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Bidirectional relationship between the Body Mass Index and Substance Use in Young Men

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ABSTRACT. *Background:* Obesity and substance use are major concern in young people**.** This study explored the bidirectional longitudinal relationships between the body mass index (BMI) of young men and their use of: 1) four classes of non-medical prescription drugs; 2) alcohol; 3) tobacco; and 4) cannabis. *Methods:* Baseline and follow-up data from the Cohort Study on Substance Use Risk Factors were used (n=5,007). A cross-lagged panel model, complemented by probit models as sensitivity analysis, was run to determine the bidirectional relationships between BMI and substance use. Alcohol was assessed using risky single-occasion drinking (RSOD); tobacco, using daily smoking; and cannabis, using hazardous cannabis use (defined as twice-weekly or more cannabis use). Non-medical prescription drugs use (NMPDU) included opioid analgesics, sedatives/sleeping pills, anxiolytics and stimulants. *Results:* Different associations were found between BMT and substance use. Only RSOD (B= -.053, p=.005) and NMPDU of anxiolytics (B=.040, p=.020) at baseline significantly predicted BMT at follow-up. Baseline RSOD predicted a lower BMI at follow-up while baseline NMPDU of anxiolytics predicted higher BMI at follow-up. Furthermore, BMI at baseline significantly predicted daily smoking (B=.050, p=.007) and hazardous cannabis use (B=.058, p=.030). *Conclusions:* Our results suggest different associations between BMI and the use of various substances by young men. However, only RSOD and NMPDU of anxiolytics predicted BMI, whereas BMI predicted daily smoking and hazardous cannabis use.

Keywords: Alcohol, BMI, cannabis, cigarette smoking, longitudinal study, NMPDU

INTRODUCTION

Obesity is a major public health problem, and its prevalence is growing at an alarming rate [1]. Relative to other industrialized countries, Switzerland's prevalence of excess weight is low [2], but nevertheless has increased over the recent years. In fact, in 2012, 41% of the Swiss population aged 15 and older were overweight or obese [3]. Although, it is low in the young Swiss population (15-24 years) compared with older age groups, overweight and obesity have increased, particularly in young men, where between 1992 and 2012 overweight has almost doubled (from 12.0% to 20.3%) and obesity has increased threefold (from 1.1% to 3.2%) [4].

Substance use is also a major concern and contributes to a variety of adverse consequences (*e.g.* impaired physical health and psychosocial maladjustment) [5]. In market economies, tobacco, alcohol and cannabis use levels in young adults are high [6, 7], and heavy substance use is estimated to cause one third of deaths in young people [8]. Both substance use and obesity are prevalent among youth, and are major risk factors in the global burden of disease [9]; they have a major impact on the health of individuals, with increased morbidity and mortality, as well as reduced life expectancy [10]. In young men, substance use and obesity rates are strongly associated, and obesity among youths has tripled in the US since 1980, [9, 11, 12]. In Switzerland, obesity - although lower than in the US or in other European countries [13, 14] - has clearly increased and Swiss substance use prevalence are generally high [15].

Studies have explored how the body mass index (BMI) of young men may be related to their substance use and several mechanisms have been put forward to explain these associations. The 'coping model' suggests that overweight or obese people may use substances as a way to

cope with the negative social and emotional consequences of bearing their excess weight [9]. The 'weight-control model' explains how those who are overweight or obese may use substances as a weight control strategy [9]. Another mechanism suggests that food intake and substance use both compete for the same brain reward sites, so that a higher BMI may be associated with lower substance use [10]. Finally, according to the 'weight gain model', substance use may increase the risk of the future weight gain, especially alcohol and cannabis use. Alcohol may have an effect on a person's energy balance as the calories in alcohol can lead to weight gain over time. Cannabis use has been linked to increased appetite, thus leading to over-consumption of calories. Additionally, cannabis use can decrease inhibitions, which could result in excessive calorie intake, or alternatively, cannabis use can dull the incentive to be physically active [9]. All of these mechanisms have been put forward to explain associations between BMI and substance use in adolescents and young people in general but could also be used to explain the same associations in young men.

Depending on the mechanism, studies on BMI and substance use have shown inconsistent results. In addition, most of these studies were cross-sectional. One important criterion for determining causality, however, is temporality [16], which commonly lacks in cross-sectional research. For example, the cross-sectional study by Blüml *et al.* [10] associated a higher BMI with lower illicit drug use among young males, but no significant associations were found between BMI and either nicotine or alcohol dependence. However, other studies have found positive associations between BMI and alcohol, cigarette and cannabis use [9, 11, 12, 17]; the cross-sectional study by Fonseca *et al.* [17] showed that obese teens were significantly more likely than their non-obese peers to report drinking alcohol daily and having been drunk more than 10 times.

The study by Pasch *et al.* [12] showed a positive cross-sectional association between BMI and binge drinking (2: 5 drinks in the same occasion), alcohol, tobacco and the use of other drugs. Some longitudinal studies have shown that BMI is predicted by binge drinking, alcohol, tobacco and the use of other drugs, but not vice versa [9, 12].

Most previous studies focused on obesity and alcohol, tobacco, and the use of illicit drugs, but little is known about the relationship between BMI and non-medical prescription drug use (NMPDU). NMPDU involves the use of standard prescription drugs either without a prescription or in ways not recommended by a medical provider [18-21]. NMPDU has increased dramatically in the US and other countries around the world [18, 20, 21] and constitutes a growing public health problem [22]. Few studies have examined the relationship between BMI and NMPDU. Some studies looking at single NMPDU have shown that people misused stimulants for a common side effect (*i.e.* appetite suppression and subsequent weight loss) [23-25]. The present study aimed to explore the relationships between BMI and the use of alcohol, tobacco and cannabis, as well as a broad range of NMPDU (involving opioid analgesics, sedatives/sleeping pills, anxiolytics and stimulants) among young adult men. The present study particularly sought to explore directional relationships, *i.e.* whether the use of those substances predicts obesity or vice versa. Finding an association between obesity and NMPDU would be helpful in targeting preventive and treatment programs that for reduce health risk factors among young adults.

METHODS

Sample

Data came from the Cohort Study on Substance Use Risk Factors (C-SURF), a longitudinal study designed to assess the substance use patterns of young Swiss men and related consequences. Enrolment took place in 3 of Switzerland's 6 army recruitment centers, located in Lausanne (French-speaking), Windisch, and Mels (German-speaking). These 3 centers cover 21 of Switzerland's 26 cantons, including all French-speaking ones. Attending army recruitment is compulsory, so virtually all men around 20 years old were eligible for inclusion in the study. 15074 Swiss men were at the army recruitment and so were eligible for study inclusion. Among them, 1829 could not be informed about the study and 13245 were informed. Among the 13245 informed, 7563 (50.2% of the eligible population) gave written consent for their participation and received the questionnaire. Participants could choose between a paper and pencil version or an online version. The questionnaires were sent to the participants' private addresses either by mail or email within two weeks after enrolment. Thus, the study was conducted outside the army environment and confidentiality, particularly with regard to the army, was assured. The study protocol (Protocol No 15/07) was approved by Lausanne University Medical School's Clinical Research Ethics Committee.

Questionnaire completion lasted about one hour. The questions asked about socio-demographics, family background, social and psychological functioning, and substance use of alcohol, tobacco, cannabis and other illicit drugs. In order to increase response rates, reminders were sent to those who failed to return the questionnaire within two weeks. If individuals still did not respond three weeks later, they were contacted by telephone. So-called encouraging

telephone calls (ETC) were conducted at this stage in order to better understand the conscripts' non- response, and to encourage them to pursue their involvement in the study. ETC aimed at getting direct person-to-person contact. Interviews were inspired by motivational interviewing techniques [26]. One of the research institutions involved in the study (the Alcohol Treatment Centre in Lausanne) has particular strengths in providing brief motivational interviewing [27, 28] and experts in motivational interviewing performed the training of interviewer staff. Training was focused on avoiding a confrontational style and on using open-ended questions to get potential participants involved in reflections on their participation instead of provoking simple "yes" or "no" answers that may have led to abrupt rejection of further participation. Thus, the interview was conducted in a form to renew or increase their initial motivation for study participation and compliance.

Baseline data were collected between September 30th 2010 and March 5th 2012, and follow-up data between January 10th 2012 and April 15th 2013, *i.e.* a time frame of about 15 months between baseline and follow-up.

A total of 5,990 participants filled in the baseline questionnaire, and 5,223 (87.2% of baseline participants) filled in the follow-up questionnaire. Missing values were deleted listwise, and the final sample consisted of 5,007 participants (95.86% of the follow-up sample).
As shown in the study of Studer et al.[29] on the same dataset, there was a certain amount of non-response bias, but this was often small and went in different directions. For example, there were more alcohol abstainers among non-respondents (11.6%) than respondents (11.2%), but there were more non-smokers (63.4%) among respondents than non-respondents (49.8%), and this was also found for non-users of cannabis (respondents: 64.8%; non-respondents: 58.0%) [29]. To

analyze non-response bias, a short, five-minute questionnaire containing questions on demography, alcohol, tobacco and cannabis use was administered to all conscripts during enrolment in the army recruitment centers, yielding a response rate of 94%. Unfortunately, the brevity necessary to ensure a high response rate from non-participants in the cohort study meant that no questions about NMPDU were asked in this short questionnaire. Given the small differences for the others drugs assessed, no major non-response bias is expected for NMPDU [29, 30].

Measurements

Non-medical prescription drug use (NMPDU). NMPDU was described to participants as use of prescription drugs without a prescription or in ways not recommended by a medical provider. Both the baseline and follow-up questionnaires assessed the frequency of NMPDU for 6 drug classes (opioid analgesics, sedatives/sleeping pills, anxiolytics, antidepressants, beta blockers and stimulants) over the last 12 months. The present study focused on the 4 most prevalent NMPDU (*i.e.* opioid analgesics, sedatives/sleeping pills, anxiolytics and stimulants). Examples were given for each class: a) sedatives/sleeping pills (*e.g.* benzodiazepines like Dalmadorm® or Rohypnol®; zopiclone or zolpidem like Imovane® or Stilnox®; chloral hydrate; barbiturates); b) anxiolytics (*e.g.* benzodiazepines like Valium®, Xanax®, Librax®; muscle relaxants); c) opioid analgesics excluding aspirin and paracetamol (*e.g.* codeine, Benylin®; opiates like fentanyl, hydrocodone; buprenorphine like Tamgesic®); d) stimulants (*e.g.* amphetamine sulfate, atomoxetine or methylphenidate). The frequency of NMPDU was dichotomized as 'use' or 'no use' in the past 12 months. NMPDU prevalence was first

calculated, for any use (*i.e.* use of at any one class of drugs at least once in the past 12 months) and then separately for each of the 4 drug classes.

Frequency of risky single-occasion drinking (RSOD). RSOD was assessed at baseline and follow-up and was defined as drinking 6 or more drinks at the same occasion. This is the most common definition of RSOD. [31] Given that standard drinks in the US contain between 12 and 14 grams of pure ethanol and that in Switzerland it is between 10 and 11 grams, the 5+ measure used in the US is comparable to the 6+ measure used in Switzerland. At risk of RSOD was coded '0' for no or less than monthly RSOD, and '1' for monthly or more frequent RSOD.

Daily smoking. The frequency of cigarette smoking was assessed and measured at baseline and follow-up and dichotomized as follows: daily smoking was coded '1' and less than daily smoking was coded '0'.

Hazardous cannabis use. Frequency of cannabis use was assessed at baseline and follow-up by asking participants how many times they had used cannabis during the past 12 months. These answers were dichotomized as follows: use once a week or less (non-hazardous cannabis use) was code '0' and twice-weekly or more frequent use (hazardous cannabis use) was coded '1'.

BMI. Participants self-reported their weight and height at both stages of the survey. These data were used to calculate BMI (kg/m^2), which is the currently accepted measure for classifying weight-related health risk. [32] Participants were categorized as underweight (BMI < 18.5), normal weight (BMI 18.5 to < 25), overweight (BMI 25 to < 30) and obesity (BMT 2:30). [33, 34] BMI was coded '0' for underweight and normal weight, and '1' for overweight and obesity. Overweight and obesity were combined in a single category due to the small prevalence of obese men, which

were also found in general population samples of young men in Switzerland, where obesity prevalence was 3.2% in 2012 compared to the overweight prevalence of 20.3% in 2012 [4].

Covariates. Demographic covariates included: age; marital status (coded 'single/divorced' or 'married/couple'); educational level (coded 'primary', < 10 years of schooling; 'secondary', 10-12 years; 'tertiary', 13 years or more); and current living arrangements (coded 'living in a family/couple' or 'alone/orphanage/foster home/homeless') at baseline. These were measured at baseline and follow-up, but only the baseline covariates were used as adjustment variables in the cross-lagged models. These variables were used because their association with substance use has been demonstrated in other studies and thus may confound the relationship with BMI [6, 35, 36].

Statistical analysis

Analyses included the descriptive demographic characteristics of the sample, followed by a cross-lagged panel model to determine the bidirectional relationships between BMI and the different types of substance use (*i.e.* RSOD, daily smoking, hazardous cannabis and NMPDU). This type of structural equation model tests the significance of the cross-lagged paths (*e.g.* baseline substance use to follow-up BMI, and baseline BMI to follow-up substance use) while controlling for the stability of the variables and covariates of interest across time (Figure 1). This technique involves computing three types of correlations between variables measured at two time points (baseline and follow-up). [37] Synchronous correlations (not presented in Figure 1, but included in the model) refer to the cross-sectional association between variables at each time point; autocorrelations refer to the association of a variable at follow-up with its own level at

baseline; and cross-lagged correlations refer to the association of a variable at follow-up with other variables at baseline. Variables were defined as categorical variables. Categorical variables were handled by means of with a weighted least squares means and variance adjusted (WLSMV) estimator in multivariate probit threshold models.

The cross-lagged panel analyses were conducted using version 7.11 of the MPlus statistical program [38]. As sensitivity analysis, suggested by an anonymous referee, a series of eight probit multiple regressions was also conducted using Stata 13 [39]: each variable at follow-up (4 NMPDU, RSOD, daily smoking, hazardous cannabis use, and BMI) was separately regressed on all baseline variables including the dependent variable at baseline (baseline adjustment). Such analyses are comparable to cross-lagged analysis in Mplus, except that correlations between residuals of the outcomes are not taken into account and that a maximum likelihood (ML) rather than WLSMV estimator is used. One advantage of this analysis is that - contrary to the cross-lagged panel model in MPlus - probit models in Stata also provide adjusted risk ratios (ARR). ARR and 95% confidence intervals (CI) were computed using the adjrr command [40] implemented in Stata because ARR are generally more easily interpretable than regression coefficients.

Insert Figure 1 about here

RESULTS

The mean age of participants was 20.0 ± 1.2 years at baseline and 21.2 ± 1.2 years at follow-up, *i.e.* about 15 months difference. Table 1 presents the distribution of the baseline and follow-up data according to the measurements included in the analyses. The majority of participants declared no NMPDU (89.79%, thus the prevalence of any use was 10.21%). The most prevalent NMPDU reported by these young adults was for opioid analgesics (6.65%). At baseline, 45.98% of participants reported at least monthly RSOD, 18.57% were daily smokers and 8.57% were hazardous cannabis users. A total of 20.31% of participants was either overweight or obese.

Insert Table 1 about here

The cross-lagged analyses examining the associations between BMI and substance use are depicted in Figure 2. For clarity, only significant autocorrelations and cross-lagged correlations from BMI at baseline to substance use variables at follow-up and from substance use variables at baseline to BMI at follow-up are presented. Cross-lagged analyses using MPlus and probit regression models conducted as sensitivity analyses with Stata yielded results that were different only in the 3rd decimal of the unstandardized and standardized coefficients. Therefore, standardized estimates obtained in cross-lagged analyses with MPlus were reported along with ARR and 95% CI obtained from probit regression models in Stata.

In cross-lagged analyses, autocorrelations were significant for all variables and indicated a certain stability over time (B ranged from .153 to .679). Besides the autocorrelation of BMT, only RSOD (B = -.053, p =.005, ARR = 0.90, 95% CI = 0.83-0.97) and NMPDU of anxiolytics (B = .040, p = .020, ARR = 1.29, 95% CT = 1.02-1.69) at baseline significantly predicted BMI at follow-up. Tn turn, BMT at baseline significantly predicted daily smoking (B = .050, p = .007, ARR = 1.13, 95% CI = 1.03-1.23) and hazardous cannabis use (B = .058, p = .030, ARR = 1.19, 95% CI = 1.01-1.40), but not NMPDU use nor RSOD.

Insert Figure 2 about here

DISCUSSION

There is an increase of overweight and obesity in many countries, including Switzerland. Overweight and obesity is becoming also a major concern in young men; our results showed a prevalence of overweight and obesity of around 20%, which is in agreement with large Swiss Health Surveys in Switzerland.

This study aimed to explore the bidirectional longitudinal relationships between the body mass index (BMI) of young men and their use of: 1) four classes of non-medical prescription drugs; 2) alcohol; 3) tobacco; and 4) cannabis. The study found clear but varying associations between BMI and substance use (*i.e.* RSOD, daily smoking, hazardous cannabis use and NMPDU). Our results showed that all these associations were unidirectional.

Alcohol (i.e. RSOD) and anxiolytics (as NMPDU) were the only two substances that predicted BMI at follow-up. Baseline RSOD predicted a lower likelihood of being overweight or obese at follow-up. This result was in accordance with the hypothesis that food intake and substance use both compete for the same brain reward sites; and that a higher BMI may be associated with lower substance use [10]. This finding is consistent with the research which showed that alcohol is inversely related to obesity [41, 42], but in contrast to Yeomans *et al.* [43], who found that binge drinking (in the absence of alcohol dependence) was linked with higher BMI.

Baseline NMPDU of anxiolytics predicted a higher likelihood of being overweight or obese at follow-up. This result is not consistent with the hypothesis that food intake and substance use compete with each other for the same brain reward sites, nor that a higher BMI may be associated with lower substance use. Furthermore, neither the coping nor the weight control strategy models manage to explain why NMPDU of anxiolytics at baseline predicted obesity in subjects. The association between BMI and NMPDU of anxiolytics might be explained by the fact that these drugs reduce the anxiety subjects feel, improving their appetite and thus increasing their BMI (in subjects where stress reduces their appetite) [44, 45].

No significant associations were found between NMPDU of opioid analgesics, sedatives/sleeping pills or stimulants and BMI. This suggests that these drugs have no prospective effects on BMI in young males. The lack of a significant association between the NMPDU of stimulants and BMI was surprising, because previous studies [23, 46] have shown that some young adults misuse stimulants for weight loss. The still low prevalence rates of these drugs in Switzerland may partly explain this lack of significance compared with higher use levels e.g. in the US. The sample size, however, is sufficient for small effect sizes. Therefore the small

prevalence rates of NMPDU may just mean that NMPDU, including NMPDU as a strategy for weight control, is not yet a widespread behavior, which may be the case in other countries with higher prevalence rates. Continued research to explore the longitudinal relationships between BMI and NMPDU in Europe is very much needed to confirm our results.

Baseline BMI predicted tobacco and cannabis use. This finding can be explained by two possible mechanisms. The coping model suggests that overweight and obese young men may use substances as a way to cope with the negative social and emotional consequences of being overweight or obese in the first place. The weight-control model explains how being overweight may increase the risk of substance use as a weight control strategy. The present study was consistent with the study by Liu *et al.* [47], who showed that smoking was associated with a higher BMI among adolescents; it was neither consistent with studies which found no association or an inverse association between BMI and nicotine or cannabis use [9, 10, 48, 49], nor was the finding consistent with Brook *et al.* [50], who showed that cannabis decreased the risk of obesity.

This study had some limitations. First, data used in this study were self-reported. Although self-reported data on risky behaviors and substance use are generally considered valid, [51] self-reported surveys could introduce various forms of bias; these include recall bias, pressure to give desirable answers and non-response bias. Concerning self-reported weight/height data to calculate BMI the literature is mixed. For some authors, data are sufficiently reliable to be used in young adults [52], but other authors come to different conclusions [53]. In Switzerland it is likely that height/weight is underreported [54], but differential underreporting is mostly related to different ages, which is a more or less constant factor in the present study. Also, when measuring associations with individual data, a main assumption in epidemiology for a reliable instrument is

that rank order should be preserved [55, 56] (i.e., despite potential underreporting of BMT the "true" overweight or obese should just weigh more than the "true" normal weight subjects). Second, the cross-lagged analysis used in this study provides an indication of temporal precedence, but cannot be considered an absolute proof of causation [37]. Finally, this study comprised only young men and cannot therefore be generalized to women, although they are known to misuse prescription drugs, too.

Conclusions

With regard to the lack of consistent studies on this topic, especially longitudinal ones, as well as to the scarcity of studies on the associations between BMI and NMPDU, the present study provides unique information about the BMI of respondents declaring NMPDU for 4 different classes of drugs. NMPDU of anxiolytics increases the chances of higher BMI, while RSOD decreases it; in the other direction, a higher BMI increases the chances of daily smoking and hazardous cannabis use. To the best of our knowledge, this is the first time that these relationships have been described within a single study and findings may be helpful in developing strategies for the prevention of weight gain, obesity, and substance use in young men.

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AUTHOR CONTRIBUTIONS

AN was primarily responsible for the design and drafted the manuscript. GG helped improve the manuscript during the process. Finally, SB, JS, SD, YH, MM and JD made contributions to the content of the manuscript. All authors read and approved the final manuscript.

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Table 1: Descriptive data on BMI, substance use and covariates at baseline and follow-up. N = 5007

Variables	Baseline Mean±SD	Follow-up Mean±SD
Age	20.0 ± 1.2	21.2 ± 1.2
Weight	73.8±11.7	75.0±11.5
Height	179.0±6.5	179.4±6.5
BMI	23.0±3.3	23.3±3.2
Alcohol per day	4.3±3.8	4.3±3.4
Cigarettes per day	7.7±7.2	8.2±7.1
Educational level	**n (%)**	**n (%)**
Primary (< 10 years)	2439 (48.71)	348 (7.0)
Secondary (10-12 years)	1244 (24.85)	2120 (42.3)
Tertiary (13 years or more)	1324 (26.44)	2539 (50.7)
Relationship status		
Single/divorced	4765 (95.2)	4701 (94.0)
Married/couple	242 (4.8)	306 (6.0)
Current living arrangements		
Family/couple	4839 (96.6)	4648 (92.8)
Other	168 (3.36)	359 (7.2)
BMI		
Underweight/normal	3990 (79.69)	3928 (78.45)
Overweight/obese	1017 (20.31)	1079 (21.55)
RSOD		
Yes	2302 (45.98)	2215 (44.24)
No	2705 (54.02)	2792 (55.76)
Daily smoking		
Yes	930 (18.57)	1042 (20.81)
No	4077 (81.43)	3965 (79.19)
Cannabis use		
Hazardous	429 (8.57)	389 (7.77)

Non-hazardous	4578 (91.43)	4618 (92.23)
Non-medical prescription drugs use		
Any use	511 (10.21)	464 (9.27)
No use	4496 (89.79)	4543 (90.73)
Kind of drugs		
Opioid analgesics	333 (6.65)	307 (6.13)
Sedatives/sleeping pills	145 (2.90)	145 (2.90)
Anxiolytics	130 (2.60)	125 (2.50)
Stimulants	94 (1.88)	85 (1.70)

BMI: body mass index RSOD: risky single-occasion drinking

Figure captions:

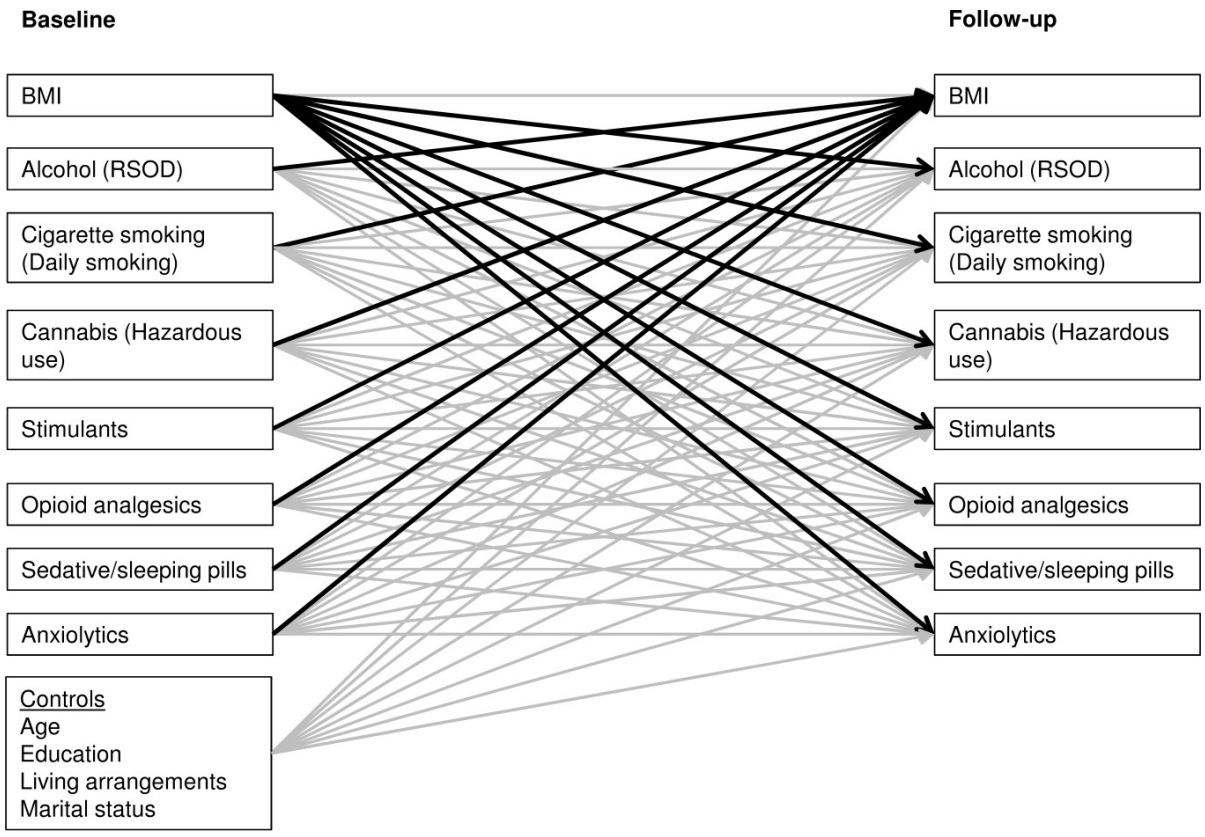

Figure 1: Conceptual model of the cross-lagged relationships between BMI and substance use

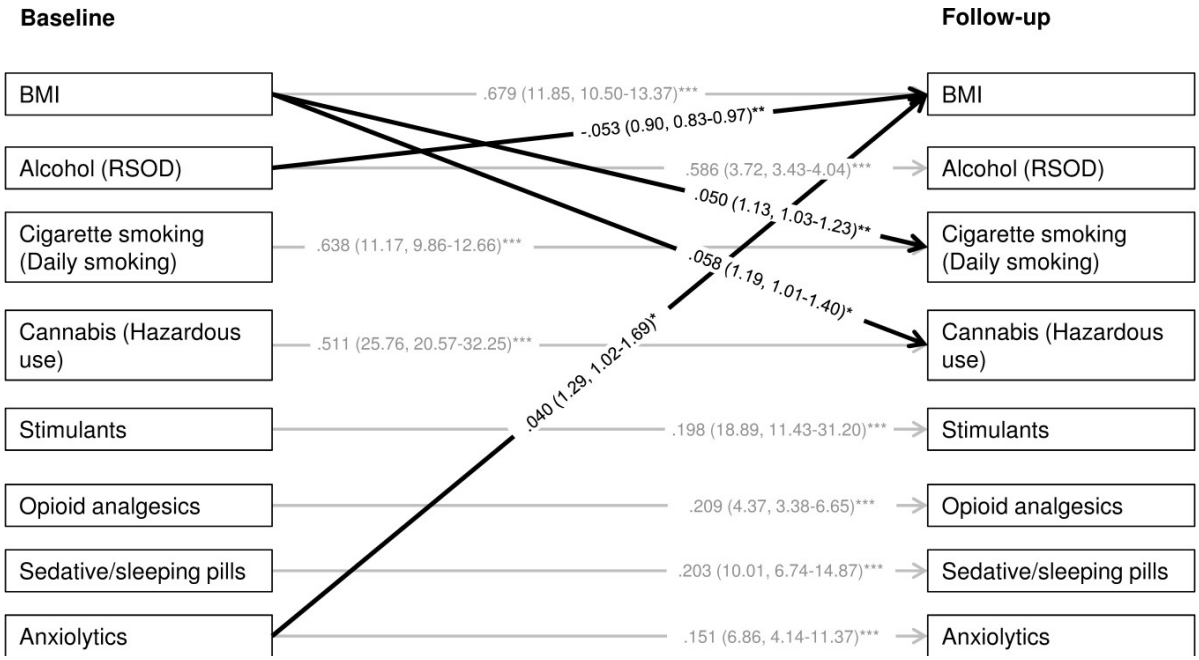

Figure 2: Cross-lagged model analyzing the longitudinal relationships between the BMI and substance use.