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ALCOHOLISM CLINICAL & EXPERIMENTAL RESEARCH

ORIGINAL ARTICLE

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

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Abstract

Background: Different forms of alcohol-related harm (e.g., hangovers, 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 characterized 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;

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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 heterogeneous 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.

KEYWORDS
adolescence, alcohol, alcohol use disorder, alcohol-related harm, transitions

INTRODUCTION

Alcohol use is the leading global risk factor for death and disability in young people aged 15 to 24 years (GBD 2016 Alcohol Collaborators, 2018; Mokdad et al., 2016). 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 (Australian Institute of Health & Welfare, 2020). Given that adolescents who engage in risky drinking tend to continue this behavior in adulthood (Lee et al., 2013; McCambridge et al., 2011; Windle, 2020), 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 (Aiken et al., 2020; Barnett et al., 2014; Lavikainen & Lintonen, 2009). Efforts to examine the risk and protective factors for alcohol-related harms have typically focused on harms in early adulthood (Little et al., 2013; Toumbourou et al., 2004). While 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 et al. (2018) found heterogeneous patterns of experiencing harms from late adolescence to adulthood in an Australian population cohort, identifying one group characterized by early onset of harms increasing until adulthood, and another group characterized 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 and 24 years (Mokdad et al., 2016), 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 (Rehm, 2001; Zinberg, 1986). Despite evidence that alcohol-related harms cluster into multiple factors (Bravo et al., 2019; Keough et al., 2016), many quantitative studies that examine alcohol-related harms aggregate factors (e.g., by summing the number of harms instead of separating by category; Little et al., 2013; McBride et al., 2004; McMorris et al., 2011; Toumbourou et al., 2004). Prince et al. (2019) reported that young adults with alcohol use disorder (AUD) experienced increasing alcohol-related consequences (e.g., passing out, interpersonal problems) each year in the 5 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.

MATERIALS AND METHODS

Participants and procedure

We used data from the Australian Parental Supply of Alcohol Longitudinal Study (APSALS; registered at ClinicalTrials.gov: NCT02280551) cohort, comprising 1927 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 minimize 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 Aiken et al., 2017 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 to 2011], Wave 3 [2012 to 2013], Wave 5 [2014 to 2015], Wave 7 [2016 to 2017], Wave 8 [2017 to 2018]; mean ages 12.9, 14.8, 16.9, 18.8, and 19.8 years, respectively; see Supplemental Information Appendix A 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 = 1828; 45.6% female). All findings are reported in accordance with STROBE guidelines (Supplemental Information Appendix B).

Measures

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 (Supplemental Information Appendix C; McBride et al., 2000). These items had six possible responses (12+ times, 5 to 11 times, 3 to 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 1 item not applicable to participants not attending school or postschool age (getting into trouble with teachers).

Alcohol abuse, alcohol dependence, and AUD

To measure alcohol abuse, we used four items adapted from the Diagnostic Interview Schedule for Children Version-IV (DISC-IV; Shaffer et al., 2000), corresponding to the Diagnostic and Statistical Manual of Mental Disorders, fouth edition (DSM-IV; American Psychiatric Association, 2000) symptoms of alcohol abuse. To measure alcohol dependence, we used seven 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; American Psychiatric Association, 2013) symptoms of AUD. Details of these items can be found in Supplemental Information Appendix D. 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 11 symptoms).

Wave 1 characteristics

We selected potential Wave 1 predictors of transitions in alcohol-related harms from a literature search (Supplemental Information Appendix E), consisting of: *child variables* (sex, externalizing), *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, 1/2 parent family, family history of alcohol problems, family conflict).

Statistical analysis

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

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 toward building the LTA model, we used latent class analysis (LCA) in Mplus version 8.3 (Muthén & Muthén, 1998–2017) to determine the number of latent statuses at each timepoint (Ryoo et al., 2018). 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 minimize the number of possible transition classes while 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 (Muthén & Muthén, 1998–2017). 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 (Degenhardt et al., 2016), 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; Lo et al., 2001) 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.

Regression analysis

Using Stata version 16 (StataCorp, 2019), 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 Supplemental Information Appendix F. 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 AUD at Wave 8, presented as RR (Zou, 2004). To align with recommendations to improve research reproducibility (Benjamin et al., 2018), 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 Supplemental Information Appendix G.

Missing data

As this is a longitudinal study, some participants had missing data from partial completion or failing to complete follow-up waves (summarized in Supplemental Information Appendix H). To reduce potential bias introduced by missingness, we imputed the data using an unrestricted H1 model (Asparouhov & Muthén, 2010) with Mplus version 8.3 (Muthén & Muthén, 1998–2017). Based on the percentage of missing information, we used $M = 20$ imputations (Graham et al., 2007). 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 Supplemental Information Appendix F) from each run of the LTA into Stata as a multiply imputed dataset for regression analyses.

Post hoc hierarchical logistic regression

While not outlined in the prepublished 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 modeled in the same cohort (Yuen et al., 2020) and research, suggesting that alcohol-related harms are highly related to heavy alcohol use (Bobak et al., 2004; Bye & Rossow, 2010; O'Dwyer et al., 2019). 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 modeled in Yuen et al. (2020)); 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 (McFadden, 1974) 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.

RESULTS

Sample characteristics

Table 1 shows the frequencies of the alcohol-related harms experienced at least once in a 12-month period at Waves 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.

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 Supplemental Information Appendix I. 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 1). Estimated proportions of Subclass 1 ($n \approx 1677$ at Wave 3; $n \approx 1231$ at Wave 5; $n \approx 405$ at Wave 7) had no more than 1%

TABLE 1 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 oncein 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%)

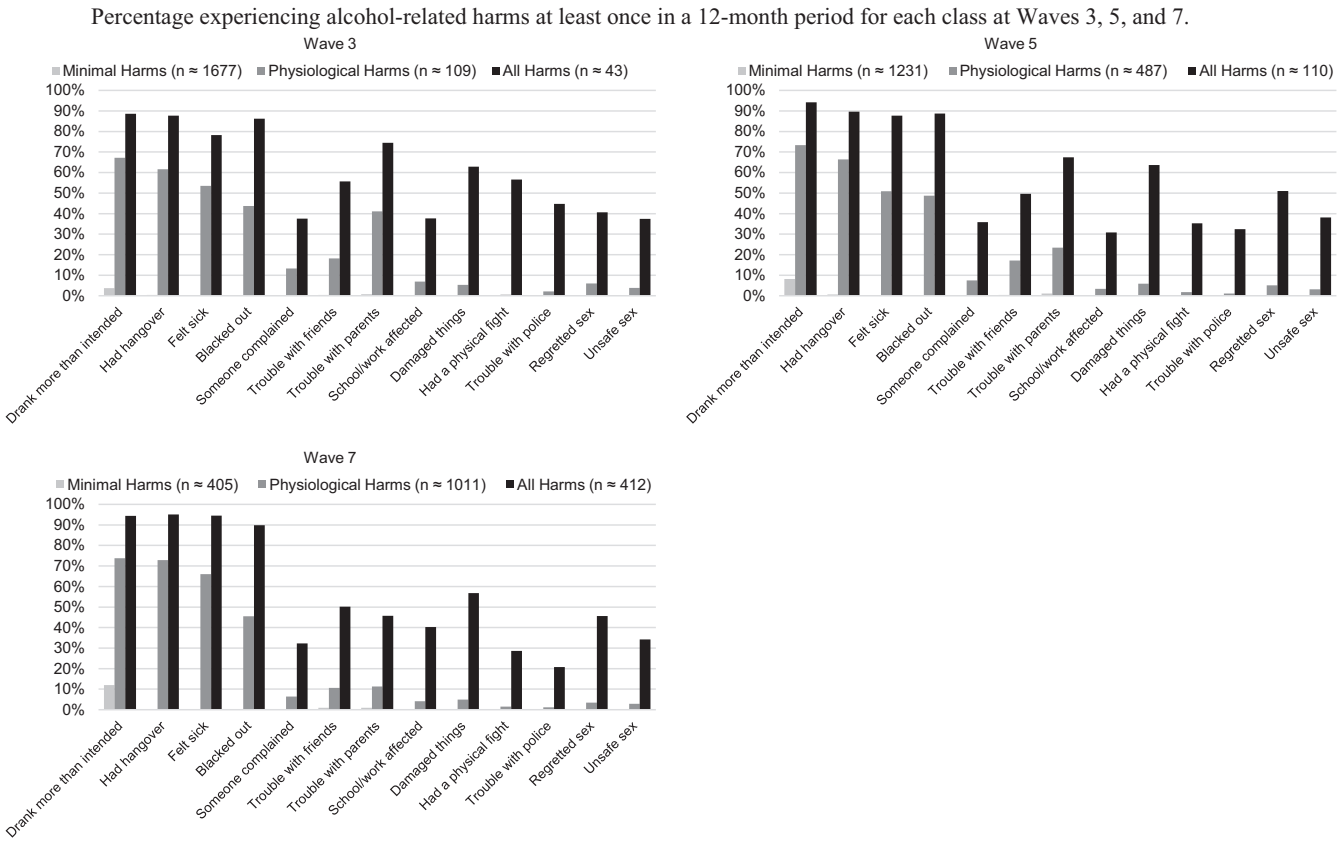

FIGURE 1 Percentage experiencing alcohol-related harms at least once in a 12-month period for each class at Waves 3, 5, and 7

of the subclass experiencing harms other than "drinking more than intended" at any timepoint and was thus labeled 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 labeled 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 labeled 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 3-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 2. Final class counts and proportions for these transition class patterns can be found in Supplemental Information Appendix J. 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 5 transition classes. These five transition classes were labeled as: (i) *minimal harms* (minimal harms across all timepoints; $n \approx 381$, 20.8%); (ii) *late escalation to physiological harms* (minimal harms in Waves 3 and 5, physiological harms in Wave 7; $n \approx 702$, 38.4%); (iii) *early escalation to physiological harms* (minimal harms in Wave 3, physiological harms in Waves 5 and 7; $n \approx 226$, 12.4%); (iv) *late escalation to all harms* (minimal harms in Waves 3 and 5, all harms in Wave 7; $n \approx 131$, 7.2%); (v) *gradual escalation to all harms* (minimal harm in Wave 3, physiological harms in Wave 5, all harms in Wave 7; $n \approx 169$, 9.2%).

Predictors of harms transition pattern

Results of the multivariable multinomial logistic regression model are presented in Table 3 (see Supplemental Information Appendix K 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 (Australian Institute of Health & Welfare, 2020) and experience of harms (Betts et al., 2018). 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 2 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

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 4 (see Supplemental Information Appendix L 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.

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 0.068 and the pseudo-R^2 for the full model including alcohol-related harms transition class was 0.142, with the harms transition classes contributing significantly to the model (χ^2 (1) = 186.79, $p < 0.001$). 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, $p < 0.001$). Adjusted logistic regression models including alcohol use trajectory membership showed the same trend of results to the planned AUD outcome models (Table 5).

DISCUSSION

We identified three distinct and consistent profiles of alcohol-related harms at ages 14 to 15, 16 to 17, and 18 to 19 years. These profiles were as follows: (i) *minimal harms*, (ii) *physiological harms* (i.e.,

TABLE 3 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 externalizing[a]	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[b]	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[c]	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[d]	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[e]	1.02	(0.90, 1.15)	0.93	(0.83, 1.05)	0.96	(0.84, 1.10)	0.90	(0.80, 1.02)
Socioeconomic 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[f]	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)

[a]RR greater than 1.00 indicates higher risk for adolescents reporting greater levels of rule-breaking and aggressive behavior.
[b]RR greater than 1.00 indicates higher risk for adolescents who report having more peers who use alcohol/tobacco.
[c]RR greater than 1.00 indicates higher risk for adolescents who report that their peers do not disapprove of alcohol/tobacco use.
[d]RR greater than 1.00 indicates higher risk for adolescents whose parents had more rules regarding alcohol use.
[e]RR greater than 1.00 indicates higher risk for adolescents whose parents are more closely monitoring their activities.
[f]RR greater than 1.00 indicates higher risk for adolescents who have easier access to alcohol in their household without parental knowledge.

TABLE 4 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 3).

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 to 17 and 18 to 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 (Australian Government Department of Health, 2019). Expanding on existing frameworks of alcohol-related harm (Rehm, 2001; Zinberg, 1986) and the patterns of harm reported by Betts et al. (2018), 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 as follows: *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 3-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

TABLE 5 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.

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 etiology 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 US study of adult men (Feingold et al., 2015), 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 (Slade et al., 2016). 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 among females (Grigsby et al., 2016). This is likely due to differences in physiology (Mumenthaler et al., 1999) 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 (Yuen et al., 2020). 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 (Leung et al., 2014) with our finding that this peer effect exposure is also associated with increased risk of experiencing alcohol-related harms earlier in life.

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 randomization, estimates may not be generalizable 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 (Aiken et al., 2017). We also note that while 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 generalizing 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 to 15 years) were excluded due to low cell size, and hence, the results are not generalizable 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 AUD found in community samples of young adults in Australia (Mewton et al., 2011) and similar high-income countries (Conway et al., 2016; Grant et al., 2015).

Conclusion

Young people experience heterogeneous patterns of alcohol-related harm during adolescence, with harms of a physiological nature being particularly common. While 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.

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CONFLICT OF INTEREST

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