at least once a month in the past 12 months at each follow-up wave.

	Wave 3		Wave 5		Wave 7	
Harm experienced at least once in past 12 months	Female (n = 796)	Male (n = 949)	Female (n = 780)	Male (n = 872)	Female (n = 718)	Male (n = 700)
Drank more than planned	86 (10.8%)	56 (5.9%)	275 (35.3%)	227 (26.0%)	502 (69.9%)	436 (62.3%)
Experienced a hangover	68 (8.5%)	35 (3.7%)	221 (28.3%)	163 (18.7%)	457 (63.6%)	423 (60.4%)
Felt sick	56 (7.0%)	29 (3.1%)	169 (21.7%)	141 (16.2%)	409 (57.0%)	414 (59.1%)
Blackout	50 (6.3%)	28 (3.0%)	180 (23.1%)	121 (13.9%)	326 (45.4%)	321 (45.9%)
Someone complained about their drinking	21 (2.6%)	11 (1.2%)	46 (5.9%)	26 (3.0%)	80 (11.1%)	69 (9.9%)
Trouble with friends	26 (3.3%)	19 (2.0%)	86 (11.0%)	42 (4.8%)	136 (18.9%)	116 (16.6%)
Trouble with parents	49 (6.2%)	32 (3.4%)	90 (11.5%)	86 (9.9%)	110 (15.3%)	120 (17.1%)
School/work affected	15 (1.9%)	8 (0.8%)	27 (3.5%)	20 (2.3%)	81 (11.3%)	78 (11.1%)
Damaged something	17 (2.1%)	13 (1.4%)	39 (5.0%)	48 (5.5%)	97 (13.5%)	116 (16.6%)
Had a physical fight	12 (1.5%)	9 (0.9%)	19 (2.4%)	21 (2.4%)	30 (4.2%)	59 (8.4%)
Trouble with police	9 (1.1%)	10 (1.1%)	18 (2.3%)	16 (1.8%)	20 (2.8%)	47 (6.7%)
Regretted having sex	16 (2.0%)	7 (0.7%)	41 (5.3%)	27 (3.1%)	93 (13.0%)	76 (10.9%)
Had unsafe sex	12 (1.5%)	7 (0.7%)	36 (4.6%)	15 (1.7%)	69 (9.6%)	56 (8.0%)
Any harm	88 (9.3%)	125 (15.7%)	303 (34.7%)	349 (44.7%)	574 (82.0%)	584 (81.3%)

4.6.2. Alcohol-related harms transitions

Model fit and classification quality statistics for the 2- to 4-class latent class models for Wave 3, Wave 5, and Wave 7 are shown in Appendix C9. As the ssaBIC and LMR-aLRT did not indicate improved model fit for the 4-class solution over the 3-class solution at each of

the three timepoints, we selected the 3-class solution for the LTA. Examination of entropy and class composition also supported selection of the 3-class solution as each class was of substantive size and showed distinct patterns of alcohol-related harms that were consistent in profile across timepoints (Figure 8). Estimated proportions of Subclass 1 (n≈1677 at Wave 3; n≈1231 at Wave 5; n≈405 at Wave 7), had no more than 1% of the subclass experiencing harms other than "drinking more than intended" at any timepoint and was thus labelled the *minimal harms* subclass. Subclass 2 (n≈109 at Wave 3; n≈487 at Wave 5; n≈1011 at Wave 7) mostly experienced harms that affected the respondent on a physiological but not necessarily interpersonal level (e.g., hangovers and blackouts), hence it was labelled as the *physiological harms* subclass. Subclass 3 (n≈43 at Wave 3; n≈110 at Wave 5; n≈412 at Wave 7), experienced a wide range of harms, including those of a physiological (e.g., blackout) and psychosocial nature (e.g., trouble with friends), as such it was labelled as the *all harms* subclass.

There were 27 possible latent transition classes in the latent transition model (i.e., each possible combination of the three subclasses across three waves). The three-timepoint latent transition model showed clear delineation of transition classes, with an average entropy of 0.89. The probabilities of transitioning across subclasses (or remaining in the same subclass) from Wave 3 to Wave 5 and from Wave 5 to Wave 7 are shown in Table 6. Final class counts and proportions for these transition class patterns can be found in Appendix C10. To reduce model complexity for all subsequent analyses, transition classes containing fewer than 5% of the original sample were excluded, resulting in approximately 1609 participants (88.02%) being retained across five transition classes. These five transition classes were labelled as: i) *minimal harms* (minimal harms across all timepoints; n≈381, 20.8%); ii) *late escalation to physiological harms* (minimal harms in Waves 3 and 5,

physiological harms in Wave 7; n≈702, 38.4%); iii) *early escalation to physiological harms* (minimal harms in Wave 3, physiological harms in Waves 5 and 7; n≈226, 12.4%); iv) *late escalation to all harms* (minimal harms in Waves 3 and 5, all harms in Wave 7; n≈131, 7.2%); v) *gradual escalation to all harms* (minimal harm in Wave 3, physiological harms in Wave 5, all harms in Wave 7; n≈169, 9.2%).

Figure 8. Percentage experiencing alcohol-related harms at least once in a 12-month period for each class at Waves 3, 5, and 7.

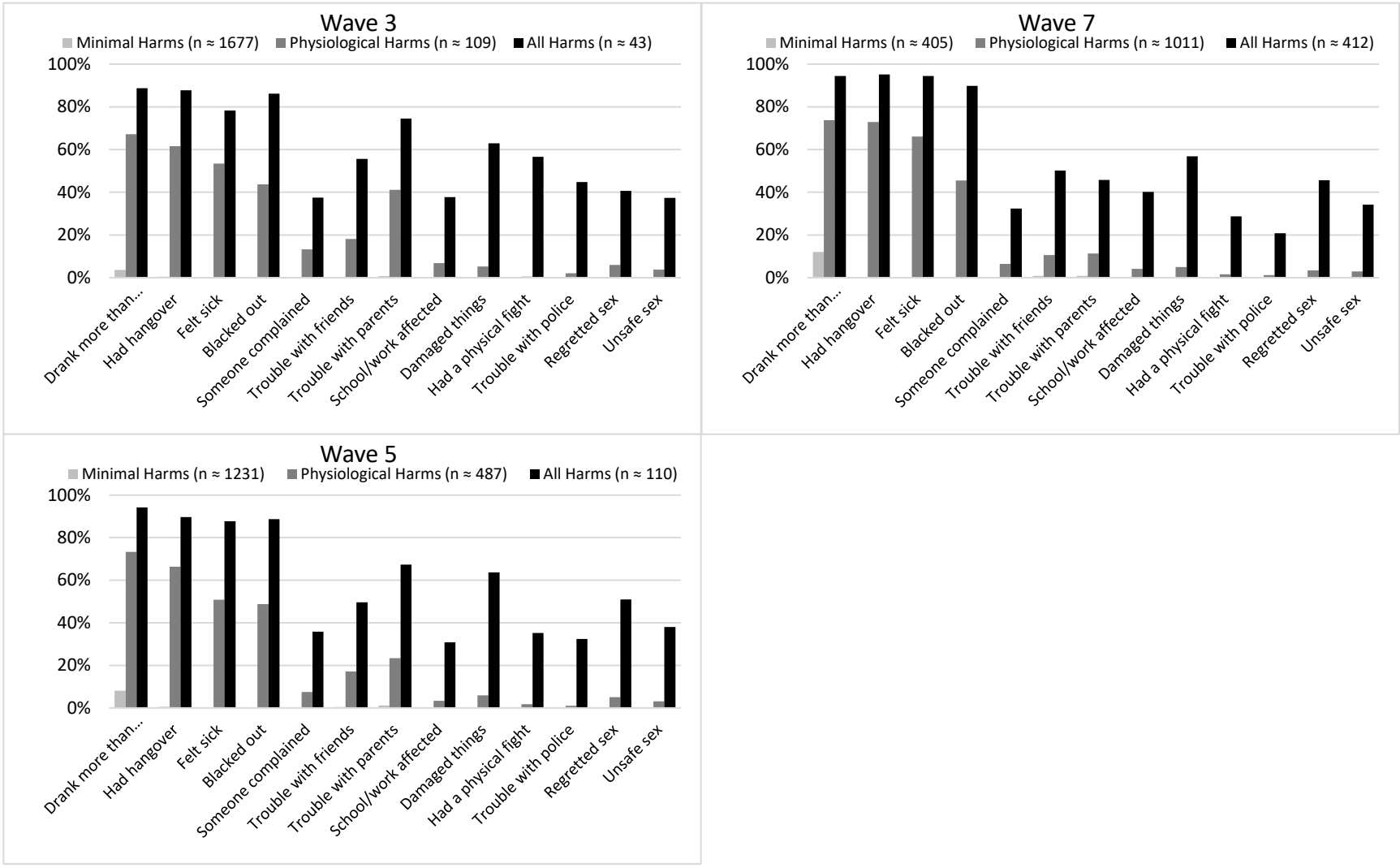

Table 6. Probabilities of moving to a different subclass in the latent transition model.

		Wave 5		
		Minimal harms	Physiological harms	All harms
Wave 3	Minimal harms	0.72	0.25	0.04
	Physiological harms	0.11	0.69	0.24
	All harms	0.11	0.20	0.65
		Wave 7		
		Minimal harms	Physiological harms	All harms
Wave 5	Minimal harms	0.33	0.56	0.11
	Physiological harms	0.03	0.77	0.39
	All harms	0.02	0.21	0.57

4.6.3. Predictors of harms transition pattern

Results of the multivariable multinomial logistic regression model are presented in Table 7 (see Appendix C11 for bivariate models). *Late escalation to physiological harm* was chosen as the reference class as it most closely reflects the Australian population in age of alcohol initiation (6) and experience of harms (14). Female sex was associated with increased risk of experiencing *early escalation to physiological harms* (RR: 2.15; 99.5% CI: 1.19, 3.90) but was not associated with other transition patterns. Peer substance use was associated with increased risk of experiencing *early escalation to physiological harms* (RR: 1.19; 99.5% CI: 1.03, 1.38) and *gradual escalation to all harms* (RR: 1.23; 99.5% CI: 1.06, 1.44) but not with *minimal harms* nor *late escalation to all harms*. Parent and other family factors were not associated with harms transition class.

Table 7. Multivariable multinomial logistic regression predicting latent class membership using Wave 1 characteristics.

	Transition Class (Ref: late escalation to physiological harms)							
	Minimal harms		Early escalation to physiological harm		Late escalation to all harms		Gradual escalation to all harms	
	RR	99.5% CI	RR	99.5% CI	RR	99.5% CI	RR	99.5% CI
Female sex	1.16	(0.68, 1.96)	2.15	(1.19, 3.90)	0.80	(0.33, 1.95)	1.55	(0.78, 3.07)
Child externalising [1]	1.01	(0.98, 1.04)	1.01	(0.98, 1.04)	1.02	(0.98, 1.06)	1.00	(0.96, 1.03)
Peer disapproval of substance use [2]	0.95	(0.80, 1.14)	0.97	(0.80, 1.18)	0.96	(0.76, 1.20)	0.96	(0.80, 1.16)
Peer substance use [3]	0.89	(0.71, 1.11)	1.19	(1.03, 1.38)	1.06	(0.86, 1.31)	1.23	(1.06, 1.44)
Parent education (Ref: High school or less)								
Diploma	0.81	(0.45, 1.45)	0.97	(0.48, 1.97)	1.07	(0.38, 3.05)	1.06	(0.40, 2.84)
University	0.95	(0.53, 1.68)	1.00	(0.49, 2.03)	1.15	(0.41, 3.21)	1.58	(0.62, 4.03)
Alcohol specific household rules [4]	0.84	(0.66, 1.07)	0.94	(0.71, 1.25)	0.85	(0.63, 1.16)	0.93	(0.69, 1.26)
Parental monitoring [5]	1.02	(0.90, 1.15)	0.93	(0.83, 1.05)	0.96	(0.84, 1.10)	0.90	(0.80, 1.02)
Socio-economic status	0.94	(0.84, 1.04)	0.97	(0.86, 1.09)	1.07	(0.89, 1.29)	1.01	(0.86, 1.19)
Single parent household	0.90	(0.46, 1.77)	1.27	(0.59, 2.71)	1.11	(0.40, 3.04)	1.44	(0.56, 3.69)
Accessibility of alcohol at home [6]	0.96	(0.89, 1.04)	1.05	(0.96, 1.15)	1.04	(0.91, 1.17)	1.09	(0.99, 1.21)
Family history of alcohol problems	0.91	(0.55, 1.48)	1.26	(0.71, 2.23)	1.17	(0.55, 2.49)	0.95	(0.46, 1.95)
Family conflict	1.04	(0.80, 1.36)	1.07	(0.74, 1.56)	1.18	(0.79, 1.77)	1.39	(0.97, 2.01)

Note. [1] RR greater than 1.00 indicates higher risk for adolescents reporting greater levels of rule-breaking and aggressive behaviour; [2] RR greater than 1.00 indicates higher risk for adolescents who report having more peers who use alcohol/tobacco; [3] RR greater than 1.00 indicates higher risk for adolescents who report that their peers do not disapprove of alcohol/tobacco use; [4] RR greater than 1.00 indicates higher risk for adolescents whose parents had more rules regarding alcohol use; [5] RR greater than 1.00 indicates higher risk for adolescents

whose parents are more closely monitoring their activities; [6] RR greater than 1.00 indicates higher risk for adolescents who have easier access to alcohol in their household without parental knowledge.

4.6.4. Harms transition pattern as predictor of meeting criteria for DSM-IV alcohol abuse and dependence, and DSM-5 AUD based on self-reported symptoms

Results of the adjusted logistic regression models are presented in Table 8 (see Appendix C12 for unadjusted models). *Minimal harms* was associated with lower risk of meeting DSM-IV criteria for alcohol dependence (RR: 0.21; 99.5% CI: 0.07, 0.61) and DSM-5 criteria for AUD (RR: 0.29; 99.5% CI: 0.12, 0.69) in Wave 8, but not with DSM-IV criteria for alcohol abuse. *Late escalation to all harms* was associated with increased risk of meeting DSM-IV criteria for alcohol dependence (RR: 3.66; 99.5% CI: 1.27, 10.49) and DSM-5 criteria for AUD (RR: 1.71; 99.5% CI: 1.19, 2.47), but not with DSM-IV criteria for alcohol abuse. *Gradual escalation to all harms* was also associated with increased risk of meeting DSM-IV criteria for alcohol dependence (RR: 4.18; 99.5% CI: 1.48, 11.79) and DSM-5 criteria for AUD (RR: 1.84; 99.5% CI: 1.37, 2.47), but not with DSM-IV criteria for alcohol abuse. *Early escalation to physiological harm* was not associated with any of the DSM outcomes in Wave 8.

Table 8. Adjusted logistic regression predicting meeting criteria for DSM-IV alcohol dependence and abuse, and DSM-5 AUD at Wave 8 by latent class.

Transition Class (Ref: late escalation to physiological harms)	DSM-IV Abuse		DSM-IV Dependence		DSM-5 AUD	
	RR	99.5% CI	RR	99.5% CI	RR	99.5% CI
Minimal harms	0.57	(0.09, 3.46)	0.21	(0.07, 0.61)	0.29	(0.12, 0.69)
Early escalation to physiological harms	0.86	(0.06, 11.50)	1.77	(0.95, 3.29)	1.34	(1.00, 1.80)
Late escalation to all harms	1.46	(0.01, 144.61)	3.66	(1.27, 10.49)	1.71	(1.19, 2.47)
Gradual escalation to all harms	1.74	(0.13, 23.71)	4.18	(1.48, 11.79)	1.84	(1.37, 2.47)

Note: Models adjust for all baseline covariates (i.e., those listed in Table 7).

4.6.5. Post-hoc hierarchical regression with DSM-IV and DSM-5 alcohol outcomes

For the DSM-IV outcome, McFadden's pseudo R^2 for the alcohol use trajectory and Wave 1 covariates model was .068 and the pseudo R^2 for the full model including alcohol-related

harms transition class was .142, with the harms transition classes contributing significantly to the model (χ^2 (1) = 186.79, p < .001). For the DSM-5 AUD outcome, pseudo R^2 for the alcohol use trajectory and Wave 1 covariates model was .040 and the pseudo R^2 for the full model was .086, with the harms transition classes also contributing significantly to the model (χ^2 (1) = 120.53, p < .001). Adjusted logistic regression models including alcohol use trajectory membership showed the same trend of results to the planned AUD outcome models (Table 9).

Table 9. Post-hoc adjusted logistic regression predicting meeting criteria for DSM-IV alcohol dependence and abuse, and DSM-5 AUD at Wave 8 by latent class.

Transition Class (Ref: late escalation to physiological harms)	DSM-IV Abuse		DSM-IV Dependence		DSM-5 AUD	
	RR	99.5% CI	RR	99.5% CI	RR	99.5% CI
Minimal harms	0.64	(0.09, 4.63)	0.24	(0.08, 0.69)	0.32	(0.13, 0.77)
Early escalation to physiological harms	0.70	(0.05, 9.96)	1.50	(0.79, 2.85)	1.24	(0.92, 1.67)
Late escalation to all harms	1.48	(0.01, 147.77)	3.63	(1.29, 10.17)	1.70	(1.20, 2.41)
Gradual escalation to all harms	1.39	(0.08, 24.71)	3.57	(1.31, 9.77)	1.71	(1.28, 2.27)

Note: Models adjust for all Wave 1 covariates and most likely class membership for alcohol use frequency and typical quantity parallel latent trajectory from Waves 2 to 6.

4.7. Discussion

We identified three distinct and consistent profiles of alcohol-related harms at ages 14-15 years, 16-17 years, and 18-19 years. These profiles were: i) *minimal harms*, ii) *physiological harms* (i.e., harms that mostly affect the individual only), and iii) *all harms* (i.e., broader range of harms including those with psychosocial consequences). Participants tended to remain within the same harms profile across timepoints, with the exception of the transition between 16-17 years and 18-19 years, where participants were more likely to shift from *minimal harms* to *physiological harms* than to stay in the *minimal harms* profile. This finding is likely explained by increases in alcohol consumption between these two timepoints due to

the legal age of purchase and drinking at a licensed venue being 18 years of age in Australia (41). Expanding on existing frameworks of alcohol-related harm (15, 16) and the patterns of harm reported by Betts, Alati (14), we also found that adolescents had heterogeneous patterns of experiencing harms across those that only affect the individual verses those that have interpersonal effects. Most of the cohort were represented across five patterns of alcohol-related harms transition. In descending order of size, these transition patterns were: *late escalation to physiological harms* (38%), *minimal harms* (21%), *early escalation to physiological harms* (12%), *gradual escalation to all harms* (9%), and *late escalation to all harms* (7%). Understanding these differing patterns of harm across adolescence and young adulthood is likely to have implications for prevention and early intervention of alcohol-related harm in young people.

With the outcomes in early adulthood, *late escalation to all harms* was associated with more than three-fold the risk of meeting DSM-IV criteria for alcohol dependence and over 1.7 times the risk of meeting DSM-5 criteria for AUD compared to *late escalation to physiological harms*. Similarly, *gradual escalation to all harms* was associated with close to four times the risk of meeting DSM-IV criteria for alcohol dependence and nearly twice the risk of meeting DSM-5 criteria for AUD. No meaningful differences were observed in meeting DSM-IV criteria for alcohol abuse between the normative *late escalation to physiological harms* class and the other four classes. As *early escalation to physiological harms* was not associated with meeting criteria for alcohol dependence nor AUD, this suggests that the experience of a broad range of harms (particularly those of a psychosocial nature) in late adolescence is what may contribute to increased risk for AUD outcomes in early adulthood. Indeed, post-hoc analyses showed that harms transition class predicted these AUD outcomes after adjusting for alcohol use consumption trajectories. This

underscores the importance of attention to the emergence of psychosocial harms in adolescence in addition to patterns of alcohol use to better understand the aetiology of alcohol harms. Experiencing physiological alcohol-related harms earlier in adolescence does not appear to predict AUD outcomes in early adulthood. Our findings are broadly consistent with those of a United States study of adult men (42), which found that alcohol problems (encompassing physiological and psychosocial harms as defined in our study) when assessed in early adolescence did not predict AUD in early adulthood, but proximal measures of alcohol problems were predictive of AUD.

Regarding the models predicting harms transition patterns, we observed differences between the groups who experienced physiological harms earlier in adolescence. Female adolescents had around twice the risk of *early escalation to physiological harms* compared to *late escalation to physiological harms*. Given the lack of sex differences across most patterns of harm, these results support findings of a convergence across young males and females in the experience of alcohol-related harms (43). Our findings show that young males and females experienced psychosocial harms at a similar rate, but not necessarily physiological harms, which continue to be more common amongst females (44). This is likely due to differences in physiology (45) rather than alcohol consumption levels (i.e., females reach higher blood alcohol concentration and greater levels of intoxication when consuming the same amount as males) given that there are no differences between males and females in our cohort in terms of alcohol use patterns (36). Having more peers who used alcohol and/or tobacco in early adolescence was associated with a small increase in risk of *early escalation to physiological harms* and similarly for *gradual escalation to all harms*, but was not associated with *late escalation to all harms*. Our model suggests that perceived peer influences in early adolescence may predict whether an adolescent experiences alcohol-

related harms earlier or later in adolescence, but do not distinguish whether they experience physiological or all types of harms in late adolescence. We add to previous reports that exposure to alcohol-using peers predicts subsequent alcohol use initiation (46) with our finding that this peer effect exposure is also associated with increased risk of experiencing alcohol-related harms earlier in life.

4.7.1. Strengths and limitations

This study adds to current knowledge on alcohol related harms in young people in three important ways: 1) we identify distinct patterns of escalation in physiological and psychosocial alcohol-related harms across adolescence; 2) we examine whether factors in early adolescence that predate any experience of harms can predict different patterns of alcohol-related harms; and 3) we examine whether these patterns of harms subsequently predict clinically-relevant alcohol-related outcomes in early adulthood. Our study's strengths also include high retention over 8 years of follow-up (74.3%), consistent 12-month follow-up intervals, and consideration of child, parent, and peer covariates associated with adolescent alcohol use.

Nonetheless, there are several important limitations. As we recruited using an opt-in process rather than population-level randomisation, estimates may not be generalisable to the wider population of young people. Although levels of alcohol use and the demographic profile of APSALS participants are similar to the Australian population, families of lower socioeconomic status are underrepresented due to the small proportion of government schools involved in the study (22). We also note that whilst we make the distinction between different types of alcohol-related harms in our study, we did not capture all possible domains of alcohol-related harm as a limitation of the scale we used. Future

analyses extending on this work should use measures encompassing a broader range of harms, although this may be challenging if assessing low prevalence harms. The harms measures were also recoded from frequency-based responses into binary variables, which may have led to biased estimates from generalising across participants who experience a harm once versus those who experience the same harm multiple times. Additionally, to reduce computational complexity, our predictor and outcome models excluded approximately 220 participants across 22 latent transition classes, which may have resulted in biased estimates for these models. Notably, all transition classes where alcohol-related harms were experienced in early-mid adolescence (age 14-15 years) were excluded due to low cell size and hence the results are not generalisable to adolescents who experience harms earlier in adolescence. Further research is needed to examine whether the findings apply to adolescents who experience alcohol-related harms earlier in life. Indeed, a larger sample size could have enabled analyses involving the classes excluded in our study. Finally, the data used in our study were self-reported and thus the AUD outcomes should not be considered a clinical diagnosis, instead representing potential clinical problems relating to alcohol use. The levels of DSM-IV alcohol abuse and alcohol dependence symptoms reported in this cohort are, however, consistent with levels of alcohol use disorders found in community samples of young adults in Australia (47) and similar high-income countries (48, 49).

4.7.2. Conclusion

Young people experience heterogenous patterns of alcohol-related harm during adolescence, with harms of a physiological nature being particularly common. Whilst factors such as sex and early-adolescent peer substance use predicted early experience of

physiological harms, this specific pattern of harm did not predict AUD in early adulthood. A combination of physiological and psychosocial harms experienced in late adolescence emerged as the strongest indicator of AUD in early adulthood, attesting to the particular significance of the latter. Our results suggest that researchers, caregivers, and clinicians should consider the importance of psychosocial harms as a risk factor for future alcohol harms.

4.8. Declarations of competing interest

RB has received untied educational grants from Mundipharma and Indivior for studies relating to pharmaceutical opioids. MF has received untied educational grants from the Australian Government Department of Health. AP has received untied educational grants from Mundipharma and Seqirus for post-marketing surveillance of pharmaceutical opioids. These parties had no role in the design, conduct, and reporting of this study. All other authors have no conflicts of interest to declare.

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national comorbidity survey-adolescent supplement. J Am Acad Child Adolesc Psychiatry. 2016;55(4):280-8. Available from: https://doi.org/10.1016/j.jaac.2016.01.006

5. CHAPTER 5: AGE AT FIRST ALCOHOL RELATED HOSPITAL SEPARATION OR EMERGENCY DEPARTMENT PRESENTATION AND RATE OF RE-ADMISSION: A RETROSPECTIVE DATA LINKAGE COHORT OF YOUNG AUSTRALIANS

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5.1. Copyright Statement

I declare that this publication occurred during my candidature as a direct result of my research towards this thesis and, to the best of my knowledge, does not breach copyright regulations nor intellectual property rights.

Yuen, W. S., Leung, J., Man, N., Chiu, V., Gisev, N., Livingston, M., Degenhardt, L., Farrell, M., Pearson, S.-A., Dobbins, T., Dunlop, A., Mattick, R. P., Peacock, A. (2022). Age at first alcohol related hospital separation or emergency department presentation and rate of re-admission: a retrospective data linkage cohort of young Australians. Drug and Alcohol Review. https://doi.org/10.1111/dar.13529

5.2. Preamble

In Chapters 3 and 4, developmental patterns of alcohol-related blackouts and patterns of experiencing different types of alcohol-related harm were identified in a longitudinal cohort of young people. Whilst the most common developmental pattern was characterised by little to no harm across adolescence, 14 to 16 percent of young people in the cohort showed developmental patterns characterised by earlier and escalating experience of harm. These latter patterns were associated with AUD in early adulthood. Females in the cohort were at increased risk of experiencing harms characterised by physiological consequences (e.g., blackouts, hangovers) earlier in adolescence.

Though Chapters 3 and 4 capture the experience of a typical cohort of young people in Australia, it is unclear whether there are similar variations in terms of age at first experience of harm and subsequent outcomes among young people who experience more severe alcohol-related harms. This can be clarified through the use of linked health administrative data.

As such, this chapter aims to address research question 4: '*Are there risk factors for experiencing clinical alcohol-related harm for the first time at a younger age in recent birth cohorts?'* and research question 5: *'Does experiencing clinical alcohol-related harm for the first time at a younger age predict greater subsequent harm in recent birth cohorts?'*. Using a retrospective linked data cohort, we examine whether certain sociodemographic and clinical characteristics are associated with the age at which a young person first experiences clinical alcohol-related harm, i.e., harms requiring medical attention through hospitals and/or emergency departments. We also examine whether age at first experience of clinical alcohol-related harm is associated with readmissions in the subsequent 12 months.

5.3. Abstract

Introduction: Alcohol is a leading risk factor for death and disease in young people. We compare age-specific characteristics of young people who experience their first ('index') alcohol-related hospitalisation or emergency department (ED) presentation, and whether age at index predicts 12-month rates of readmission.

Methods: We used a retrospective linked-data cohort of 10,300 people aged 12-20 years with an index alcohol-related hospital and/or ED record in New South Wales, Australia from 2005-2013. Age group (early adolescent [12-14 years], late adolescent [15-17 years], young adult [18-20 years]) and diagnosis fields were used in logistic regression analyses and to calculate incidence rates with adjustment for year of index event, sex, socioeconomic disadvantage, and residence remoteness.

Results: People who experienced their index event in early adolescence (adjusted relative risk ratio [ARRR] = 0.45 [95% confidence interval = 0.39, 0.52]) or late adolescence (ARRR = 0.82 [0.74, 0.90]) were less likely to be male compared to young adults. Early adolescents (ARRR = 0.60 [0.51, 0.70]) and late adolescents (ARRR = 0.84 [0.76, 0.93]) were less likely to have a hospitalisation index event. Early adolescents (adjusted incidence rate ratio [AIRR] = 1.40 [1.15, 1.71]) and late adolescents (AIRR = 1.16 [1.01, 1.34]) were more likely than young adults to have a subsequent 12-month non-poisoning injury ED presentation.

Discussion and Conclusions: We identified potential healthcare needs for young people who have experienced an alcohol-related ED presentation or hospitalisation, with age-specific characteristics and outcomes that can be used to inform future health policy and service planning.

Keywords: alcohol, young people, record linkage, emergency department, hospitalisation

5.4. Introduction

Alcohol use has been the leading global risk factor for death and disease since 1990 in adolescents and young adults (hereafter 'young people', aged between 12 to 20 years) (1). Indeed, nearly 10% of deaths in young people worldwide in 2016 were attributable to alcohol consumption (2). In Australia, people aged 18-24 years are more likely to exceed the single-occasion risk guideline (4 standard drinks) than any other age group (3).

Across the population, people typically initiate alcohol use in mid-adolescence (4) and subsequently escalate alcohol use until their mid-twenties (5). However, cohort studies show that development of alcohol use usually varies among young people (6-10). Whilst some initiate alcohol use in early adolescence (i.e., before age 15 years), others abstain until adulthood (age 18 years or older) (6, 7, 9). Once initiated, some young people rapidly increase the frequency and quantity of their drinking, whereas others remain infrequent and/or moderate drinkers (6-9). Longitudinal cohort studies show that certain factors in early adolescence, such as peer alcohol use, can predict alcohol development patterns (6, 10). Importantly, patterns involving earlier initiation and/or rapid escalation are linked to future adverse health outcomes such as alcohol-use disorders (6, 10, 11). It is unclear, however, whether the timing of the experience of alcohol-related harm can be similarly predicted and whether this timing confers differential risk of further harm.

While young people with alcohol use problems such as alcohol dependence rarely seek treatment (12, 13), there has been an increase in young people accessing health services for acute (e.g. injuries) and/or chronic health problems (e.g. liver disease) due to problematic alcohol use (14-16). Examining young people at their first-ever presentation to inpatient and emergency department (ED) services with an alcohol-related problem (hereafter 'index

event') can inform targeted interventions to reduce re-presentation and longer-term costs to the health of these people. Indeed, adults hospitalised for alcohol-related problems in Denmark were far more likely than the general population to be readmitted for a wide range of diagnoses (e.g. alcohol poisoning, liver disease, stroke, injuries) and to also die from various causes of death (e.g. liver cancer, cardiovascular disease, suicide, and accidental injury) (17). However, it is currently unknown whether people who experience their first alcohol-related health service event (hospitalisation or ED presentation) earlier in adolescence have different profiles and outcomes to people who experience their first event later in adolescence or in early adulthood.

As such, the aim of this study was to identify young people at their index alcohol-related hospital separation or ED presentation and examine differences by age group (early adolescent [12-14 years], late adolescent [15-17 years], young adult [18-20 years]). Specifically, this study examines: 1) sociodemographic and clinical characteristics by age group at index event; and 2) age group at index event as a predictor of rates of subsequent health service utilisation (including alcohol-related and other-substance related utilisation) within 12 months of index event separation.

5.5. Methods

5.5.1. Participants

We used data from a subset of people from the existing Data-Linkage Alcohol Cohort Study (DACS) (18). This set of linked administrative data consists of hospital and ED records from people in New South Wales (NSW), Australia, who were admitted to hospital or presented to an ED with evidence of an alcohol-related diagnosis between January 1st, 2005 and December 31st, 2014. An alcohol-related diagnosis was defined as one or more of the

conditions in Table 10, presented as International Classification of Diseases Version 10 Australian Modification (ICD-10-AM) codes. ICD 9th Version Clinical Modification (ICD-9-CM) and Systematized Nomenclature of Medicine Clinical Terms Australian version (SNOMED CT-AU) equivalent codes are shown in Appendix D1. For hospital separations, a principal diagnosis and up to 50 additional diagnoses could be provided. For ED presentations, only the principal diagnosis field was provided. Data linkage was completed by the Centre for Health Record Linkage using ChoiceMaker, a probabilistic record linkage software (19). Ethics approval was provided by the NSW Population and Health Services Research Ethics Committee (18).

We restricted the DACS cohort to people born between 1992 and 2001 with their first alcohol-related hospital separation or ED presentation record between 2005 and 2013. We considered this record as their index event. If a person had both an ED presentation and hospital separation record on the same day, the record with an alcohol-related diagnosis was used as their index event. If both records had an alcohol flag, the ED presentation was used. This ensured that the sample consisted of people aged between 12 and 20 years that have not had any prior alcohol-related hospital separations or ED presentations between age 12 years and the age of their index event (see Appendix D2 for the number of people entering the cohort each year by age at cohort entry). We chose the age of 12 years for the lower bound for this subset as the mean age of initiation of alcohol in Australia was 14.7 years in 2001 and has since steadily risen (20), so it is unlikely that people below age 12 years would have experienced alcohol-related harm. Studies in hospital and ED settings in the UK and Australia have also reported that adolescents who present with alcohol intoxication tend to be aged 12 years or older (21, 22). This method of truncating the cohort also ensures that there is at least one person-year of follow-up for each person during the

period of 2005 to 2013. A flowchart of the cohort formation can be found in Appendix D3.

5.5.2. Data sources

5.5.2.1. Hospital data

The Admitted Patient Data Collection (APDC) is administered by the NSW Health Department and contains records of all hospital separations provided by public hospitals, public psychiatric hospitals, public multi-purpose services (e.g., integrated health and aged care services), private hospitals, and private day procedure centres in NSW. Primary and secondary diagnoses were coded using the ICD-10-AM codeset.

5.5.2.2. Emergency department data

The Emergency Department Data Collection (EDDC) is administered by the NSW Health Department and contains records of all patient presentations to participating public hospital EDs in NSW. The number of participating EDs increased over time from 46 (30%) in 1996 to 90 (60%) in 2010. Diagnoses were coded using the ICD-9-CM, ICD-10-AM, and SNOMED-CT-AU codesets.

5.5.2.3. Mortality data

The NSW Registry of Births, Deaths and Marriages and the Australian Coordinating Registry Cause of Death Unit Record File are two datasets containing mortality information for deaths that were recorded in NSW. The former provides information regarding date of birth and fact of death, whereas the latter includes additional information such as cause of death. In this study, these data were used solely for the purposes of adjusting for mortality when deriving person years for our 12-month follow-up analysis for Aim 2.

5.5.3. Measures

5.5.3.1. Age at index event

Age at index event was calculated from the date of birth and date of separation (APDC) or presentation (EDDC) variables. This was then recoded into 3-year age groups (early adolescent [12-14 years; prior to median age of alcohol use onset (4, 20)], late adolescent [15-17 years; post-median age of alcohol use onset], young adult [18-20 years; age of legal alcohol purchase and consumption at licensed venue in Australia, which commences from 18 years onwards]).

5.5.3.2. Sociodemographic characteristics

To examine sociodemographic characteristics, we used variables from the APDC and EDDC datasets including sex (male, female), remoteness area of usual residence (major city, inner regional, outer regional, remote, very remote; collapsed into two categories: major city, regional/remote) (23), and Index of Relative Socio-economic Disadvantage which ranks geographical area of usual residence by relative disadvantage based on the Australian Bureau of Statistics Census (24) in quintiles.

5.5.3.3. Clinical characteristics

To examine clinical characteristics at the index event, we grouped diagnosis codes into the categories of 'alcohol poisoning', 'mental/behavioural condition', and 'other physical condition' based on ICD-10-AM labelling. We created binary variables that flagged any records for these categories across all diagnosis fields (see Table 10 for list of codes). As the APDC dataset has multiple diagnosis fields, people may have more than one type of alcohol-related diagnosis.

Table 10. List of alcohol-related diagnoses.

Note. ICD-10-AM = International Classification of Diseases Version 10 Australian Modification. Equivalent codes for ICD 9th Version Clinical Modification and Systematized Nomenclature of Medicine Clinical Terms Australian version are shown in Appendix D1.

Category	ICD-10 AM Code	Condition
Alcohol poisoning	R78.0	Finding of alcohol in blood
	T51	Toxic effect of alcohol
	X45	Accidental poisoning by and exposure to alcohol
	X65	Intentional self-poisoning by and exposure to alcohol
	Y15	Poisoning by and exposure to alcohol, undetermined intent
	Y90	Evidence of alcohol involvement determined by blood alcohol level
	Y91	Evidence of alcohol involvement determined by level of intoxication
Mental/behavioural condition	F10.0	Acute intoxication
	F10.1	Harmful use of alcohol
	F10.2	Alcohol dependence
	F10.3	Alcohol withdrawal
	F10.4-F10.9	Other alcohol-induced mental conditions
Other physical condition	E24.4	Alcohol-induced pseudo-Cushing's syndrome
	E51.2	Wernicke encephalopathy
	G31.2	Degeneration of nervous system due to alcohol
	G62.1	Alcoholic polyneuropathy
	G72.1	Alcoholic myopathy
	I42.6	Alcoholic cardiomyopathy
	K29.2	Alcoholic gastritis
	K70.0-K70.4, K70.9	Alcohol-induced liver diseases
	K85.2, K86.0	Alcohol-induced pancreatitis

5.5.3.4. Subsequent hospital and ED events

To examine 12-month utilisation of health services after the index event, we calculated person-years by adding 365 days to the date of separation (APDC) or date of presentation (EDDC). People who died within 12 months of their index event were censored using the date of death variable from the RBDM and COD URF datasets. Using APDC and EDDC diagnosis fields, subsequent hospital separations and ED presentations were broadly classified as: 1) any hospital separation or ED presentation; 2) ED presentation; and 3) hospital separation. These were further classified into alcohol-specific, other substance-specific, non-substance mental disorder, and other accidental injury for hospital separations and ED presentations (see Appendix D4 for list of codes). SNOMED-CT-AU codes from the EDDC were mapped to ICD-10-AM equivalent codes using the Commonwealth Scientific and Industrial Research Organisation snoMAP Starter tool and the National Library of Medicine Unified Medical Language System mapping project. Of the 7,583 SNOMED-CT-AU codes we attempted to map to ICD-10-AM in this cohort, 287 (3.8%) were unable to be matched.

5.5.4. Statistical analysis

We conducted all analyses in SAS v9.4 (SAS Institute Inc. Cary, NC, USA) using complete-case data. These analyses were not pre-registered and should thus be considered exploratory. Reporting is consistent with the RECORD guidelines (Appendix D5).

5.5.4.1. Association between sociodemographic and clinical characteristics and age at index

We used multinomial logistic regression models to determine whether the sociodemographic and clinical characteristics described above were associated with age group at index event. To account for potential year effects, we adjusted for year of index

event. Results are presented as adjusted relative risk ratios (ARRR) with 95% confidence intervals.

5.5.4.2. Subsequent hospital and ED events by age at index

We calculated rates per person-years (PY) and incidence rates for subsequent 12-month hospital and ED events from the date of index separation, disaggregated by age group at index event. Incidence rates per 100 PY were calculated using Poisson or negative binomial regression models (depending on the estimated over-dispersion of the variable) to examine subsequent hospital and ED events. Comparisons of the incidence rates are presented as adjusted incidence rate ratios (AIRR) with 95% confidence intervals. Models were adjusted for sex, year of index event, socioeconomic status, and remoteness area of usual residence. SNOMED-CT-AU codes from the EDDC that were unable to be mapped to ICD-10-AM codes were retained for 'any' episode analyses and dropped for cause-specific analyses.

5.6. Results

Our study included 10,300 young people. Table 11 shows the demographic characteristics of the overall cohort and by age group. The largest age group was the late adolescent group, comprising 48.4% (*n* = 4984) of the cohort, followed by the young adult (35.5%; *n* = 3656) and early adolescent (16.1%; *n* = 1660) groups. There were marginally more males than females overall (51.5% male; *n* = 5303). Half of the cohort were in the two most disadvantaged socio-economic quintiles (52.1%; *n* = 5366) and the majority resided in major cities (63.0%; *n* = 6490). Index records predominantly consisted of ED presentations (64.0%; *n* = 6587), with acute intoxication being the most common reason for hospital separations and ED presentations (66.6%; *n* = 6856).

Table 11. Sociodemographic and clinical characteristics at index event for people aged 12 to 20 years with a hospital contact for an alcohol-related problem in NSW, Australia from 2005 to 2013.

Note: Bolded statistics indicate *P* < 0.05. Percentages rounded to one decimal place. Adjusted correlate models adjust for year of index event. * suppressed due to low cell size (n < 10). ** coded as three separate binary variables as diagnosis types are not mutually exclusive, people in the APDC may present with more than one alcohol-related diagnosis. RRR = relative risk ratio; CI = confidence interval

	Total n = 10300 (%)	**A. Early adolescent (12-14 years) n = 1660 (%)**	**B. Late adolescent (15-17 years) n = 4984 (%)**	**C. Young adult (18-20 years) n = 3656 (%)**	**A vs C (ref.) RRR (95% CI)**	**A vs C (ref.) Adjusted RRR (95% CI)**	**B vs C (ref.) RRR (95% CI)**	**B vs C (ref.) Adjusted RRR (95% CI)**
Sex								
Male	5301 (51.5)	646 (38.9)	2594 (52.1)	2061 (56.4)	**0.49 (0.44, 0.55)**	**0.45 (0.39, 0.52)**	**0.84 (0.77, 0.91)**	**0.82 (0.74, 0.90)**
Female	4996 (48.5)	1014 (61.1)	2389 (47.9)	1593 (43.6)	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Socio-economic Disadvantage Quintile								
1 (Most disadvantaged)	2788 (27.1)	468 (28.2)	1333 (26.8)	987 (27.0)	*Ref.*	*Ref.*	*Ref.*	*Ref.*
2	2578 (25.0)	428 (25.8)	1219 (24.5)	931 (25.5)	0.97 (0.83, 1.14)	1.03 (0.85, 1.25)	0.97 (0.86, 1.09)	0.99 (0.87, 1.14)
3	1681 (16.3)	252 (15.2)	790 (15.9)	639 (17.5)	0.83 (0.69, 1.00)	0.85 (0.68, 1.06)	0.92 (0.80, 1.05)	0.92 (0.79, 1.07)
4	1176 (11.4)	184 (11.1)	569 (11.4)	423 (11.6)	0.92 (0.75, 1.13)	1.00 (0.78, 1.28)	1.00 (0.86, 1.16)	1.02 (0.86, 1.22)
5 (Least disadvantaged)	2074 (20.1)	327 (19.7)	1072 (21.5)	675 (18.5)	1.02 (0.86, 1.21)	1.16 (0.94, 1.43)	**1.18 (1.04, 1.33)**	**1.29 (1.12, 1.49)**
Missing	*	*	*	*				
Remoteness Area of Usual Residence								
Major city	6490 (63.0)	1031 (62.1)	3176 (63.7)	2283 (62.5)	0.99 (0.87, 1.11)	1.02 (0.89, 1.18)	1.06 (0.97, 1.15)	1.08 (0.98, 1.20)
Regional/remote	3810 (37.0)	629 (37.9)	1808 (36.3)	1373 (37.6)	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Service Accessed								
Hospital separation	3713 (36.0)	487 (29.3)	1810 (36.3)	1416 (38.8)	**0.66 (0.58, 0.74)**	**0.60 (0.51, 0.70)**	**0.90 (0.83, 0.99)**	**0.84 (0.76, 0.93)**
Emergency department	6587 (64.0)	1173 (70.7)	3174 (63.7)	2240 (61.3)	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Diagnosis Type **								

Alcohol poisoning	612 (5.9%)	94 (5.7%)	282 (5.7%)	236 (6.5%)	0.87 (0.68, 1.11)	0.83 (0.61, 1.13)	0.87 (0.73, 1.04)	0.90 (0.74, 1.11)
Mental/behavioural condition	9568 (92.9%)	1561 (94.0%)	4674 (93.8%)	3333 (91.2%)	**1.53 (1.21, 1.93)**	**1.59 (1.19, 2.13)**	**1.46 (1.24, 1.72)**	**1.45 (1.20, 1.75)**
Other physical condition	225 (2.2%)	11 (0.7%)	66 (1.3%)	148 (4.1%)	**0.16 (0.09, 0.29)**	**0.21 (0.10, 0.41)**	**0.32 (0.24, 0.43)**	**0.34 (0.24, 0.49)**

5.6.1. Association between sociodemographic and clinical characteristics and age at index

For all regression models (Table 11), we chose the young adult group as the reference as it is the age group that has the highest prevalence of alcohol-related harms in the population. After adjusting for year of index event, relative to females, males were less likely to be in the early adolescent group (ARRR = 0.45 [0.39, 0.52]) and late adolescent group (ARRR = 0.82 [0.74, 0.90]) compared to young adult group. With the most disadvantaged socio-economic quintile as the reference, adjusted analyses showed that people in the least disadvantaged quintile were more likely to be in the late adolescent group compared to the young adult group (ARRR = 1.29 [1.12, 1.49]). There was a lack of clear evidence of an association between the early adolescent group and the young adult group with respect to socio-economic disadvantage. Likewise, associations between remoteness area of usual residence and index age group were inconclusive.

Adjusted analyses showed that people whose index event was a hospital separation (versus an ED presentation) were less likely to be in the early adolescent group compared to the young adult group (ARRR = 0.60 [0.51, 0.70]). Adjusted analyses also showed that people whose index event was a hospital separation were less likely to be in the late adolescent group compared to the young adult group (ARRR = 0.84 [0.76, 0.93]). People whose index event included a 'mental/behavioural condition' diagnosis code were more likely to be in the early adolescent group (ARRR = 1.59 [1.19, 2.13]) and the late adolescent group (ARRR = 1.45 [1.20, 1.75]) compared to the young adult group. People whose index event included an 'other physical condition' diagnosis code were less likely to be in the early adolescent group (ARRR = 0.21 [0.10, 0.41]) and the late adolescent group (ARRR = 0.34 [0.24, 0.49])

compared to the young adult group. Associations between the presence of the 'alcohol poisoning' diagnoses and index age group were inconclusive for both the unadjusted and adjusted models.

5.6.2. Subsequent hospital separations and ED presentations by age at index

Table 12 shows the number and rates per 100 person years (PY) of ED presentations and hospital separations across the cohort in the 12 months following cohort entry. In the early adolescent group, there were 2063 ED presentations and 1001 hospital separations across 1660.0 PY. These were accounted for by 716 (43.1% of age group) and 594 (35.8%) people, respectively. In the late adolescent group, there were 5911 ED presentations (n people = 2201, 44.2% of age group) and 3217 hospital separations (n people = 1663, 33.4%) across 4977.6 PY. In the young adult group, there were 4672 ED presentations (n people = 1669, 45.7%) and 2573 hospital separations (n people = 1243, 34.0%) across 3646.0 PY. Across all age groups, 403 people (3.9%) experienced at least one and 39 (0.4%) experienced at least two subsequent alcohol-related ED presentations. For alcohol-related hospitalisations, 1829 people (17.8%) experienced at least one and 192 (1.9%) experienced at least two subsequent hospital separations.

After adjusting for year of cohort entry, sex, socioeconomic status, and remoteness of usual residence, analyses showed that people in the early adolescent group (AIRR = 1.40 [1.15, 1.71]) and late adolescent group (AIRR = 1.16 [1.01, 1.34]) had higher rates of non-poisoning injury ED presentations compared to the young adult group. The early adolescent group had lower rates of any hospital separation (AIRR = 0.80 [0.70, 0.92]) and non-alcohol substance-related hospital separation (AIRR = 0.65 [0.44, 0.95]) compared to the young adult group. Similarly, the late adolescent group had lower rates of any hospital separation compared to

the young adult group (AIRR = 0.89 [0.81, 0.98]).

Table 12. Rates of subsequent 12-month emergency department presentations and hospital presentations per 100 person years by age group at index event.

Note: Bolded statistics indicate P < 0.05. * Estimated for a balanced population using least squares means in SAS adjusting for sex, year of index event, socioeconomic status, and remoteness area of usual residence; ** excludes overdose and poisoning. PY = person years of observation; IR = incidence rate; IRR = incidence rate ratio; CI = confidence interval.

	A. Early-mid adolescent (12-14 years; PY = 1660)			**B. Mid-late adolescent (15-17 years; PY = 4977.55)**			**C. Young adult (18-20 years; PY = 3646.02)**			**A vs C (ref)**		**B vs C (ref)**	
	n People (Events)	**IR (95% CI)**	**Adjusted IR* (95% CI)**	**n People (Events)**	**IR (95% CI)**	**Adjusted IR* (95% CI)**	**n People (Events)**	**IR (95% CI)**	**Adjusted IR* (95% CI)**	**IRR (95% CI)**	**Adjusted IRR* (95% CI)**	**IRR (95% CI)**	**Adjusted IRR* (95% CI)**
Any ED/hospital contact	957 (3064)	184.58 (170.63, 199.67)	179.40 (164.55, 195.60)	2739 (9128)	183.48 (175.33, 192.00)	180.51 (172.50, 188.89)	2059 (7245)	200.19 (189.91, 211.02)	194.09 (183.19, 205.64)	0.92 (0.84, 1.01)	0.92 (0.83, 1.03)	**0.92 (0.85, 0.98)**	0.93 (0.86, 1.00)
Any emergency department presentation	716 (2063)	124.28 (113.88, 135.62)	121.36 (110.30, 133.53)	2201 (5911)	118.84 (112.96, 125.02)	115.02 (109.35, 120.99)	1669 (4672)	128.89 (121.53, 136.69)	120.67 (113.16, 128.68)	0.96 (0.87, 1.07)	1.01 (0.89, 1.14)	0.92 (0.85, 1.00)	0.95 (0.88, 1.04)
Alcohol-specific ED presentation	82 (96)	5.78 (4.54, 7.36)	6.05 (4.62, 7.91)	175 (193)	3.88 (3.30, 4.56)	3.88 (3.30, 4.57)	146 (193)	5.29 (4.47, 6.26)	4.90 (4.05, 5.93)	1.09 (0.81, 1.47)	1.23 (0.86, 1.76)	**0.73 (0.58, 0.92)**	0.79 (0.61, 1.02)
Other substance-specific ED presentation	13 (14)	0.84 (0.50, 1.42)	1.16 (0.58, 2.32)	46 (50)	1.00 (0.76, 1.33)	0.93 (0.65, 1.34)	41 (90)	2.47 (2.01, 3.04)	1.16 (0.75, 1.78)	**0.34 (0.19, 0.60)**	1.00 (0.42, 2.38)	**0.41 (0.29, 0.57)**	0.80 (0.47, 1.38)
Non-substance mental disorder ED presentation	60 (109)	6.57 (4.94, 8.72)	6.68 (4.88, 9.15)	181 (250)	5.02 (4.22, 5.98)	4.74 (3.97, 5.66)	156 (252)	6.93 (5.73, 8.37)	5.75 (4.64, 7.11)	0.95 (0.67, 1.33)	1.16 (0.77, 1.75)	**0.72 (0.56, 0.94)**	0.83 (0.62, 1.09)
Other injuries of external causes ED presentation**	217 (319)	19.22 (16.67, 22.15)	20.56 (17.65, 23.96)	649 (905)	18.19 (16.73, 19.77)	17.07 (15.69, 18.58)	476 (631)	17.30 (15.67, 19.10)	14.67 (13.14, 16.38)	1.11 (0.93, 1.32)	**1.40 (1.15, 1.71)**	1.05 (0.92, 1.20)	**1.16 (1.01, 1.34)**
Any hospitalisation	594 (1001)	60.30 (54.65, 66.53)	57.52 (51.59, 64.14)	1663 (3217)	64.63 (61.11, 68.35)	63.97 (60.45, 67.69)	1243 (2573)	70.87 (66.45, 75.59)	71.81 (66.87, 77.13)	**0.85 (0.76, 0.96)**	**0.80 (0.70, 0.92)**	**0.91 (0.84, 0.99)**	**0.89 (0.81, 0.98)**

Alcohol-specific hospitalisation	376 (413)	24.88 (22.25, 27.82)	23.94 (21.11, 27.14)	862 (1024)	20.57 (19.19, 22.05)	20.38 (19.00, 21.86)	591 (777)	21.32 (19.69, 23.10)	21.79 (19.96, 23.80)	**1.17 (1.02, 1.34)**	1.10 (0.93, 1.30)	0.96 (0.87, 1.07)	0.94 (0.83, 1.05)
Other substance-specific hospitalisation	76 (108)	6.51 (4.93, 8.58)	7.01 (5.17, 9.52)	276 (462)	9.28 (8.00, 10.76)	9.21 (7.94, 10.69)	210 (426)	11.69 (9.90, 13.81)	10.87 (9.00, 13.13)	**0.56 (0.40, 0.77)**	**0.65 (0.44, 0.95)**	0.79 (0.63, 0.99)	0.85 (0.66, 1.08)
Non-substance mental disorder hospitalisation	134 (302)	18.19 (14.57, 22.72)	16.74 (13.04, 21.50)	431 (982)	19.74 (17.39, 22.41)	18.00 (15.86, 20.43)	318 (731)	20.15 (17.38, 23.37)	19.36 (16.47, 22.75)	0.90 (0.69, 1.18)	0.86 (0.63, 1.20)	0.98 (0.81, 1.19)	0.93 (0.75, 1.15)
Other injuries of external causes hospitalisation**	123 (174)	10.48 (8.73, 12.59)	10.52 (8.61, 12.86)	399 (498)	10.00 (8.99, 11.14)	9.73 (8.73, 10.85)	339 (447)	12.30 (10.94, 13.84)	11.49 (10.07, 13.12)	0.85 (0.69, 1.06)	0.92 (0.71, 1.19)	**0.81 (0.69, 0.95)**	0.85 (0.71, 1.01)

5.7. Discussion

Our study used linked administrative data to examine the characteristics and 12-month readmission rates of a cohort of young people who presented to an ED or were hospitalised for an alcohol-related problem in NSW, Australia for the first time since age 12 years. Correlates of younger age at index event included: female sex, presenting to an ED (versus hospital separation), and presenting with a mental/behavioural condition (e.g., acute intoxication). In the 12-months following index, non-poisoning injury ED presentation rates were higher among adolescents compared to young adults and overall rates of hospitalisation were slightly lower among adolescents compared to young adults.

Males were much more likely to be older at their first event, being 55% less likely to be in the early adolescent group and 18% less likely to be late adolescent group compared to the young adult group. This finding contrasts with existing reports of early adolescent alcohol consumption, where no sex differences in levels of alcohol use have been found in Australia, (6, 25) nor in other regions such as the UK (26). A potential explanation could be that while females have similar rates of binge drinking to males in early adolescence, females tend to reach higher levels of intoxication compared to males when consuming the same amount of alcohol, and are thus more likely to experience alcohol problems requiring hospitalisation (27). Indeed, the majority of alcohol-related diagnoses in our cohort were related to intoxication and our findings mirror that of a Dutch study (28) and a Welsh study (29) on adolescents admitted to hospital for alcohol problems, where people aged 16 and younger were less likely to be male but older adolescents were more likely to be male. Importantly, qualitative studies have found that young people tend to be unaware that the effect of alcohol can depend on physical differences in body size and sex (30, 31). Accordingly,

strategies to reduce alcohol-related harms in young people should consider improving education messaging for adolescents and young adults to elucidate the role of physiological differences in how alcohol affects the body.

Late adolescents in our cohort were less likely to be disadvantaged than younger adults, but no differences were found between early-adolescents and young adults. A possible explanation for late adolescents being less likely to be disadvantaged than young adults is that there is an influx of young people at this age who: 1) are consuming alcohol for the first time, with most adolescents starting to use alcohol at the ages encompassed by our late-adolescent group (15-17 years) (4) and 2) are less disadvantaged and thus have more discretionary funds to experiment with alcohol. Overall, however, our cohort was skewed towards people who were more disadvantaged, with 52% of the cohort being in the lowest two quintiles. In addition, a higher proportion of our cohort resided outside of major cities (37%) compared to the general NSW population of the same age (25%)(32), which does not necessarily mean that our sample is not representative, but is likely explained by higher rates of alcohol use among young people residing in rural Australia (33). This is consistent with emergency department (29) and linked cohort (34) studies that have found greater socioeconomic disadvantage to be associated with greater alcohol-related harm, disproportionate in contrast to findings that less socioeconomic disadvantage is associated with heavy episodic drinking (35). The reasons for this discrepancy between consumption and harm are complex (36), and potential strategies to address this inequity include licensing changes that target the over-representation of alcohol outlets in disadvantaged areas and interventions that target vulnerable populations (37).

Most of our cohort experienced their first alcohol-related event as an ED presentation

rather than a hospital separation, with ED presentations being more likely in the adolescent groups compared to young adults. This suggests that people who experience their first alcohol-related event at a younger age are more likely to have an acute problem compared to people who are older. Much of our cohort received an acute intoxication diagnosis, with relatively few being diagnosed with alcohol poisoning or other physical conditions. Younger adolescents compared to young adults were 45-59% more likely to be diagnosed with mental/behavioural conditions such as acute intoxication and were 66-79% less likely to be diagnosed with other physical conditions such as alcoholic liver disease. This is expected as young adults tend to have had longer exposure to alcohol and therefore had the opportunity to develop conditions associated with chronic alcohol use.

In the 12 months following the index event, non-poisoning injury ED presentations were 40% higher in people who experienced their index event in early adolescence and 16% higher in late adolescence compared to young adulthood after controlling for other sociodemographic characteristics. Given the dose-response relationship between alcohol use and injury (38) and the under-detection of alcohol involvement in injury ED presentations (39), it is likely that a substantial number of these injury ED presentations in our cohort were related to alcohol use. Indeed, there is evidence from NSW that the introduction of alcohol licensing regulations significantly reduced the rate of serious injury in the same area by 24.8% (40). Thus, addressing alcohol-related issues in young people, especially adolescents, can have the added benefit of reducing overall rates of injury. Indeed, a record linkage study of young people in NSW who were treated for alcohol problems between 2001 to 2016 showed that those who spent at least 30 days in treatment were much less likely to be subsequently hospitalised for physical injuries (HR = 0.77 [95% CI = 0.61-0.98]) and also range of other reasons (41). This is particularly important given that

accidental injuries are one of the leading causes of death among 15 to 24 year-olds in Australia, contributing to 32% of deaths in this age group from 2017 to 2019 (42).

Hospitalisation rates for any cause in the 12 months following the index event were 20% lower in the early adolescent group and 11% lower in the late adolescent group compared to the young adult group. This may be in part due to rates of all-cause hospitalisations being lower across adolescents in the NSW population compared to young adults (43) rather than cohort-specific effects. Compared to age-matched 12-month NSW population estimates, however, ED presentation rates in our cohort in the 12 months subsequent to the index event were at least 3 times higher (44) and hospitalisation rates in our cohort at least 4 times higher (43). Evidence from Denmark suggests that adults who have been hospitalised for alcohol problems were much more likely to have subsequent admissions compared to the general population (17), though it is unclear whether this varies by age and whether similar results can be found in the Australian population. Extensions to our current work would benefit from comparisons in rates of cause-specific and all-cause ED presentations and hospitalisations between the Australian population of young people and young people who have previously had an alcohol-related issue to identify whether there are differences in morbidity.

5.7.1. Limitations

Due to the nature of linked administrative data, our study has several limitations that should be considered. As the data were not collected for the purposes of this study, we were unable to adjust for confounders such as parent/family alcohol use. ED records only included those from public hospitals and the proportion of participating EDs has increased over time, from around 30% in 1996 to around 60% in 2010. Additionally, secondary

diagnosis fields were not provided in ED records and alcohol-related diagnoses may not be recorded by staff at EDs. Given that most alcohol-related events for young people are ED presentations, it is likely due to the aforementioned limitations that there has been under-ascertainment of ED cases for alcohol-related problems (45). Diagnosis codes collected from routine administrative data may be inaccurate due to errors such as poor communication between patients and clinicians, as well as lack of clinician experience and code-specific training (46). Diagnosis codesets also differed between APDC (ICD-10-AM) and EDDC (SNOMED-CT-AU) which may have impacted diagnosis groupings as we were unable to match all SNOMED-CT-AU to ICD-10-AM codes, although minimal records were impacted. Finally, our follow-up was restricted to 12 months, which may be insufficient to examine the effect of age at first event on subsequent health outcomes for younger people in our cohort. Future work should extend the follow-up period and examine outcomes in adulthood.

5.7.2. Conclusions

Young people who present to an ED or are hospitalised for the first time with an alcohol-related reason at a younger age are more likely to be female, experience an ED presentation, and to present with mental or behavioural condition. Adolescents are also subsequently more likely to present to an ED for a non-poisoning injury compared to young adults. Our findings highlight potential healthcare needs for young people who have experienced an alcohol-related ED presentation or hospitalisation, with age-specific clinical characteristics and outcomes that can be used to inform future health policy and service planning.

5.8. Declarations of competing interest

MF has received untied educational grants from the Australian Government Department of

Health. LD has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Indivior, Reckitt Benckiser, Mundipharma and Seqirus. AP has received investigator-initiated untied educational grants from Mundipharma and Seqirus for post-marketing surveillance of pharmaceutical opioids. These parties had no role in the study design, conduct, and reporting. All other authors have no conflicts of interest to declare.

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6. CHAPTER 6: GENERAL DISCUSSION

6.1. Overview

This thesis examined trajectories of alcohol-related harm in young people aged 12 to 24 years, a population with the highest prevalence of risky drinking and experience of acute harms due to alcohol (1). While evidence suggests that alcohol consumption has been declining in this age group (2-4), there have been conflicting accounts regarding whether rates of alcohol-related harm have declined in concert (5-8). Regardless, alcohol remains the leading risk factor for death and disease for young people worldwide (9). There is a need to clarify recent trends in alcohol-related harm at the population level and subsequently identify high risk developmental patterns of harm in recent cohorts of young people who have shown declines in consumption (i.e., born during or after 1990s), including whether there are any modifiable risk factors to these patterns.

Conceptualising alcohol-related harm can be challenging as there are a myriad of ways in which harms can be measured, ranging from surveys to health service records. Whereas the latter facilitates study of severe harms and access of health services, the former presents the opportunity to capture broader populations, including people who experience sub-clinical harms or do not use health services for problems due to alcohol. These forms of data are not without their disadvantages, however. Surveys tend to underestimate alcohol consumption due to various biases (e.g., social desirability, non-response, sampling frames; 10, 11, 12), and are thus likely to do the same for alcohol-related harm. Administrative data only includes specific forms of harm (e.g., poisoning), which are rare in the population, and only captures those who seek medical attention. Key variables such as the involvement of alcohol are also often underreported in administrative data due to systematic issues with

coding systems and/or practitioner error (13, 14). As such, examination of a wide range of data sources is necessary to provide a more holistic understanding of the current state of alcohol-related harm amongst young people.

Thus, this thesis contains four studies that each aim to investigate the issue of alcohol-related harm in recent cohorts of young people focusing on a variety of types of harms and using multiple approaches to measurement (see Table 13 for summary of key findings).

Study 1 (Chapter 2) was aimed at answering research question 1: '*Are self-reported harms among young people less prevalent in recent birth cohorts, in line with previous findings on declining alcohol consumption?'* and research question 2: '*What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving declines in alcohol consumption?'*. This study is an age, period, cohort analysis of trends in alcohol-related risky behaviours across the Australian population, including a comparison of trends between males and females. Using data from 6 cross-sectional surveys of a general population sample from 2001 to 2016 (*n*=121,281), the results have high generalisability to the Australian population and relevancy in examining trends parallel to those reported on alcohol consumption (15, 16). Though the prevalence of alcohol-related risky behaviours declined with more recent birth cohorts, people in late adolescence and early adulthood reported the highest prevalence of these behaviours compared to older ages. Similar to trends in alcohol consumption (17, 18), there is evidence of a closing male-female gap in risky behaviours amongst young people and recent birth cohorts that appears to be driven by greater declines for males than females.

Studies 2 and 3 (Chapters 3 and 4) were aimed at answering research question 2: '*What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving*

declines in alcohol consumption?' and research question 3: *'In recent birth cohorts, are there early adolescent factors that predict high-risk developmental patterns of harm?'*. These studies use data from the Australian Parental Supply of Alcohol Longitudinal Study (APSALS), a cohort of people born between the 1990s and early 2000s and followed up in repeated annual surveys, to identify patterns of alcohol-related harm experienced across the span of adolescence and early adulthood. First, trajectories of blackouts, a common alcohol-related harm, are examined (Chapter 3; *n*=1,821), followed by an examination of transitions between different types of alcohol-related harm (Chapter 4; *n*=1,828). These chapters identified that young people typically experienced minimal harm or only physiological harms (e.g., blackouts) on rare occasions throughout adolescence. Though less common, developmental patterns characterised by early experience of blackouts and psychosocial harms (e.g., getting into fights) were associated with greater risk of later alcohol use disorder (AUD). Female adolescents were consistently at higher risk of experiencing physiological harms at a younger age.

Study 4 (Chapter 5) was aimed at answering research question 4: '*Are there risk factors for experiencing clinical alcohol-related harm for the first time at a younger age in recent birth cohorts?'* and research question 5: *'Does experiencing clinical alcohol-related harm for the first time at a younger age predict greater subsequent harm in recent birth cohorts?'.* This study uses data from a subset of the Data-linkage Alcohol Cohort Study (DACS), specifically young people aged 12 to 20 years born during the same period as that of the cohort featured in Studies 2 and 3 (*n*=10,300). We examine whether the age at which a young person first experienced an alcohol-related hospital admission or emergency department (ED) presentation can be predicted by sociodemographic factors, and whether those presenting at a younger age were more likely to be readmitted subsequently for both

alcohol-related and unrelated reasons. In line with the findings of Studies 2 and 3, people experiencing clinical alcohol-related harm for the first time at an earlier age were more likely to be female. Younger age at first experience of clinical alcohol-related harm was associated with higher 12-month rates of injury-related ED presentation and lower rates of any hospitalisation. In the 12 months following their first experience of clinically significant alcohol-related harm, young people in our cohort had higher rates of any ED presentation and hospital admission compared to young people in the population.

A notable theme that emerged across the results of all four studies was age-specific differences between males and females. To preface, the terms 'male' and 'female' are used as recorded in surveys or reported in existing literature. These terms are generally lack specific definitions within the literature and are poorly specified in survey measurements. For instance, the national survey data used in Study 1 used the following phrasing from 2001 to 2013 with binary response options: "Are you male or female?" This was changed in 2016 to include an 'other' category with the question phrased as: "What is your sex?" The following discussion will consider the terms 'male' and 'female' in reference to sex recorded at birth.

The remainder of this chapter will situate the findings of this thesis with the literature by emphasising two broad themes: 1) trends in alcohol-related harms among young people; and 2) development of alcohol-related harm in recent cohorts of young people. Strengths and limitations of the dissertation will be considered, followed by implications of the findings and suggestions for future directions.

Table 13. Summary of key findings for each research question addressed in this thesis.

Research Question	Chapter(s)	Data Source	Design	Sample characteristics	Key Findings
1: Are self-reported harms among young people less prevalent in recent birth cohorts, in line with previous findings on declining alcohol consumption?	2	National Drug Strategy Household Survey (2001-2016)	Repeated cross-sectional	General population household survey of Australian residents aged 14 to 80 years.	Alcohol-related risky behaviours are declining in prevalence with time across the population of drinkers. Risky behaviours peaked in 1950s birth cohorts, then steadily declined with recent birth cohorts. Risky behaviours increase in prevalence from adolescence, peak at age 21 years, then decline with age. Males are twice as likely as females to report risky behaviours, but this gap is closing in younger people and in more recent birth cohorts.
2: What are the typical developmental patterns of alcohol-related harm in birth cohorts who are driving declines in alcohol consumption?	3, 4	Australian Parental Supply of Alcohol Longitudinal Study (2010-2018)	Longitudinal cohort	Cohort of young people recruited from Grade 7 in 2010-2011 from schools across New South Wales, Western Australia, and Tasmania.	The most common pattern of harm involves minimal harm in adolescence that is followed by some experience of physiological harm in early adulthood. Patterns involving early and/or escalating experience of alcohol-related harm are less common in a typical cohort of adolescents.
3: In recent birth cohorts, are there early adolescent factors that predict high-risk developmental patterns of harm?	3, 4	Australian Parental Supply of Alcohol Longitudinal Study (2010-2018)	Longitudinal cohort	Cohort of young people recruited from Grade 7 in 2010-2011 from schools across New South Wales, Western Australia, and Tasmania.	Females were more likely to experience early and/or escalating physiological harms compared to males. Having more peers who use substances in early adolescence increased risk of earlier alcohol initiation and also earlier experience of physiological harms.

Research Question	Chapter(s)	Data Source	Design	Sample characteristics	Key Findings
4: Are there risk factors for experiencing clinical alcohol-related harm for the first time at a younger age in recent birth cohorts?	5	Data-Linkage Alcohol Cohort Study (2005-2013)	Retrospective linked administrative data cohort	People aged 12 to 20 years who experienced an alcohol-related ED presentation or hospital admission for the first time since age 12 years in New South Wales, Australia.	Females were more likely to access hospital services with an alcohol problem for the first time at a younger age compared to males. Young people who first accessed hospital services for an alcohol problem in the form of an ED presentation rather than a hospitalisation were more likely to be younger.
5: Does experiencing clinical alcohol-related harm for the first time at a younger age predict greater subsequent harm in recent birth cohorts?	5	Data-Linkage Alcohol Cohort Study (2005-2013)	Linked administrative data cohort	People aged 12 to 20 years who experienced an alcohol-related ED presentation or hospital admission for the first time since age 12 years in New South Wales, Australia.	Accessing hospital services with an alcohol problem for the first time at a younger age was associated with greater risk of 12-month ED presentations for injuries but lower risk of 12-month hospitalisations for any reason. Young people who have previously accessed hospital services for an alcohol problem have much higher subsequent 12-month rates of any hospital service access compared to the general population of young people.

6.2. Trends in alcohol-related harms among young people

6.2.1. Prevalence of harms among young people in recent birth cohorts

Comparison of birth cohorts in Study 1 indicate that recent generations of Australians are much less likely to report engaging in risky behaviours while under the influence of alcohol compared to older generations. This is commensurate with reports of declining prevalence and volume of alcohol use among people born during or after the 1990s (2, 19-21). As Study 1 only included people who had consumed alcohol in the past 12 months, these trends reflect decreased risky behaviour among young drinkers rather than decreased risky behaviour due to the declining prevalence of young drinkers. This means that when we consider the prevalence of alcohol-related risky behaviours across the entire population, these behaviours have declined even more than Study 1 suggests since the prevalence of people who abstain from drinking has been increasing. However, there is also the possibility that these young people are simply more reluctant to divulge their engagement in risky behaviours. Indeed, social desirability can substantially bias results relating to risky alcohol use and harms (10). It has been proposed that the decline of alcohol use in recent generations of young people may be partly due to changes in social norms and increasing consciousness regarding the health risks of alcohol use (22, 23). If this is the case, these trends in alcohol-related risky behaviours may be partially driven by impression management rather than solely by changes in prevalence of risky behaviour.

Despite recent declines, reporting of alcohol-related risky behaviours has historically been, and continues to be, most common in adolescence and early adulthood compared to later adulthood. Age effects in Study 1 showed increasing prevalence of risky behaviours with age until a lifetime peak at age 21 years, at which point the prevalence decreases steadily with

age. Developmental factors rather than social factors could explain this persistent age effect, especially in light of the strong birth cohort effects. For instance, it has been well-established that people have increased propensity for risk-taking in late adolescence and early adulthood (24) and that psychosocial maturity (e.g., impulse control, resistance to peer influence) continues to develop well into the late 20s (25). This is reflected by drinking patterns in young people. Whilst the proportion of Australian adults aged 18 to 24 years exceeding the single occasion risk guidelines (> 4 standard drinks on one occasion; 26) decreased between 2007 and 2019, they remained the age group most likely to engage in this pattern of drinking (27). Additionally, although more recent birth cohorts are less likely to drink or engage in risky drinking in adolescence compared to earlier birth cohorts, by early adulthood these differences in birth cohort are much smaller (28). As such, risky patterns of alcohol use and alcohol-related risky behaviours among young people continue to be a public health issue despite recent periods of decline.

While Study 1 examines trends in risky behaviours (e.g., driving, swimming) rather than harms per se, these behaviours can be a precursor to acute alcohol-related harms such as poisoning and injury. These acute harms can typically be captured by health service data such as hospital and ED records. The age effects reported in Study 1 are corroborated by the rates of ED presentations for alcohol problems in New South Wales (NSW) Australia, which are also historically and currently highest among people aged 18-24 years (29). In the linked administrative cohort used in Study 4, around 1200 people under the age of 18 years accessed hospital and/or ED services for the first time with an alcohol problem each year in NSW. This is relatively substantial considering that these young people are not able to legally purchase alcohol or consume alcohol in licensed venues. Although adolescents have much lower rates of alcohol-attributable hospitalisations compared to adults, the age group

with the second highest rates of ED presentations for alcohol problems in NSW are 15- to 17-year-olds (29, 30). Thus, it appears that young people are experiencing disproportionate rates of acute alcohol-related harm compared to the population.

Though trends in alcohol-related hospital and ED access across Australia have thus far only been examined descriptively, studies in similar countries such as England and Canada have reported increasing rates of alcohol-related ED and hospital visits among adolescents and young adults between the early 2000s and late 2010s (31, 32). These trends should be interpreted with caution, however, as recording of alcohol involvement in hospitals and EDs with the commonly used International Classification of Diseases (ICD) system can be unreliable, particularly in cases where alcohol is a contributing factor rather than the primary reason for admission/presentation (14). A recent study of Western Australia (WA) data found that linking subsequent hospitalisation data to ED data resulted in double the number of alcohol-related ED presentations being identified among people aged 12 to 24 years (33). The same study also found vastly different trends when comparing ED-only data to linked data, with subpopulations such as Aboriginal and Torres Strait Islander persons shifting from an increasing trend to stable trend after linkage (33). These findings highlight the need to incorporate multiple data sources when examining patterns of alcohol-related harm to minimise bias.

6.2.2. Shifting prevalence of alcohol-related harms between males and females

In Study 1, comparison of the prevalence of alcohol-related risky behaviours showed that males were overall twice as likely to report risky behaviours compared to females across the period of 2001 to 2016. However, cohort effects showed that the male-female ratio declined with birth year, approaching a ratio of 1 in the most recent birth cohorts (i.e.,

1990s to 2000s). This suggests that the prevalence of alcohol-related risky behaviours is becoming more similar between recent generations of males and females, whereas in earlier cohorts these behaviours were more common amongst males. These findings are likely associated with recent shifts in alcohol use and risky drinking amongst males and females, as the prevalence of these drinking behaviours have also been converging in recent birth cohorts around the world (17, 34). This convergence varies by age, with the trend among young people in the Europe and the United States typically being driven by males decreasing consumption and heavy episodic drinking at a greater rate than females (18, 34), whereas the convergence in people aged 30 years and older appears to be a result of increases in consumption and heavy episodic drinking amongst females (18). This does not appear to be the case in Australia, however, with evidence that the male-female convergence across the population applies for lifetime risky drinking but not single-occasion risky drinking (35).

A critique of cohort comparisons between males and females raised by Livingston, Callinan (35) is that age-specific patterns in drinking behaviours are often overlooked. Namely, male-female differences in alcohol consumption are typically minimal in early adolescence (36, 37) and the gap widens substantially with age (38). Thus, comparison of cohorts alone could lead to cohort effects being mistaken for or confounded by age effects (i.e., people in different birth cohorts at a single point in time would be of different ages). Indeed, whilst there appeared to be a cohort effect in Australian lifetime risky drinking, male-female convergence was evident only among 50- to 69-year-olds when examining by age group (35). An advantage of the modelling approach in Study 1 is that the cohort effects adjust for the effect of age, and vice-versa. This suggests that the male-female convergence in alcohol-related risky behaviours across birth cohorts is unlikely to be a result of age differences.

Indeed, the convergence found in Study 1 appears to be driven by steeper declines among males compared to females, with health service data similarly showing greater improvements in harm prevalence amongst young males compared to females (6, 33). Whilst alcohol-related ED presentations in WA have declined among males aged 12 to 24 years between 2005 and 2017, there is much greater age variation in young females (33). Specifically, ED presentation rates amongst females in WA declined in the 12- to 17-year-old group, were stable in the 18- to-20-year-old group, and increased in the 21- to 24-year-old group over this period (33). Between 2014 and 2021 in NSW, alcohol-related ED presentation rates increased among 15- to 17-year-old females but were stable among males (29). Though alcohol-related ED presentation rates in NSW declined among both males and females aged 18 to 24 years, males showed a sharper decline (29). Nationally, rates of alcohol-attributable hospitalisations have declined in males aged 15 to 34 years but have remained stable in same-aged females between 2010 and 2017 (6). Overall, these trends in hospital service use suggest a closing male-female gap in alcohol-related harm which appear to be driven primarily by decreases in harm among males.

Given that these converging patterns of alcohol use and harms are largely cohort effects, the reasons for these changes are likely related to cultural shifts. Whilst alcohol use, particularly heavy drinking, has historically been a ‘masculine’ activity (39), these norms have been changing. In response, alcohol marketing is increasingly targeting females (40). Since the 2010s, social media has emerged as a marketing platform with high reach and relatively low cost, in addition to being a space where people can promote a specific image of oneself and engage with countless others. As social media is predominantly used by young people, relative increases in risky drinking and alcohol-related harms among recent cohorts of females may be closely linked to the portrayal of alcohol in social media. Indeed,

recent marketing strategies have used concepts of celebrating female empowerment and gender equality to promote alcohol to females (41). In the context of peer interactions, young people often choose to present a specific tailored image of alcohol use that omits experiences that are negative (42, 43), particularly amongst females who are often more heavily scrutinised in the way they present themselves in a drinking context (44, 45). With emerging research showing that social media engagement in alcohol-related content increases likelihood of alcohol use and risky drinking (46, 47), these gendered aspects of social media with overtly positive depictions of alcohol may be contributing to the recent increases in alcohol use and resultant harms among females.

6.3. Development of alcohol-related harm in recent cohorts of young people

6.3.1. Trajectories of alcohol-related harm

Patterns of transitioning between minimal, physiological only (e.g. blacking out), and physiological plus psychosocial (e.g. getting into fights) harm profiles in Study 3 indicated that young people were typically more likely to experience the same types of harm from age 15 to age 19 years than to experience different types of harm. The exception was between age 17 years and age 19 years, where people were more likely to shift from experiencing minimal harms to experiencing physiological harms than they were to continue experiencing minimal harms. Indeed, across the developmental trajectories of harm identified in Study 2 and Study 3, experience of physiological harms at age 18-19 years emerged as the most common trajectory. In other words, young people in this Australian cohort typically did not experience any alcohol-related harm until early adulthood, at which point they experienced some physiological harms. This is unsurprising as recent birth cohorts tend to try alcohol for the first time later in adolescence compared to earlier cohorts (e.g., mean age has risen by

least 1 year between the early 2000s and late 2010s in Australia and U.S.; 27, 48), meaning physiological harms in adolescence are less likely. Analyses of alcohol use trajectories in recent cohorts of young people also typically find that most young people abstain from drinking or drink at low levels in early adolescence, before escalating to binge drinking in late adolescence and early adulthood (49, 50). Whilst minimal harms across the whole population would be ideal, it is reassuring that the second most common trajectory in both Study 2 and Study 3 are the trajectories with very minimal harm. The remaining higher-risk trajectories combined (i.e., those showing escalating experience of harm) constituted less than half of the cohort in each of the studies. Thus, in this recent cohort of young Australians, the normative trajectories of alcohol-related harms appear to be relatively low-risk.

Study 3 found no differences in early adulthood AUD symptoms between young people who experienced physiological harm earlier in adolescence versus later. However, when examining the trajectory of one specific physiological harm, blackouts, Study 2 found that experiencing increasing numbers of blackouts during adolescence was a significant predictor of subsequent AUD. Similar studies examining blackouts in older adolescents and young adults also report that blackouts predict future AUDs (51) and other alcohol-related harms such as injury (52). These differences between Study 2 and Study 3 may be due to the unique characteristics of a blackout compared to the other physiological harms assessed in the cohort (drinking more than planned, having a hangover, feeling sick), as blackouts signify a level of intoxication that interferes with neurological functioning (53, 54). This does not necessarily imply that other physiological harms are not indicative of alcohol problems, as the lack of difference between AUD symptoms in adolescents who experience physiological harms earlier versus later may also be an unintended consequence of omitting the

frequency of harms in favour of a binary any harm/no harm approach to reduce model complexity in Study 3.

As expected of a non-clinical sample of young people, a low proportion (< 25%) of adolescents experienced psychosocial harms. Of the young people who experienced psychosocial harms, most did not see onset of these harms until they were 19 years of age. Experiencing both physiological and psychosocial harms at age 19 years predicted AUD symptoms at age 20 years. Though psychosocial harms are often associated with heavy drinking patterns (55, 56) that are known to predict later AUD symptoms (49, 57), differences in drinking levels between different trajectories of harms is unlikely to be the reason for the findings of Study 3. Indeed, the association between psychosocial harms and later AUD symptoms in Study 3 held even after adjusting for trajectories of alcohol use frequency and quantity. The most parsimonious explanation for these findings is that the harms as measured in Study 3 substantially overlap with the DSM-5 definition of AUD, as the criteria includes both physiological (e.g., "Spent a lot of time drinking or being sick or getting over other aftereffects") and psychosocial symptoms (e.g., "Continued to drink even though it was causing trouble with your family or friends"; 58). Notably, experience of psychosocial harms predicted AUD irrespective of whether a result of gradual escalation via physiological harms or sudden escalation from minimal harms. Thus, the results of Study 3 suggest that, whilst the experience of any psychosocial harm is a risk factor for AUD, the trajectory of escalation into psychosocial harm may be less important in the prediction of AUD.

6.3.2. Risk factors for alcohol-related harm

6.3.2.1. Parent and peer influences

Adolescents who reported having peers in early adolescence who use alcohol or tobacco

were more likely to initiate alcohol use at a younger age (Study 2) and experience physiological harm at a younger age (Study 3). These findings are consistent with the well-established role of peers in young peoples' drinking behaviours (59). While the actual prevalence of alcohol-consuming peers is a risk factor for alcohol use among adolescents (60), adolescents often overestimate how many of their peers consume alcohol (61). Indeed, mere perception of peer alcohol use has been associated with increased alcohol use (62, 63). This applies to Study 2 and Study 3, as these studies assessed the respondents' perception of how many of their friends use alcohol, with a previous study using the same cohort reporting that perceptions of peer alcohol use also increased the risk of early-onset heavy drinking (49). Interestingly, this peer effect was not associated with escalating blackouts in Study 2 nor psychosocial harms at age 19 years in Study 3. Given that these studies examined peer substance use at age 13 rather than at each year, this may be due to changing social circles and/or influence of peers as young people age. That is, peer influences at age 13 years may have had a stronger influence on alcohol-related harms in early adolescence but this effect was not captured in Study 2 nor Study 3 because harms in the cohort predominantly emerged in early adulthood. Regardless, as young peoples' social norms around alcohol change, these peer effects could become less apparent. There is preliminary evidence that drinking is becoming less normative among adolescents (64), with young people being increasingly aware of the health risks (22, 23) and social impact (65) of alcohol use.

Having easier access to alcohol at home without parental knowledge in early adolescence also predicted earlier initiation to alcohol use in Study 2. This is consistent with other longitudinal studies that have identified restricting access to alcohol at home as a parenting factor that reduces the likelihood of alcohol use initiation in early adolescence (66).

However, availability of alcohol at home was not associated with the escalation of blackouts in Study 2 nor patterns of harm in Study 3. Again, this may relate to differing life stages. It may be the case that having unrestricted access to alcohol at home provides adolescents with an easy way to try alcohol earlier, but once initiated, they source alcohol by other means, especially by late adolescence and early adulthood. A survey of Australian secondary students found that the percentage of adolescents who obtained alcohol from home as their primary source was much higher among adolescents aged 12 to 15 years compared to those aged 16 to 17 years (3). Indeed, as young people age into adulthood, the influence of parenting factors on alcohol use behaviour diminishes (67). The cohort in Study 2 and 3 also report that supply of alcohol from non-parental sources increased over time (68), lending credence to the theory that adolescents source their first drink of alcohol from unrestricted stores at home but subsequently source their alcohol from elsewhere. Though the studies in this thesis found no direct association between home accessibility to alcohol and alcohol-related harms, it is still an important parenting factor as earlier age of initiation and experience of being drunk is associated with riskier patterns of alcohol use in adolescents (69-71).

6.3.2.2. Males and females

In addition to the changes in prevalence of alcohol-related harms between males and females discussed in Section 6.2.2., Study 2, Study 3, and Study 4 each found significant associations between sex and experience of harm. In the longitudinal cohort of young people, female adolescents were nearly three times as likely as male adolescents to experience escalating blackouts (Study 2) and twice as likely to experience early physiological harms (Study 3). As previously discussed, these studies each control for alcohol

use frequency and quantity, so the effects are likely due to the experience of harm rather than variations in levels of drinking. Specifically, this appears to be unique to physiological harms, as male-female status was not associated with psychosocial harms at age 19 years in Study 3. Likewise, the linked administrative cohort of young people in Study 4 showed that young people who experienced their first alcohol-related hospitalisation or ED presentation at a younger age were more likely to be female and have an intoxication diagnosis. A similar finding has also been observed in Dutch (72) and Welsh (73) hospital data, where people who are hospitalised for alcohol intoxication in early adolescence are more likely to be female. Together, these findings suggest that there is a widespread phenomenon of female sex as a risk factor for earlier experience of alcohol-related harm that is not limited to the Australian context.

Given that the results pertain to physiological harms, the reasons for these findings are likely related to the differential effects of alcohol on males versus females. Indeed, while male and female alcohol use levels are typically very similar in adolescence (36, 37), people assigned female at birth tend to reach higher levels of blood alcohol content (BAC) compared to people assigned male at birth when consuming the same amount of alcohol due to differences in body mass and metabolism (74). Neuroimaging studies also report significant differences between male and female adolescents who consume alcohol. In a study of young people aged 16 to 19 years, binge drinking was associated with deficits in areas associated with attention, working memory, visuospatial ability, and inhibition among females but not males (75). Similarly, female adolescents aged 14 to 17 years with AUD appeared to require greater brain activity when performing the same working memory task as female adolescents without AUD, but this effect was absent in male adolescents (76). In later adolescence and early adulthood however, the gap between male and female alcohol

use increases slightly, with the ratio of harms prevalence shifting towards males as evidenced by Study 4 and similar hospital data (72, 73). This is likely due to greater increases in drinking among males compared to females that typically occurs when aging into adulthood (37). Late adolescence and early adulthood is also associated with greater increases in risk-taking behaviour among males compared to females, which may contribute to higher rates of hospitalisation (e.g., motor vehicle accidents; 77, 78). In sum, both self-report and hospital administrative data identify female status as a risk factor for early physiological harm even after consideration of differences in levels of alcohol use.

6.4. Strengths and limitations of the dissertation

6.4.1. Data sources

The four studies in this thesis use a range of datasets to examine alcohol-related harms in young people. The large sample sizes of these datasets, ranging from 1,821 to 121,281 people, enables higher precision in examining effects and provides greater representation across the population. However, one main limitation of this thesis is that populations with high prevalence of risky drinking and alcohol-related harms, such as Aboriginal and Torres Strait Islander peoples and people of diverse sexualities and genders (27), are not explicitly examined in these studies. Rather, the thesis has focused on broader trends and patterns across the population. Suggestions for further research in these areas are raised in Section 6.5.

Study 1, Study 2, and Study 3 each use self-reported data from samples that have comparable characteristics and drinking rates to the broader population, lending confidence to the generalisability of the results. It should be noted that the NDSHS sample in Study 1 does not include people in non-permanent housing (79) and the APSALS cohort in Study 2

and Study 3 has an overrepresentation of young people attending private and independent schools (80). Thus, these samples are likely skewed towards people of higher socio-economic status. Self-reported data on alcohol behaviours are also liable to biases relating to recall (12) and social desirability (10), which may result in underestimations of alcohol-related harm. Despite these limitations, self-reported surveys are one of the few data collection methods that provide broad reach with minimal participant and researcher burden and have been shown to broadly match consumption trends measured via objective sources (15, 81).

Study 4 uses linked administrative hospital and ED data, allowing for the examination of alcohol-related harms in a clinical cohort. This type of data enables researchers to analyse pre-existing healthcare records at a state-wide or nation-wide level. This is both a benefit and limitation of linked data, as whilst there is no researcher or participant burden in terms of collecting the data, the data are collected for administrative rather than research purposes. Variables that would be recorded in a research study are often absent in administrative data as they are irrelevant to the healthcare service being provided (e.g., peer substance use, parental practices). Any information recorded in linked administrative data is also at the clinicians' discretion and is subject to human error, particularly in the case of EDs in NSW which do not require personnel trained in clinical coding to record diagnoses (82). Indeed, alcohol-related presentations are often underreported in health data (13). Particularly in the case of EDs, where alcohol-related presentations are perceived by clinical staff as being highly stressful due to the potentially physically and verbally aggressive nature of patients (83), there is also the possibility of incorrect coding due to human error. Across both hospitals and EDs, there are also issues with recording alcohol involvement in coding instruments such as the ICD when alcohol is not the primary cause for seeking medical

attention (14). As the acute problems that young people can access health services for do not always explicitly involve alcohol (e.g., injury), the prevalence of alcohol-related ED presentations and hospital separations are likely to be under ascertained in Study 4. Despite these limitations, linked administrative data remain the most comprehensive source of information about the use of health services across the population.

6.4.2. Analysis methods

This thesis used a variety of robust analytic approaches that were chosen based on the key research questions. To examine trends in alcohol-related risky behaviours as well as potential male-female effects on these trends, Study 1 uses age-period-cohort (APC) modelling. Since the components of an APC model (i.e., age, period, and birth cohort) are interrelated, there needs to be some way of examining each component whilst adjusting for the others. This often involves assumptions about one or more of the components, for example, assuming that birth cohort has minimal effects on the outcome of interest (84). Though there is no perfect solution to this problem, critiques of APC modelling approaches suggest examining non-linear effects and making assumptions that are based on theory rather than from a mathematical basis (85). As such, Study 1 uses Rutherford's adaptation (86) of Carstensen's APC approach (87), which enables non-linear trends to be modelled with clearly stated assumptions. Namely, two models are estimated for the age function: 1) linear temporal changes are attributed to period whilst cohort is held constant to examine differences among people of different ages in a particular reference year; and 2) linear temporal changes are attributed to cohort whilst period is held constant to examine differences as people in a particular reference cohort age. Additionally, Rutherford's APC approach accommodates an interaction term in the model (86), which allowed examination

of differences in age and cohort trends of alcohol-related risky behaviours between males and females. The downside to the inclusion of an interaction term is that one component of the APC needs to be excluded, in this case, period. However, examination of the period effect in separate male and female APC models showed extremely similar trends and extant literature suggests that the convergence in male and female alcohol consumption is dependent on age and cohort rather than period (18, 35). Thus, exclusion of the period component was justifiable as it would have had negligible effect in the male-female interaction models.

Study 2 and Study 3 each use person-centred analysis approaches to examine developmental patterns of alcohol-related harms, namely latent class growth analysis (Study 2) and latent transition analysis (Study 3). These variations of latent class modelling focus on identifying clusters of people who have similar trajectories of growth based on a specified outcome or similar patterns of transitioning across a set of outcomes. The benefit of these approaches is that it allows researchers to identify common clusters that exist amongst participants. Thus, patterns that are identified in this manner are occurring 'naturally' rather than being grouped based on arbitrary specifications. However, it should be noted that there can be wide variations amongst individuals assigned to the same latent class. Some individuals may fit poorly in all of the identified classes, though the likelihood of this can be reduced through the model selection process (i.e., by favouring models that have higher posterior probabilities which indicates greater classification accuracy). The examination of predictors and outcomes of these latent classes in Study 2 and Study 3 also take into consideration various confounders relevant to alcohol use in young people, including parenting, peer, and child factors.

Consistent with other studies examining hospital and ED data (e.g., 88, 89, 90), Study 4 uses the well-established metric of incidence rates to quantify alcohol-related hospitalisations and ED presentations among young people. To ensure that the sample consisted only of people who accessed hospital services with an alcohol-related problem for the first time in their lives, we examined similar linked administrative cohorts to identify a minimum age for alcohol-related harm. This was confirmed with examination of the DACS cohort, where young people below this age (12 years) were predominantly accessing hospital services for issues relating to fetal alcohol syndrome rather than their own use of alcohol. Whilst Study 4 adjusts for variations due to the period, covariates relevant to alcohol use and harms such as family history of substance use, peer substance use, and prior treatment access are absent in linked administrative data. Thus, we were not able to adjust for these factors in Study 4 as was possible in Study 2 and Study 3.

6.5. Implications and future directions

6.5.1. Examining and synthesising broader aspects of alcohol-related harm

Though the results of Study 1 imply that there have been reductions in alcohol-related risky behaviours among young people, there remains a paucity of research examining trends in harm. Alcohol-related harms span a wide range of outcomes resulting from alcohol use, ranging in severity, chronicity, and impacts beyond the individual (e.g., family, friends, healthcare service utilisation, law enforcement). Given that there is no singular source of data that captures all aspects of alcohol-related harm, assessment of trends and other harms patterns necessitates incorporation of a variety of data sources. Different methods of measuring alcohol-related harm can show different trends (e.g., as shown in Sims, Preen (33)), which indicates that there is merit in developing more robust and standardised

approaches to quantifying harm.

Documentation of alcohol-related hospitalisations and ED presentations across Australia have thus far been limited to reports of rates and trends at the population level (91). Where disaggregated by age, groupings generally span large ranges that obscure age-specific trends (e.g., 15 to 34 years; 6). An examination of APC trends in rates of hospital service access will supplement the results of Study 1, ideally utilising both hospitalisation and ED data to minimise underestimations of alcohol-related harm (33). Similar APC modelling should be extended to mortality data, though given that deaths with alcohol as a contributing factor tend to be a result of chronic conditions (1), it is likely that the effects of recent trends in alcohol consumption on deaths will not be apparent for at least another decade unless specifically examining deaths due to injury, which are also influenced by non-alcohol factors. Given that declines in adolescent drinking appear to be partly maintained into early adulthood (28), there may indeed be noticeable reductions in alcohol-related mortality. Trends in treatment for alcohol problems should also be assessed, as this is a population affected by chronic alcohol-related harm but are not necessarily captured by hospital service data. Only one study has examined Australian trends in alcohol treatment episodes, though as age and cohort trends were modelled separately it is unclear whether trends in cohort are affected by age and vice versa (92).

Incorporating additional sources of data (e.g., treatment, mortality) also expands our understanding of the impact of alcohol use outside of trends. The harms captured in the longitudinal cohort in Study 2 and Study 3 were limited by nature of being self-reported, whereas the harms captured in the linkage cohort in Study 4 were limited as they were restricted to harms captured in through hospital or emergency department access.

Combining these and other measures of alcohol-related harm can, for instance, enhance our understanding of the individual level associations between self-reported measures of harm and clinical measures.

One aspect of alcohol-related harm that has been the focus of increasing attention since the 1990s is quantifying alcohol's harm to others, that is, the impact of someone else's use of alcohol (93). This can range from physical harm such as injuries due to assault, to financial harm such as needing to divert family funds to pay for alcohol or related legal/healthcare costs (94, 95). In Australia, the annual cost of alcohol's harm to others was estimated to exceed AU$34 billion when considering costs relating to healthcare, criminal justice, child protection, treatment and helpline services, and productivity (96). A survey of alcohol's harm to others in 2008 showed that the group with the largest contribution to harming others was males in their 20s (93). Given the declines in alcohol consumption and alcohol-related risky behaviours among young people, particularly young males, further research can clarify questions such as whether alcohol's harm to others has also declined and what factors increase risk of perpetrating harm to others while under the influence of alcohol.

6.5.2. Shifting public health strategies to target alcohol use in young females

As discussed in Section 6.2.2., there appears to be a closing male-female gap in alcohol-related risky behaviour and harm that may be driven by decreasing prevalence of harms amongst adolescent and young adult males and increasing prevalence amongst young adult females. Section 6.3.2.2. highlights the consistent finding of female sex as a risk factor for earlier experience of alcohol-related harm in recent survey and linked data cohort studies. Thus, there is a need to adjust existing public health strategies or create new strategies to reduce alcohol-related harm, particularly among females in recent birth cohorts.

Population-wide policies aimed at reducing alcohol-related harm often unintentionally have different effect sizes for males compared to females (97). For instance, a modelling study found that increases in alcohol taxation and minimum unit prices in the United Kingdom would substantially reduce alcohol use and hospitalisation rates in males, but among females these simulated policies resulted in only very minor reductions (97). In certain regions of Australia, laws that have been implemented to restrict trading hours of licensed venues (e.g., pubs) have resulted in noticeable reductions to non-domestic assaults (98-100). However, the victims of these assaults are predominantly male (98, 101), meaning that the impact of trading hour policies are likely to reduce harm amongst males than females. Conversely, extension of takeaway liquor trading hours (e.g., bottle shops) appear to have increased incidents of domestic violence assaults (102), the victims of whom are predominantly female (103). Examination of Australian and Swedish alcohol policy find that explicit mentions of females tend to either focus on reproductive aspects (e.g., drinking while pregnant or breastfeeding) or aspects of victimisation due to harm from others (104, 105), although Swedish policy does include mentions of rising alcohol use in young females and need to target this demographic (105). Current Australian policy lacks consideration of how females' own alcohol use can impact their health at an individual level (e.g., physiological conditions due to prolonged alcohol use, injuries resulting from risky behaviours). Therefore, policies aimed at reducing alcohol-related harm should carefully consider both the unintentional effects that population-wide strategies have on females versus males, in addition to broadening the focus of female-centric policies outside of reproductive and victim narratives.

As evidenced by the studies in this thesis, alcohol-related harms can be experienced by young people early in life, particularly for females. Recent qualitative studies have reported

that many young people are unaware that the effects of alcohol can depend on physiological differences such as variations in body size and sex (106, 107). Though young people appear to be becoming increasingly aware of the health risks associated with alcohol use, this knowledge appears to be focused on developmental risks, with gendered aspects focusing on harm from others rather than physiological differences (23). However, current evidence on young peoples' knowledge of the effects of alcohol remains sparse, which calls for further research in this area. Research on whether young peoples' knowledge varies between males and females is also lacking. As children and adolescents have been shown to benefit from education programs aimed at reducing alcohol-related harm (108, 109), similar early education programs focusing on how alcohol can affect people differently based on their physiological makeup may also be effective in reducing alcohol-related harm.

6.5.3. Emerging avenues of alcohol promotion to young people

A potential reason for the increase in alcohol-related harms amongst young adult females raised in Section 6.2.2. is the impact of changing alcohol norms and role of social media. These changes are also likely to impact adolescents, with a recent survey reporting that Australians aged 12 to 17 years use an average of four social media services (110). A social media platform with rising popularity, TikTok (110), often has overwhelmingly positive representations of alcohol (111). Though alcohol marketing tends to be age-restricted on social media, this can be circumvented via promotion through popular social media users ('influencers'; 41, 112). Indeed, many influencers with adolescent audiences post positively about alcohol experiences, often without disclosing sponsorships where relevant (112). Greater engagement in alcohol-related social media has been associated with higher levels of drinking and alcohol-related problems among young people (113, 114). Though there is

very little research on interventions delivered via social media, a recent study found that intentions to purchase alcohol can be reduced through comments on social media that detail negative consequences of alcohol use or promote abstinence (115). Thus, there is the potential to implement social media interventions aimed at reducing alcohol-related harms in adolescents such as regulating alcohol promotion from influencers.

6.6. Conclusions

Acute alcohol-related harms are becoming less prevalent among young people, but many people in recent birth cohorts continue to be impacted by these harms at a young age. As trends in alcohol-related harm appear to vary between different sources of data, research examining trends across a variety of sources (e.g., treatment and morbidity data) and developing standardised methods of measuring harm can help further clarify the impact of recent declines in alcohol. The identification of a closing male-female gap in harms driven by steeper declines in males and of female status as a risk factor for early harm suggest alcohol-related cultural shifts that also warrant further research. These developments in recent cohorts of young people call for improvements to early intervention strategies that are aimed at reducing alcohol-related harm in young people and refinement of approaches to quantifying alcohol-related harm.

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7. APPENDICES

7.1. Appendix A: Appendices for Chapter 2

7.1.1. Appendix A1. STROBE Checklist.

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	7-8

7.1.3. Appendix A2. Model selection details.

7.1.3.1. Appendix A2.1. APC model

In selecting the APC model with the best fit, lower AIC values indicate that the model is a closer approximation of the data, where the model is losing less information than a model with higher AIC. Lower BIC values are interpreted in the same way as AIC, with the key difference being that BIC penalises more complex models (i.e., more components or more cubic spline knots in this context) compared to AIC. To determine the number of equally spaced internal knots in the cubic spline functions of the final APC models, we compared AIC and BIC values for a model with four internal knots for age, period, and cohort versus models with increased knots for age and cohort (given the high number of age and cohort data points available). We increased the knots for age and cohort until AIC and BIC both showed no substantial improvement.

Appendix C shows the fit statistics for the full APC models, the age-cohort models, and the age-period models for different numbers of internal knots. While AIC indicated that the APC, AP, and AC models were similar, BIC and deviance statistics consistently showed that the full APC model had improved fit over the reduced models irrespective of the number of internal knots. AC models consistently had better fit than the AP models, indicating that cohort had a more pronounced effect than period irrespective of the number of internal knots.

As the number of internal knots increased for the age and cohort components, both AIC and BIC showed improvements up to nine internal knots, although BIC more clearly showed that the nine-knot model had improved fit over other combinations of internal knots for age and cohort (Appendix C). The model containing four internal knots for age and nine internal knots for each of age and cohort was thus chosen for our primary analyses. Appendix C

shows fitted values for models using other numbers of internal knots.

7.1.3.2. Appendix A2.2. Male-female APC interaction model

Due to the weighting method used for drift extraction in this APC modelling approach (31), a full interaction with all the APC terms may result in overfitting and skewed estimates, particularly when the male-female ratio of cases is uneven (Table 1). Therefore, we reduced the number of splines to model the interactions, decreasing the knots for age and cohort until AIC and BIC both showed no substantial improvement.

Though AIC was similar between the models, BIC showed that three internal knots for the age and cohort components had improved fit over other combinations with the reduced spline interaction, as well as improved fit over the full interaction model (Appendix F). Thus, for each of the age and cohort components, three equally spaced internal knots were used to describe non-linear effects in the reduced-spline male-female interaction models.

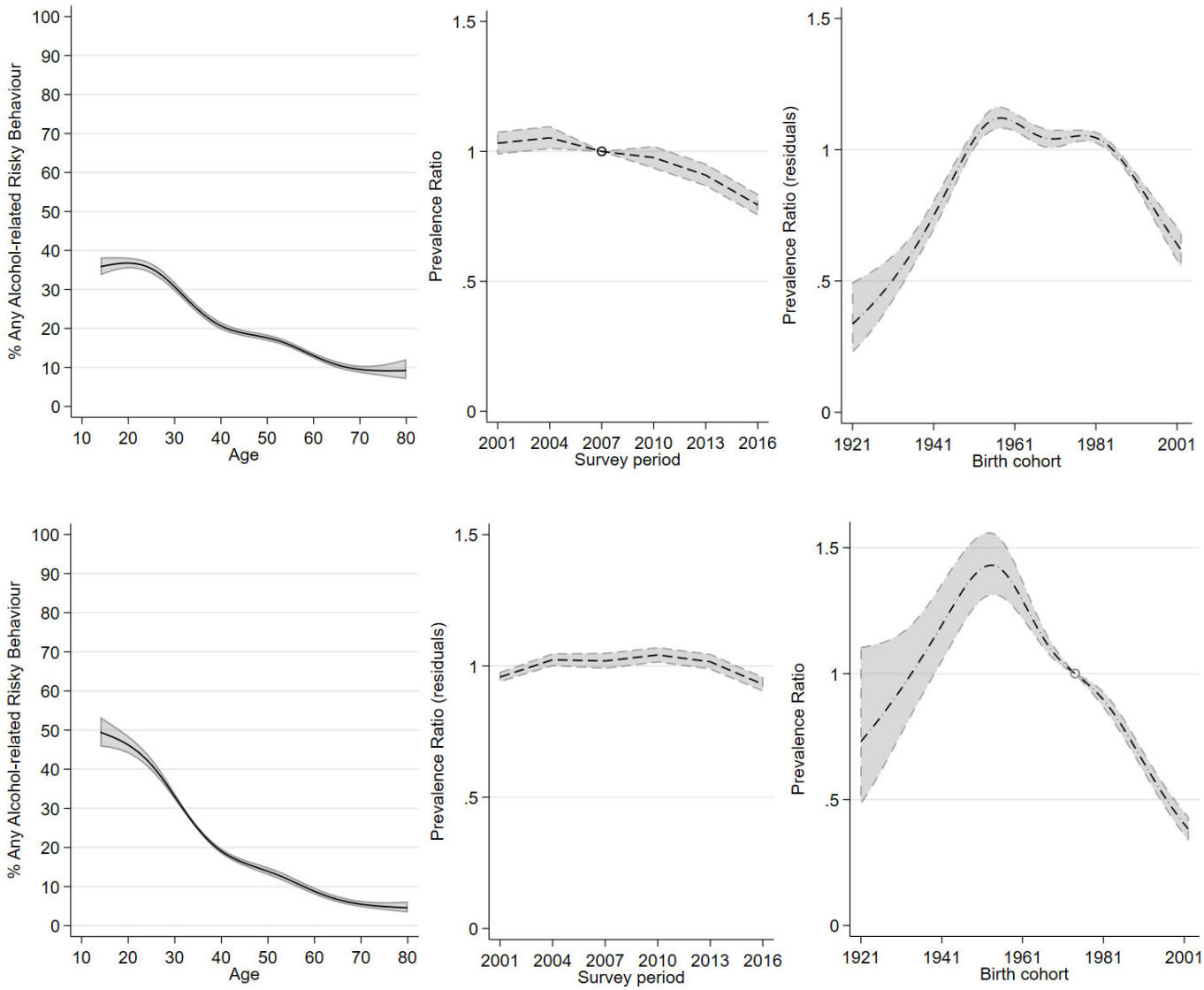
7.1.4. Appendix A3. Fit statistics for age, period, and cohort models.

Knots	Model	AIC	BIC	Log-likelihood	d.f.	Deviance	p
4	APC	7.375	-1605.314	-1460.02	385		
	AC	7.449	-1591.593	-1478.86	389	37.686394	< 0.001
	AP	7.710	-1487.293	-1531.01	389	141.986348	< 0.001
5	APC	7.169	-1679.791	-1416.79	383		
	AC	7.241	-1666.869	-1435.23	387	36.887268	< 0.001
	AP	7.481	-1575.100	-1484.12	388	134.648566	< 0.001
6	APC	6.982	-1746.545	-1377.42	381		
	AC	7.049	-1735.767	-1394.79	385	34.743834	< 0.001
	AP	7.295	-1645.464	-1445.94	387	137.029758	< 0.001
7	APC	6.876	-1780.892	-1354.26	379		
	AC	6.936	-1772.922	-1370.23	383	31.935712	< 0.001
	AP	7.213	-1674.260	-1428.54	386	148.571966	< 0.001
8	APC	6.833	-1790.323	-1343.55	377		
	AC	6.891	-1783.014	-1359.19	381	31.274904	< 0.001
	AP	7.161	-1691.023	-1417.17	385	147.232056	< 0.001
9	**APC**	**6.799**	**-1795.811**	**-1334.82**	**375**		
	AC	**6.858**	**-1788.334**	**-1350.54**	**379**	**31.4431**	**< 0.001**
	AP	**7.129**	**-1699.770**	**-1409.8**	**384**	**149.96434**	**< 0.001**
10	APC	6.800	-1787.529	-1332.96	373		
	AC	6.858	-1780.106	-1348.66	377	31.388934	< 0.001
	AP	7.124	-1697.621	-1407.88	383	149.822736	< 0.001

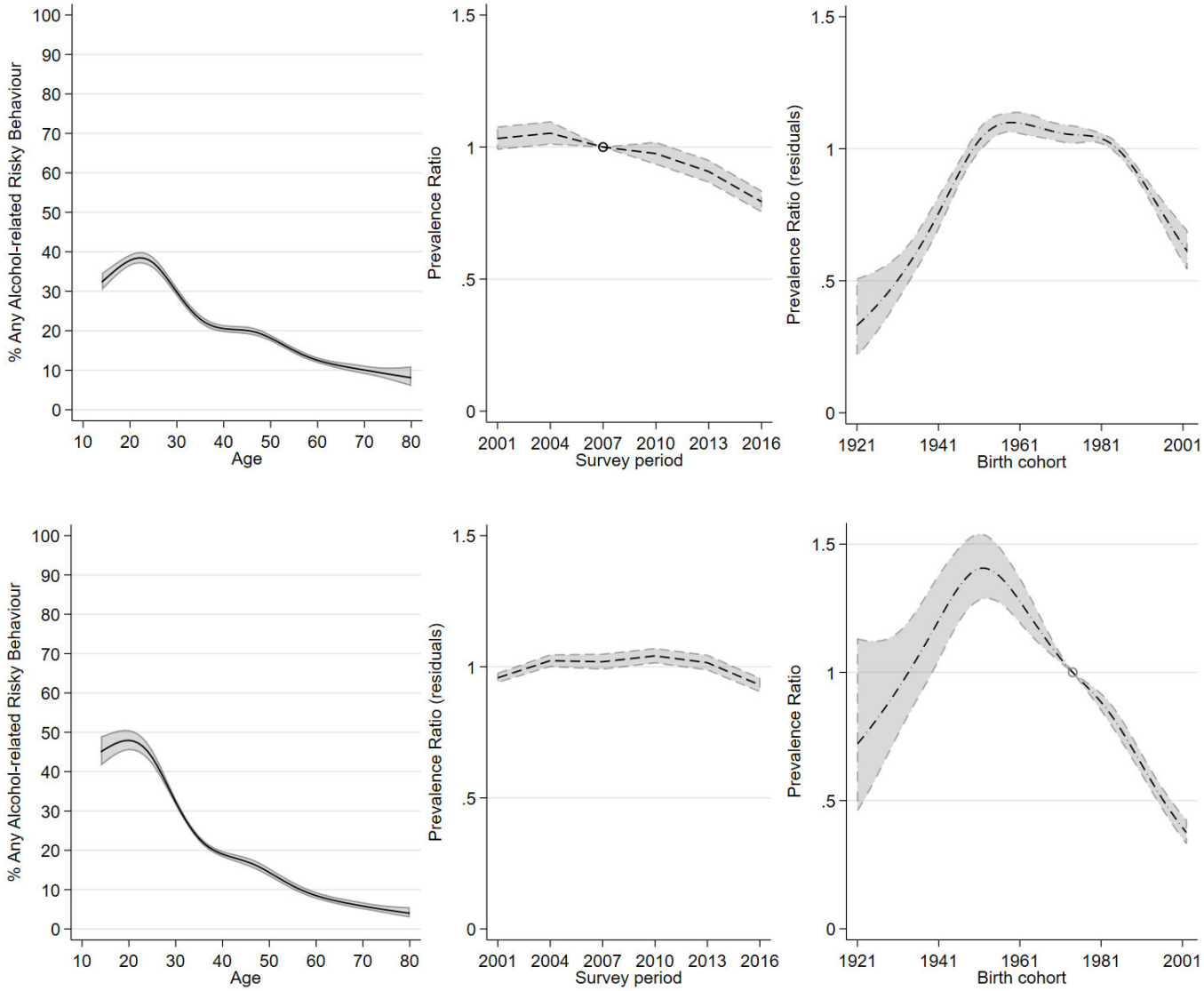
Note. Knots = number of equally spaced internal knots for age and cohort, number of knots for period is 4 for all models; APC = age-period-cohort; AP = age-period; AC = age-cohort; AIC = Akaike Information Criterion, smaller values indicate better model fit; BIC = Bayesian Information Criterion, smaller values indicate better model fit; d.f. = degrees of freedom. Bolded rows indicate chosen model.

7.1.5. Appendix A4. Fitted AP-C (top) and AC-P (bottom) functions from the APC model using other internal knots for age, period, and cohort.

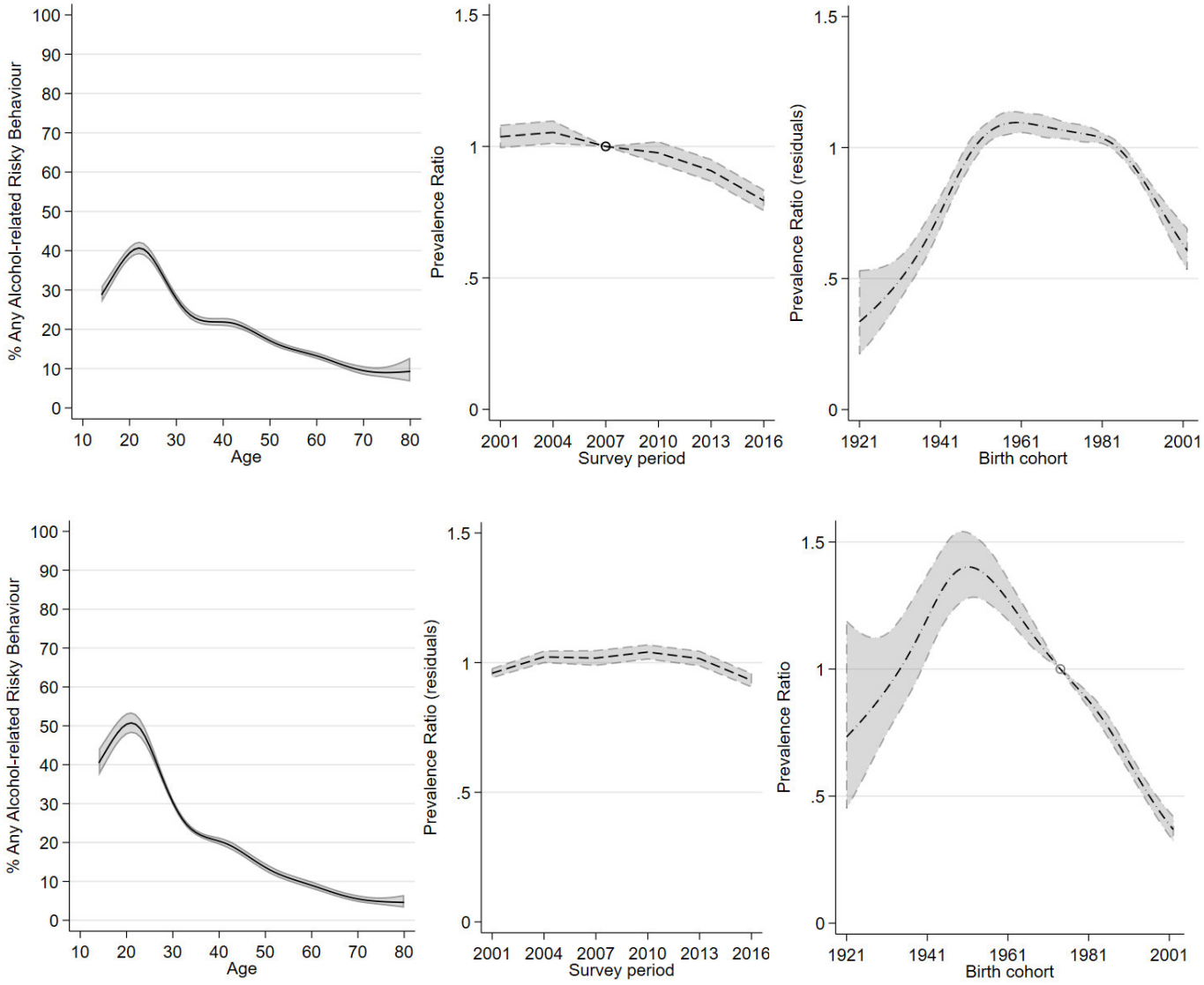
7.1.5.1. Appendix A4.1. 4 internal knots for age, period, and cohort.



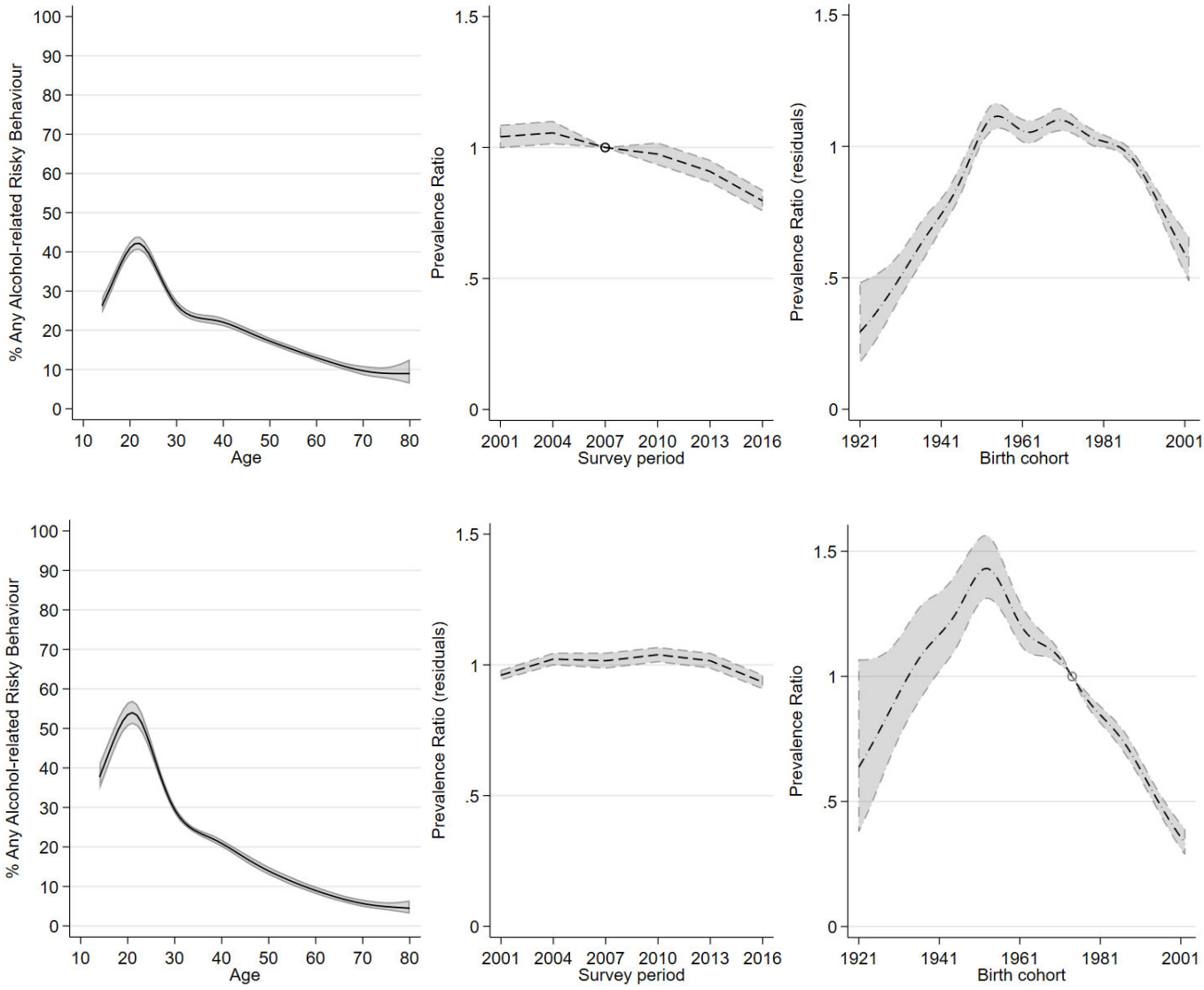
7.1.5.2. Appendix A4.2. 4 internal knots for period, 5 internal knots for age and cohort.



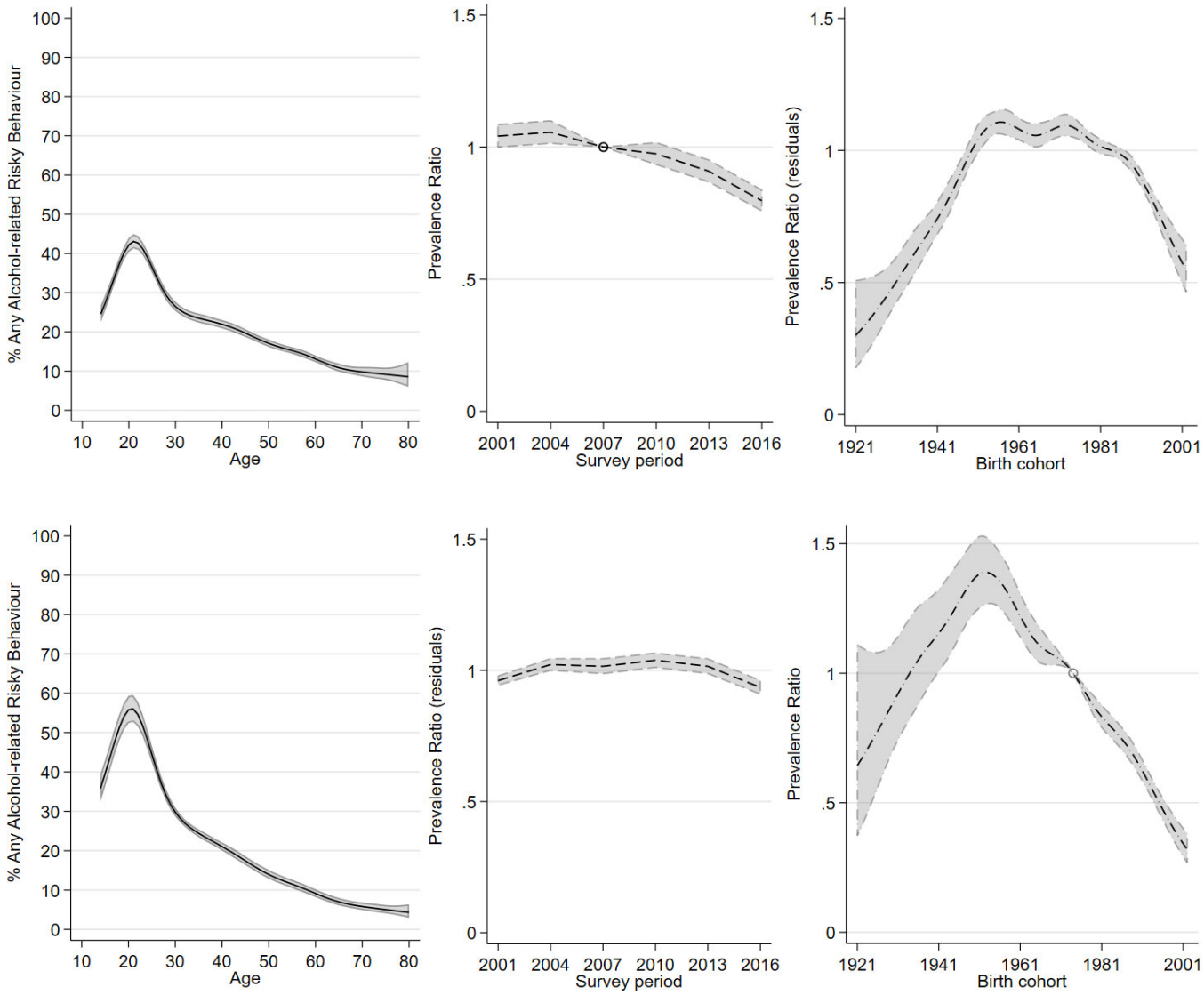
7.1.5.3. Appendix A4.3. 4 internal knots for period, 6 internal knots for age and cohort.



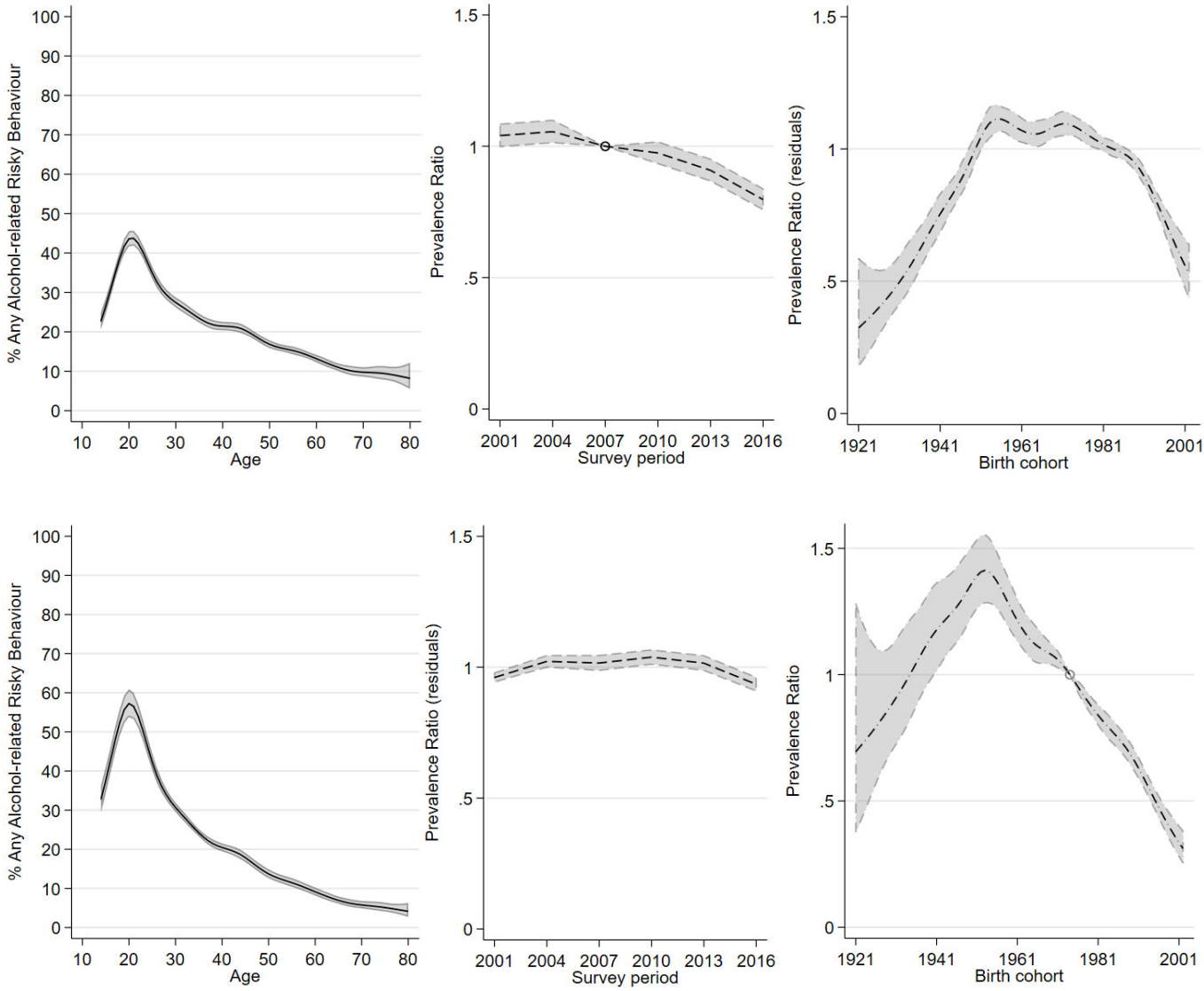
7.1.5.4. Appendix A4.4. 4 internal knots for period, 7 internal knots for age and cohort.



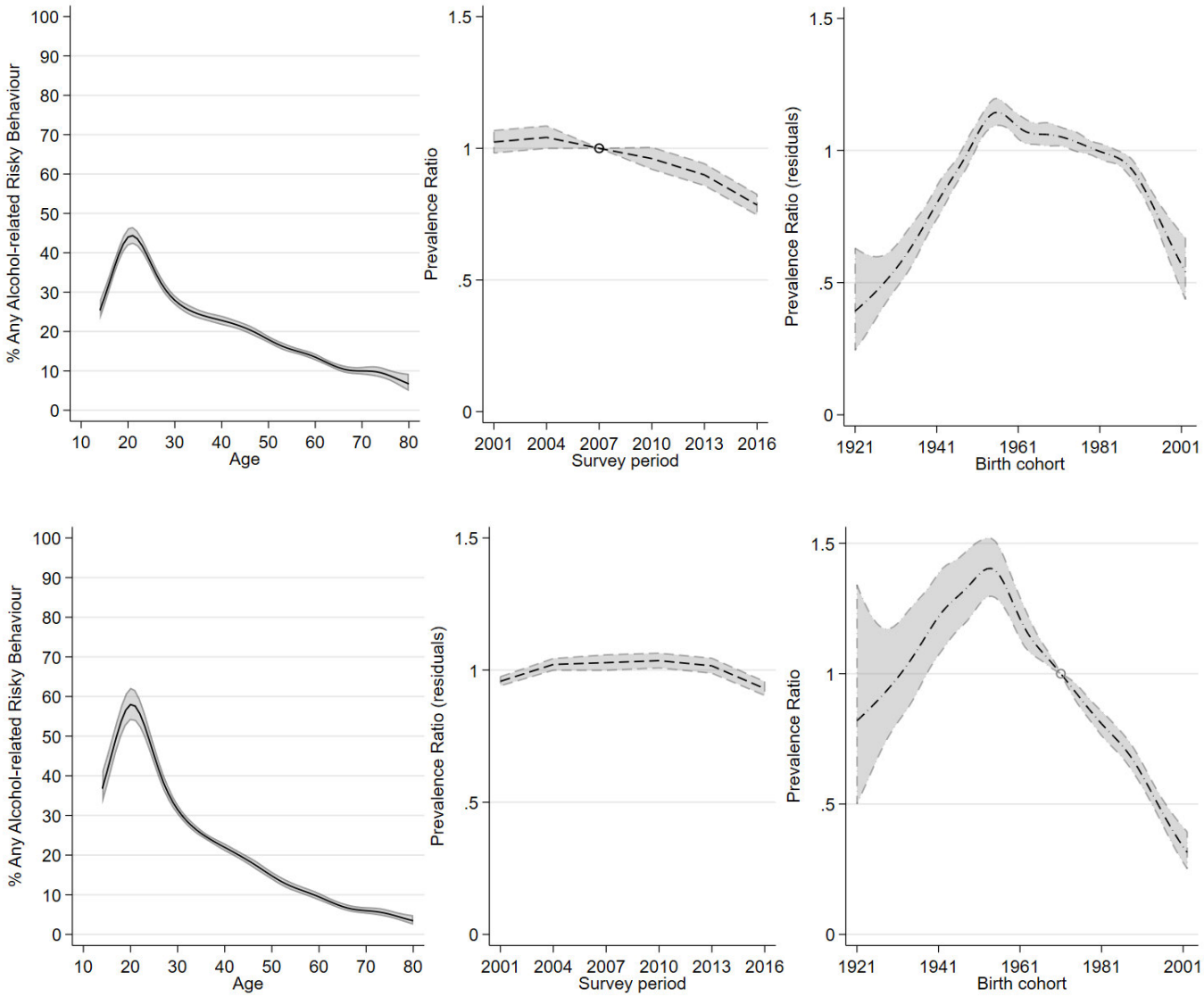
7.1.5.5. Appendix A4.5. 4 internal knots for period, 8 internal knots for age and cohort.



7.1.5.6. Appendix A4.6. 4 internal knots for period, 10 internal knots for age and cohort.



7.1.6. Appendix A5. Fitted AP-C (top) and AC-P (bottom) functions from the APC model using 4 internal knots for period, 9 internal knots for age and cohort using an unweighted sample



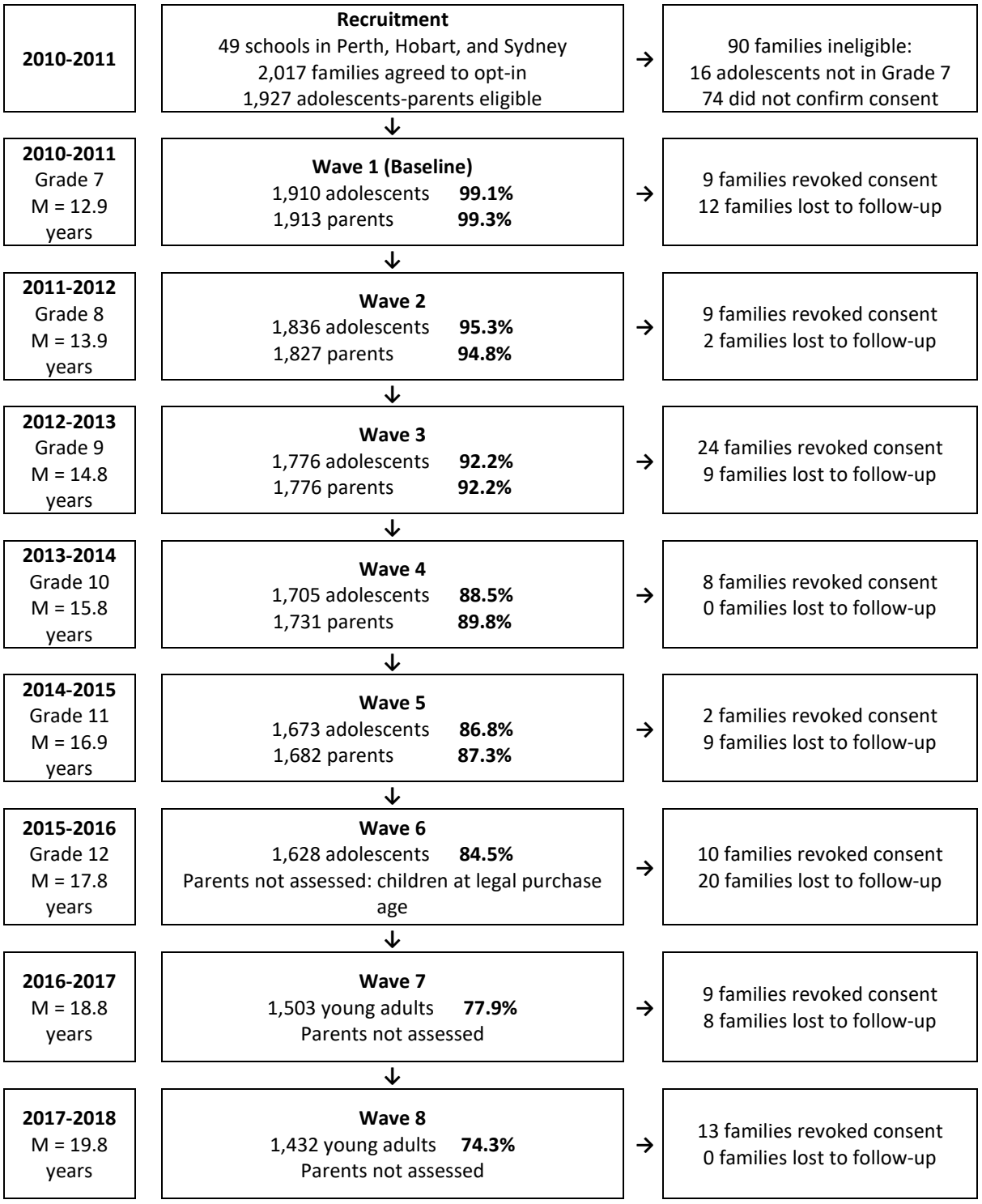
7.1.7. Appendix A6. Fit statistics for male-female interaction models.

Model	Knots	AIC	BIC	Log-likelihood	d.f.
Full interaction	9	5.876	-4195.266	-2300.33	750
Reduced Splines	8	5.876	-4223.02	-2306.51	756
	7	5.872	-4235.548	-2306.93	758
	6	5.868	-4248.282	-2307.24	760
	5	5.864	-4260.768	-2307.69	762
	4	5.862	-4271.726	-2308.89	764
	3	**5.860**	**-4283.122**	**-2309.88**	**766**
	2	5.901	-4259.363	-2328.44	768

Note. Knots = number of equally spaced internal knots for age and cohort; AIC = Akaike Information Criterion, smaller values indicate better model fit; BIC = Bayesian Information Criterion, smaller values indicate better model fit; d.f. = degrees of freedom. Bolded row indicates chosen model.

7.2. Appendix B: Appendices for Chapter 3

7.2.1. Appendix B1. Cohort retention flowchart.



7.2.2. Appendix B2. STROBE Checklist.

	Item No.	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	✓
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	✓
Study size	10	Explain how the study size was arrived at	✓
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓
		(*b*) Describe any methods used to examine subgroups and interactions	✓
		(*c*) Explain how missing data were addressed	✓
		(*d*) If applicable, explain how loss to follow-up was addressed	✓
		(*e*) Describe any sensitivity analyses	✓
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	✓
		(c) Consider use of a flow diagram	✓
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	✓
		(c) Summarise follow-up time (eg, average and total amount)	✓
Outcome data	15*	Report numbers of outcome events or summary measures over time	✓
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	✓
		(*b*) Report category boundaries when continuous variables were categorized	N/A

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	✓
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

7.2.3. Appendix B3. Wave 1 predictors of blackouts identified from the literature.

Baseline predictor	Measurement	Reported by	Comments	Reference(s)
Child variables				
Sex	Single item (Are you: *Male; Female*).	Child	Mixed findings; most studies report females experience more blackouts, but some reported that males experience more blackouts.	Schuckit, Smith (1), Chartier, Hesselbrock (2), Bonar, Goldstick (3)
Externalising	Standardised t-score based on the rule-breaking and aggressive behaviour subscales of the Achenbach Youth Self Report (4).	Child	Externalising symptoms associated with increased blackouts.	Schuckit, Smith (1)
Peer variables				

Baseline predictor	Measurement	Reported by	Comments	Reference(s)
Peer alcohol use/disapproval of use	Adapted from the 2011 Monitoring the Future (MTF) survey (5). Single item for disapproval (How do you think your close friends would feel about you drinking alcohol: *Not disapprove; Disapprove; Strongly disapprove*). Single item for use (How many of your friends drink alcohol: *None; Very few; Quite a few; Most; All*).	Child	Having peers who use/approve of alcohol associated with increased blackouts.	Schuckit, Smith (1), Merrill, Treloar (6)
Peer tobacco use/disapproval of use	Adapted from the 2011 Monitoring the Future (MTF) survey (5). Single item for disapproval (How do you think your close friends would feel about you smoking cigarettes: *Not disapprove; Disapprove; Strongly disapprove*). Single item for use (How many of your friends smoke cigarettes: *None; Very few; Quite a few; Most; All*).	Child	Having peers who use/approve of tobacco associated with increased blackouts.	Schuckit, Smith (1), Bonar, Goldstick (3)
Parent variables				

Baseline predictor	Measurement	Reported by	Comments	Reference(s)
Highest level of education	Single item (What is your highest educational qualification: *School certificate; Diploma, trade or non-trade certificate; Undergraduate degree; Postgraduate degree; None of the above*).	Parent	Higher parental education associated with lower risk of child binge drinking; no studies have examined association with blackouts.	Melotti, Heron (7)
Alcohol-specific rules	Adapted from van der Vorst, Engels (8). Ten items (I'm allowed to…drink alcohol at home when my parents are around; drink alcohol at home when my parents are not around; drink more than one glass of alcohol at home when my parents are around; drink more than one glass of alcohol at home when my parents are not around; drink as much alcohol as I'd like outside the house; drink alcohol with my friends at a party; come home drunk; become drunk when I go out with friends; drink alcohol on the weekend; drink alcohol during the week: *Never; Rarely, Sometimes, Often; Always*). Responses were summed, with higher scores indicating stricter alcohol-specific rules (range 10-50).	Child	Alcohol-specific rules associated with lower likelihood of alcohol use initiation; no studies have examined association with blackouts.	van der Vorst, Engels (8), Van Der Vorst, Engels (9)

Baseline predictor	Measurement	Reported by	Comments	Reference(s)
Monitoring of child's activities	Adapted from Small and Kerns (10). Six items (My parent(s) usually know what I am doing after school; My parent(s) know who my friends are; My parent(s) know where I am after school; If I am going to be home late, I am expected to call my parent(s) to let them know; I tell my parent(s) who I'm going to be with before I go out; I talk to my parent(s) about the plans I have with my friends: *Never; Rarely; Sometimes; Often; Always*). Responses were summed, with higher scores indicating stricter monitoring (range 6-30).	Child	Low parental monitoring associated with child binge drinking in adolescence; no studies have examined association with blackouts.	Donaldson, Handren (11)
Family variables				
Socioeconomic status	Single item (Index of Relative Socio-economic Advantage and Disadvantage [IRSAD]; a population measure standardised to a mean of 1,000 (12) scored as low SES [deciles 1-3], medium SES [deciles 4-7], and high SES [deciles 8-10]).	Parent	Low SES associated with child alcohol use but not associated with binge drinking; no studies have examined association with blackouts.	Melotti, Heron (7), Kwok and Yuan (13)

Baseline predictor	Measurement	Reported by	Comments	Reference(s)
One/two parent household	Single item (Who do you live with most of the time: *Father; Step-father; Mother; Step-mother; Brother(s) and/or sister(s); Grandparent(s) and/or other relatives*). Responses were collapsed into a binary variable of two-parent or one-parent household.	Child	Single-parent household associated with child binge drinking in adolescence but not adulthood, no studies have examined association with blackouts.	Barrett and Turner (14), Merline, Jager (15)
Alcohol accessibly at home without parental knowledge	Adapted from Komro, Maldonado-Molina (16). Single item (In the last 6 months, how easy do you think it would have been for you to take alcohol without parents knowing: *Very easy; Pretty easy; Not very easy; Impossible*). Responses were summed, with higher scores indicating increased levels of access to alcohol in the home (range 6-20).	Child	Increased accessibility to alcohol at home associated with increased child alcohol use and intention to use alcohol, no studies have examined association with blackouts.	Komro, Maldonado-Molina (16)

Baseline predictor	Measurement	Reported by	Comments	Reference(s)
Family history of alcohol problems	Single item (Did your natural father or mother ever have any problems with drinking, not limited to isolated incidents: *yes; no*).	Parent	Presence of biological relatives with alcohol problems associated with experience of blackouts, maternal family history may be better predictor than paternal family history.	LaBrie, Hummer (17), Marino and Fromme (18)
Family conflict	Adapted from Ary, Duncan (19). 6 items (Family members have big arguments over little things; Family members get angry with each other daily; Family members get angry with each other three times a week; Family members support one another; There are feelings of togetherness in our house; Family members get along well: *true; false*). Responses were summed, with a higher score indicating greater levels of conflict (score range: 3-6).	Parent	Greater family conflict associated with increased child alcohol use; no studies have examined association with blackouts.	Ary, Duncan (19), Chaplin, Sinha (20)

7.2.3.1. References for Appendix B3

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7.2.4. Appendix B4. Ten most common missing data patterns.

Variable	Pattern of Missing Data										Missing
Child externalising at baseline											16
Peer approval of substance use at baseline											16
Peer substance use at baseline											18
Alcohol-specific household rules at baseline											20
Parental monitoring at baseline											17
Single parent household at baseline											14
Home access to alcohol at baseline											26
Family history of alcohol problem at baseline										X	107
Family positive relations at baseline											28
Parent education at baseline											32
Socio-economic Index For Area at baseline											25
Child sex											14
DSM-IV Alcohol abuse at Wave 8					X	X	X	X	X		377
DSM-5 AUD at Wave 8				X	X	X	X	X	X		461
DSM-IV Alcohol dependence at Wave 8				X	X	X	X	X	X		462
Blackouts at Wave 2											39
Blackouts at Wave 3											68
Blackouts at Wave 4									X		129
Blackouts at Wave 5								X	X		163
Blackouts at Wave 6			X				X	X	X		213
Blackouts at Wave 7		X				X	X		X		331
Frequency*quantity of alcohol use at Wave 2											41
Frequency*quantity of alcohol use at Wave 3											67
Frequency*quantity of alcohol use at Wave 4									X		130
Frequency*quantity of alcohol use at Wave 5								X	X		167
Frequency*quantity of alcohol use at Wave 6			X				X	X	X		208
Frequency*quantity of alcohol use at Wave 7		X				X	X		X		330
Number of cases (N=1821)	1046	60	28	44	114	60	32	28	28	42	

Note: Row totals indicate total number missing for variable; Column totals indicate number missing in specific pattern; X indicates missing data for that variable in that pattern.

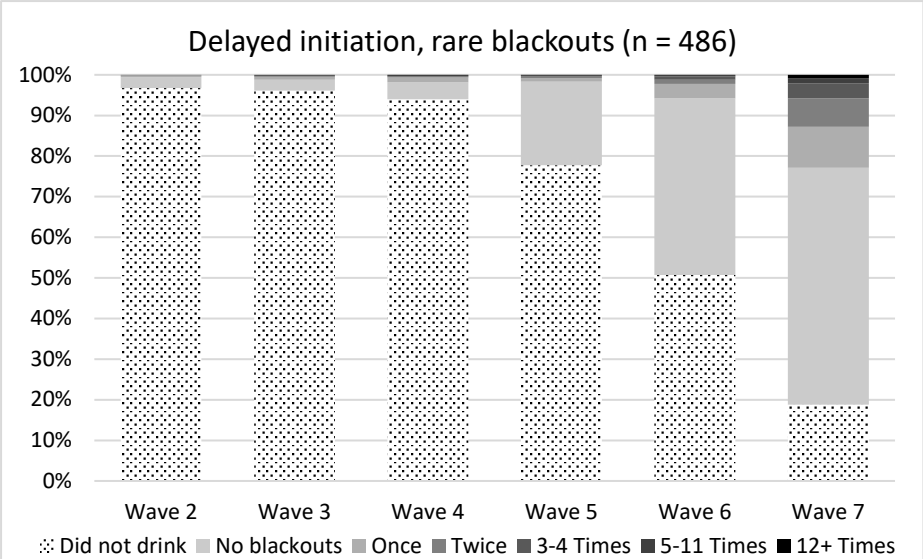
7.2.5. Appendix B5. Complete case latent class growth analysis fit statistics.

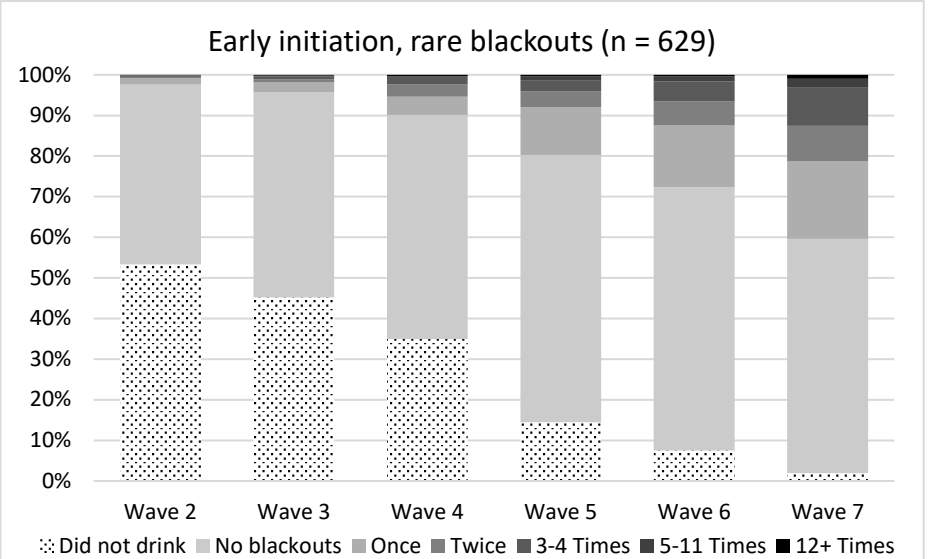
						Proportion in each latent class			
Class Solution	**AIC**	**BIC**	**SSABIC**	**LMR-ALRT**	**BLRT**	**Class 1**	**Class 2**	**Class 3**	**Class 4**
2	13251.35	13334.20	13283.38	< .001	< .001	0.518	0.482	-	-
3	13085.61	13183.98	13123.62	< .001	< .001	0.371	0.481	0.148	-
4	13084.39	13198.30	13128.42	0.7098	< .001	0.343	0.479	0.053	0.124

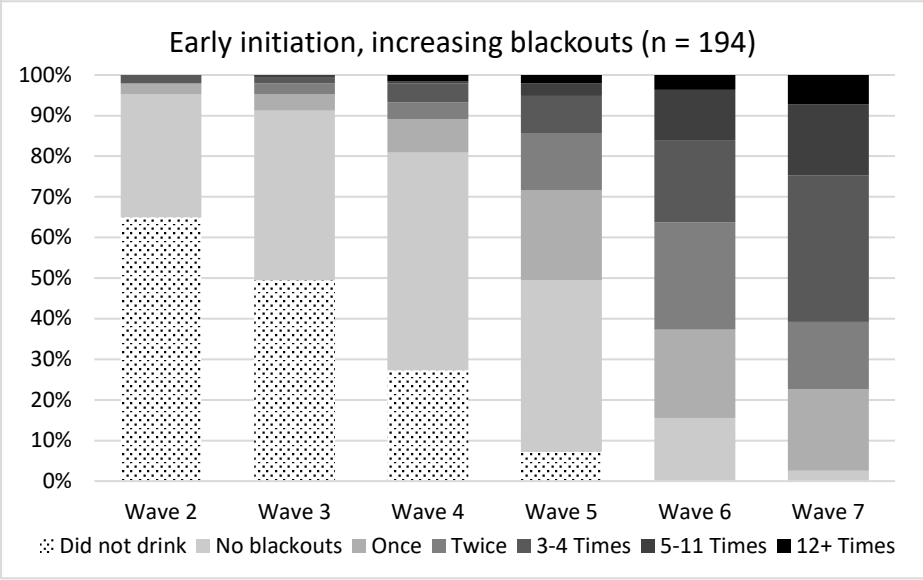
7.2.6. Appendix B6. Complete case average latent class probabilities for most likely latent class membership by latent class.

	Latent Class		
Most likely latent class membership	Delayed initiation, rare blackouts	Early initiation, rare blackouts	Early initiation, increasing blackouts
Delayed initiation, rare blackouts	0.822	0.169	0.009
Early initiation, rare blackouts	0.108	0.798	0.094
Early initiation, increasing blackouts	0.014	0.173	0.813

7.2.7. Appendix B7. Complete case probabilities of endorsing different numbers of blackouts for each class, 3-class solution.







7.2.8. Appendix B8. Complete case bivariate multinomial logistic regression predicting latent class membership using baseline characteristics.

	Reference: Delayed initiation, rare blackouts				Reference: Early initiation, rare blackouts	
	Early initiation, rare blackouts		Early initiation, increasing blackouts		Early initiation, increasing blackouts	
	RRR	99.5% CI	RRR	99.5% CI	RRR	99.5% CI
Female sex	1.38	(0.88, 2.16)	3.40	(1.73, 6.71)	2.47	(1.27, 4.79)
Child externalising	1.04	(1.01, 1.06)	1.02	(0.99, 1.05)	0.99	(0.96, 1.02)
Peer disapproval of substance use	0.91	(0.80, 1.03)	0.88	(0.75, 1.03)	0.97	(0.84, 1.11)
Peer substance use	1.47	(1.09, 1.98)	1.45	(1.07, 1.96)	0.99	(0.90, 1.08)
Parent education (Reference: High school or less)						
Diploma	0.81	(0.46, 1.43)	0.94	(0.43, 2.08)	1.15	(0.53, 2.51)
University	0.81	(0.47, 1.40)	1.08	(0.51, 2.29)	1.34	(0.64, 2.80)
Alcohol specific household rules	0.74	(0.45, 1.22)	0.73	(0.44, 1.23)	0.99	(0.85, 1.15)
Parental monitoring	0.89	(0.80, 0.98)	0.89	(0.80, 1.01)	1.01	(0.93, 1.10)
Socio-economic status	0.88	(0.80, 0.96)	0.97	(0.85, 1.11)	1.11	(0.98, 1.25)
Single parent household	2.22	(1.17, 4.23)	1.86	(0.80, 4.31)	0.84	(0.40, 1.75)
Accessibility of alcohol at home	1.02	(0.96, 1.09)	1.11	(1.01, 1.22)	1.09	(0.99, 1.19)
Family history of alcohol problems	1.10	(0.69, 1.73)	0.91	(0.49, 1.69)	0.83	(0.45, 1.52)
Family conflict	1.29	(0.99, 1.68)	1.28	(0.91, 1.81)	1.00	(0.73, 1.37)

7.2.9. Appendix B9. Complete case multivariate multinomial logistic regression predicting latent class membership using baseline characteristics.

	Reference: Delayed initiation, rare blackouts				Reference: Early initiation, rare blackouts	
	Early initiation, rare blackouts		Early initiation, increasing blackouts		Early initiation, increasing blackouts	
	RRR	99.5% CI	RRR	99.5% CI	RRR	99.5% CI
Female sex	1.75	(1.01, 3.04)	4.51	(2.07, 9.81)	2.58	(1.24, 5.34)
Child externalising	1.02	(0.99, 1.05)	1.00	(0.96, 1.04)	0.98	(0.95, 1.01)
Peer disapproval of substance use	1.06	(0.90, 1.26)	0.94	(0.79, 1.13)	0.89	(0.74, 1.06)
Peer substance use	1.39	(1.01, 1.93)	1.41	(1.00, 1.97)	1.01	(0.91, 1.12)
Parent education (Reference: High school or less)						
Diploma	0.87	(0.45, 1.70)	1.03	(0.42, 2.56)	1.18	(0.51, 2.76)
University	0.98	(0.51, 1.88)	1.19	(0.50, 2.85)	1.22	(0.54, 2.77)
Alcohol specific household rules	0.98	(0.68, 1.42)	0.98	(0.66, 1.44)	1.00	(0.84, 1.18)
Parental monitoring	0.94	(0.84, 1.06)	0.93	(0.82, 1.06)	0.99	(0.89, 1.10)
Socio-economic status	0.90	(0.81, 1.01)	0.98	(0.84, 1.15)	1.08	(0.94, 1.25)
Single parent household	1.90	(0.91, 3.95)	1.95	(0.77, 4.89)	1.03	(0.45, 2.31)
Accessibility of alcohol at home	1.04	(0.97, 1.13)	1.13	(1.01, 1.26)	1.08	(0.97, 1.20)
Family history of alcohol problems	0.95	(0.56, 1.60)	0.77	(0.39, 1.54)	0.82	(0.43, 1.56)
Family conflict	1.23	(0.90, 1.68)	1.24	(0.84, 1.83)	1.01	(0.72, 1.43)

7.2.10. Appendix B10. Complete case unadjusted logistic regression predicting meeting criteria for DSM-IV alcohol dependence and abuse, and DSM-5 AUD by latent class.

	Dependence		Abuse		AUD	
	OR	99.5% CI	OR	99.5% CI	OR	99.5% CI
Reference: Delayed initiation, rare blackouts						
Early initiation, rare blackouts	1.90	(0.98, 3.69)	0.82	(0.30, 2.27)	1.97	(1.17, 3.31)
Early initiation, increasing blackouts	3.97	(1.83, 8.60)	0.54	(0.10, 2.78)	4.68	(2.27, 9.64)
Reference: Early initiation, rare blackouts						
Early initiation, increasing blackouts	2.09	(1.07, 4.08)	0.65	(0.13, 3.38)	2.38	(1.20, 4.71)

7.2.11. Appendix B11. Complete case adjusted logistic regression predicting meeting criteria for DSM-IV alcohol dependence and abuse, and DSM-5 AUD by latent class.

	Dependence		Abuse		AUD	
	OR	99.5% CI	OR	99.5% CI	OR	99.5% CI
Reference: Delayed initiation, rare blackouts						
Early initiation, rare blackouts	1.77	(0.85, 3.69)	0.93	(0.26, 3.24)	1.98	(1.09, 3.58)
Early initiation, increasing blackouts	3.51	(1.46, 8.42)	0.47	(0.05, 4.03)	4.76	(2.10, 10.76)
Reference: Early initiation, rare blackouts						
Early initiation, increasing blackouts	1.98	(0.94, 4.19)	0.51	(0.07, 3.58)	2.40	(1.15, 5.03)

7.2.12. Appendix B12. Latent class growth analysis fit statistics.

						Proportion in each latent class			
Class Solution	**AIC**	**BIC**	**SSABIC**	**LMR-ALRT**	**BLRT**	**Class 1**	**Class 2**	**Class 3**	**Class 4**
2	19171.25	19259.36	19208.53	<.001	<.001	0.494	0.506	-	-
3	19011.06	19115.70	19055.34	<.001	<.001	0.385	0.477	0.138	-
4	18955.85	19077.01	19007.12	0.106	<.001	0.340	0.078	0.464	0.118

Note: Values averaged across 20 imputations. AIC = Akaike Information Criteria; BIC = Bayesian Information Criteria; SSABIC = Sample-Size Adjusted Bayesian Information Criteria; LMR-ALRT = Lo-Mendell-Rubin Adjusted Likelihood Ratio Test; BLRT = Bootstrapped Likelihood Ratio Test.

7.2.13. Appendix B13. Average latent class probabilities for most likely latent class membership by latent class.

	Latent Class		
Most likely latent class membership	Delayed initiation, rare blackouts	Early initiation, rare blackouts	Early initiation, increasing blackouts
Delayed initiation, rare blackouts	0.830	0.162	0.050
Early initiation, rare blackouts	0.246	0.765	0.098
Early initiation, escalating frequent blackouts	0.118	0.223	0.749

Note: Averaged across 20 imputations. Diagonals represent the average latent class classification probability for participants' assigned class, i.e. those assigned to the *delayed initiation, rare blackouts* class had an average classification probability of 0.83 for that class. Non-diagonals represent the average latent class classification probability for the additional classes, i.e. those assigned to the e*arly initiation, rare blackouts* class had an average misclassification probability of 0.098 for the *early initiation, increasing blackouts* class.

7.2.14. Appendix B14. Bivariate multinomial logistic regression predicting latent class membership using baseline characteristics.

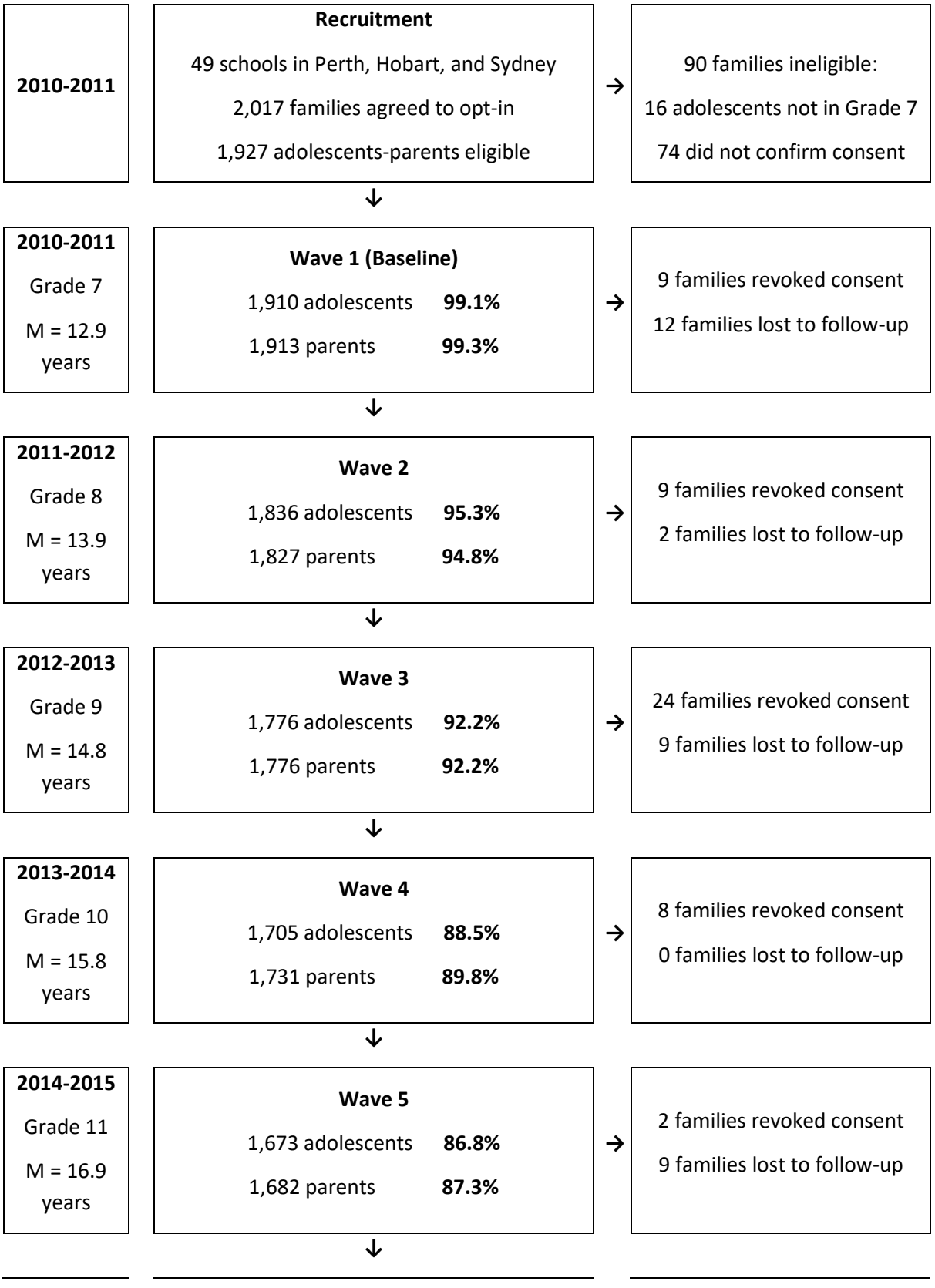
	Class (Reference: Delayed initiation, rare blackouts)				Class (Reference: Early initiation, rare blackouts)	
	Early initiation, rare blackouts		Early initiation, increasing blackouts		Early initiation, increasing blackouts	
	RRR	99.5% CI	RRR	99.5% CI	RRR	99.5% CI
Female sex	1.15	(0.75, 1.75)	2.96	(1.59, 5.53)	2.58	(1.30, 5.10)
Child externalising	1.03	(1.01, 1.06)	1.02	(0.99, 1.05)	0.99	(0.96, 1.02)
Peer disapproval of substance use	0.90	(0.80, 1.01)	0.89	(0.76, 1.05)	0.99	(0.85, 1.16)
Peer substance use	1.41	(1.13, 1.76)	1.41	(1.12, 1.78)	1.00	(0.90, 1.12)
Parent education (Reference: High school or less)						
Diploma	0.88	(0.52, 1.47)	1.07	(0.49, 2.34)	1.22	(0.54, 2.73)
University	0.85	(0.51, 1.44)	1.33	(0.63, 2.79)	1.55	(0.70, 3.47)
Alcohol specific household rules	0.63	(0.35, 1.15)	0.65	(0.36, 1.16)	1.02	(0.85, 1.24)
Parental monitoring	0.87	(0.79, 0.95)	0.87	(0.78, 0.98)	1.01	(0.92, 1.10)
Socio-economic status	0.92	(0.85, 1.00)	0.99	(0.87, 1.13)	1.07	(0.95, 1.22)
Single parent household	1.93	(1.06, 3.52)	1.42	(0.63, 3.18)	0.74	(0.33, 1.64)
Accessibility of alcohol at home	1.05	(0.99, 1.11)	1.11	(1.01, 1.22)	1.06	(0.96, 1.16)
Family history of alcohol problems	1.11	(0.72, 1.73)	1.07	(0.60, 1.91)	0.96	(0.51, 1.81)
Family conflict	1.26	(0.74, 1.61)	1.21	(0.86, 1.70)	0.96	(0.70, 1.33)

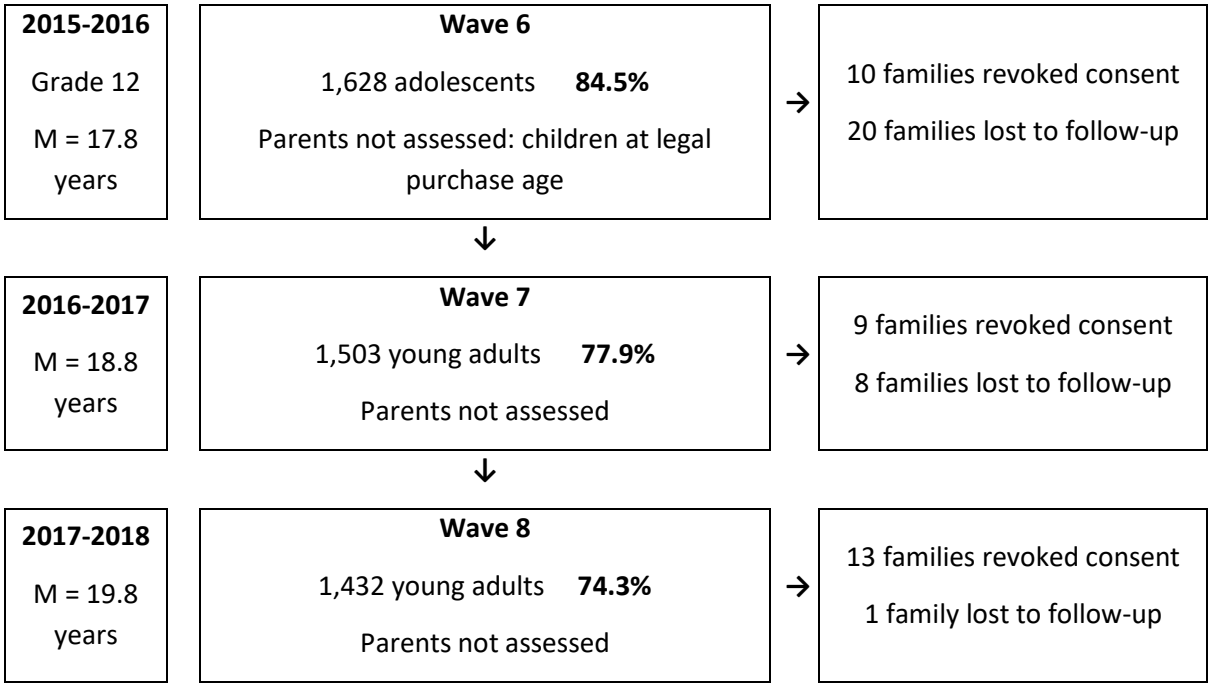
7.2.15. Appendix B15. Unadjusted logistic regression predicting meeting criteria for DSM-IV alcohol dependence and abuse, and DSM-5 AUD by latent class.

	Dependence		Abuse		AUD	
Class	OR	99.5% CI	OR	99.5% CI	OR	99.5% CI
Reference: Delayed initiation, rare blackouts						
Early initiation, rare blackouts	1.81	(1.02, 3.22)	1.00	(0.30, 3.36)	1.96	(1.25, 3.08)
Early initiation, increasing blackouts	3.38	(1.72, 6.66)	0.38	(0.03, 4.77)	4.64	(2.32, 9.28)
Reference: Early initiation, rare blackouts						
Early initiation, increasing blackouts	1.87	(1.01, 3.45)	0.38	(0.02, 6.09)	2.37	(1.15, 4.87)

7.3. Appendix C: Appendices for Chapter 4

7.3.1. Appendix C1. Cohort retention flowchart.




2015-2016
Grade 12
M = 17.8 years
Wave 6
1,628 adolescents 84.5%
Parents not assessed: children at legal purchase age
10 families revoked consent
20 families lost to follow-up
2016-2017
M = 18.8 years
Wave 7
1,503 young adults 77.9%
Parents not assessed
9 families revoked consent
8 families lost to follow-up
2017-2018
M = 19.8 years
Wave 8
1,432 young adults 74.3%
Parents not assessed
13 families revoked consent
1 family lost to follow-up

7.3.2. Appendix C2. STROBE Checklist.

	Item No.	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	✓
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	✓
Study size	10	Explain how the study size was arrived at	✓
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓
		(*b*) Describe any methods used to examine subgroups and interactions	✓
		(*c*) Explain how missing data were addressed	✓
		(*d*) If applicable, explain how loss to follow-up was addressed	✓
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	✓
		(c) Consider use of a flow diagram	✓
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	✓
		(c) Summarise follow-up time (eg, average and total amount)	✓
Outcome data	15	Report numbers of outcome events or summary measures over time	✓
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	✓
		(*b*) Report category boundaries when continuous variables were categorized	N/A

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	✓
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

7.3.3. Appendix C3. Alcohol-related harms items.

Item as it appears in survey (In the last 12 months, how many times:)	Short form
Did you drink more than you planned?	Drank more than planned
Did you have a hangover after drinking?	Experienced a hangover
Were you sick after drinking?	Felt sick
Have you been unable to remember what had happened while you had been drinking?	Blackout
Did someone you were going out with complain about your drinking?	Someone complained about their drinking
Did you get into trouble with your friends because of alcohol (your friends got annoyed with you)?	Trouble with friends
Did you get into trouble with your parents because of your drinking?	Trouble with parents
Did you damage something because you were affected by alcohol?	Damaged something
Did you get in a physical fight with someone because you were affected by alcohol?	Had a physical fight
Did you get into trouble with police because of your drinking?	Trouble with police
When affected by alcohol, did you have sex that you later regretted?	Regretted having sex
When affected by alcohol, did you have sex you were afraid would lead to pregnancy or sexually transmitted disease?	Had unsafe sex

7.3.4. Appendix C4. Alcohol abuse, alcohol dependence, and alcohol use disorder items.

Item as it appears in survey:	Criterion for:	Symptom (In the past year, have you):
In the last year, did you miss uni/TAFE/work etc. to go drinking or because you were hung-over? IF YES Did you miss uni/TAFE/work etc. more than once because of drinking?	DSM-IV alcohol abuse DSM-5 alcohol use disorder	Found that drinking—or being sick from drinking—often interfered with taking care of your home or family? Or caused job troubles? Or school problems?
In the last year, did you go to uni/TAFE/work etc. right after you had been drinking or drink while you were at uni/TAFE/work? IF YES Did you do this more than once?	DSM-IV alcohol abuse DSM-5 alcohol use disorder	
In the last year, did you get into trouble at uni/TAFE/work etc. or did you have problems with your school/work because of your drinking? IF YES Did this happen more than once?	DSM-IV alcohol abuse DSM-5 alcohol use disorder	
In the last year, did you drink before you did something important or while you were doing something important... like babysitting or working? IF YES Did you do this more than once?	DSM-IV alcohol abuse DSM-5 alcohol use disorder	
In the last year, did you get into arguments with your family or friends because of drinking? IF YES Even though you had problems with your family or friends, did you drink anyway?	DSM-IV alcohol abuse DSM-5 alcohol use disorder	Continued to drink even though it was causing trouble with your family or friends?
In the last year, did you get into physical fights while drinking? IF YES Did this happen more than once? IF YES Even though you got into physical fights, did you drink alcohol anyway?	DSM-IV alcohol abuse DSM-5 alcohol use disorder	More than once gotten into situations while or after drinking that increased your chances of getting hurt (such as driving, swimming, using machinery, walking in a dangerous area, or having unsafe sex)?

In the last year, did you ever drink in situations where you could get hurt, like right before or while you were riding a bike, swimming or driving a motorcycle? IF YES Did you do this more than once?	DSM-IV alcohol abuse DSM-5 alcohol use disorder	
In the last year, did you get into trouble with the police when you were drunk or because you had been drinking? IF YES Did this happen more than once?	DSM-IV alcohol abuse	More than once gotten arrested, been held at a police station, or had other legal problems because of your drinking?
In the last year, did you often drink more than you thought you would?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	Had times when you ended up drinking more, or longer, than you intended?
Did you often end up drinking for a longer time than you thought you would?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	
In the last year, did you ever try to quit or cut down on your drinking? IF YES When you decided to quit or cut down in the last year, were you always able to do so for at least one month?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	More than once wanted to cut down or stop drinking, or tried to, but couldn't?
In the last year, have you often felt you should quit or cut down?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	
In the last year, could you drink a lot more alcohol than you used to before you got drunk?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	Had to drink much more than you once did to get the effect you want? Or found that your usual number of drinks had much less effect than before?
Did it seem the same amount of alcohol had less effect on you?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	
In the last year, were there many days when you felt sick or hung-over after drinking? IF YES In the last year did you spend a lot of time drinking? IF YES In the last year did you spend a lot of time planning how you would get alcohol?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	Spent a lot of time drinking? Or being sick or getting over other aftereffects?
Did you ever want a drink so badly that you could not think about anything else?	DSM-5 alcohol use disorder	Wanted a drink so badly you couldn't think of anything else?

In the last year, were there often things you cut down on or did not do because of drinking, for example, things that you used to like to do?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	Given up or cut back on activities that were important or interesting to you, or gave you pleasure, in order to drink?
In the last year, did drinking cause you to have any physical health problems or did drinking make a health problem worse? IF YES Did you continue drinking even though it was causing you a physical problem?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	Continued to drink even though it was making you feel depressed or anxious or adding to another health problem? Or after having had a memory blackout?
In the last year, did drinking cause you to get very sad or depressed or irritable? IF YES Did you continue drinking even though it made you feel this way?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	
When you didn't drink or when you cut down in the last year, did you feel bad or feel sick? IF YES Did you become nervous or worried? Did you feel restless, like you couldn't sit still? Did you feel your heart beating fast? Did you feel sick to your stomach or have to vomit or throw up? Did you have trouble sleeping? Did you get headaches? Did you sweat a lot? Did you feel weak? Did you ever have any fits or seizures? Did your hands shake? ONLY IF NO to the previous question, did your tongue tremble or eyes twitch? Did you see, feel, or hear things that other people couldn't?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	Found that when the effects of alcohol were wearing off, you had withdrawal symptoms, such as trouble sleeping, shakiness, restlessness, nausea, sweating, a racing heart, or a seizure? Or sensed things that were not there?
In the last year, did you ever drink alcohol or take any medicines like tranquilisers or sedatives so that you wouldn't feel bad or sick from cutting down?	DSM-IV alcohol dependence DSM-5 alcohol use disorder	

7.3.5. Appendix C5. Wave 1 predictors of alcohol-related risk factors and harms identified from the literature.

Wave 1 predictor	Measurement	Reported by	Comments	Reference(s)
Child variables				
Sex	Single item (Are you: *Male; Female*)	Child	Females more likely to experience physiological harms, males more likely to experience psychosocial harms. Evidence of sex convergence across all alcohol-related harms, sex ratio is close to 1 for cohorts of similar age to APSALS.	Slade, Chapman (1), Grigsby, Forster (2)
Externalising	Standardised t-score based on the rule-breaking and aggressive behaviour subscales of the Achenbach Youth Self Report (3).	Child	Externalising behaviours predict AUD onset and alcohol-related harm in early adulthood.	Farmer, Gau (4), Little, Hawkins (5)

Peer alcohol use/approval of use	Single item for approval (How do you think your close friends would feel about you drinking alcohol: *Not disapprove; Disapprove; Strongly disapprove*) Single item for use (How many of your friends drink alcohol: *None; Very few; Quite a few; Most; All*)	Child	Having peers who use alcohol and/or approve of alcohol use is associated with later harms.	Grigsby, Forster (2)
Peer tobacco use/approval of use	Single item for approval (How do you think your close friends would feel about you smoking cigarettes: *Not disapprove; Disapprove; Strongly disapprove*) Single item for use (How many of your friends smoke cigarettes: *None; Very few; Quite a few; Most; All*)	Child	Mixed findings regarding peer tobacco use and association with alcohol use, unable to find studies examining association with alcohol-related harms.	Lundborg (6), Wang, Hipp (7)
Parent variables				
Highest level of education	Single item (What is your highest educational qualification: *School certificate; Diploma, trade or non-trade certificate; Undergraduate degree; Postgraduate degree; None of the above*)	Parent	Higher parental education protective against alcohol-related harm.	Kendler, Gardner (8)

Alcohol use	Typical quantity of drinks between the reporting parent or their partner (whichever is higher), single item (On a day that you have an alcoholic drink, how many standard drinks do you usually have: *13 or more drinks; 11-12 drinks; 7-10 drinks; 5-6 drinks; 3-4 drinks; 1-2 drinks*)	Parent	Parent alcohol use, particularly paternal drinking level, predicts alcohol-related harms in early adulthood.	Grigsby, Forster (2), Little, Hawkins (5)
Alcohol accessibly at home without parental knowledge	Single item (In the last 6 months, how easy do you think it would have been for you to take alcohol without parents knowing: *Very easy; Pretty easy; Not very easy; Impossible*)	Child	Associated with child alcohol use levels, unable to find studies examining association with alcohol-related harms.	Swendsen, Burstein (9)

Alcohol-specific rules	10 items (I'm allowed to…drink alcohol at home when my parents are around; drink alcohol at home when my parents are not around; drink more than one glass of alcohol at home when my parents are around; drink more than one glass of alcohol at home when my parents are not around; drink as much alcohol as I'd like outside the house; drink alcohol with my friends at a party; come home drunk; become drunk when I go out with friends; drink alcohol on the weekend; drink alcohol during the week: *Never; Rarely, Sometimes, Often; Always*)	Child	Permissive messages towards alcohol use from parents (i.e. allowing child to drink when parent is present) predicted alcohol-related harms.	Reimuller, Hussong (10)
Monitoring of child's activities	6 items (My parent(s) usually know what I am doing after school; My parent(s) know who my friends are; My parent(s) know where I am after school; If I am going to be home late, I am expected to call my parent(s) to let them know; I tell my parent(s) who I'm going to be with before I go out; I talk to my parent(s) about the plans I have with my friends: *Never; Rarely; Sometimes; Often; Always*)	Child	Mixed findings; Ham and Hope (11) found increased parental monitoring to be protective against alcohol-related harm whereas Maldonado-Molina, Reingle (12) found that increased parental involvement predicts alcohol-related violence.	Ham and Hope (11), Maldonado-Molina, Reingle (12)

Family variables				
Socioeconomic status	Single item (Index of Relative Socio-economic Advantage and Disadvantage [IRSAD]; scored as low SES [deciles 1-3], medium SES [deciles 4-7], and high SES [deciles 8-10].	Parent	High SES predicts heavy episodic drinking, low SES predicts alcohol-related behavioural problems.	Kendler, Gardner (8)
One/two parent household	Single item (Who do you live with most of the time: *Father; Step-father; Mother; Step-mother; Brother(s) and/or sister(s); Grandparent(s) and/or other relatives*)	Child	Associated with child alcohol use levels, unable to find studies examining association with alcohol-related harms.	Alati, Maloney (13)
Family history of alcohol problems	Single item (Did your natural father or mother ever have any problems with drinking, not limited to isolated incidents: *yes; no*)	Parent	Having a family history of alcohol problems predicts alcohol-related harms.	Grigsby, Forster (2)
Family conflict	6 items (Family members have big arguments over little things; Family members get angry with each other daily; Family members get angry with each other three times a week; Family members support one another; There are feelings of togetherness in our house; Family members get along well: *true; false*)	Parent	Higher quality parent-adolescent relationships protective against alcohol-related harm.	Kuntsche, van der Vorst (14)

7.3.5.1. References for Appendix C5.

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7.3.6. Appendix C6. Accounting for latent transition class classification uncertainty.

We used the modified three-step Bolck-Croon-Hagenaars estimation method (BCH; 1, 2, 3) to account for the uncertainty of class membership categorisation in the LTA model for regression analyses. First, a latent class transition model was estimated. Next, an expanded data file with one record for each latent class for each individual was created. For example, in a 3-class model, each individual will have three records that are identical with the exception of a "latent class" variable and a weighting variable. This BCH weighting variable was calculated from the inverse of a matrix containing the classification probabilities for most likely latent transition class membership by latent transition class (4). Finally, associations between latent transition class membership and other variables were estimated as a multiple group model using the BCH weighting variable.

7.3.6.1. References for Appendix C6.

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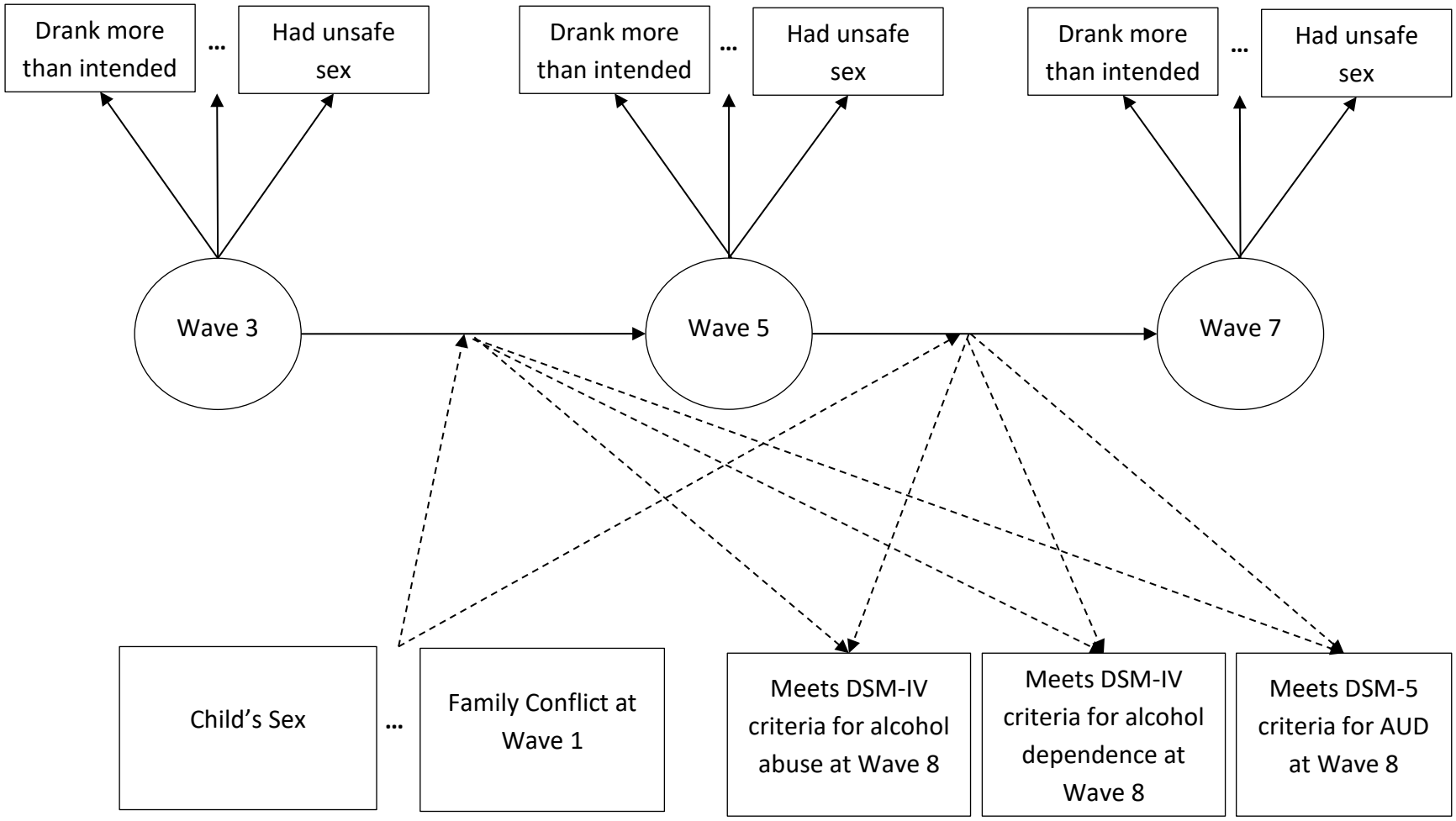
7.3.7. Appendix C7. Latent transition model for three time points with Wave 1 predictors and distal outcomes.



7.3.8. Appendix C8. Ten most common missing data patterns.

Variable	Pattern of Missing Data							Missing (%)
Child sex								14 (0.8)
Child externalising at Wave 1								16 (0.9)
Peer disapproval of substance use at Wave 1								16 (0.9)
Peer substance use at Wave 1								18 (1)
Parent education at Wave 1								32 (1.8)
Alcohol-specific household rules at Wave 1								20 (1.1)
Parental monitoring at Wave 1								17 (0.9)
Socio-economic Index For Area at Wave 1								25 (1.4)
Single parent household at Wave 1								14 (0.8)
Home access to alcohol at Wave 1								26 (1.4)
Family history of alcohol problems at Wave 1						X		107 (5.9)
Family conflict at Wave 1								28 (1.5)
DSM-IV Alcohol abuse at Wave 8		X	X	X			X	414 (22.6)
DSM-IV Alcohol dependence at Wave 8		X	X	X			X	411 (22.5)
DSM-5 AUD at Wave 8		X	X	X			X	410 (22.4)
Drank more than intended at Wave 3								71 (3.9)
Had hangover at Wave 3								71 (3.9)
Felt sick at Wave 3								71 (3.9)
Blacked out at Wave 3								72 (3.9)
Someone complained at Wave 3								71 (3.9)
Trouble with friends at Wave 3								72 (3.9)
Trouble with parents at Wave 3								71 (3.9)
School/work affected at Wave 3								71 (3.9)
Damaged things at Wave 3								71 (3.9)
Had a physical fight at Wave 3								72 (3.9)
Trouble with police at Wave 3								71 (3.9)
Regretted sex at Wave 3								71 (3.9)
Unsafe sex at Wave 3								71 (3.9)
Drank more than intended at Wave 5				X		X		166 (9.1)
Had hangover at Wave 5				X		X		166 (9.1)
Felt sick at Wave 5				X		X		167 (9.1)
Blacked out at Wave 5				X		X		166 (9.1)
Someone complained at Wave 5				X		X		166 (9.1)
Trouble with friends at Wave 5				X		X		166 (9.1)
Trouble with parents at Wave 5				X		X		166 (9.1)
School/work affected at Wave 5				X		X		166 (9.1)
Damaged things at Wave 5				X		X		166 (9.1)
Had a physical fight at Wave 5	X			X	X	X	X	440 (24.1)
Trouble with police at Wave 5				X		X		166 (9.1)
Regretted sex at Wave 5				X		X		166 (9.1)

Unsafe sex at Wave 5						X			X		166 (9.1)
Drank more than intended at Wave 7				X	X	X	X				401 (21.9)
Had hangover at Wave 7				X	X	X	X				401 (21.9)
Felt sick at Wave 7				X	X	X	X				401 (21.9)
Blacked out at Wave 7				X	X	X	X				401 (21.9)
Someone complained at Wave 7				X	X	X	X				401 (21.9)
Trouble with friends at Wave 7				X	X	X	X				401 (21.9)
Trouble with parents at Wave 7				X	X	X	X				401 (21.9)
School/work affected at Wave 7				X	X	X	X				401 (21.9)
Damaged things at Wave 7				X	X	X	X				401 (21.9)
Had a physical fight at Wave 7				X	X	X	X				401 (21.9)
Trouble with police at Wave 7				X	X	X	X				401 (21.9)
Regretted sex at Wave 7				X	X	X	X				401 (21.9)
Unsafe sex at Wave 7				X	X	X	X				401 (21.9)
Number of cases (N=1828)	**935**	**175**	**122**	**105**	**89**	**75**	**44**	**38**	**27**	**20**	

Note: Row totals indicate total number missing for variable; Column totals indicate number missing in specific pattern; X indicates missing data for that variable in that pattern.

7.3.9. Appendix C9. Latent class analysis model fit and classification quality statistics.

Model		Fit and classification quality						Proportion in each latent class			
Wave	Class Solution	AIC	BIC	SSABIC	LMR-ALRT	BLRT	Entropy	Class 1	Class 2	Class 3	Class 4
3	2	4000.45	4149.25	4063.47	<.001	<.001	0.98	0.08	0.92	-	-
	3	3838.86	4064.81	3934.55	0.003	<.001	0.98	0.92	0.02	0.07	-
	4	3865.66	4168.77	3994.03	0.078	<.001	0.95	0.01	0.05	0.03	0.92
5	2	10319.86	10468.66	10382.88	<.001	<.001	0.91	0.27	0.73	-	-
	3	9868.05	10094.00	9963.74	<.001	<.001	0.92	0.26	0.04	0.71	-
	4	9945.00	10248.11	10073.37	0.14	<.001	0.90	0.03	0.70	0.03	0.23
7	2	18034.62	18183.42	18097.64	<.001	<.001	0.81	0.45	0.55	-	-
	3	17367.04	17592.99	17462.74	<.001	<.001	0.81	0.49	0.40	0.12	-
	4	17371.49	17674.59	17499.86	0.02	<.001	0.80	0.10	0.35	0.07	0.48

Note: Averaged across M = 20 imputations. AIC = Akaike Information Criteria; BIC = Bayesian Information Criteria; SSABIC = Sample-Size Adjusted Bayesian Information Criteria; LMR-ALRT = Lo-Mendell-Rubin Adjusted Likelihood Ratio Test; BLRT = Bootstrapped Likelihood Ratio Test.

7.3.10. Appendix C10. Final class counts and proportions for all latent transition class patterns based on their most likely latent transition class pattern.

Transition Class	Wave 3 Latent Class	Wave 5 Latent Class	Wave 7 Latent Class	n (%)*
1	**No harms**	**No harms**	**No harms**	**381 (20.87)**
2	**No harms**	**No harms**	**Physiological harms**	**702 (38.39)**
3	**No harms**	**No harms**	**All harms**	**131 (7.16)**
4	No harms	Physiological harms	No harms	14 (0.75)
5	**No harms**	**Physiological harms**	**Physiological harms**	**226 (12.34)**
6	**No harms**	**Physiological harms**	**All harms**	**169 (9.25)**
7	No harms	All harms	No harms	1 (0.05)
8	No harms	All harms	Physiological harms	10 (0.54)
9	No harms	All harms	All harms	43 (2.36)
10	Physiological harms	No harms	No harms	2 (0.10)
11	Physiological harms	No harms	Physiological harms	7 (0.39)
12	Physiological harms	No harms	All harms	2 (0.14)
13	Physiological harms	Physiological harms	No harms	2 (0.12)
14	Physiological harms	Physiological harms	Physiological harms	46 (2.54)
15	Physiological harms	Physiological harms	All harms	23 (1.23)
16	Physiological harms	All harms	No harms	1 (0.05)
17	Physiological harms	All harms	Physiological harms	5

				(0.30)
18	Physiological harms	All harms	All harms	20 (1.07)
19	All harms	No harms	No harms	2 (0.10)
20	All harms	No harms	Physiological harms	3 (0.16)
21	All harms	No harms	All harms	0 (0.01)
22	All harms	Physiological harms	No harms	0 (0.00)
23	All harms	Physiological harms	Physiological harms	6 (0.30)
24	All harms	Physiological harms	All harms	2 (0.11)
25	All harms	All harms	No harms	0 (0.00)
26	All harms	All harms	Physiological harms	7 (0.37)
27	All harms	All harms	All harms	24 (1.30)

Note: Class counts calculated from proportions averaged across M = 20 imputations.

7.3.11. Appendix C11. Bivariate multinomial logistic regression predicting latent class membership using Wave 1 characteristics.

	Transition Class (Ref: late escalation to physiological harms)							
	No harms		Early escalation to physiological harm		Late escalation to all harms		Gradual escalation to all harms	
	RR	99.5% CI	RR	99.5% CI	RR	99.5% CI	RR	99.5% CI
Female sex	1.19	(0.74, 1.92)	1.79	(1.04, 3.07)	0.7	(0.30, 1.65)	1.19	(0.63, 2.22)
Child externalising	1.01	(0.98, 1.03)	1.02	(0.99, 1.05)	1.03	(0.99, 1.07)	1.02	(0.98, 1.06)
Peer disapproval of substance use	0.95	(0.81, 1.11)	0.91	(0.77, 1.09)	0.91	(0.74, 1.10)	0.88	(0.76, 1.03)
Peer substance use	0.95	(0.77, 1.16)	1.22	(1.06, 1.41)	1.11	(0.92, 1.34)	1.25	(1.09, 1.44)
Parent education (Ref: High school or less)								
Diploma	0.75	(0.43, 1.33)	0.83	(0.43, 1.63)	1.1	(0.40, 3.06)	0.94	(0.38, 2.31)
University	0.81	(0.47, 1.39)	0.87	(0.45, 1.70)	1.3	(0.48, 3.48)	1.54	(0.70, 3.53)
Alcohol specific household rules	0.83	(0.64, 1.09)	0.82	(0.63, 1.07)	0.8	(0.60, 1.08)	0.79	(0.60, 1.04)
Parental monitoring	1.01	(0.90, 1.14)	0.9	(0.81, 1.01)	0.91	(0.81, 1.02)	0.86	(0.77, 0.96)
Socio-economic status	0.93	(0.84, 1.01)	0.94	(0.85, 1.04)	1.07	(0.90, 1.27)	1.01	(0.88, 1.15)
Single parent household	1.03	(0.55, 1.96)	1.39	(0.68, 2.84)	1.18	(0.44, 3.15)	1.52	(0.66, 3.49)
Accessibility of alcohol at home	0.95	(0.89, 1.03)	1.04	(0.95, 1.13)	1.05	(0.93, 1.18)	1.09	(0.99, 1.20)
Family history of alcohol problems	0.92	(0.57, 1.47)	1.3	(0.76, 2.23)	1.16	(0.55, 2.41)	0.98	(0.49, 1.95)
Family conflict	1.05	(0.81, 1.37)	1.14	(0.81, 1.60)	1.28	(0.88, 1.85)	1.43	(1.02, 2.01)

Note: RR = Relative risk ratio; CI = Confidence interval.

7.3.12. Appendix C12. Unadjusted logistic regression predicting meeting criteria for DSM-IV alcohol dependence and abuse, and DSM-5 AUD at Wave 8 by latent class.

	DSM-IV				DSM-5	
Transition Class (Ref: late escalation to physiological harms)	Abuse		Dependence		AUD	
	RR	99.5% CI	RR	99.5% CI	RR	99.5% CI
No harms	0.48	(0.08, 2.90)	0.21	(0.07, 0.60)	0.29	(0.12, 0.68)
Early escalation to physiological harms	0.88	(0.07, 10.44)	1.74	(0.95, 3.18)	1.31	(0.98, 1.75)
Late escalation to all harms	1.73	(0.18, 164.27)	3.81	(1.35, 10.74)	1.76	(1.23, 2.51)
Gradual escalation to all harms	2.33	(0.19, 29.22)	4.18	(1.54, 11.34)	1.82	(1.37, 2.41)

7.4. Appendix D: Appendices for Chapter 5

7.4.1. Appendix D1. SNOMED-CT-AU codes and corresponding conditions mapped to approximate ICD-10-AM and ICD-9-CM codes

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
E24.4	*No alcohol-specific code available*	237738005	Pseudo-Cushing's syndrome due to alcohol
E51.2	291.1	21007002	Wernicke's disease
F10	291 303 305.0	191477001 42344001 25702006 228315001 18653004 21000000 228341007 32553006 228357007 228316000 268645007 228354000 228317009	Pathological alcohol intoxication Alcohol-induced psychosis Alcohol intoxication Binge drinker Alcohol intoxication delirium Idiosyncratic intoxication Unable to abstain from drinking Hangover Persistent effect of alcohol Alcoholic binges exceeding sensible amounts Nondependent alcohol abuse Drink driving Alcoholic binges exceeding safe amounts

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		191883007	Nondependent alcohol abuse, episodic
		169942003	Maternal alcohol abuse
		304605000	Methanol abuse
		288021000119107	Disorder due to alcohol abuse
		191882002	Nondependent alcohol abuse, continuous
		15167005	Alcohol abuse
		284591009	Persistent alcohol abuse
		228310006	Drinks in morning to get rid of hangover
		41083005	Alcohol-induced sleep disorder
		191884001	Nondependent alcohol abuse in remission
		86325007	Non megaloblastic anaemia due to alcoholism
		191805002	Episodic acute alcoholic intoxication in alcoholism
		191802004	Acute alcoholic intoxication in alcoholism
		7200002	Alcoholism
		235955000	Drug-induced chronic

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			pancreatitis
		66590003	Alcohol dependence
		713583005	Mild alcohol dependence
		2403008	Psychoactive substance dependence
		25702006	Alcohol intoxication
		7200002	Alcoholism
		308742005	Alcohol withdrawal-induced convulsion
		713862009	Severe alcohol dependence
		10755041000119100	Alcohol dependence in childbirth
		191812006	Episodic chronic alcoholism
		2403008	Psychoactive substance dependence
		154211000119108	Chronic pancreatitis due to chronic alcoholism
		191804003	Continuous acute alcoholic intoxication in alcoholism
		191813001	Chronic alcoholism in remission
		7200002	Alcoholism
		87810006	Megaloblastic anaemia due to alcoholism

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		66590003	Alcohol dependence
		231467000	Absinthe addiction
		300939009	Abstinent alcoholic
		191811004	Continuous chronic alcoholism
		714829008	Moderate alcohol dependence
		235952002	Chronic pancreatitis due to acute alcohol intoxication
		97571000119109	Thrombocytopenia co-occurrent and due to alcoholism
		66590003	Alcohol dependence
		10741871000119101	Alcohol dependence in pregnancy
		288041000119101	Perceptual disturbance due to alcohol withdrawal
		191480000	Alcohol withdrawal syndrome
		85561006	Uncomplicated alcohol withdrawal
		191480000	Alcohol withdrawal syndrome
		8635005	Alcohol withdrawal delirium
		79578000	Alcohol paranoia
		61144001	Alcohol-induced psychotic disorder with delusions

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		191476005	Alcohol withdrawal hallucinosis
		7052005	Alcohol hallucinosis
		42344001	Alcohol-induced psychosis
		191480000	Alcohol withdrawal syndrome
		191478006	Alcoholic paranoia
		191471000	Korsakov's alcoholic psychosis with peripheral neuritis
		73097000	Alcohol amnestic disorder
		192811002	Alcoholic encephalopathy
		69482004	Korsakoff's psychosis
		42344001	Alcohol-induced psychosis
		281004	Dementia associated with alcoholism
		231463001	Alcoholic dementia NOS (disorder)
		191475009	Chronic alcoholic brain syndrome
		78524005	Alcohol-induced sexual dysfunction
		34938008	Alcohol-induced anxiety disorder
		228353006	Reverse tolerance to alcohol
		228351008	Physical tolerance to alcohol

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		228350009	Behavioural tolerance to alcohol
		53936005	Alcohol-induced mood disorder
		228323004	Drinking bout
		29212009	Alcohol-induced organic mental disorder
		228322009	Drinking episode
		192206005	Mental and behavioral disorders due to use of alcohol (disorder)
		192207001	Mental and behavioral disorders due to use of alcohol: acute intoxication (disorder)
		192208006	Mental and behavioral disorders due to use of alcohol: harmful use (disorder)
		192209003	Mental and behavioural disorders due to use of alcohol: dependence syndrome) or (chronic alcoholism [& (addiction) or (dipsomania)]) (disorder)
		192210008	Mental and behavioral disorders due to use of alcohol:

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			withdrawal state (disorder)
		192211007	Mental and behavioral disorders due to use of alcohol: withdrawal state with delirium (disorder)
		192212000	Mental and behavioural disorders due to use of alcohol: psychotic disorder (& [hallucinosis] or [jealousy] or [paranoia] or [psychosis NOS]
		192213005	Mental and behavioral disorders due to use of alcohol: amnesic syndrome (disorder)
		192214004	Mental and behavioural disorders due to use of alcohol: residual and late-onset psychotic disorder) or (chronic alcoholic brain syndrome [& dementia NOS]
		192215003	Mental and behavioral disorders due to use of alcohol: other mental and behavioral disorders

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			(disorder)
		268639004	Chronic alcoholism (disorder)
		268683008	Mental and behavioral disorders due to use of alcohol: dependence syndrome (disorder)
		268684002	Mental and behavioral disorders due to use of alcohol: psychotic disorder (disorder)
		304606004	Ethanol abuse (finding)
		268685001	Mental and behavioral disorders due to use of alcohol: residual and late-onset psychotic disorder (disorder)
		192216002	Mental and behavioral disorders due to use of alcohol: unspecified mental and behavioral disorder (disorder)
		160592001	Alcohol intake above recommended sensible limits
		191806001	Acute alcoholic intoxication in remission, in alcoholism

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
G31.2	303	192811002 133301000119102 300992002 361272001 135761000119101 230353003 361273006	Alcoholic encephalopathy Degenerative brain disorder due to alcohol Alcohol-induced cerebellar ataxia Cerebellar ataxia due to alcoholism Cerebral degeneration due to alcoholism Morel laminar sclerosis Alcoholic cerebellar degeneration
G62.1	357.5	192811002 69482004 191471000 7916009 191472007	Alcoholic encephalopathy Korsakoff's psychosis Korsakov's alcoholic psychosis with peripheral neuritis Alcoholic polyneuropathy #Wernicke-Korsakov syndrome (disorder)
G72.1	*No alcohol-specific code available*	19303008	Alcohol myopathy

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
I42.6	425.5	83521008	Dilated cardiomyopathy caused by alcohol
K29.2	535.3	2043009 40241000119109	Alcoholic gastritis Gastric haemorrhage due to alcoholic gastritis
K70.0 K70.1 K70.2 K70.3 K70.4 K70.9	571.0 571.1 571.2 571.3 	50325005 9953008 235875008 307757001 235880004 309783001 420054005 1085021000119106 235881000 1082611000119101 41309000 307757001 235880004 420054005	Alcoholic fatty liver Acute alcoholic liver disease Alcoholic hepatitis Chronic alcoholic hepatitis Alcoholic fibrosis and sclerosis of liver Acute alcoholic liver disease Alcoholic cirrhosis Hepatic ascites due to chronic alcoholic hepatitis Alcoholic hepatic failure Ascites due to alcoholic hepatitis Alcoholic liver damage Chronic alcoholic hepatitis Alcoholic fibrosis and sclerosis of liver Alcoholic cirrhosis

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		309783001	Oesophageal varices in alcoholic cirrhosis of the liver
		1082601000119104	Ascites due to alcoholic cirrhosis
		1082621000119108	Hepatic coma due to alcoholic liver failure
		713370005	Acute on chronic alcoholic liver disease
		713181003	Chronic alcoholic liver disease
K85.2	*No alcohol-specific code available*	235942001	Alcohol-induced acute pancreatitis
		445507008	Alcohol-induced pancreatitis
K86.0	*No alcohol-specific code available*	235952002	Chronic pancreatitis due to acute alcohol intoxication
		154211000119108	Chronic pancreatitis due to chronic alcoholism
R78.0	790.3	442766007	Alcohol in blood specimen above reference range
		442669008	Ethanol in blood specimen above legal threshold for operating vehicle

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		441685000	Ethanol in blood specimen above reference range
		274776000	Finding of alcohol in blood
		207273009	Alcohol blood level excessive (situation)
		160592001	Alcohol intake above recommended sensible limits
T51	980	216633005	Accidental poisoning by alcoholic beverage
		216635003	Accidental poisoning by denatured alcohol
		95906008	Drug interaction with alcohol
		287166006	Accidental poisoning with ethyl alcohol
		442764005	Poisoning by benzene
		82782008	Alcohol poisoning
		212807002	Grain alcohol causing toxic effect
		216636002	Accidental poisoning by methylated spirit
		315226008	Pain in lymph nodes after alcohol consumption
		89507002	Toxic effect of denatured alcohol

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		25966003	Metabolic acidosis due to methanol
		212809004	Methyl alcohol causing toxic effect
		216640006	Accidental poisoning by methanol
		212813006	Toxic effect of isopropyl alcohol
		6749002	Toxic effect of propyl alcohol
		216645001	Accidental poisoning by isopropyl alcohol
		216648004	Accidental poisoning by rubbing alcohol substitute
		4953006	Toxic effect of butyl alcohol
		6749002	Toxic effect of propyl alcohol
		57346004	Toxic effect of fusel oil
		216651006	Accidental poisoning by fusel oil
		87460008	Toxic effect of amyl alcohol
		67426006	Toxic effect of alcohol
		82047000	Diarrhoea due to alcohol intake
		314539001	Alcohol related optic neuropathy
		269765000	Accidental poisoning by alcohol
		212816003	Rubbing alcohol causing toxic

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			effect (disorder)
		212817007	Isopropyl alcohol causing toxic effect NOS (disorder)
		212818002	Fusel oil causing toxic effect NOS (disorder)
		212819005	Other alcohol causing toxic effect (disorder)
		212820004	Alcohol causing toxic effect NOS (disorder)
		213687005	Toxic effect of other alcohols (disorder)
		212815004	Isopropanol causing toxic effect (disorder)
		212814000	Dimethyl carbinol causing toxic effect (disorder)
		212811008	Wood alcohol causing toxic effect (disorder)
		212808007	Ethyl alcohol causing toxic effect NOS (disorder)
		212806006	Ethyl alcohol causing toxic effect (disorder)
		699208000	Thrombocytopenia due to

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			alcohol
X45	E860	212813006	Toxic effect of isopropyl alcohol
		216640006	Accidental poisoning by methanol
		82782008	Alcohol poisoning
		216635003	Accidental poisoning by denatured alcohol
		6749002	Toxic effect of propyl alcohol
		212809004	Methyl alcohol causing toxic effect
		242263000	Accidental exposure to alcohol
		216633005	Accidental poisoning by alcoholic beverage
		212813006	Toxic effect of isopropyl alcohol
		242265007	Accidental exposure to ethanol
		278363000	Alcoholic macrocytosis
		442764005	Poisoning by benzene
		4953006	Toxic effect of butyl alcohol
		287166006	Accidental poisoning with ethyl alcohol
		699208000	Thrombocytopenia due to alcohol

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		212809004	Methyl alcohol causing toxic effect
		67426006	Toxic effect of alcohol
		6749002	Toxic effect of propyl alcohol
		216645001	Accidental poisoning by isopropyl alcohol
		89507002	Toxic effect of denatured alcohol
		212807002	Grain alcohol causing toxic effect
		216648004	Accidental poisoning by rubbing alcohol substitute
		216651006	Accidental poisoning by fusel oil
		216636002	Accidental poisoning by methylated spirit
		89507002	Toxic effect of denatured alcohol
		442764005	Poisoning by benzene
		87460008	Toxic effect of amyl alcohol
		269765000	Accidental poisoning by alcohol
		57346004	Toxic effect of fusel oil
		221843007	Accidental poisoning by and exposure to alcohol, occurrence at home (event)
		221844001	Accidental poisoning by and

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			exposure to alcohol, occurrence in residential institution (event)
		221845000	Accidental poisoning by and exposure to alcohol, occurrence at school, other institution and public administrative area (event)
		221846004	Accidental poisoning by and exposure to alcohol, occurrence at sports and athletics area (event)
		221847008	Accidental poisoning by and exposure to alcohol, occurrence on street and highway (event)
		221848003	Accidental poisoning by and exposure to alcohol, occurrence at trade and service area (event)
		221849006	Accidental poisoning by and exposure to alcohol, occurrence at industrial and construction area (event)
		221850006	Accidental poisoning by and

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			exposure to alcohol, occurrence on farm (event)
		221851005	Accidental poisoning by and exposure to alcohol, occurrence at other specified place (event)
		221852003	Accidental poisoning by and exposure to alcohol, occurrence at unspecified place (event)
		57346004	Toxic effect of fusel oil
X65 (*note that no generalised mapping matches were available with SNO-MED although lexical matching suggest use of the above codes*)	*No alcohol-specific code available*	222103001	Intentional self-poisoning by and exposure to alcohol (event)
		222104007	Intentional self-poisoning by and exposure to alcohol, occurrence at home (event)
		222105008	Intentional self-poisoning by and

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			exposure to alcohol, occurrence in residential institution (event)
		222106009	Intentional self-poisoning by and exposure to alcohol, occurrence at school, other institution and public administrative area (event)
		222107000	Intentional self-poisoning by and exposure to alcohol, occurrence at sports and athletics area (event)
		222108005	Intentional self-poisoning by and exposure to alcohol, occurrence on street and highway (event)
		222110007	Intentional self-poisoning by and exposure to alcohol, occurrence at trade and service area (event)
		222111006	Intentional self-poisoning by and exposure to alcohol, occurrence at industrial and construction area (event)
		222112004	Intentional self-poisoning by and

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			exposure to alcohol, occurrence on farm (event)
		222113009	Intentional self-poisoning by and exposure to alcohol, occurrence at other specified place (event)
		222114003	Intentional self-poisoning by and exposure to alcohol, occurrence at unspecified place (event)
		312963001	Methanol retinopathy
Y15	E860	222702003	Poisoning by and exposure to alcohol, undetermined intent (event)
	980	222703008	Poisoning by and exposure to alcohol, occurrence at home, undetermined intent (event)
		222704002	Poisoning by and exposure to alcohol, occurrence in residential institution, undetermined intent (event)
		222705001	Poisoning by and exposure to alcohol, occurrence at school, other institution and public

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			administrative area, undetermined intent (event)
		222706000	Poisoning by and exposure to alcohol, occurrence at sports and athletics area, undetermined intent (event)
		222707009	Poisoning by and exposure to alcohol, occurrence on street and highway, undetermined intent (event)
		222708004	Poisoning by and exposure to alcohol, occurrence at trade and service area, undetermined intent (event)
		222709007	Poisoning by and exposure to alcohol, occurrence at industrial and construction area, undetermined intent (event)
		222710002	Poisoning by and exposure to alcohol, occurrence on farm, undetermined intent (event)
		222711003	Poisoning by and exposure to

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			alcohol, occurrence at other specified place, undetermined intent (event)
		222713000	Poisoning by and exposure to alcohol, occurrence at unspecified place, undetermined intent (event)
		274776000	Finding of alcohol in blood
Y90 (*note that no generalised mapping matches were available with SNO-MED although lexical matching suggest use of the 'Finding of alcohol in blood' code*)	*No alcohol-specific code available*	223333005	Evidence of alcohol involvement determined by blood alcohol level (navigational concept)
		223334004	Evidence of alcohol involvement determined by blood alcohol level of less than 20 mg/100 ml (navigational concept)

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
		223335003	Evidence of alcohol involvement determined by blood alcohol level of 20-39 mg/100 ml (navigational concept)
		223336002	Evidence of alcohol involvement determined by blood alcohol level of 40-59 mg/100 ml (navigational concept)
		223337006	Evidence of alcohol involvement determined by blood alcohol level of 60-79 mg/100 ml (navigational concept)
		223338001	Evidence of alcohol involvement determined by blood alcohol level of 80-99 mg/100 ml (navigational concept)
		223339009	Evidence of alcohol involvement determined by blood alcohol level of 100-119 mg/100 ml (navigational concept)
		223340006	Evidence of alcohol involvement determined by blood alcohol

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			level of 120-199 mg/100 ml (navigational concept)
		223341005	Evidence of alcohol involvement determined by blood alcohol level of 200-239 mg/100 ml (navigational concept)
		223342003	Evidence of alcohol involvement determined by blood alcohol level of 240 mg/100 ml or more (navigational concept)
		223343008	Evidence of alcohol involvement determined by presence of alcohol in blood, level not specified (navigational concept)
		25702006	Alcohol intoxication
Y91 (*note that generalised mapping matches were only available for Y91.1 and Y91.9 with SNO-MED*	*No alcohol-specific code available*	230800004	Alcoholic coma

ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
although lexical matching suggest use of 'Alcohol intoxication' code)			
		82047000	Diarrhoea due to alcohol intake
		361267005	Alcohol-related fit
		223344002	Evidence of alcohol involvement determined by level of intoxication (navigational concept)
		223345001	Evidence of alcohol involvement determined by level of intoxication, mild alcohol intoxication (navigational concept)
		223346000	Evidence of alcohol involvement determined by level of intoxication, moderate alcohol intoxication (navigational concept)
		223347009	Evidence of alcohol involvement determined by level of

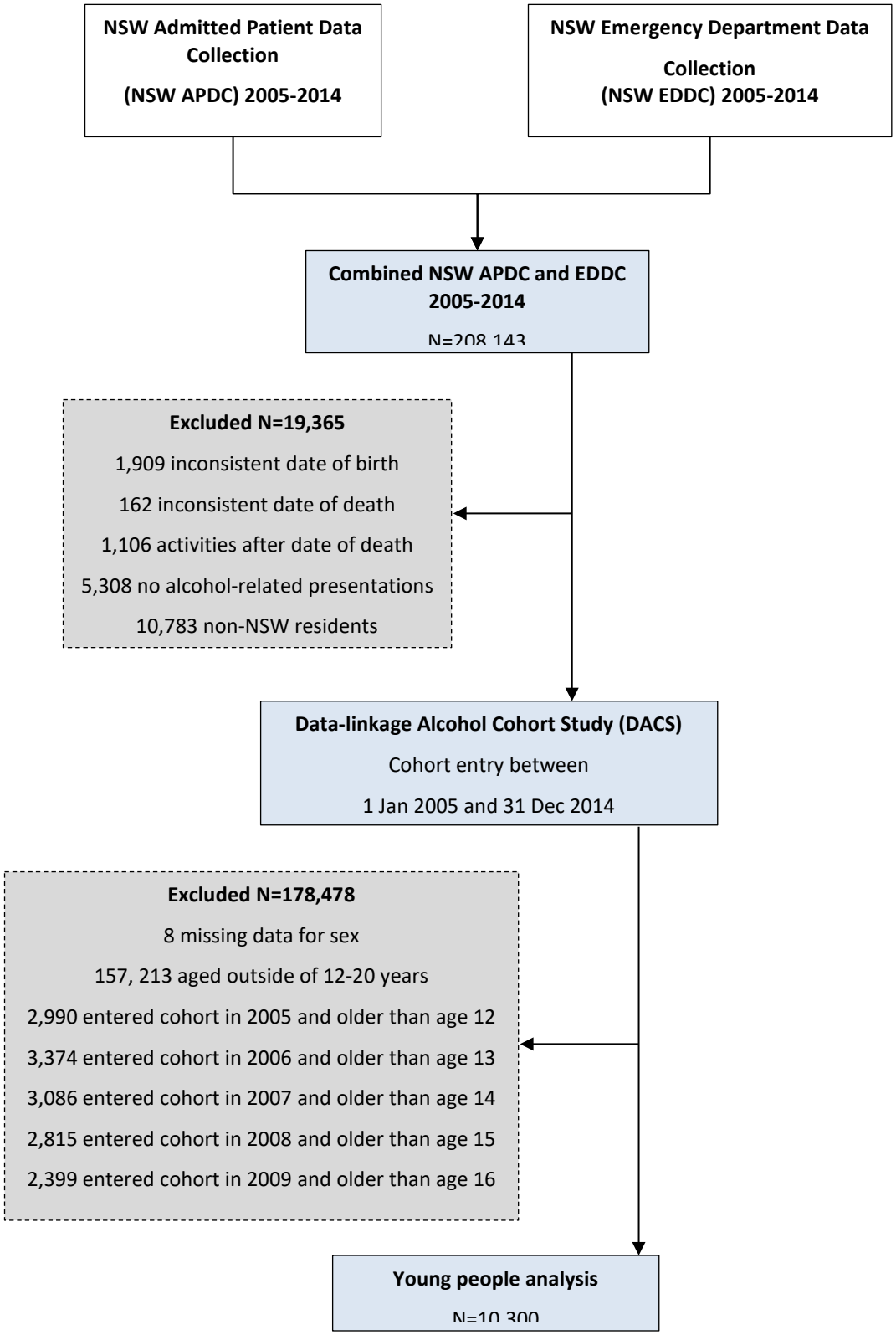
ICD-10-AM	ICD-9-CM	SNOMED-CT-AU	Condition
			intoxication, severe alcohol intoxication (navigational concept)
		223348004	Evidence of alcohol involvement determined by level of intoxication, very severe alcohol intoxication (navigational concept)
		223349007	Evidence of alcohol involvement determined by level of intoxication, alcohol involvement, not otherwise specified (navigational concept)

7.4.2. Appendix D2. Number of patients entering the cohort each year from 2005 to 2013 by age at cohort entry.

	Year of cohort entry									
Age at cohort entry (years)	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**Total**
12	10	18	13	13	12	12	*	10	11	108
13	-	51	61	68	62	72	46	46	38	444
14	-	-	156	173	196	164	143	150	126	1108
15	-	-	-	288	297	254	220	280	257	1596
16	-	-	-	-	395	385	324	316	341	1761
17	-	-	-	-	-	433	366	433	395	1627
18	-	-	-	-	-	-	626	683	681	1990
19	-	-	-	-	-	-	-	550	587	1137
20	-	-	-	-	-	-	-	-	529	529
Total	10	69	230	542	962	1320	1734	2468	2965	10300

Note. * = suppressed due to low cell size (n < 10).

7.4.3. Appendix D3. Flowchart of cohort formation.



7.4.4. Appendix D4. List of ICD-10-AM and SNOMED-CT-AU codes for subsequent 12-month ED presentations and hospital separations.

Category	ICD-10-AM	SNOMED-CT-AU	Condition
Alcohol-specific	*See Appendix A above*		
Other substance-specific	F11	5602001 14784000 52866005 75544000 77721001 87132004 191819002 231477003 231478008 231479000 426001001 428819003 429512006	Mental and behavioural disorders due to use of opioids
	F12	23527004 26714005 37344009 39807006 39951001 63649001 77355000 85005007 191838006 191839003 191891003 268641003 428823006 703848005	Mental and behavioural disorders due to use of cannabinoids

Category	ICD-10-AM	SNOMED-CT-AU	Condition
	F13	231473004	Mental and behavioural disorders due to use of sedatives
	F14	27956007 31956009 46975003 51493001 78267003 80868005 429782000	Mental and behavioural disorders due to use of cocaine
	F15	45421006 8837000 84758004 21647008 428370001	Mental and behavioural disorders due to use of other stimulants, including caffeine
	F16	-	Mental and behavioural disorders due to use of hallucinogens
	F17	56294008 90755006	Mental and behavioural disorders due to use of tobacco
	F18	60901005 105549004 426095000 191853003 191856006	Mental and behavioural disorders due to use of volatile solvents
	F19	2403008 6525002 9769006 11061003 11387009 26416006 28368009 32709003	Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		43242008 50026000 51339003 66214007 70545002 74934004 84584008 88320008 91388009 105546006 110281001 191483003 191484009 191485005 191486006 191492000 191494004 191495003 191496002 191816009 191865004 191873008 191939002 228371004 228372006 228373001 228375008 228438002 231451006 231466009 231481003 231482005	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		247702001 361049005 361055000 363101005 363314000 365984004 396344000 416119007 425533007 426590003 429299000 429672007 442351006 445273005	
	T40.1	13187008 216463005 242829007 290182008 290183003 295174006 295175007 295176008	Poisoning by heroin
	T40.2	242828004 295165009 295170002 295171003 295172005 295173000 295184007 295186009	Poisoning by other opioids
	T40.3	60199004 216464004	Poisoning by methadone

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		242831003 295161000 295163002 295164008	
	T40.4	295154004 295167001 295169003 295190006 295193008 295194002	Poisoning by other synthetic narcotics
	T40.5	290544006 290545007 296321004 296322006 296323001	Poisoning by cocaine
	T40.6	11196001 242253008 290220008 290221007 290222000 295213004 297199006	Poisoning by other and unspecified narcotics
	T43.6	-	Poisoning by psychostimulants with abuse potential
	T43.8	-	Poisoning by other psychotropic drugs, not elsewhere classified
	T43.9	-	Poisoning by psychotropic drug, unspecified
Non-substance mental disorder	F20	4926007 12939007 16990005 26025008	Schizophrenia

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		29599000 30336007 31658008 35218008 35252006 46153004 58214004 64905009 71103003 79204003 79866005 83746006 88975006 102909009 111483008 111484002 191526005 191527001 191530008 191531007 191538001 191539009 191542003 191548004 191554003 191555002 231485007 247917007	
	F22	216004 2073000 48500005 64514005	Persistent delusional disorders

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		67348001 82791007 89809008 191667009 191668004 225452001 231487004 238973003 247667002 247677000 268622001 276243003 416611006 417233008 427975003	
	F23		Acute and transient psychotic disorders
	F24		Induced delusional disorder
	F25	38368003 68890003 84760002 191567000 191570001 191571002 191572009 270901009 271428004	Schizoaffective disorders
	F28	73917004	Other nonorganic psychotic disorders
	F29	69322001 191525009 280427006	Unspecified nonorganic psychosis

Category	ICD-10-AM	SNOMED-CT-AU	Condition
	F30	191586008 191595000 191658009 231494001 231496004 268619003 281257007 284512001 405273008	Manic episode
	F31	1196001 4441000 5703000 9340000 13313007 13746004 20960007 26530004 31446002 41836007 48937005 49468007 51637008 53049002 54761006 68569003 71294008 75752004 79584002 82998009 83225003 85248005 111485001	Bipolar affective disorder

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		191590005 191618007 191620005 191621009 191623007 191625000 191627008 191629006 191630001 191632009 191634005 191636007 191639000 191641004 192362008 371596008 371599001 371600003	
	F32	48589009 79298009 310495003 310496002 832007 30605009 70747007 83458005 87512008 310497006 320751009 370143000 73867007 77911002	Depressive episode

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		191676002 192080009 413296003 35489007 36923009 87414006 162722001	
	F33	28475009 66344007 191616006 268621008 274948002 300706003	Recurrent depressive disorder
	F40	19887002 25501002 54587008 102916005 102932008 191733007 225631001 247822006 247832004 277820005 277821009 277822002 277824001 277826004 277827008 277829006 386808001 386810004	Phobic anxiety disorders
	F41	5874002	Other anxiety disorders

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		11458009 21897009 35429005 36646009 37868008 48694002 61387006 70997004 79823003 80583007 126943008 129869000 162723006 191708009 191709001 197480006 198288003 207363009 225624000 225635005 225636006 225637002 225642005 225644006 231502005 231503000 231504006 231506008 247808006 247825008 277823007 277828003	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		277833004 277834005 300894000 300895004 304896009 371631005 395017009 417676004	
	F42	67698009 191736004 247963001 271559000 271953006 373658006 416661002	Obsessive-compulsive disorder
	F43	9674006 17226007 32937002 39093002 47372000 47505003 53339009 55668003 57194009 66381006 67195008 84984002 162218007 162318009 192037000 192041001 192042008	Reaction to severe stress, and adjustment disorders

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		192044009 192046006 192056005 192057001 225021007 271952001 300979000 309838005 313182004 317816007 386822001 423136007 428687006	
	F44	3586005 20734000 44376007 88984006 191677006 191713008 191714002 246537007 246538002 276300008	Dissociative disorders
	X70 X71 X78 X79 X80 X81 X82 X83 X84	274228002 269808005 287189003 288311002 287181000 287190007 287182007 287183002 287184008	Self-harm

Category	ICD-10-AM	SNOMED-CT-AU	Condition
	Y87.0	287193009 287185009 287194003 287186005 287195002 36153001 44301001 53846008 55554002 82313006 418420002	
Other injuries of external causes	S00-S99	274181002 210989006 271109002 60506006 211022009 22562004 429059007 439461004 231814009 423145008 63943002 110165004 231815005 283050005 431583000 269210000 283027004 283052002 72512006 86821006 60897004	Injury to body (incl. specified and unspecified body regions)

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283026008 283051009 283070004 283325003 44921007 283144003 85140006 110245004 50228009 76362004 3097002 40194002 10920005 110159004 262630008 262632000 2825006 47222000 63811003 30888005 13114007 45974008 284584006 6045004 110248002 110250005 110252002 110256004 110258003 262635003 262637006 262643008	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		262649007 262653009 262654003 64458007 211024005 274180001 44422006 110164000 210987008 110166003 110168002 111703006 283053007 66176005 66578000 75767000 271107000 70166002 211008009 283148000 423428008 4821001 52945003 125668004 110237009 110240009 110242001 110243006 110244000 110247007 110249005 307214007	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		423051001 210985000 283025007 283049005 283115000 283321007 262528003 110067005 274166008 110068000 110069008 110070009 210323002 283399001 60076001 71491003 231816006 314535007 110032005 110033000 110034006 14997005 210343008 21051006 231817002 231845008 262749000 269164007 283360009 314536008 447350003 373602003	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		110072001 110074000 110076003 210325009 283692004 283742006 283361008 11386000 210294003 283403005 283691006 283741004 32550009 50683006 110064003 110062004 110063009 110065002 110066001 110037004 283362001 110038009 110039001 110042007 110044008 210341005 283454005 283693009 283743001 210345001 210358000 283355005	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283744007 312655004 74066007 262628006 283363006 20509003 210344002 262662006 29256009 446896007 110099004 110100007 110101006 262627001 210361004 286622004 110084004 110086002 110087006 110089009 110091001 135874008 210363001 262659008 286623009 110130004 110094009 110096006 210347009 110052006 110055008 110077007	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		210339009 283359004 283738008 284476005 370247008 110047001 110049003 110053001 110054007 110057000 110058005 110059002 110060007 110078002 110079005 110080008 210342003 2419001 283400008 283401007 283450001 283501005 283502003 283687001 283792007 313261004 73973007 79167003 38354005 262544007 283192003 283398009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283499002 283685009 283736007 283790004 40883004 428088000 775008 111593004 207705002 25424007 445493000 48466003 69866009 83385002 24063002 111601003 127281000 127284008 1739001 232277004 232279001 263149000 27644009 38567007 428099003 55798004 76542006 83969004 81639003 263171005 232375005 40613008	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		413878002 414944000 427773004 427904000 207787008 263167007 3421000 49346003 110017003 110018008 110019000 110020006 110021005 110023008 110024002 110027009 207782002 207788003 263151001 263156006 263157002 263158007 263161008 263163006 263164000 263165004 269057007 31187005 34649000 44916009 4788002 63669006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		65648007 84111004 109683005 109747007 109748002 109751009 109752002 109753007 210374005 263270004 269166009 36202009 66517001 207753003 263172003 207755005 23611004 429194003 86559007 207759004 207771005 263173008 263174002 76174009 263175001 263064003 69425000 207763006 207776000 20714001 207785000 207881000	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		263152008 49128003 56863004 297158000 263162001 263168002 263169005 263170006 95851007 27477003 95850008 111609001 111611005 111613008 371161001 371162008 418764009 430984009 4807003 71642004 77295000 302964004 34622000 8135006 81629009 232376006 249358001 109671008 109678002 210366009 23415000 304838007	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		1852004 53933002 85848002 231863008 314506004 371123004 164033006 21549001 231864002 231867009 371066008 371124005 417750006 62635000 110262009 211483007 231954005 42697001 95799000 231795004 231791008 231851003 231852005 44199000 315296002 12193006 284691000 41658006 78598000 367423000 231878001 231939004	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		231950001 231956007 231980006 404649002 416713004 416952000 80744008 95725002 314533000 231794000 262754009 282752000 85100000 110030002 62106007 76418009 127298000 282750008 62564004 127299008 311825006 262693007 209834008 209922004 262689001 34663006 90768003 127304009 32415004 51101002 450418003 25689009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		262691009 78914008 91589002 23713006 5886004 262949005 315048006 315049003 43216008 82999001 209947002 209987007 26205001 262952002 315046005 371050006 40135004 428561000 87345009 209940000 262955000 28048009 35672006 111668007 111671004 127301001 127308007 127309004 18485009 301764006 37955001 431266005	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		78477003 54355006 127294003 127295002 127302008 207728001 275382005 28188001 39020005 53267002 79228001 9015001 283854002 67070005 90465004 262576002 110071008 210305005 212451003 307497002 212483009 29264003 57998008 58020007 284575006 95817008 21763005 82271004 125593007 274164006 282756002 397869004	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		404199004 109746003 127276009 19491003 212400009 231813003 262758007 282448001 282449009 282751007 282754004 282755003 282757006 282758001 282781004 282783001 284002000 285059008 285661003 2999009 314661000 314662007 33931005 38372004 427782005 429433004 430937009 65759007 95848000 211476000 283029001 283056004	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		271113009 429174007 262773008 274182009 9375000 283055000 211009001 283151007 424959007 59212007 447220009 8513005 210386008 110141002 210395000 275489000 110135009 283356006 283365004 283364000 110144005 110146007 110148008 125644007 283457003 283508004 283745008 428152007 85336009 263180005 11782000 207984009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		269064009 281910003 269066006 87804006 269068007 21573009 13498003 207985005 208122008 32497008 8840000 125606003 207906009 207907000 207908005 207909002 208001004 269062008 274153008 274156000 281914007 281915008 281918005 31235003 53868003 61386002 78687007 209134006 44264009 11008006 209137004 209048009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		360444002 39848009 405561009 209557005 445760005 262697008 405754008 405759003 282787000 405757001 405758006 405755009 212197005 212202003 212205001 74297002 95671001 6836001 6956001 210779003 262937009 212399002 360437006 360450007 283856000 50001009 212486001 262522002 90460009 125588009 125591009 282759009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		58189007 111722002 211056003 10050004 428016006 429665006 431044006 211042000 38484003 211153009 274187003 30223005 36990001 211039006 283090008 7739007 271118000 5473002 86926000 211104009 39573000 210454002 283376000 21441000 269169002 274171001 283422001 283472004 283523009 283760006 370241009 274167004	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		127314000 210407001 283473009 283524003 283816002 370242002 61196003 125607007 14493003 18960007 207938004 207939007 207940009 208029001 208034002 263071008 274154002 281922000 281923005 281924004 44434003 72513001 78211006 89825003 208215006 311814002 263256004 66112004 78516000 33737001 45356009 60667009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		20274005 12204004 1261007 28081005 3291007 31693001 57577003 79546008 17633000 20121009 39335003 51760006 68650003 89636007 90863004 311408004 78011002 129165008 209075002 125612008 209122003 209218003 263259006 274162005 66540002 209799008 209807005 28238002 54942004 59201007 430894003 36838006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		212210002 233888009 17414004 262782002 210060006 86175003 3903005 22897006 90070003 33072005 42458003 44599007 42434002 59190009 262784001 48424004 282726006 233746005 210087005 262790002 262792005 262793000 307218005 320934008 33847006 211547001 212456008 438505003 212487005 432754003 282770002 262523007	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		262525000 282767001 282768006 282769003 422916003 62112002 65978000 211492005 276465001 283137007 284062002 68893001 307390004 211486004 308154003 37907001 447096000 60211009 14992004 23287003 237331002 307579008 36160007 39716001 89966002 274183004 283039007 29440002 49435000 62586003 211048001 18823009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		211041007 211043005 211046002 211051008 211063003 211064009 283061002 300935003 35655004 90947008 17039000 271127004 271143006 34403004 452002 211110009 35057008 10868000 211144002 283259002 43263005 45822009 283037009 439598000 283351001 210421004 210483004 210484005 237339000 269170001 283383007 283431001	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283532006 283631009 283768004 5715001 8577002 91325009 16809003 210456000 210457009 210469001 210472008 269172009 274170000 67267004 285399003 135869000 210426009 210427000 283949007 285398006 210430007 210434003 283945001 283954003 237332009 249221003 262935001 274169001 410062001 283381009 283529008 283717002	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		212488000 283475002 275431006 282077009 283378004 283526001 283762003 443183003 20784007 125608002 207957008 281932007 281933002 17463000 207958003 207959006 207962009 208054001 274158004 281934008 281936005 281937001 426646004 125872003 207974008 125871005 17616007 208184007 263217005 39408006 426679004 7687006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		208150008 33118001 64455005 13695006 208164008 208165009 208166005 263218000 263219008 301032005 301033000 36127009 207986006 207993005 59962009 263220002 263221003 77493009 15474008 209390009 91037003 263222005 209180008 129164007 49891002 263012009 209548004 309710005 12519004 209565008 209566009 209571002	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		209810003 209812006 262524001 24300005 230614002 405753002 212359000 10392004 56515006 14180000 210180009 234506007 234507003 23589004 210190001 262820001 262822009 262823004 210192009 61014001 43756009 15151004 39400004 262799001 431674004 262802005 13891000 210176004 235887001 262804006 262827003 61823004	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		125626004 262841007 64834002 262845003 125629006 50008003 210130003 262885009 47771009 49011004 210197003 40095003 210206008 262891006 70092007 262893009 405584002 74324004 9264002 24850009 262898000 77165001 283916003 22724000 262913009 125638008 125637003 237090005 7395000 210260000 262833007 262682005	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		285834000 275420003 78508009 283859007 68565009 283952004 262965006 212457004 262962009 285348005 300956001 110016007 283170002 373596001 11805005 128069005 282766005 110015006 127277000 235999009 24257003 262921003 276464002 282764008 282771003 282772005 282782006 283976007 424270008 42479003 424863004 72073003	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		40257000 211500005 211501009 80907003 85636003 211235006 211189001 211192002 211197008 211200009 428167006 64831005 66371007 211215005 283156002 87843005 211186008 274191008 45915002 47117005 88212009 125645008 210502009 283367007 283460005 283748005 283369005 125648005 283462002 283513000 283701008 283750002	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		82085002 125647000 14649006 283368002 283749002 33173003 58150001 111637008 41972004 52784000 56642004 48561006 71039006 87376003 1658003 263099004 29749002 47864008 9682006 208227009 208228004 40643005 427803007 111639006 8704005 208225001 208229007 56299003 42636007 127286005 208240004 208244008	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		208245009 208250003 86844009 208254007 413875004 73244003 263191003 208241000 208242007 43295006 66308002 23741005 50890004 89294002 90235006 208272001 263192005 269080004 269081000 58580000 263193000 62356006 208267005 208271008 281525005 21419000 281526006 440366004 80767005 208273006 208285003 208270009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		208274000 209239005 209401004 263074000 263076003 209238002 209244003 209245002 263077007 275337006 416833005 417039001 417076003 125614009 125615005 208754006 22911007 263051004 269105005 263021005 263022003 46307004 269106006 125616006 208759001 208769007 208775003 263019000 263049003 209118008 263009006 3199001	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		209413009 209417005 275334004 74779009 209576007 27182002 209410007 212362002 47185005 7680008 212361009 429432009 10129005 210833003 307731004 209416001 86319008 209419008 262979003 210517008 428539005 212421009 281540007 211550003 211551004 211552006 211555008 2591000 40368002 202141001 202329003 263122000	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283154004 283197009 125594001 125595000 282760004 428192009 68152007 69301007 91613004 211504001 39812007 211290004 211252005 111712008 211250002 211251003 211256008 211257004 211258009 283081001 271161002 271166007 43956002 60298004 283157006 283158001 283248006 76348006 84485007 111713003 12250001 283032003	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283033008 283370006 125650002 283463007 283613008 283751003 446395003 61526004 85218007 212490004 283371005 125649002 210538002 210552000 210553005 283414008 283464001 283515007 283614002 283703006 283752005 283807001 445724000 58399008 6154004 85135003 302222008 208294009 208298007 209252000 209255003 209257006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		209258001 263078002 263203001 302232001 309464009 33041006 68819003 64902007 281528007 63948006 263195007 71139009 68854005 263196008 442448003 69427008 111641007 263197004 72497001 263204007 37449000 42760000 53792000 54556006 71555008 123973009 111640008 12676007 3228009 390986009 42945005 429655000	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		66246007 208322000 271576001 208309008 208312006 263207000 17222009 208325003 208326002 25529004 263199001 123971006 123972004 269083002 80411001 208321007 208340001 307713000 54645004 281527002 263208005 33192001 88116004 19259001 208513000 263206009 53627009 75857000 81966000 50397009 2295008 263205008	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		281530009 33141009 35442005 41036008 6163002 649002 78980006 28078000 65966004 91419009 125617002 208782004 2651006 417558002 95854004 208785002 3019000 208796005 4273008 208790004 209585007 405275001 263128001 209429001 269134004 442130003 209453007 209581003 212261007 212265003 62745008 212255009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		212258006 67279004 212270005 212271009 87450004 35709005 210837002 34173009 210855006 212459001 212462003 210543009 212458009 442265005 211565002 111693009 211563009 211564003 211566001 283198004 283199007 125596004 125597008 69787006 211515006 288286000 76437000 211514005 25546001 5662003 211506004 211509006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		211507008 211508003 211510001 211511002 48123002 211291000 211305001 211319001 283059006 211253000 211304002 211306000 211317004 211318009 211320007 283058003 283083003 283084009 373580004 40762003 271162009 271170004 271172007 283126006 283127002 34441006 74631009 76430003 287115001 211274004 283331000 283332007	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283334008 283348008 428762009 44352004 69743002 298083004 211311003 211312005 211325002 26363007 275454002 283163002 283201009 283202002 283203007 283204001 283205000 283250003 283290000 283293003 283294009 287116000 428363001 69531000 62573007 17415003 274192001 274193006 274194000 283034002 283035001 283036000	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		75504007 274172008 274173003 275457009 370243007 370245000 125653000 125654006 210579001 210580003 210597009 23777003 2630008 269177003 283419003 283420009 283520007 283521006 283619007 283664009 283665005 283708002 283709005 283757004 283758009 283812000 32348000 446361002 446456003 125655007 262545008 430981001	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		438480008 446314003 446451008 60959003 74196000 210599007 395002005 283373008 283374002 210535004 210563002 210564008 210573000 283417001 283418006 283467008 283518009 283519001 283617009 283706003 283755007 283756008 125652005 219152002 283372003 283415009 283517004 284549007 370244001 125651003 13736001 15550007	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		210560004 210565009 210571003 283416005 283465000 283466004 283516008 283616000 283661001 283705004 283753000 283754006 283809003 28547009 429418007 446393005 73059000 9798005 42818005 208371005 208370006 208372003 208373008 208374002 209271003 31975004 68076002 281513007 29014003 82065001 9468002 2012002	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		281517008 37633006 30632004 7585008 43767005 84030002 74465000 14916000 57114005 73316002 208369005 37174005 85922006 208375001 263211006 208390002 208403005 208420009 32311009 111642000 208396008 208404004 61653009 67730008 69916004 208405003 208406002 208408001 208393000 208401007 1370007 208394006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		208418006 54641008 208397004 263209002 55716004 698056009 46422008 78292000 7551007 208399001 263210007 3331008 55874001 208400008 208417001 9275003 208402000 208441003 208436006 208437002 208438007 208443000 209308006 209316002 263086002 274160002 208434009 208435005 208467008 208471006 297133005 208439004	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		208440002 208472004 208474003 208475002 297132000 18171007 405817008 208463007 209302007 209318001 21698002 22713002 24424003 263085003 417474005 208444006 297130008 208445007 208446008 208447004 208448009 208449001 208477005 208478000 209307001 208450001 14505003 208451002 208452009 208453004 208454005 208455006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		208483008 208484002 208485001 208487009 208488004 297131007 76865005 208456007 208457003 208458008 208459000 208489007 208490003 208491004 208492006 208493001 36778005 41511005 416176009 208430000 208461009 68360003 76974008 20511007 37418005 208388003 208499002 208500006 209263002 209264008 209265009 209268006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		209273000 209283001 209287000 209304008 263079005 307171000 125618007 12588000 208811007 38556006 57467003 20026002 208818001 208842002 281503004 45634004 73387003 110029007 208820003 263026000 125619004 125620005 208866008 263054007 263055008 269111008 38301007 54420005 75137002 29818001 312844001 7669008	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		125802004 208873003 208881002 409765008 416143005 416352009 209492000 70704007 209469000 209441008 441702008 287097007 209612008 263129009 263130004 209479003 209464005 209470004 209472007 32128001 209473002 209482008 209485005 38540001 209471000 209480000 209481001 209483003 209484009 209496002 209499009 87778004	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		209463004 212269009 212274001 212284000 212282001 428233007 210843000 210838007 210848009 210845007 429421009 209497006 209498001 210583001 210596000 209775008 209502008 210549008 210585008 210594002 441885003 210584007 314665009 446313009 210569003 209494004 210550008 210566005 210567001 210568006 262971000 441932009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		10380004 211582000 211583005 211584004 211585003 211586002 211587006 283858004 211569008 211571008 211572001 211574000 211575004 211578002 211579005 47814001 50793006 210611002 210617003 210619000 125657004 210627009 210628004 210629007 210632005 210633000 210634006 210635007 262580007 262596005 50248002 95855003	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		210630002 8918008 247503008 263125003 282761000 282763002 422444006 423657003 439052006 441886002 52011008 125598003 125599006 282762007 262520005 427914009 44801007 307391000 84416003 211519000 211330003 211331004 211337000 211338005 56809002 61341000 271174008 85763007 211359003 446132009 49277003 274196003	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283384001 125658009 210665002 283482003 283769007 283770008 125659001 210666001 283385000 283483008 283534007 283633007 446455004 210772007 5913000 263225007 209335002 359820003 361119006 20100009 208528000 208529008 263226008 275338001 208521006 263227004 52450003 79484004 1705000 263228009 208526001 209337005	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		263088001 359817006 208548007 275340006 301034006 426382004 127287001 208550004 208552007 89820008 208551000 263229001 26442006 54441004 208579006 208580009 208582001 208591002 263232003 263233008 19652000 263236000 66926007 263235001 30905007 208581008 208590001 208731002 25415003 28576007 71620000 125621009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		157265008 208892001 63975004 17883008 86269002 7449006 52984008 429722003 209507002 209508007 210697002 415748002 212468004 262976005 135851009 209509004 262992000 212467009 281543009 430906009 212469007 11730002 211592008 74270009 125600009 7523003 22878006 211521005 45613006 211384000 211332006 211333001	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		211339002 211340000 271176005 271177001 271184009 86540005 211361007 283179001 283268000 283310003 283103004 446869009 283040009 283041008 283386004 125660006 283434009 283771007 44140000 446367003 212491000 283388003 283389006 283774004 283219000 283436006 283487009 283537000 283538005 125661005 283387008 210682000	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		210688001 210693003 210702006 283435005 283485001 283536009 283672006 283772000 283827000 80756009 111643005 208596007 208597003 208598008 208600002 208601003 209340005 209342002 209344001 263113001 307178006 428151000 51037009 208612003 23900009 111645003 20433007 208610006 208611005 208613008 208614002 263237009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		281843000 428256003 428257007 428798001 47848000 208629000 208631009 208632002 271577005 413877007 414293001 414943006 69166006 31978002 22234005 28012007 446979005 447139008 6990005 445410003 208634001 208635000 208636004 208637008 208638003 263240009 278537006 75591007 447395005 28359007 208615001 21867001	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		281533006 59639009 111646002 67394003 77803008 15385006 54530004 281531008 263242001 281535004 308153009 208657007 208658002 208659005 208660000 307727005 34268009 4673003 208732009 208662008 208663003 208664009 25899002 263244000 26908008 281532001 123975002 208666006 208668007 6698000 90338005 16114001	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		209348003 209349006 209350006 209351005 263089009 263091001 263115008 42188001 48187004 413876003 111644004 208627003 414292006 414942001 208929003 263029007 263059002 1544005 208959008 269112001 35106007 58320001 281504005 19494006 208915004 208917007 208921000 239720000 269113006 275326005 302932006 302933001	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		208976007 209515004 209517007 35726004 81902001 239728007 209626004 209519005 209627008 239729004 127292004 127293009 54888009 209625000 263139003 281523003 208977003 81884004 212317001 275335003 210698007 22817005 262988007 429513001 209523002 269138001 285395009 212471007 212472000 212473005 212470008 441933004	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		211597002 211599004 38128008 211596006 40874009 282773000 433162006 438582003 444158007 444159004 444448004 125601008 125602001 282774006 282775007 428881005 438479005 55042009 58075000 211438006 17048005 74814004 90244007 283138002 29298007 211385004 211334007 211341001 211402004 211403009 211406001 211407005	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		24328004 269202001 283134000 78360004 1525003 15290006 271185005 271188007 271189004 271191007 271192000 283132001 53960009 78561001 283354009 269205004 283341002 283353003 38189003 68765006 801006 211426002 211429009 211432007 283183001 283184007 283185008 283187000 283272001 283275004 283276003 283277007	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283314007 283315008 283316009 287121002 298105007 62516008 87711004 88524003 111715005 14158003 211400007 274195004 274199005 283046003 80691007 283390002 125662003 283222003 283775003 447419001 51639006 283677000 370239008 125664002 210729001 210730006 283391003 283440002 283441003 283541001 283640008 283678005	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283777006 284552004 54461005 88977003 210734002 275461003 276496005 430903001 446859003 283394006 284551006 125663008 17288006 210711006 210712004 210713009 210714003 210715002 210720002 210721003 210723000 283223008 283228004 283393000 283395007 283439004 283442005 283443000 283444006 283542008 283543003 283544009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		283639006 283676009 283680004 283776002 283779009 283834003 370240005 446359006 91368005 208677000 208678005 24948002 263247007 428018007 64665009 208684008 208685009 208686005 263246003 429664005 79626009 263245004 263248002 75308009 263249005 26646003 9808005 281536003 41977005 42306005 67422008 18724009	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		36924003 54013005 70204006 208687001 263251009 111647006 11254008 208688006 208689003 208690007 208701008 208702001 208703006 263252002 424648000 424817005 71790003 77551005 311821002 208719004 311822009 21351003 81576005 208710000 208711001 208712008 208713003 208715005 208716006 208717002 209359007 209375005	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		263093003 302036006 74395007 208691006 208733004 209360002 269100000 41608004 342070009 15574005 209353008 209354002 209357009 263092008 263250005 367527001 125622002 281506007 54394007 263030002 263062004 85646001 86899000 208994001 209536002 209633004 125623007 209013002 63141004 44465007 82788007 88906006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		24730004 209533005 307139007 74383007 263133002 209531007 209532000 209635006 262998001 209540006 24864009 49388007 212335005 210716001 212476002 209544002 210717005 430206002 281544003 212475003 66885008 74204001 65896005 211609000 283861003 74682007 211602009 211604005 211606007 283862005 43422002 65504006	

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		95858001 210706009 1378000 283224002 125603006 282776008 282777004 282780003 125604000 282778009 282779001	
	V01-V09	214206004 214218008 214227009 214230002 214744007	Pedestrian injured in transport accident
	V10-V99	386662004 386663009 214096002 242161009 297186008 216291004 214150008 214345006 214538005 214593004 242122001 127350007 214031005 242089005 277135009 418399005	Injured in transport accident (incl. pedal cyclist, motorcycle rider, vehicle occupant)

Category	ICD-10-AM	SNOMED-CT-AU	Condition
	W00-W19	288296009 17886000 86591008 2617007 82947003 49905000 1912002 40104005 68062003 78361000 217082002 225054009	Fall
	W20-W99 X00-X29 X50-X59	217898008 218017003 218073006 78427001 217835008 269794007 269795008 242605002 217876004 217879006 23361001 217706007 242635009 242648008 242649000 242650000 262551003 217756002 217748000 217399009	Other external causes of accidental injury (excl. poisoning)

Category	ICD-10-AM	SNOMED-CT-AU	Condition
		242430009 269776001 217571001 217585006 217176002 218141002 274924006 218135009 218138006 218144005 238457002 242627006 242592000 274920002 242598001 242594004 420008001 269703005 417981005 17542004 55566008	

Note. Only includes SNOMED-CT-AU codes that were identified in the cohort.

7.4.5. Appendix D5. RECORD Statement.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	In title and abstract.	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	In title and abstract.
Introduction					
Background rationale	2	Explain the scientific background and rationale for	In Background section (pg. 3-4).		

		the investigation being reported			
Objectives	3	State specific objectives, including any prespecified hypotheses	In Background section (pg. 4).		
Methods					
Study Design	4	Present key elements of study design early in the paper	In Methods section (pg. 4-7).		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	In Methods section (pg. 4-5).		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be	Diagnosis codes used to select the population are provided in Table 1 and Appendix A. Flow diagram in Appendix C.

		sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	In Measures section (pg. 6-7).	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Diagnosis codes used to classify the outcomes are provided in Appendix D.
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	In Measures section (pg. 6-7).		
Bias	9	Describe any efforts to address potential sources of bias	Potential biases identified in the		

			Limitations (pg. 12).		
Study size	10	Explain how the study size was arrived at	N/A		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	In Measures and Statistical analysis sections (pg. 6-7).		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of	In Statistical analysis section (pg. 7).		

		sampling strategy (e) Describe any sensitivity analyses			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	In methods section (pg. 4-6) and Appendix C.
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	In methods section (pg. 4-6).
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and	In Participants section (pg. 4-5).	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text	In Participants section (pg. 4-5).

		analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		and/or by means of the study flow diagram.	
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	In Results section (pg. 8) and Table 2.		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	In Results section (pg. 8-9) and Tables 2 and 3.		

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	In Results section (pg. 8-9) and Tables 2 and 3.		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	N/A		
Discussion					
Key results	18	Summarise key results with reference to study objectives	In Discussion section (pg. 9-10).		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	In Limitations section (pg. 12)	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility	In Limitations section (pg. 12)

				over time, as they pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	In Discussion section (pg. 9-12).		
Generalisability	21	Discuss the generalisability (external validity) of the study results	In Discussion section (pg. 9-12).		
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	In Funding section (pg. 13).		
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Supplemental information provided in appendices. The study protocol has been referenced in-text (#19) and is also accessible

					here: https://bmjopen.bmj.com/content/9/8/e030605