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ASSOCIATIONS BETWEEN ALCOHOL USE-RELATED OUTCOMES AND PSYCHOPATHOLOGICAL SYMPTOMS: PERSON- AND VARIABLE-ORIENTED APPROACHES

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I. Preface

Alcohol consumption has a detrimental effect on health: morbidity and mortality due to various disease and injury types can be attributable to alcohol use. Globally, alcohol consumption was responsible for approximately 5% of all deaths and 5% of all disability-adjusted life years lost due to mortality and disability in 2016 (Shield et al., 2020). Alcohol use contributes to a significant public health problem in Hungary among adults and adolescents due to the high levels of alcohol consumption, problematic forms of alcohol use and alcohol-attributable health burden. (Inchley et al., 2020; Shield et al., 2020; World Health Organization, 2018a).

The societal costs of alcohol use highlight the importance of investigating further alcohol consumption patterns in Hungary to identify more precisely individuals with harmful alcohol use as well as to gain more accurate knowledge on the risk mechanisms underlying adverse alcohol use-related outcomes. To address these issues, the present dissertation examines the co-occurrence of psychopathological symptoms and outcomes of alcohol use from different perspectives. It was expected that the present dissertation can contribute to broaden our epidemiological and psychopathological-motivational knowledge of Hungarian alcohol users.

II. Introduction

II/1. Comorbidity between AUD and different types of psychiatric disorders

The simultaneous or consecutive co-occurrence of alcohol use disorder (AUD) and other psychiatric disorders is highly prevalent, which can contribute to significant health burden, for example, by leading to adverse treatment outcomes and increased mortality rates (Bradizza et al., 2006; Castillo-Carniglia et al., 2019; Hjorthøj et al., 2015).

Extensive cross-sectional and longitudinal findings suggest positive associations and high comorbidity rates between AUD and other externalizing psychiatric disorders, such as substance use disorders (SUDs), attention deficit hyperactivity disorder (ADHD) and antisocial personality disorder (ASPD) (Castillo-Carniglia et al., 2019; Groenman et al., 2017; Guy et al., 2018). Moreover, it is also important to discuss the associations between behavior addictions (i.e., gaming [GD] and gambling disorder are considered by the large taxonomic systems of mental disorders) and AUD. Meta-analytic findings showed high comorbidity levels between gambling disorder and AUD in clinical as well as in community samples (Dowling et al., 2015; Lorains et al., 2011). On the other hand, the existing literature were inconclusive on the association between GD and alcohol consumption and problems: significant and positive links between GD and alcohol use-related outcomes were reported in addition to other findings with non-significant associations between the two risk behaviors (Burleigh et al., 2019; Erevik et al., 2019; Ream et al., 2011). A possible explanation for these comorbidities is that there are shared and non-disorder-specific etiologic and psychopathological factors across these disorders, such as similarities in genetic correlations, neurobiological characteristics (e.g., areas responsible for behavioral regulation, reward mechanisms, stress response), environmental risk factors (e.g., child abuse and trauma), psychological mechanisms (e.g., impulsivity, emotional dysregulation, sensation seeking) as well as in symptomatic features (e.g., symptoms representing impaired control over behavior) (Estévez et al., 2017; Helle et al., 2019; Kotyuk et al., 2020; Lee et al., 2011; Vanyukov et al., 2012; Walther et al., 2012).

Increased rates of comorbidity and significant and positive associations were shown between AUD and various forms of internalizing psychiatric disorders, such as major depressive disorder (MDD) and different types of anxiety disorders (ADs), including generalized anxiety disorder (GAD), social anxiety disorder (SAD), panic disorders, obsessive-compulsive disorder (OCD) and posttraumatic stress disorder (PTSD) (Boden & Fergusson, 2011; Castillo-Carniglia et al., 2019; Cuzen et al., 2014; Debell et al., 2014; Lai et al., 2015; Schry & White, 2013). Similar psychopathological mechanisms with AUD were suggested across these internalizing disorders (Anker & Kushner, 2019; Kotov et al., 2017). For example, the self-medication hypothesis proposes that symptoms of MDD and ADs have a predictive effect on alcohol use and problems via coping drinking motives. On the other hand, other findings suggested that the AUD can lead to the subsequent presence of MDD and various types of ADs (Boden & Fergusson, 2011; Smith & Randall, 2012; Straus et al., 2018; Turner et al., 2018).

The broad diagnostic category of eating disorders (EDs) incorporates multiple and distinct psychiatric disorders, such as anorexia nervosa (AN), bulimia nervosa (BN) or binge eating disorder (BED) (World Health Organization, 2018b). The meta-analytic findings showed positive, weak and moderate associations between AUD and different types of EDs, in addition to higher rates of comorbidity for those types of EDs which are characterized with binge eating and purging behavior compared to EDs with restrictive features (Bahji et al., 2019; Bogusz et al., 2021; Gadalla & Piran, 2007). In the case of the comorbidity between AUD and EDs with binge eating, common etiological risk mechanisms were identified: shared neurobiological correlates (e.g., reward processes, behavioral control) and psychological and affective characteristics (e.g., both disorders positively associated with internalizing symptoms, emotion dysregulation, impulsivity) can explain the positive correlation between AUD and EDs with binge eating (e.g., BED, BN) (Ferriter & Ray, 2011; Schulte et al., 2016). Moreover, similar coping and reward-seeking motivations can determine eating and alcohol use: both behaviors can be used to gain pleasurable experiences, and to cope with negative affectivity (in absence of adaptive emotion regulation) (Ferriter & Ray, 2011; Schulte et al., 2016).

II/2. Classification models of alcohol use and AUD

Alcohol users and individuals with AUD are highly diverse groups, substantial differences can be captured in both groups in the patterns of alcohol consumption, AUD symptomatology and in other risk factors (e.g., family history, age of onset of AUD, comorbid psychiatric disorders). Therefore, the goal of the alcohol classification models is to establish typologies of alcohol users or AUD (Babor & Caetano, 2006; Hesselbrock & Hesselbrock, 2006; Leggio et al., 2009).

Findings of the previous empirically based classification models based on AUD symptoms were divergent. On the one hand, numerous studies identified classes of alcohol users which differ in the overall severity level of AUD symptoms in clinical as well as in community samples. That is, in accordance with the AUD subtypes of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), these quantitatively different subgroups can be placed along a severity continuum and they are distinguished by an increasing overall probability of the presence of AUD symptoms and not by the presence of specific symptoms (Casey et al., 2013; Ko et al., 2010). On the other hand, some studies also identified qualitatively different classes of AUD, which showed distinct symptomatic profiles with high probabilities to experience

specific types of symptoms (e.g., subgroups of AUD which were characterized primarily by drinking alcohol larger amounts than intended) (Castaldelli-Maia et al., 2014). However, other classification models proposed that different measures of alcohol consumption (e.g., frequency, quantity, binging) should be also considered as indicators of alcohol typologies in addition to symptoms of AUD to explore subgroups of at-risk alcohol users in a wider range of severity levels. Studies with this approach repeatedly discriminated classes of alcohol users with an increasing risk for harmful alcohol consumption, for example, by identifying classes of low, moderate and high risks (Jackson et al., 2014; Smith & Shevlin, 2008). To the Author's best knowledge, previous studies did not investigate alcohol user typologies in representative adult samples in Central-Eastern European (CEE) countries as well as specifically in Hungary (see: Aim 1/a). Moreover, considering the high rates of comorbidity between AUD and other psychiatric disorders, investigation of the associations between latent classes of alcohol users and various dimensions of psychopathological symptoms can contribute to describing more precisely characteristics of alcohol drinking subgroups (see: Aim 1/b).

However, it is important to note that several typologies were not restricted to classify alcohol users solely based on indicators of alcohol consumption and AUD symptoms, rather considered a wider range of risk characteristics (e.g., family history, age of onset of AUD, comorbid psychiatric disorders). Binary classification models (e.g., classification models of Jellineck, Cloninger et al., Babor et al.) suggested that individuals with AUD can be classified into a less and a more severe subgroup based on, amongst others, levels of alcohol use and problems, onset of AUD, family history of AUD, childhood and personality risk factors, comorbid psychopathology, treatment outcomes (Babor & Caetano, 2006; Leggio et al., 2009). Moreover, other classification models suggested more than two subtypes of AUD and in some cases the identified classes of AUD overlapped and showed similar. Based on these findings the following subtypes of AUD were distinguished repeatedly: (i) low severity of alcohol-related impairment and comorbid psychopathological symptoms, (ii) chronic severe subtypes in terms of AUD symptoms and comorbid psychiatric problems, (iii) negative affect classes, and (iv) antisocial subtypes (Hildebrandt et al., 2017; Leggio et al., 2009; Moss et al., 2007).

Overall, these classification solutions highlighted that co-occurring externalizing and internalizing psychopathology can explain the heterogeneity among individuals with AUD (Hildebrandt et al., 2017). In line with this, other classification models attempted to account for the differences in severity levels and distinct constellations of comorbid psychiatric disorders among individuals with AUD. Four classes of AUD were repeatedly identified across these studies: (i) classes with overall low levels of comorbid psychiatric disorders, (ii) classes with moderate-high levels of comorbid internalizing psychiatric disorders, (iii) subgroups which showed primarily comorbid externalizing psychiatric disorders, and (iv) classes with moderate-high levels of both internalizing and externalizing comorbid psychiatric disorder presence. (Glass et al., 2014; Müller et al., 2020; Sintov et al., 2010; Urbanoski et al., 2015). However, to the Author's best knowledge, existing studies which aimed to identify subgroups of AUD based on symptomatic levels or presence of comorbid psychiatric disorders used cross-sectional design and did not focus on the changes of comorbid psychiatric disorder severity (e.g., due to attendance in a treatment program) in different latent classes of AUD (see: Aim 2/a).

Finally, other classification models attempted to classify adolescents based on their use of alcohol as well as other psychoactive substances. Studies that used such an approach discriminated predominantly alcohol user classes with increasing severity levels (e.g., experimental users, moderate risk users, binge drinkers); however, considering a wider range of psychoactive substances can allow to identify subgroups with polysubstance use patterns (e.g., adolescents with concurrent use of alcohol and cannabis or other illicit drugs) (Davoren et al., 2016; Halladay et al., 2020; Tomczyk et al., 2016). To the best of the Author's knowledge, little is known about the latent classes of alcohol and illicit drug use among adolescents in CEE countries and specifically in Hungary (Göbel et al., 2016; Halladay et al., 2020; Tomczyk et al., 2016) (see: Aim 3/a). Previous latent class analytic findings consistently showed that polysubstance users show high levels of externalizing and internalizing psychopathological symptoms and behaviors (e.g., antisocial behaviors, depressive symptoms) compared to less severe subgroups (Tomczyk et al., 2016). However, to the best of the Author's knowledge, existing studies did not examine the association between latent classes of alcohol and illicit drug use and potentially addictive behaviors, such as GD. Therefore, it might be possible that a more accurate interpretation can be obtained by comparing levels of GD symptom severity and specific GD criteria between empirically-based subgroups which simultaneously considers alcohol use and illicit drug use (see: Aim 3/b).

II/3. The role of drinking motives on the relationships between psychopathological symptoms and alcohol use-related outcomes

The motivational model of alcohol use (Cox & Klinger, 1988) differentiates four distinct types of drinking motives based on the valence and source of the motivations: (i) enhancement (positive valence with an internal source), (ii) social (positive valence with an external source), (iii) coping (negative valence with an internal source) and (iv) conformity motives (negative valence with an external source) (Cooper et al., 2015; Kuntsche et al., 2005). Meta-analytic findings showed that enhancement motives presented the strongest associations with outcomes of alcohol consumption, whereas alcohol use-related problems were linked to enhancement and coping motives with the highest levels of magnitude (Bresin & Mekawi, 2021).

Existing research also reported that different drinking motives are associated with distinct patterns of distal psychopathological antecedents (Cooper et al., 2015; Kuntsche et al., 2006b). Psychopathological variables most consistently were associated with coping, enhancement and conformity motives (Cooper et al., 2015). Coping motives were positively associated with negative affectivity and internalizing symptomatology, affective dysregulation and problematic eating behaviors (e.g., BN, BED) (Allan et al., 2015; Bakhshaie et al., 2021; Bravo et al., 2018; Cooper et al., 2015; Luce et al., 2007; Schry & White, 2013). Enhancement motives showed positive links with personality characteristics of sensation seeking, reward sensitivity, low self-control, psychopathological features with impulsive characteristics (e.g., ADHD, binge eating, cluster B personality disorders) (Cooper et al., 2015; Grazioli et al., 2019; Tragesser et al., 2007; Trojanowski et al., 2019). In the case of conformity motives, significant and positive relationships were shown with personality and psychopathology factors which can indicate interpersonal difficulties, such as symptoms of SAD, anxiety sensitivity and attachment anxiety (Cooper et al., 2015; Schry & White, 2013).

The present dissertation examined further the role of drinking motives on the relationships between psychopathological symptoms and alcohol use-related outcomes in two aspects. First, it has been noted that more research would be needed to examine the motivational background of individuals with clinically diagnosed AUD (Cooper et al., 2015). Specifically, little is known about motivational differences between subgroups of AUD with distinct profiles of co-occurring psychopathological symptoms (e.g., subgroups with low vs. high overall levels of symptom severity, subgroups with predominantly internalizing vs. externalizing psychopathologies) (see: Aim 2/b). Second, previous studies highlighted that similar motivational processes determine some forms of eating behavior (e.g., binge eating) and alcohol use (i.e., reward-seeking and coping tendencies) (Ferriter & Ray, 2011; Schulte et al., 2016; Trojanowski et al., 2019). In line with these, individuals with different forms of EDs (e.g., BN, BED) consistently showed higher levels of coping motives and enhancement drinking motives (Anderson et al., 2006; Luce et al., 2007; Mikheeva & Tragesser, 2016; Trojanowski et al., 2019). However, to the Author's best knowledge, existing studies did not explore whether drinking motives with internal source (i.e., coping and enhancement motives) mediate the relationship between symptoms of EDs and alcohol use (see: Aim 4).

III. Aims of the dissertation

The present dissertation aimed to examine co-occurrence of psychopathological symptoms and outcomes of alcohol use from different perspectives. Specifically, the present dissertation aimed to (i) identify empirically-based subgroups of alcohol users in clinical and general adult and adolescent samples and to examine their associations with various dimensions of psychopathological symptoms, and (ii) to investigate the role of drinking motives on the relationships between psychopathological symptoms and outcomes of alcohol use.

Study 1 aimed to explore distinct subgroups of alcohol users in a representative Hungarian adult sample (Aim 1/a) and to examine associations between these alcohol drinking latent classes and various dimensions of psychopathological symptoms (Aim 1/b). The aim of Study 2 was to identify latent classes of AUD inpatients in a treatment program with distinct profiles and change patterns of psychopathological symptoms (Aim 2/a) and to investigate differences between these subgroups in terms of drinking motives (Aim 2/b). Study 3 aimed to identify latent classes of alcohol and illicit drug use in a representative Hungarian adolescent sample (Aim 3/a) and to compare these substance-using subgroups in terms of GD symptom severity and criteria (Aim 3/b). Finally, Study 4 aimed to test the mediating role of drinking motives with internal source (i.e., coping and enhancement motives) on the relationship between symptoms of EDs and alcohol use among adolescents (Aim 4).

IV. Study 1: An Empirically Based Typology of Alcohol Users in a Community Sample Using Latent Class Analysis[1,]

IV/1. Material and methods

IV/1/1. Participants and procedure

The present study utilized data from a nationally representative sample of the National Survey on Addiction Problems in Hungary 2015 (Paksi et al., 2017). The study sample ensured proportional distribution of the participants in terms of age (between 18-64 years), regional geographic locations, and size of residence (net sample: $N = 2274$). Participants who had used alcohol in the past 12 months and showed non-missing data were selected for further analysis ($N = 1520$; 52.2% male [$N = 794$]; mean age = 33.14 years; [SD = 12.32]).

IV/1/2. Measures

IV/1/2/1. Alcohol Use Disorders Identification Test (AUDIT). The 10-item AUDIT was used to assess the patterns of alcohol consumption and problems in the past 12 months (Gerevich et al., 2006; Saunders et al., 1993). The instrument displayed acceptable internal consistency (Cronbach's $\alpha = 0.82$). Due to the very high level of floor effect on the original response scales, items were transformed into dichotomous variables for further analysis.

IV/1/2/2. Brief Symptom Inventory (BSI). A 27-item long, abbreviated version of the BSI (Derogatis & Savitz, 2000; Unoka et al., 2004) was used to assess symptoms of anxiety, depression, hostility, interpersonal sensitivity, and obsessive-compulsivity. Subscales of the questionnaire presented satisfactory internal consistencies (Cronbach's $\alpha = 0.80 – 0.87$).

IV/1/3. Data analysis

In order to identify homogenous subgroups of participants based on their characteristics of alcohol consumption, a Latent Class Analysis (LCA) was conducted (Collins & Lanza, 2009). AUDIT items were specified as dichotomous indicator variables. To retain the best fitting model, the results of multiple model fit indices were taken into account: the Akaike Information Criteria (AIC), the Bayesian Information Criteria (BIC), the Sample Size Adjusted Bayesian Information Criteria (SSA-BIC), the index of Entropy and the Lo-Mendel-Rubin Adjusted Likelihood Ratio Test (LMRT). Next, multinomial logistic regression were performed with R3Step (Muthén & Muthén, 2017) to explore the effects of gender, age, level of education, employment status, age of onset of alcohol use, and symptom levels of anxiety, depression, hostility, interpersonal sensitivity, and obsessive-compulsivity on class memberships. Mplus 8.0 statistical software was used in the analyses (Muthén & Muthén, 2017).

IV/2. Results

IV/2/1. Latent Class Analysis (LCA)

[1] Originally published as: Horváth, Zs., Paksi, B., Felvinczi, K., Griffiths, M. D., Demetrovics, Zs., & Urbán, R. (2019). An empirically based typology of alcohol users in a community sample using latent class analysis. *European Addiction Research, 25*(6), 293-302. https://doi.org/10.1159/000501516

Models with one to four latent classes were estimated. Overall, the three-class solution provided the most adequate degree of model fit and retained for further analyses.

IV/Figure 1. Class-based probability of endorsing each dichotomous items of the AUDIT.

Response patterns of the three latent classes are presented in IV/Figure 1. Participants assigned to Class 1 ('Light alcohol drinkers') demonstrated the lowest rates of item endorsement probability related to indicators of alcohol consumption and negative consequences. Class 2 ('Alcohol drinkers with low risk of dependence') was described with medium to high probability of item endorsement on alcohol consumption indicators, and low probability of item endorsement related to negative consequences. The subgroup of Class 3 ('Alcohol drinkers with severe dependence symptoms') showed high probabilities of item endorsement on alcohol consumption and negative consequences.

IV/2/2. Validation of the latent classes

Multinomial logistic regression was conducted to validate the identified latent classes (IV/Table 1). The latent class of 'Light alcohol drinkers' was specified as a reference category. Male gender, younger age, economically active status, earlier onset of alcohol use, and a higher level of depression significantly increased the odds of the membership of 'Alcohol drinkers with low risk of dependence' compared to Class 1. Significantly higher odds of membership were displayed for 'Alcohol drinkers with severe dependence symptoms' compared to the reference category if the participant was male, had a lower level of educational achievement, reported earlier onset related to the first alcoholic drink, and showed a higher level of hostility.

IV/Table 1. Predictors of class memberships: a multinomial logistic regression.

	Class 2 'Alcohol drinkers with low risk of dependence' Crude OR [95% CI]	Class 3 'Alcohol drinkers with severe dependence symptoms' Crude OR [95% CI]
Gender[1]	**4.45 [2.47 – 8.04]**	**3.75 [1.73 – 8.10]**
Age	**0.94 [0.91 – 0.96]**	0.98 [0.96 – 1.00]
Level of education[2]	1.24 [0.69 – 2.20]	**3.73 [1.97 – 7.07]**
Employment status[3]	**1.91 [1.02 – 3.56]**	1.12 [0.56 – 2.24]
Young age of onset: first drink[4]	**2.14 [1.16 – 3.94]**	**3.01 [1.57 – 5.76]**
Depression	**1.10 [1.02 – 1.20]**	1.02 [0.91 – 1.15]
Hostility	1.14 [0.97 – 1.33]	**1.24 [1.07 – 1.43]**
Interpersonal sensitivity	0.97 [0.85 – 1.11]	0.89 [0.74 – 1.07]
Obsessive-compulsive	0.93 [0.82 – 1.05]	1.02 [0.89 – 1.18]

Note. Crude Odds Ratios (95% confidence intervals) of the association between validating covariates and latent class membership relative to Class 1 ('Light alcohol drinkers'). Odds ratios presented by bold figures are significant at least $p < 0.05$ level. [1]Gender: 0 = Female, 1 = Male; [2]Level of education: 0 = Participant had a graduation at vocational or high-school at least, 1 = Participant did not have vocational or high-school graduation; [3]Employment status: 0 = Unemployed, economically inactive, 1 = Working, economically active; [4]Age of onset: first alcoholic drink: 0 = At least at the age of 15 years, or none, 1 = At the age of 14 years or earlier. Anxiety was not included in the final analysis as a predictor, due to the negative suppressor effect of depression.

V. Study 2: Patterns and temporal change of psychopathological symptoms among inpatients with alcohol use disorder undergoing a twelve-step based treatment[2,]

V/1. Methods

V/1/1. Participants and procedure

The present study was conducted between 2013 and 2018 at the Nyírő Gyula National Institute of Psychiatry and Addictions, Budapest, Hungary. The study specifically focused on the eight week-long Minnesota Model treatment program which harmonizes professional treatment approaches and principles of the twelve-step based self-help group of Alcoholics Anonymous (AA). During the treatment, various group and individual psychotherapeutic techniques are applied, including daily AA meetings, specific group meetings based on the principles of AA, assertiveness training, relaxation and stress management training, art therapeutic sessions, group meetings for affected family members, and psycho-education.

Overall, 303 inpatients (males: 59.41% [*N* = 180]; mean age: 46.43 years [SD=10.32]) with AUD participated in the present study. A total of 218 participants (71.95%) successfully

[2] Originally published as: Horváth, Zs., Tremkó, M., Fazekas, Zs., Tóth, A., Petke, Zs., Farkas, J., Griffiths, M. D., Demetrovics, Zs., & Urbán, R. (2020). Patterns and temporal change of psychopathological symptoms among inpatients with alcohol use disorder undergoing a twelve-step based treatment. *Addictive Behaviors Reports, 12*, 100302. https://doi.org/10.1016/j.abrep.2020.100302

completed the eight-week long program. A semi-structured interview was administered by the treatment staff before treatment enrollment. Data were collected during the interview concerning socio-demographics (e.g., age, gender, education), and psychiatric anamnesis (e.g., family history of substance misuse, previous suicide attempts, treatment involvement history, pre-care). Standardized questionnaires were used at two measurement points. On first entering the treatment program, alcohol consumption (e.g., harmful alcohol consumption, drinking motives), and psychopathological-related aspects were assessed. At the end of the treatment program, the levels of psychopathological symptoms were re-assessed.

V/1/2. Measures

V/1/2/1. Alcohol Use Disorders Identification Test (AUDIT). The 10-item AUDIT was used to assess the degree of harmful alcohol consumption (Gerevich et al., 2006; Saunders et al., 1993). The scale had sufficient internal consistency (Cronbach's $\alpha = 0.72$).

V/1/2/2. Brief Symptom Inventory (BSI). The present study assessed psychopathological symptom severity using the 53-item BSI (Derogatis & Savitz, 2000; Unoka et al., 2004). General symptom severity, anxiety, depression, hostility, interpersonal sensitivity, obsessive-compulsive, paranoid ideation, phobic anxiety, psychoticism, and somatization scale scores were considered for analyses. The subscales of the BSI displayed acceptable levels of internal consistency at both measurement points (pre-treatment: Cronbach's $\alpha = 0.73 – 0.89$; post-treatment: Cronbach's $\alpha = 0.68 – 0.86$).

V/1/2/3. Drinking Motivations Questionnaire–Revised (DMQ-R). The 20-item DMQ-R was used to assess drinking motives (Kuntsche et al., 2006a; Németh, Urbán, et al., 2011). The subscales of conformity, coping, enhancement, and social motives provided satisfactory degree of internal consistency (Cronbach's $\alpha = 0.79 – 0.90$).

V/1/3. Data analysis

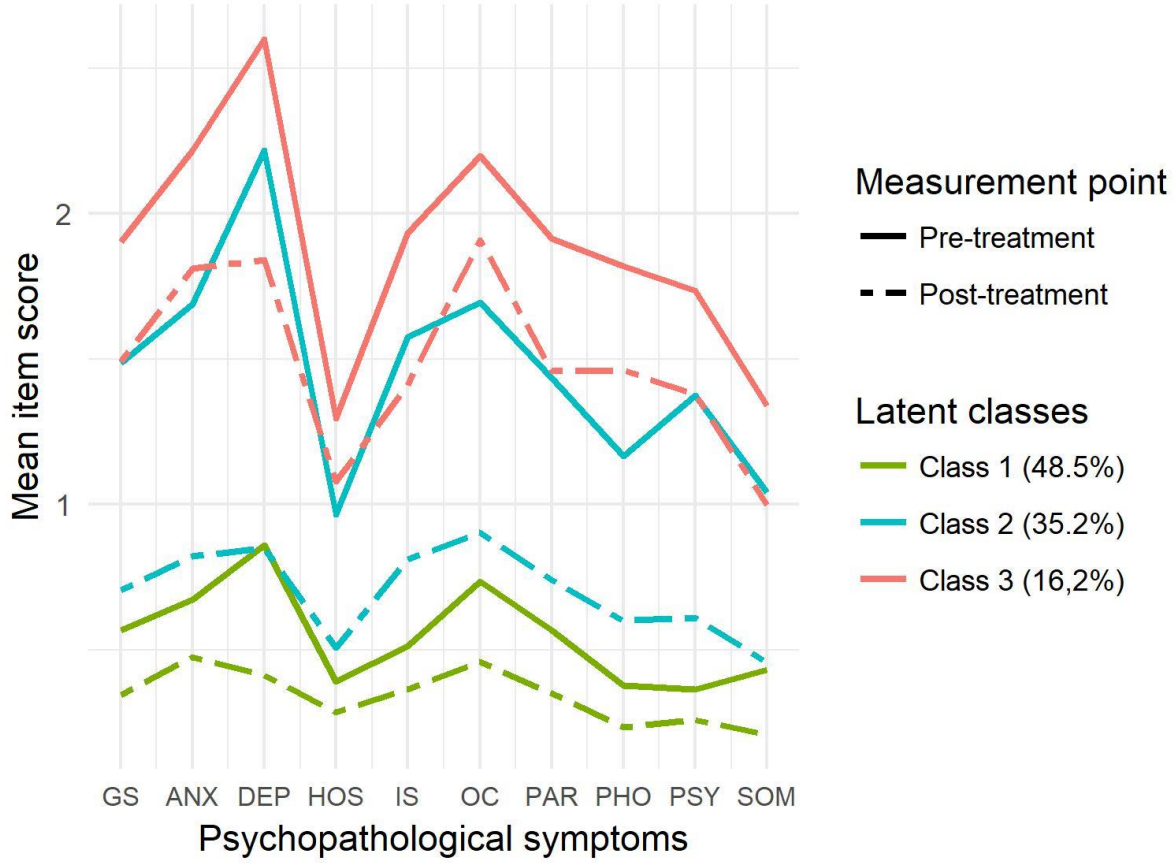
Latent class growth analysis (LCGA) was used to identify subgroups of participants based on psychopathological symptom profiles and change trajectories (Jung & Wickrama, 2008). Average item scores of the BSI subscales assessed at the beginning and at the end of the treatment were specified as indicator variables. The level of model fit was evaluated based on the AIC, the BIC, the SSA-BIC, the index of entropy and the LMRT. Next, multinomial logistic regression (with R3Step method) was used to analyze the link between latent class membership and age, gender, family history of substance misuse, previous suicide attempt, pre-care before the treatment program, level of harmful alcohol consumption, drinking motives (Asparouhov & Muthén, 2013). Mplus 8.0 statistical software was used to perform the analyses.

V/2. Results

V/2/1. Latent class growth analysis (LCGA)

Models with one to four latent classes were estimated. Overall, the three-class solution provided the most adequate degree of model fit and retained for further analyses.

V/Figure 1 demonstrates the symptom profiles of the three identified latent classes at the beginning and the end of the treatment program. Apart from the change of hostility for Class 3, latent classes showed significant decreases in each dimension of psychopathological symptoms. Individuals assigned to Class 1 ("low severity symptomatic subgroup with mild decrease") had low-severity symptom profiles at both measurement points. Individuals assigned to Class 2 ("moderate severity symptomatic subgroup with strong decrease") had moderate levels of symptomatic severity at the beginning of the treatment, but low levels of symptomatic severity by the end of the program. Individuals assigned to Class 3 ("high severity symptomatic subgroup with moderate decrease") had high levels of symptomatic severity at the beginning of the treatment program, but moderate levels of symptomatic severity by the end of the program.



V/Figure 1. Mean item scores of the three latent classes on the subscales of the BSI before and after the treatment program. Abbreviations: GS = Global symptom severity, ANX = Anxiety; DEP = Depression; HOS = Hostility; IS = Interpersonal sensitivity; OC = Obsessive-compulsive; PAR = Paranoid ideation; PHO = Phobic anxiety; PSY = Psychoticism; SOM = Somatization.

V/2/2. Validation of the latent classes

Multinomial logistic regression analysis was performed to examine the association between latent class membership and psychopathological history-related and alcohol consumption-

related covariates (V/Table 1). The "low severity" subgroup was selected as the reference category. The presence of family history of substance misuse, absence of pre-care before the treatment program, higher rates of coping drinking motives and harmful alcohol consumption all significantly increased the odds of being in the "moderate severity" subgroup membership compared to the reference category. In the case of the "high severity" subgroup, higher rates of conformity and coping drinking motives significantly contributed to the class membership compared to the reference category.

V/Table 1. Association between validating covariates and latent class membership

	Class 2 "Moderate severity symptomatic subgroup with strong decrease" *N* = 105; 34.9% OR [95% CI]	Class 3 "High severity symptomatic subgroup with moderate decrease" *N* = 49; 16.2% OR [95% CI]
Age	1.01 [0.98 – 1.05]	1.02 [0.97 – 1.08]
Gender[1]	1.36 [0.66 – 2.82]	1.99 [0.75 – 5.29]
Family history of substance misuse[2]	**2.13 [1.04 – 4.33]**	2.25 [0.91 – 5.58]
Previous suicide attempt[2]	1.39 [0.60 – 3.19]	1.75 [0.66 – 4.67]
Psychiatric-, AUD- or SUD-related pre-care shortly before the treatment program [2]	**0.36 [0.14 – 0.90]**	0.35 [0.11 – 1.13]
Harmful alcohol consumption	**1.48 [1.00 – 2.19]**	1.31 [0.72 – 2.38]
Conformity drinking motive	1.50 [0.93 – 2.40]	**1.81 [1.06 – 3.08]**
Coping drinking motive	**2.53 [1.65 – 3.88]**	**1.85 [1.03 – 3.31]**
Enhancement drinking motive	1.10 [0.70 – 1.72]	1.36 [0.64 – 2.91]
Social drinking motive	1.19 [0.74 – 1.92]	1.65 [0.79 – 3.46]

Note. Reference category: "Low severe symptomatic subgroups with mild decrease" class. Odds ratios (OR) presented by bold figures are significant at least $p < 0.05$ level. [1]Gender: 0 = Female, 1 = Male; [2]Categorical variables coded as 0 = No, 1 = Yes.

VI. Study 3: Polysubstance use is positively associated with gaming disorder symptom severity: A latent class analytical study[3]

VI/1. Materials and methods

VI/1/1. Participants and procedure

Data from a representative Hungarian sample of the Health Behaviour in School-aged Children survey in 2018 were used in the present study (Németh, 2019). Stratification was used during sampling according to the type of education, school grade, maintainer of the school, geographical region and settlement type. Data collection was performed among students

[3] Originally published as: Horváth, Zs., Király, O., Demetrovics, Zs., Németh, Á., Várnai, D., & Urbán, R. (2021). Polysubstance use is positively associated with gaming disorder symptom severity: A latent class analytical study. *European Addiction Research.* https://doi.org/10.1159/000517042

attending fifth-, seventh-, ninth and eleventh grades (*N* = 6003). However, because data regarding illicit drug use was only collected among students in the ninth and eleventh grades, adolescents in lower grades were excluded from the present analyses. (*N* = 2768; Females: 52.08% [*N* = 1439]; mean age 16.73 years [SD = 1.21]).

VI/1/2. Measures

VI/1/2/1. Alcohol and illicit drug use. Separate variables were constructed to measure the frequency of alcohol use, drunkenness and cannabis use in the participants' lifetime and past month (0 = *Lifetime abstinence*, 1 = *Lifetime presence but not in the past month*, 2 = *Past month presence*). Moreover, lifetime use of other illicit drug types were also considered: ecstasy or MDMA, amphetamines, medications with non-medical purpose, designer drugs, concurrent use of alcohol and medications (0 = *No use at all*; 1 = *Consumption at least once*).

VI/1/2/2. Gaming behavior. An abbreviated, five-item version of the Ten-Item Internet Gaming Disorder Test (IGDT-10) (Király et al., 2017, 2019) was applied to measure the overall symptomatic severity of GD and the criteria of GD as proposed in the ICD-11: loss of control, giving up other activities, continuation, and negative consequences. A satisfactory level of internal consistency was presented ($\omega = 0.87$). Moreover, principal component analysis was used to create a composite score of gaming frequency based on two separate questions measuring the frequency of gaming on average schooldays and weekend days.

VI/1/2/3. Life satisfaction. By using the one-item Cantril ladder (Levin & Currie, 2014), adolescents rated their level of satisfaction with life on an eleven-point scale.

VI/1/3. Data analysis

Latent class analysis (LCA) was performed to distinguish subgroups with distinct patterns of alcohol consumption and drunkenness and use of various illicit drug types. The optimal solution was selected based on the AIC, the BIC, the SSA-BIC, the index of entropy, the LMRT. Next, the relationships between latent classes and GD symptom severity and criteria were also assessed via multinomial logistic regression among gamers (R3Step method) (Asparouhov & Muthén, 2014) while controlling for the effects of gender, school grade, life satisfaction and frequency of gaming. Analyses were conducted using Mplus 8.0 (Muthén & Muthén, 2017).

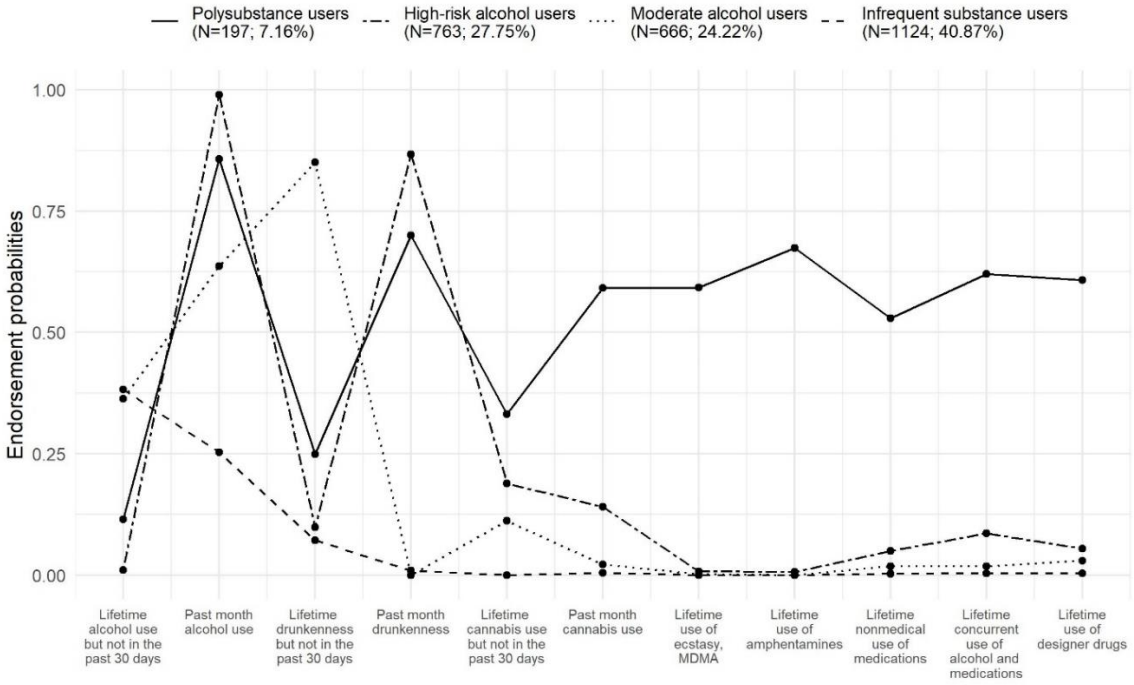
VI/2. Results

VI/2/1. Latent class analysis

LCA with one to five latent classes was performed. Overall, the four-class solution provided the most adequate degree of model fit and retained for further analyses.

Class-based profile characteristics are summarized in VI/Figure 1. Class 1 ('Polysubstance users') had moderately high-very high probabilities for drinking alcohol, drunkenness and using cannabis in the past month, in addition to the high probabilities of lifetime use of all other types of illicit drugs. Class 2 ('High-risk alcohol users') showed very high probabilities for consuming alcohol and drunkenness in the past month, and low-very low probabilities for illicit drug use. Class 3 ('Moderate alcohol users') showed very high probabilities for drinking alcohol in the past month and lifetime drunkenness (but not in the past month) whereas any form of

lifetime illicit drug use was extremely unlikely. Finally, Class 4 ('Infrequent substance users') demonstrated low–very low probabilities for alcohol use, drunkenness, and illicit drug use.



VI/Figure 1. Profile characteristics of the latent classes of alcohol and illicit drug use.

VI/2/2. Association between latent classes of alcohol and illicit drug use and GD

The findings of the multinomial regression analyses are displayed in VI/Table 1. The polysubstance users presented significantly higher rates of GD symptom severity and the GD criteria of 'negative consequences' (in both cases compared to the other three latent classes) and 'giving up other activities' (compared to high-risk and moderate alcohol users), while controlling for the effects of the included covariates.

VI/Table 1. Multinomial logistic regression: Predictors of alcohol and illicit drug use-related latent class memberships

Model 1 – Gaming disorder symptom severity			
	High-risk alcohol users OR [95% CI]	Moderate alcohol users OR [95% CI]	Infrequent substance users OR [95% CI]
Gender[1]	1.00 [0.61 – 1.65]	0.77 [0.47 – 1.27]	0.66 [0.41 – 1.07]
School grade[2]	1.02 [0.66 – 1.57]	1.05 [0.68 – 1.62]	**0.27 [0.18 – 0.42]**
Life satisfaction	**1.17 [1.03 – 1.33]**	**1.16 [1.02 – 1.31]**	**1.23 [1.09 – 1.39]**
Frequency of gaming	1.12 [0.85 – 1.46]	1.07 [0.82 – 1.40]	0.92 [0.72 – 1.19]
Gaming disorder symptom severity	**0.82 [0.73 – 0.93]**	**0.82 [0.73 – 0.92]**	**0.87 [0.78 – 0.98]**

Model 2 – Criterion: Giving up other activities			
	High-risk alcohol users OR [95% CI]	Moderate alcohol users OR [95% CI]	Infrequent substance users OR [95% CI]
Gender[1]	0.87 [0.54 – 1.40]	0.66 [0.41 – 1.06]	**0.60 [0.38 – 0.94]**
School grade[2]	1.01 [0.66 – 1.56]	1.04 [0.67 – 1.60]	**0.27 [0.18 – 0.42]**
Life satisfaction	**1.18 [1.04 – 1.33]**	**1.17 [1.04 – 1.32]**	**1.23 [1.10 – 1.38]**
Frequency of gaming	1.04 [0.81 – 1.32]	0.99 [0.78 – 1.26]	0.86 [0.69 – 1.08]
Criterion: Giving up other activities[3]	**0.35 [0.17 – 0.75]**	**0.34 [0.16 – 0.74]**	0.64 [0.33 – 1.25]
Model 3 – Criterion: Continuation			
	High-risk alcohol users OR [95% CI]	Moderate alcohol users OR [95% CI]	Infrequent substance users OR [95% CI]
Gender[1]	0.85 [0.53 – 1.37]	0.65 [0.40 – 1.04]	**0.57 [0.36 – 0.90]**
School grade[2]	1.01 [0.66 – 1.56]	1.04 [0.67 – 1.60]	**0.27 [0.18 – 0.41]**
Life satisfaction	**1.18 [1.05 – 1.34]**	**1.18 [1.04 – 1.33]**	**1.25 [1.11 – 1.40]**
Frequency of gaming	1.02 [0.79 – 1.30]	0.98 [0.77 – 1.24]	0.81 [0.65 – 1.03]
Criterion: Continuation[3]	0.61 [0.33 – 1.13]	0.55 [0.29 – 1.04]	1.12 [0.64 – 1.97]
Model 4 – Criterion: Negative consequences			
	High-risk alcohol users OR [95% CI]	Moderate alcohol users OR [95% CI]	Infrequent substance users OR [95% CI]
Gender[1]	0.67 [0.41 – 1.08]	0.87 [0.54 – 1.41]	**0.61 [0.39 – 0.97]**
School grade[2]	1.03 [0.67 – 1.60]	1.01 [0.65 – 1.56]	**0.27 [0.18 – 0.42]**
Life satisfaction	**1.17 [1.03 – 1.32]**	**1.18 [1.04 – 1.33]**	**1.23 [1.09 – 1.38]**
Frequency of gaming	0.98 [0.77 – 1.24]	1.01 [0.79 – 1.29]	0.88 [0.70 – 1.10]
Criterion: Negative consequences[3]	**0.39 [0.19 – 0.77]**	**0.48 [0.26 – 0.91]**	**0.45 [0.25 – 0.81]**

Note. Reference category = polysubstance users. Analyses were performed among gamers. Significant ($p < 0.05$) regression coefficients (odds ratios with 95% confidence intervals) are presented as bold values. [1]Coded as: 0 = Female; 1 = Male. [2]Coded as: 0 = ninth graders; 1 = eleventh graders. [3]Coded as: 0 = *Never or sometimes*; 1 = *Often*.

VII. Study 4: Alcohol consumption and risk for feeding and eating disorders in adolescence: The mediating role of drinking motives[4]

VII/1. Methods

VII/1/1. Participants and procedure

The present study's data derived from the Hungarian data of the European School Survey Project on Alcohol and Other Drugs from 2015 (Elekes, 2016). The target population of this study consisted of ninth- and tenth-grade students in general and vocational secondary schools.

[4] Originally published as: Horváth, Zs., Román, N., Elekes, Zs., Griffiths, M. D., Demetrovics, Zs., & Urbán, R. (2020). Alcohol consumption and risk for feeding and eating disorders in adolescence: The mediating role of drinking motives. *Addictive behaviors, 107,* 106431. https://doi.org/10.1016/j.addbeh.2020.106431

Stratified cluster sampling assured representativeness of the sample in terms of geographic region, grade, and school type (N = 6664). Only data were considered for the final analyses from those adolescents who reported alcohol consumption in their lifetime (N = 5457; proportion of males: 50.0% [N = 2731]; mean age = 16.62 [SD = 0.94]).

VII/1/2. Measures

VII/1/2/1. Alcohol consumption. A composite latent variable with high internal consistency was defined based on the frequency of alcohol use and drunkenness in the past 12 months and 30 days, the frequency of binge drinking in the past 30 days, and the self-reported drunkenness level on the last drinking occasion ($\omega = 0.89$).

VII/1/2/2. Center of Epidemiological Studies Depression-Scale (CES-D). Depressive symptomatology in the past seven days was assessed using the short, six-item version of the CES-D (Demetrovics, 2007; Kokkevi & Fotiou, 2009). The scale presented a good level of internal consistency ($\omega = 0.89$).

*VII/1/2/3. Drinking Motives Questionnaire – Short Form (DMQ-SF).*The 12-item DMQ-SF assessed participants' reasons for alcohol use (Kuntsche & Kuntsche, 2009; Németh, Kuntsche, et al., 2011). Only coping and enhancement motives were involved in the current analyses, but due to the high level of correlation between them (r = 0.86), a composite latent factor of 'internal drinking motives' was specified with very high internal consistency ($\omega = 0.94$).

VII/1/2/4. SCOFF Questionnaire. To assess the risk for feeding and eating disorders (FEDs), the five-item SCOFF Questionnaire was used (Dukay-Szabó et al., 2016; Morgan et al., 1999). Based on the items of the scale, the level of risk for FEDs was measured by a one-factor latent variable with adequate internal consistency ($\omega = 0.78$).

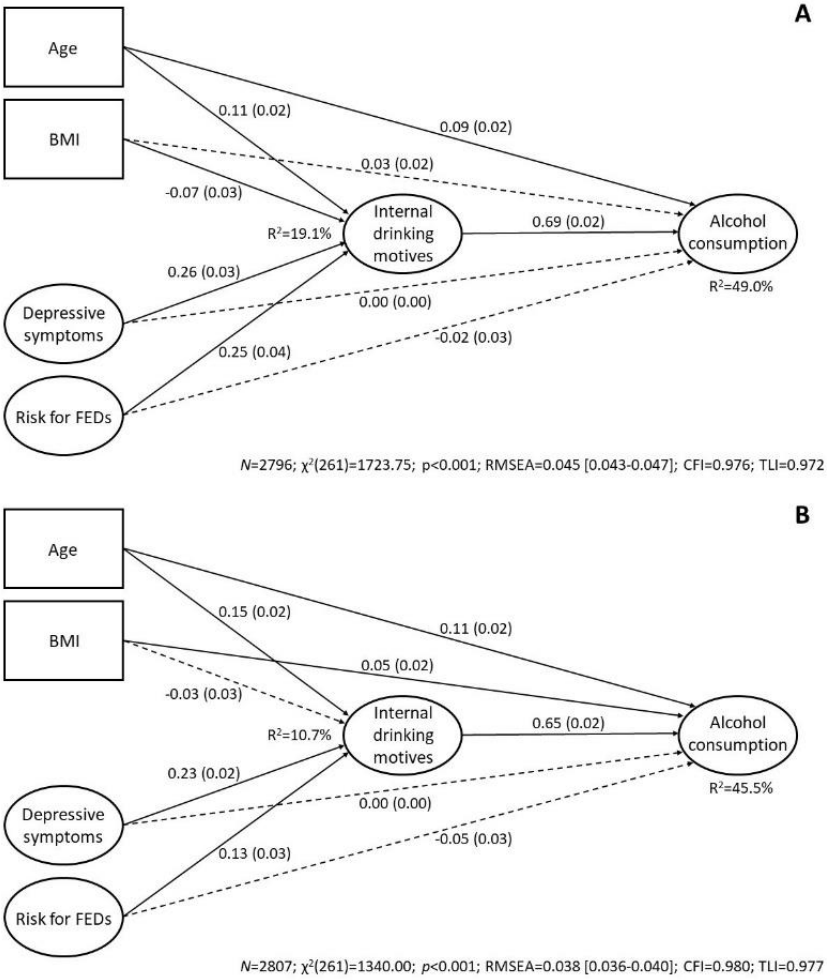
VII/1/3. Data analysis

Structural equation modeling was performed to examine the indirect effect of risk for FEDs on alcohol use via internal drinking motives (all specified as latent variables). The analysis was performed separately for males and females. The effects of age, BMI, and depressive symptoms were also taken into account during the analyses. The model estimation was based on the Weighted Least Squares Mean and Variance technique. Degree of model fit was determined based on the Comparative Fit Index (CFI), the Tucker-Lewis Index (TLI), the Root Mean Squared Error of Approximation (RMSEA). Analyses were performed using MPlus 8.0 (Muthén & Muthén, 2017).

VII/2. Results

Regression path coefficients between the predictor and outcome variables are shown in VII/Figure 1A for females and in VII/Figure 1B for males. Optimal level of model fit was presented for males and females. For both gender groups, in the final model the regression path coefficient between depressive symptoms and alcohol use was fixed at 0 to avoid negative suppressor effects. Risk for FEDs and depressive symptoms presented a significant and positive predictive effect on internal drinking motives among males and females. The direct effect between risk for FEDs and alcohol use was non-significant in both groups. Internal drinking

motives demonstrated a significant, positive and strong relationship with alcohol consumption irrespective of gender.



VII/Figure 1. Standardized regression coefficients representing the association between risk for FEDs, internal drinking motives and alcohol consumption among females (A) and males (B). Note. Solid lines represent significant ($p < 0.05$) standardized (β) regression coefficients. Dashed lines represent non-significant ($p > 0.05$) standardized (β) regression coefficients. Related to each regression coefficients, standard error (S.E.) values are presented in brackets. Regression coefficient between depressive symptoms and alcohol consumption was fixed at 0.

Effect size indices relating to the total, direct, and indirect effects from risk for FEDs upon alcohol consumption are shown in VII/Table 1. The total effect of risk for FEDs on alcohol use was significant among females, but it was non-significant for males. Therefore, for males, the indirect effect from risk for FEDs to alcohol consumption was not estimated. Among both genders, the direct effect of risk for FEDs did not remain significant after taking into account the effect of drinking motives. The indirect effect was significant via internal drinking motives among females.

VII/Table 1. Standardized and unstandardized effect size indices related to the total, direct and indirect effects from risk for FEDs to alcohol consumption among males and females

	Males		Females	
	B (S.E.)	*β* (S.E.)	*B* (S.E.)	*β* (S.E.)
Total effect	0.05 (0.05)	0.03 (0.04)	**0.22 (0.05)**	**0.16 (0.04)**
Direct effect	-0.07 (0.05)	-0.05 (0.03)	-0.02 (0.05)	-0.02 (0.03)
Indirect effect through internal drinking motives	-[1]	-[1]	**0.24 (0.04)**	**0.17 (0.03)**

Note. Unstandardized (*B*) and standardized (*β*) effect size measures presented with bold figures are significant at least $p < 0.05$ level. [1]Indirect effect from risk for FEDs to alcohol consumption was not estimated among males due to non-significant total effect.

VIII. General discussion

VIII/1. Classification models of alcohol use and AUD

In Studies 1 and 3 we used representative and population-based samples to identify subgroups of adult alcohol users and adolescent alcohol and illicit drug users. Both latent class models suggested that subgroups show increasing levels of risk for hazardous alcohol and substance use, and they can be placed along continuums of severity (Davoren et al., 2016; Halladay et al., 2020; Jackson et al., 2014; Sacco et al., 2009; Tomczyk et al., 2016). Specifically, latent classes in Study 1 were discriminated along a dimension of alcohol involvement severity ranging from infrequent to problematic alcohol drinking. Subgroups in Study 3 formed a dimension of severity of substance use ranging from infrequent alcohol use to polysubstance use. The identified latent classes in Studies 1 and 3 correspond to previous findings regarding subgroups of adult alcohol use and adolescent substance use. For example, previous classification models among adults repeatedly discriminated classes of infrequent alcohol users, regular and/or heavy episodic users without AUD symptoms, and high-risk alcohol users who experience negative consequences (Jackson et al., 2014; Sacco et al., 2009). The classification model of alcohol users in Study 1 can also be harmonized with the DSM-5's severity-based distinction of AUD (American Psychiatric Association, 2013). Moreover, classification models of adolescent alcohol and illicit drug use consistently identified subgroups of light alcohol drinkers, regular-moderate alcohol users, heavy and excessive alcohol users, and polysubstance users (Dauber et al., 2009; Davoren et al., 2016; Gohari et al., 2020; Halladay et al., 2020; Tomczyk et al., 2016).

The latent classes of AUD in Study 2 highlighted the importance of considering co-occurring psychopathological disorders and symptoms in typologies of AUD. Similarly, previous binary and multiclass taxonomies of AUD also emphasized that co-occurring externalizing and internalizing psychopathology (e.g., subgroups with marked negative affectivity and/or antisocial characteristics) can explain at least party the heterogeneity among individuals with AUD (Hildebrandt et al., 2017; Leggio et al., 2009; Moss et al., 2007). The classification model in Study 2 suggested severity-based and quantitative differences between subgroups of AUD: subgroups differed in the overall severity level of psychopathological symptoms and there were

no classes with predominantly internalizing or externalizing psychopathology. The retained typology is also comparable with previous studies which attempted to identify subgroups of AUD by considering exclusively levels of co-occurring psychopathologies. Some of these taxonomies also proposed severity-based discrimination between classes of AUD ranging between mild and severe psychopathological levels, whereas classes with overall low and moderate-high comorbid psychopathological severity were also repeatedly identified in the literature (Glass et al., 2014; Müller et al., 2020; Sintov et al., 2010; Urbanoski et al., 2015; Villalobos-Gallegos et al., 2017). Moreover, the retained subgroups also differed in terms of changes in symptomatic levels. Specifically, the 'Moderate severity symptomatic subgroup with strong decrease' class presented higher levels of psychopathological symptomatic improvement. Although methodological limitations did not allow to specify treatment effects on the symptomatic changes, this classification model highlighted the importance of investigating longitudinal, psychopathology-related changes and treatment differences between AUD classes (Roos et al., 2017).

VIII/2. Associations between psychopathological symptoms and alcohol use-related outcomes

VIII/2/1. Externalizing psychopathological characteristics

Studies 1 and 2 showed significant and positive associations between hostility and subgroups with higher levels of consumption and negative consequences. The measured construct of hostility in both studies encompassed symptoms of aggressive tendencies, difficulties to regulate distress and irritability (Derogatis & Savitz, 2000). It might be possible that hostility, alcohol use and problems are all indicators of a higher-order and transdiagnostic dimension of externalizing disorders which explains the co-occurrence between them and represents a shared liability to externalizing behaviors (e.g., neurobiological and psychological features of negative affectivity, stress regulation, impulsivity) (Krueger & South, 2009). Moreover, causal explanations can also be assumed, such as one can use alcohol as a means for coping with the distressful affective states of irritability and aggressive urges, whereas symptoms of hostility can also emerge as a consequence of problematic alcohol use (i.e., as withdrawal symptoms).

In Study 3, the latent class of 'Polysubstance users' provided support for the co-occurrence of high levels of alcohol use and illicit drug use. As a possible explanation for the background of this co-occurrence, the common liability to addiction (CLA) model suggests that there are shared, non-substance-specific etiologic risk factors that contribute to the CLA as well as can be accounted for the concurrent use of these substances (Vanyukov et al., 2012). Moreover, the 'Polysubstance users' class was not only characterized by the concurrent use of alcohol and illicit drugs, but these adolescents also showed elevated rates of GD symptom severity and criteria endorsement. Therefore, these findings show similarities with previous studies which reported significant and positive associations between levels of GD and outcomes of alcohol and drug use (Burleigh et al., 2019; Estévez et al., 2017; Marmet, Studer, Wicki, et al., 2019). Previous empirical findings and theoretical models of addictions highlighted that there are shared and common genetic, neurobiological (e.g., areas responsible for reward functions, executive functions) and psychological precursors (e.g., impulsivity, negative affectivity, maladaptive emotion regulation) and similar symptomatic characteristics (e.g., obsessive-

compulsive features in symptomatology) between substance use-related problems and GD (Burleigh et al., 2019; Estévez et al., 2017; Kotyuk et al., 2020; Marmet, Studer, Lemoine, et al., 2019; Walther et al., 2012). Alternatively, causal pathways can also be assumed, such as substance use before and during gaming might promote decreased control over gaming and might lead to negative consequences, whereas those who experience adverse consequences due to gaming can also start to use alcohol and illicit drugs in order to dampen stress and negative emotional states due to these gaming problems (Cowlishaw et al., 2014; Škařupová et al., 2018).

VIII/2/2. Internalizing psychopathological characteristics

In Study 1 it was possible to assess the unique associations between levels of alcohol consumption and symptoms of MDD and ADs by investigating the differences between the classes of 'Light alcohol drinkers' and 'Alcohol drinkers with low risk of dependence'. The findings highlighted that the presence of non-symptomatic alcohol use was associated with elevated symptom severity of MDD. However, previous classification models rather suggested negative and non-significant associations between MDD levels and non-symptomatic classes with moderate-high alcohol consumption (Sacco et al., 2009; Smith & Shevlin, 2008). In these typologies MDD and GAD levels rather varied as a function of alcohol problems and not by the levels of alcohol consumption per se (Sacco et al., 2009; Smith & Shevlin, 2008).

Studies 1 and 2 allowed to explore associations between alcohol problems and symptoms of MDD and different types of ADs in the adult general population and clinical samples. Study 1 showed non-significant associations between 'Alcohol drinkers with severe dependence symptoms' and symptomatic levels of MDD, GAD and OCD. Previous classification models reported significant and positive associations between MDD, GAD and class memberships of alcohol users with high rates of alcohol use and problems (Casey et al., 2013; Kuo et al., 2008).

Study 2 demonstrated that latent classes of AUD with at least moderate psychopathological symptomatic severity at the baseline (experiencing MDD, GAD and OCD symptoms at highest) showed significantly higher levels of harmful alcohol consumption compared to the low severity subgroup. Previous studies also reported that classes with more severe comorbid psychopathologies showed higher levels of alcohol consumption and AUD symptom compared to subgroups with lower severities (Glass et al., 2014; Müller et al., 2020). Taken together, these findings are at least partly in line with previous literature which suggested that AUD is positively associated with MDD and different types of ADs (Boden & Fergusson, 2011; Castillo-Carniglia et al., 2019; Cuzen et al., 2014; Lai et al., 2015). Moreover, other studies also highlighted the importance of considering co-occurring internalizing psychopathological symptoms as an important element of classification models of alcohol use and AUD (Hildebrandt et al., 2017; Leggio et al., 2009; Moss et al., 2007). The positive association between harmful alcohol use and subgroups of AUD with increasing overall (predominantly internalizing) psychopathological severity might indicate the possible presence of a higher-order, general psychopathological factor (e.g., the p-factor or the super spectra level in the Hierarchical Taxonomy of Psychopathology) (Caspi et al., 2014; Kotov et al., 2017). Such transdiagnostic factor can represent a non-specific, common liability factor to suffer from various forms of psychiatric disorders and can account for the covariation of internalizing and externalizing psychiatric disorders, increased psychopathological impairment and shared

etiology (Caspi et al., 2014; Kotov et al., 2017). However, causal models can also be assumed to explain the links between MDD, ADs and alcohol use outcomes in Studies 1 and 2. For example, based on the self-medication hypothesis, symptoms of MDD and ADs can predict subsequent alcohol use and problems via the motivation to cope with internalizing symptoms. Alternatively, increased and problematic alcohol use can lead to the subsequent presence of symptoms of MDD and various types of ADs via neurobiological changes and adverse social consequences (Boden & Fergusson, 2011; Smith & Randall, 2012; Turner et al., 2018).

Finally, in Study 4, higher levels of symptom severity of EDs (i.e., AN, BN) were associated with higher rates of alcohol consumption among female adolescents even over the effects of age, BMI and depressive symptoms. This finding is in accordance with previous empirical data which presented significant and positive links between alcohol use and symptoms of EDs (e.g., drive for thinness, body dissatisfaction, symptoms of BN) (Arias et al., 2009; Baker et al., 2017, 2018). Shared neurobiological (e.g., reward processes, behavioral control) and psychological-affective characteristics (e.g., elevated levels of internalizing symptoms, maladaptive emotion regulation, impulsivity and similar motivational mechanisms) can explain the aforementioned positive correlation (Ferriter & Ray, 2011; Schulte et al., 2016). Alternatively, the concept of 'food and alcohol disturbance' suggested that symptoms of EDs (e.g., restrictive and bulimic tendencies) and alcohol use can be associated functionally (Choquette et al., 2018).

VIII/3. The role of drinking motives on the relationships between psychopathological symptoms and alcohol use-related outcomes

Study 2 showed that compared to AUD individuals with low overall psychopathological severity, those with moderate and high baseline severity levels (experiencing MDD, GAD, OCD and interpersonal sensitivity at highest) showed elevated rates of coping and conformity motives. In coping motives, alcohol drinking aims to alleviate and mitigate negative emotional states, whereas alcohol use due to conformity motives aims to avoid social disapproval or rejection (Cooper et al., 2015; Cox & Klinger, 1988; Kuntsche et al., 2005). The significant and positive associations between these latent classes of AUD and coping motives are congruous with previous literature data: higher levels of coping motives were associated with elevated rates of internalizing symptomatology, such as MDD, GAD, SAD, and OCD symptoms (Allan et al., 2015; Bakhshaie et al., 2021; Bravo et al., 2018; Cooper et al., 2015; Schry & White, 2013). Moreover, the self-medication hypothesis proposes that symptoms of MDD and ADs can predict subsequent alcohol use and problems via the alcohol drinking motivation to cope with symptoms of MDD and ADs (Hussong et al., 2011; Smith & Randall, 2012; Turner et al., 2018). Existing research also reported that conformity drinking motives are positively associated with anxiety sensitivity, SAD and BPD symptoms (Cooper et al., 2015; Kaufman et al., 2020; Schry & White, 2013). It might indicate that drinking to avoid social disapproval and rejection can be explained by the lack of effective interpersonal skills, difficulties in interpersonal relationships and assertiveness (Kaufman et al., 2020; Schry & White, 2013).

Study 4 showed the mediating function of internal drinking motives (i.e., comprising enhancement and coping motives) on the relationship between symptoms of EDs and alcohol consumption among female adolescents. Existing literature data also demonstrated that individuals with different forms of EDs (e.g., BN, BED) showed higher levels of coping

motives and enhancement drinking motives (Anderson et al., 2006; Luce et al., 2007; Mikheeva & Tragesser, 2016; Trojanowski et al., 2019). It might be possible that high levels of enhancement and coping drinking motives can indicate that alcohol drinking is used as a dominant way to regulate positive and negative emotional states (e.g., to experience or to enhance intensity of positive emotions, to cope with negative affectivity) as the alcohol using person might be short of adaptive emotion regulation strategies (Cheetham et al., 2010; Cooper et al., 2015). Alternatively, it is also possible that the symptoms of EDs can contribute to high rates of psychological distress and adverse intra- and interpersonal outcomes which might subsequently lead to elevated rates of alcohol use via coping drinking motives.

VIII/4. Limitations

The findings of the dissertation should be interpreted cautiously due to various methodological limitations. First, samples used in the dissertation might bias the findings. For example, although Studies 1, 3 and 4 used representative samples of the Hungarian adult and adolescent population, it might be possible that prevalence of alcohol use and alcohol problems were underestimated. The applied convenience and non-representative sampling in Study 2 might have influenced characteristics and limited generalizability of the AUD classes (e.g., less severe or non-treatment-seeking AUD individuals were not included). Second, the methodological designs of Studies 1-4 impeded the exploration of causal mechanisms between alcohol use-related variables and psychopathological symptoms. For example, cross-sectional design of Studies 1, 3 and 4 did not allow to determine whether different forms of psychopathological symptoms precede alcohol use or rather induced by alcohol use (i.e., bidirectional relationships). The applied before-after design of Study 2 (i.e., absence of control group, blinding, randomization, and long-term follow-up) was also insufficient to determine the specific treatment effects on psychopathological changes. Third, cross-cultural generalizability of the latent class models in Studies 1 and 3 was not tested. Fourth, the measurement of alcohol use- and psychopathology-related constructs was biased in several aspects (e.g., the possibility of recall and social desirability bias due to the use of self-report measures). The measurement of alcohol use and psychopathologies was not complete, such as not measuring specific symptoms of AUD (e.g., in Studies 1-4), alcohol problems among adolescent (e.g., in Studies 3 and 4), assessing only a limited number of psychiatric disorders (e.g., in Studies 1 and 2), not covering all aspects and symptoms of psychiatric disorders by the applied measurements (e.g., in Studies 3 and 4), using non-specific constructs of alcohol use, drinking motives and psychiatric disorders (e.g., in Studies 2 and 4). Moreover, all the studies in the dissertation were limited by not including relevant confounding or third variables which can account for the associations between alcohol use-related outcomes and psychopathological symptoms (e.g., impulsivity, sensation seeking, emotion regulation, alcohol expectancies).

VIII/5. Conclusions and practical implications

The present dissertation aimed to examine associations between alcohol consumption and various forms of psychopathological symptoms by (i) identifying empirically-based subgroups of alcohol users in clinical and general adult and adolescent samples and examining their associations with various dimensions of psychopathological symptoms and by (ii) investigating the role of drinking motives on the relationships between psychopathological symptoms and

outcomes of alcohol use. Studies 1-3 identified latent classes of alcohol use and AUD with increasing severity levels and highlighted the role of externalizing and internalizing psychopathological symptoms in alcohol classification models. Moreover, Studies 2 and 4 highlighted the role of negative reinforcement and internal drinking motives on the associations between outcomes of alcohol use and psychopathological symptoms.

By using representative, population-based samples in Studies 1 and 3, it was possible to assess and identify individuals who show hazardous patterns of alcohol and illicit drug use. Specifically, approximately 9% of the adult alcohol users showed high levels of AUD symptoms, whereas approximately 7% of the adolescent population was characterized by polysubstance use patterns. Exploring the prevalence of high-risk alcohol users in the adult and adolescent population and describing their psychological characteristics might be informative for policymakers to design more tailored prevention and intervention programs. For example, performing brief screening programs for harmful alcohol use among clients at general practitioner services, emergency departments and school-level might have a potential to identify at-risk individuals who might require assistance regarding their difficulties on alcohol use.

Findings of the present dissertation indicated that higher levels of alcohol use and problems are co-occurring with various psychopathological symptoms. Therefore, intervention and prevention programs regarding alcohol consumption might use broader focus which simultaneously covers domains of substance use and mental health (Teesson et al., 2020). Similarly, existing literature on treatment for individuals with co-occurring AUD and other psychiatric disorders proposed integrated treatment forms which is characterized by simultaneous and unified treatment of AUD and the co-occurring psychiatric disorder by the same treatment team (Flanagan et al., 2018; Smith & Randall, 2012; Yule & Kelly, 2019). Such treatment programs might include elements of motivational enhancement therapies, twelve-step-related approaches, relapse prevention focused therapies, cognitive behavioral therapies as well as address functional associations and transdiagnostic characteristics which might explain the interrelationship between the comorbid disorders, such as focusing on processes regarding emotion regulation, drinking motives, reward dysfunction, behavioral control, social skills (Flanagan et al., 2018; Helle et al., 2019; Smith & Randall, 2012; Yule & Kelly, 2019).

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[5] Publications which are presented with bold are included in the dissertation.