Title: Association between nonmedical prescription drug use and health status among young Swiss men.
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Journal: The Journal of adolescent health : official publication of the Society for Adolescent Medicine
Year: 2014 Oct
Volume: 55
Issue: 4
Pages: 549-55
DOI: 10.1016/j.jadohealth.2014.04.004

Associations between Non-Medical Prescription Drug Use and Health status among young men: a prospective study in Switzerland.

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Acknowledgements

This work was supported by Swiss National Science Foundation (SNSF) grant FN 33CS30_139467.

Conflict of interest

The authors declare no conflicts of interest.

Word count: 3,484 words

Number of tables: 3

Abstract (250 words)

Purpose Examine the relationship between the non-medical prescription drug use (NMPDU) of 6 drug classes and health.

Methods Data from the baseline and follow-up of the Cohort Study on Substance Use Risk Factors (C-SURF) were used (n = 4,958). Two sets of logistic regression models were fitted to examine the associations between NMPDU of opioid analgesics, sedatives/sleeping pills, anxiolytics, antidepressants, beta blockers and stimulants, and health status *(SF-12v2).* We first computed odds ratios (ORs) between NMPDU at baseline and poor mental and physical health at follow-up, adjusting for poor mental or physical health at baseline. We then computed ORs between poor mental and physical health at baseline and NMPDU at follow-up, adjusting for NMPDU at baseline.

Results Three key findings regarding mental health were: first, there was a reciprocal risk between poor mental health and sedatives and anxiolytics; second, poor mental health increased NMPDU of opioid analgesics and antidepressants, but not vice versa; and third, there were no associations with stimulants.

Three key findings regarding physical health were: first, poor physical health increased the risk of NMPDU of anxiolytics; second, the only reciprocal risk was between physical health and NMPDU of opioid analgesics; and third, there were no associations with stimulants.

Conclusion These results, among the first ever on reciprocal effects between NMPDU and mental and physical health status, give unique information concerning the adverse

effects of NMPDU on health and vice versa. The study shows that NMPDU is not only a sign of self-medication, but may induce health problems.

Key words: Longitudinal study, mental health, NMPDU, physical health, Switzerland, young men

Implications and Contribution (49 words)

This study is among the first to examine the longitudinal association of non-medical prescription drug use (NMPDU) and poor health status. Findings suggest that there is a reciprocal risk between NMPDU of sedatives and anxiolytics and poor mental health; there is no association with stimulants and poor health status.

1. INTRODUCTION

Prescription drugs such as opioid analgesics, sedatives/sleeping pills, anxiolytics and stimulants are all considered medically sound and effective in treating a wide range of disorders (1). However, because of the potential for abusing or becoming dependent on them (2-5), non-medical prescription drug use (NMPDU) can occur. NMPDU involves either using a drug without a prescription or in ways not recommended by a doctor (2, 6-8). NMPDU is on the rise in the United States (US) (2, 5), concerns many drug classes and constitutes a growing public health problem (9). Furthermore, NMPDU of opioid analgesics is the second most frequent illicit use of drugs, after cannabis (8, 10, 11). In the US, in 2010, 3.6% of those aged 12 or older were current users of illicit drugs other than cannabis, with the majority of them non-medical users of psychotherapeutic drugs (8, 12, 13). Young adults now misuse prescription drugs at higher rates than illegal drugs with the exception of cannabis (9), and men commonly use drugs more often than women (14). However, there have been few studies outside the US—particularly few in Europe and Switzerland (10, 15-17). NMPDU in Switzerland is also a major concern and, for males, ranks just after alcohol, tobacco and cannabis use (10). The present study looks at NMPDU and related health issues in Swiss young men from a longitudinal perspective.

Prescription drugs can increase the risk of psychiatric and other medical disorders (2); excessive or inappropriate drug use, whether continuous or intermittent, may have detrimental consequences for the physical or mental health of the consumer/patient (18). For example, NMPDU of opioids increases the risk of developing opioid-use disorder (7, 8). It is well known, and unsurprising, that individuals in poor health use

more medicine (19), but there is also an association between health and substance use in adolescents who choose to cope with their pressures by abusing both licit and illicit substances (20). However, little is known about NMPDU. Studies in this field are commonly cross-sectional and focus on relationships between substance abuse and health status (21, 22). Few studies have examined the specific associations between NMPDU and health status, and their cross-sectional design prevented them from drawing any causal interpretations. Furthermore, the few studies on the relationships between NMPDU and health status generally focused on NMPDU of opioid analgesics, benzodiazepines or stimulants alone (8, 13), showing positive associations with pain, but also with psychiatric disorders (7, 13, 23, 24). However, a longitudinal study by Martins *et al.* (8) showed that the association between mood/anxiety disorders and non-medical prescription opioid use could arise in one or more non-mutually exclusive ways: non-medical prescription opioid use lead to mood/anxiety disorders (the 'precipitation' hypothesis); mood/anxiety disorders lead to non-medical prescription opioid use (the 'self-medication' hypothesis); and/or a third factor influences vulnerability to both ('shared vulnerability'). The present study looks at NMPDU among twenty-year-old men in Switzerland. In addition to the commonly studied drug classes, it also looks at the NMPDU of: 1) beta blockers (which may be misused for their anti-tremor and, perhaps to a lesser degree, anti-anxiety effects) (25); and 2) antidepressants widely used against symptoms of depressive disorders and increasingly for anxiety disorders (26). Moreover, these two substances are among those used by healthy individuals trying to enhance their cognitive function (*e.g.* increased concentration and focus) for specific reasons (*e.g.* reduce anxiety and fear), particularly students facing exams (17, 27).

Hence, it would be valuable to know whether and how these two drug classes are related to mental and physical health.

To the best of our knowledge, no single longitudinal study has yet examined the relationships between the NMPDU of six drug classes and physical and mental health in young men. It thus remains unclear whether all NMPDU induces poor mental and physical health, or *vice versa*, whether there is a reciprocal risk association, and what the nature of the associations might be. The present study investigates the associations between poor health (*i.e.* mental and physical) and six NMPDU classes (*i.e.* opioid analgesics, sedatives/sleeping pills, anxiolytics, antidepressants, beta blockers and stimulants) instead of just focusing on the most studied drugs (*i.e.* opioid analgesics, benzodiazepines and stimulants). Further, it investigates the bidirectional relationships between NMPDU and poor mental and physical health using a large sample of young men in Switzerland.

2. METHODS

2.1. Sample

Data came from the Cohort Study on Substance Use Risk Factors (C-SURF), a longitudinal study designed to assess substance use patterns among young Swiss men and the related consequences. Enrolment took place in 3 of 6 national Swiss army recruitment centers, located in Lausanne (French-speaking), Windisch and Mels (German-speaking). Including all 6 centers would have proved logistically infeasible (*e.g.* including the Italian-speaking center would have required questionnaires in a third language, despite less than 5% of Swiss speaking Italian; each center required its own research team for enrolling participants throughout the year; and, for administrative reasons, the army was unwilling to give access to all its centers, but provide it for the largest). These 3 centers cover 21 of Switzerland's 26 cantons, including all French-speaking cantons.

Attending army recruitment is compulsory, so virtually all 20-year-old men in these regions were eligible for study inclusion. Thus, there were no complex sampling design features (*e.g.* related to oversampling of age groups or cantons). It is important to note that this study was conducted outside any military context. Contrary to most existing studies on substance use among young adults, whose samples consist essentially of college students, C-SURF had the unique advantage of enrolling a highly representative sample of the general population of young Swiss men. Women were not eligible for inclusion in C-SURF. Because their military recruitment is voluntary, the small number of women who enroll in the army is not representative of the general female population in this age group.

Questionnaires in French or German (see: http://www.c-surf.ch/en/30.html) were sent to the 7,563 private addresses of those who gave written consent to participate. Baseline data were collected between September 30th 2010 and March 5th 2012; follow-up data between January 10th 2012 and April 15th 2013. The baseline and follow-up timeframe was thus about 15 months. A total of 5,990 participants filled in the baseline questionnaire; 5,223 (87.2%) filled in the follow-up questionnaire. Missing values were deleted listwise; the final sample consisted of 4,958 participants (94.9% of the follow-up sample). As shown in the study of *Studer et al.*, there was a certain amount of non-response bias, but this was often small and went in different directions. For the Francophone sample, 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 found for cannabis non-users too (respondents, 64.8%; non-respondents, 58.0%) (28). To analyse non-response bias, a short, five-minute questionnaire containing questions on demography, alcohol, tobacco and cannabis use was administered to all conscripts in the recruitment process, 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, we did not expect a major non-response bias for NMPDU (28, 29).

The study protocol (Protocol No 15/07) was approved by Lausanne University Medical School's Clinical Research Ethics Committee.

2.2. Measurements

2.2.1. NMPDU

NMPDU was described to participants as use of prescription drugs without a prescription or in ways not recommended by a doctor.

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. 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) antidepressants (*e.g.* Fluoxetine®, Remeron®); e) stimulants (*e.g.* amphetamine sulfate, atomoxetine or methylphenidate); and f) beta blockers (*e.g.* propranolol, atenolol or metoprolol). The frequency of NMPDU was dichotomized as ‘use’/‘no use’ over the past 12 months. NMPDU prevalence was first calculated for any use (*i.e.* use of at least one class at least once in the past 12 months) and then separately for each of the 6 drug classes.

2.2.2. Health Status

Health was assessed using the *‘Medical Outcomes Study 12-Item Short Form Survey Instrument’ (SF-12 v2)(30)*. This is a multipurpose, short form survey with 12 questions, all selected from the SF-36 Health Survey (31). The SF-12 is a generic measure and does not target a specific age or disease group. It was developed to provide a shorter,

yet valid alternative to the SF-36, and is weighted and summed to provide easily interpretable scales for physical and mental health. Its scoring guidelines allow two summary scores to be derived: the 'physical health summary' score and the 'mental health summary' score. These range from 0 to 100 and are computed using the scores from 12 questions; zero and 100 indicate the lowest and highest levels of health measured by the scale, respectively. Linear transformations were performed to obtain norm-based scores (mean = 50; SD = 10). Due to the non-normal distribution of these standardized summary scores, we dichotomized them into 'good health' (≥ 45, coded '0') and 'poor health' (< 45, coded '1') based upon clinical meaningfulness (32, 33) defining ½ a standard deviation (SD; *i.e.* 5).

2.2.3. Covariates

Demographic covariates included: age; alcohol use with binge drinking classed as frequency of 6 drinks or more (non binge drinking coded '0'; binge drinking coded '1'); tobacco (less than daily smoking coded '0'; daily smoking coded '1'); cannabis (used once a week or less, i.e. non-hazardous cannabis use, coded '0'; twice weekly use or more, i.e. hazardous cannabis use, coded '1'); marital status (coded 'single/divorced' or 'married/couple'); educational level (< 10 years of schooling, coded 'primary'; 10–12 years, coded 'secondary'; 13 years or more, coded 'tertiary'); and current living arrangements (coded 'living in a family/couple' or 'living alone/orphanage/foster home/homeless').

2.3. Statistical analyses

All analyses were performed using Stata software, version 12. Analyses included descriptive demographic characteristics of the sample, followed by logistic regression

models to assess: 1) associations between any and specific NMPDU at baseline and poor health (separately for mental and physical health) at follow-up; and 2) associations between poor health (separately for mental and physical health) at baseline and any and specific NMPDU at follow up.

To examine the causal effects of NMPDU on poor mental and physical health, two sets of models were fitted. Odds ratios (ORs) were computed between NMPDU at baseline and poor mental and physical health at follow-up, adjusting for poor mental or physical health at baseline and for the other covariates. All participants with poor mental or physical health at baseline were then excluded in order to establish the causal relationship between NMPDU at baseline and the incidence of poor mental or physical health at follow-up. Accordingly, 1,265 participants in poor mental health at baseline were excluded (N = 3,693) from the models predicting poor mental health at follow-up, and 247 participants in poor physical health at baseline were excluded (N = 4,711) from the models predicting poor physical health at follow-up. The rates for any NMPDU between those excluded and those who participated did not vary.

Two sets of models were also fitted to examine the causal effects of poor mental and physical health on NMPDU. ORs between poor mental or physical health at baseline and NMPDU at follow-up were estimated, adjusting for NMPDU at baseline and for the other covariates. In order to establish any causal relationships between mental/physical health at baseline and incidence of NMPDU at follow up, the models were fitted again, excluding all participants with NMPDU at baseline. NMPDU of each drug class and of any NMPDU (*i.e.* the use of at least one class) were assessed, respectively. All analyses were made separately for mental and physical health.

In order to carry out a sensitivity analysis, all these calculations were repeated using the continuous scores. Those results tended towards the same conclusions; however we choose to use dichotomized variables for clearer clinical meanings.

3. RESULTS

The mean age of participants was 19.96 ± 1.19 years at baseline and 21.25 ± 1.21 years at follow-up, *i.e.* about 15 months difference.

Table 1 presents the distribution of the baseline cohort according to the measures analyzed. The majority of participants declared no NMPDU (89.49%, thus prevalence of any use was 10.51%). The most prevalent NMPDU reported by these young adults were for opioid analgesics (6.53%), sedatives/sleeping pills (2.88%) and anxiolytics (2.56%).

A total of 25.51% had poor mental health and 4.98% had poor physical health.

Insert Table 1 about here

Examining the effects of NMPDU at baseline on poor health status at follow-up, after adjustment (Table 2), the only positive and significant relationships were for any NMPDU, sedatives/sleeping pills and anxiolytics, with adjusted ORs (AORs) of 1.26 [1.03–1.54], 1.45 [1.01–2.08], and 1.52 [1.04–2.24], respectively. After excluding participants with poor mental health at baseline, NMPDU of anxiolytics and beta blockers at baseline was significantly associated with an increased risk of poor mental health (AORs were 2.11 [1.25–3.56] and 2.97 [1.04–8.51], respectively). Generally, NMPDU at baseline increased the risk of poor mental health at follow-up, even if the association was not always significant.

Concerning poor physical health, a positive and significant association with the NMPDU of opioid analgesics was only observed in the adjusted model; AOR was 1.55 [1.00–

2.42] in the adjusted model. Generally, NMPDU at baseline did not increase the risk of poor mental health at follow-up.

Insert Table 2 about here

The effects of poor mental health status at baseline was significantly and positively related to any NMPDU and to 4 classes of NMPDU at follow-up, but not to stimulant and beta blocker use (Table 3). Results remained the same in both the adjusted model and after excluding participants with NMPDU at baseline. There was a reciprocal risk between poor mental health and anxiolytics and sedatives/sleeping pills; opioid analgesics, antidepressants and beta blockers showed a unidirectional association; and there was no association between poor mental health and stimulants.

In the adjusted model, the only significant and positive associations between poor physical health at baseline and NMPDU at follow-up, were with the NMPDU of opioid analgesics and anxiolytics; AORs were 1.82 [1.18–2.81] and 2.10 [1.07–3.77], respectively. Excluding NMPD users at baseline, the AOR between poor physical health at baseline and NMPDU incidence was significant for all classes of NMPDU except for any NMPDU and stimulants. Therefore, the only reciprocal risk was between poor physical health and NMPDU of opioid analgesics; poor physical health increased the risk of almost all incidences of NMPDU.

Insert Table 3 about here

These analyses were repeated with continuous instead of dichotomous health scores; the direction and size of effects remained basically the same.

4. DISCUSSION

This study finds a clear association between NMPDU and health status. However, the associations between NMPDU and health status arise in one or more non-mutually exclusive ways.

Poor mental health

For the association of NMPDU and poor mental health, there are 3 key findings. First, no association was found between poor mental health and NMPDU of stimulants. Second, there were 2 unidirectional associations: poor mental health increased NMPDU of opioid analgesics and antidepressants. The finding that poor mental health increased NMPDU of opioid analgesics is consistent with Zullig *et al.*'s cross-sectional study(13) and with the self-medication hypothesis in Martins *et al.*'s study(8). In this hypothesis, NMPDU occurs after mental health problems have occurred, *i.e.* individuals with poor mental health engage in NMPDU to relieve their symptoms (8). The fact that poor mental health increased NMPDU of antidepressants can also be interpreted as self-medication, but this is only speculation. Therefore, developing prevention strategies about self-medication and its consequences on mental health problems are important. Third, there were reciprocal associations between any NMPDU, NMPDU of sedatives/sleeping pills and NMPDU of anxiolytics, and poor mental health. This suggests that NMPDU of sedatives/sleeping pills and anxiolytics at baseline increased the risk of poor mental health at follow-up, and *vice versa*. We can interpret this to mean that NMPDU occurs not only to self-medicate poor mental health, but that NMPDU for other reasons may lead to poor mental health. Although not all associations remained

significant, this interpretation is bolstered by the fact that the strength of associations remained consistent even after excluding men with poor mental health at baseline. Comparisons with earlier findings are difficult. To our knowledge, this is the first study published using prospective data to examine reciprocal effects between NMPDU for 6 different classes of drugs and health status. Our findings show that NMPDU is a predictor of poor mental health; this is consistent with the fact that illicit drug use/NMPDU is widely thought to have a negative effect on health status in general (21, 34). They also confirm previous studies indicating that poor health is a predictor of (both any and specific) NMPDU (7, 35-37).

The present study's findings suggested that young men in poor health may self-medicate, and those declaring NMPDU may worsen their health status over time due to side effects (from the frequencies or quantities of drugs taken). Confirming these results will require future studies to look at usage frequencies, quantities taken and motives for NMPDU. The present study's data failed to demonstrate that the NMPDU of stimulants was associated with poor mental health and *vice versa.* However, the lack of their effects on health may result from the lower prevalence rates of NMPDU of stimulants in this study. It is possible that men with mental health problems do not self-medicate using stimulants, because this may make them even more restless and uneasy. It is notable that, besides antidepressants, other drug classes were more 'downers' than 'uppers'. It is possible that people receiving stimulants in stimulant treatment do not use them non-medically. Finally, it may be that stimulants used as drugs for their perceived effects are easily accessible on the illicit drug market; hence, due to much lower stimulant doses, and thus weaker effects, NMPDU may just not be as attractive as is in

the US. However, we can only speculate about this finding. Due to inconclusive data on this issue, further research will be needed to confirm these results.

Poor physical health

For the association of NMPDU and poor physical health, there are 3 key findings. First, poor physical health at baseline increased the risk of NMPDU of anxiolytics at follow-up, but not *vice versa*. Second, only NMPDU of opioid analgesics and poor physical health showed reciprocal risk. Third, there was no association between poor physical health and the NMPDU of stimulants. Results showing that poor physical health may be a precursor for NMPDU are consistent with Simoni-Wastila *et al.*'s study (38). This is explained by the self-medication hypothesis: it is well known that people self-medicate when they are not well. For example, studies have shown positive associations between NMPDU of opioids and pain (7, 23). Stogner and Gibson (20) described a link between illicit drugs and health problems that is consistent with our results; we also found a link between NMPDU and physical health problems. We suggest that regardless of the kind of drug used, there is a link with physical health.

Generally, the mechanisms which influence adolescent medicinal drug use are not well understood, but our findings suggested that self-medication as a coping strategy may be an important factor, *i.e.* a response to internal or external strain.

Limitations

This study had some limitations. First, study data were self-reported. Although self-reported data on risky behaviors and substance use are generally considered valid (39), self-reported surveys could introduce various forms of bias, including recall bias,

pressure to give desirable answers and non-response bias. Second, this study's sample inclusion criteria meant it comprised only men. Therefore generalizations about health status and NMPDU for women cannot be made, although they are known to misuse prescriptions drugs too.

Finally, we did not use diagnostic criteria to classify men's mental health, but a self-reported screening tool, which might explain the rather low poor mental and physical health prevalence rates obtained.

Conclusion

Due to the lack of longitudinal studies on this topic, this study provides unique information about the mental and physical health status of respondents declaring NMPDU for 6 different classes of drugs. To our knowledge, this is the first time that these relationships have been described in the same study. Our findings showed that NMPDU of most classes of drugs were linked with health status (both mental and physical), however no association was found with NMPDU of stimulants. These results could help address prevention strategies to young adults about the growing public health problem of NMPDU.

Authors' contributions

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

References

1. McCabe SE, West BT, Cranford JA, et al. Medical misuse of controlled medications among adolescents. Arch Pediatr Adolesc Med. 2011;165(8):729-35.
2. Blanco C, Alderson D, Ogburn E, et al. Changes in the prevalence of non-medical prescription drug use and drug use disorders in the United States: 1991–1992 and 2001–2002. Drug Alcohol Depend 2007;90(2–3):252–60.
3. Compton WM, Volkow ND. Abuse of prescription drugs and the risk of addiction. Drug Alcohol Depend. 2006;83(Supplement 1):S4–S7.
4. Stoops W, Tindall M, Mateyoke-Scrivner A, Leukefeld C. Methamphetamine Use in Nonurban and Urban Drug Court Clients. Int J Offender Ther Comp Criminol. 2005;49(3):260-76.
5. Zacny J, Bigelow G, Compton P, Foley K, Iguchi M, Sannerud C. College on problems of drug dependence taskforce on prescription opioid non-medical use and abuse: position statement Drug Alcohol Depend. 2003;69(3):215-32.
6. Ghandour LA, El Sayed DS, Martins SS. Prevalence and patterns of commonly abused psychoactive prescription drugs in a sample of university students from Lebanon: an opportunity for cross-cultural comparisons. Drug Alcohol Depend. 2012; 121(1–2):110–7.
7. Huang B, Dawson DA, Stinson FS, et al. Prevalence, correlates, and comorbidity of nonmedical prescription drug use and drug use disorders in the United States: Results of the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2006;67(7):1062-73.
8. Martins SS, Fenton MC, Keyes KM, Blanco C, Zhu H, Storr CL. Mood and anxiety disorders and their association with non-medical prescription opioid use and prescription opioid-use disorder: longitudinal evidence from the National epidemiologic Study on Alcohol and Related Conditions. Psychol Med. 2012;42(6):1261-72.
9. Kelly BC, Wells BE, Leclair A, D T, Parsons JT, Golub SA. Prevalence and correlates of prescription drug misuse among socially active young adults. Int J Drug Policy. 2012;(in press).
10. Baggio S, Studer J, Mohler-Kuo M, Daeppen JB, Gmel G. Profiles of drug users in Switzerland and effects of early-onset intensive use of alcohol, tobacco and cannabis on other illicit drug use. Swiss Med Wkly. 2013;143:w13805.
11. Ford JA. Nonmedical Prescription Drug Use Among Adolescents The Influence of Bonds to Family and School. Youth & Society. 2009;40(3):336-52.
12. Blanco C, Secades-Villa R, García-Rodríguez O, Labrador-Mendez M, Wang S, Schwartz RP. Probability and predictors of remission from life-time prescription drug use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Psychiat Res. 2013;47(1):42–9.
13. Zullig KJ, Divin AL. The association between non-medical prescription drug use, depressive symptoms, and suicidality among college students. Addict Behav. 2012;37(8):890-9.
14. Haberstick BC, Young SE, Zeiger JS, Lessem JM, Hewitt JK, Hopfer CJ. Prevalence and correlates of alcohol and cannabis use disorders in the United States: Results from the national longitudinal study of adolescent health. Drug and Alcohol Dependence. 2013.
15. Franke A, Bonertz C, Christmann M, et al. Non-medical use of prescription stimulants and illicit use of stimulants for cognitive enhancement in pupils and students in Germany. Pharmacopsychiatry. 2011;44(02):60-6.
16. Kokkevi A, Fotiou A, Arapaki A, Richardson C. Prevalence, patterns, and correlates of tranquilizer and sedative use among European adolescents. Journal of adolescent health. 2008;43(6):584-92.
17. Maier LJ, Liechti ME, Herzig F, Schaub MP. To Dope or Not to Dope: Neuroenhancement with Prescription Drugs and Drugs of Abuse among Swiss University Students. PloS one. 2013;8(11):e77967. doi:10.1371/journal.pone.0077967

18. Berland-Benhaïm C, Giocanti D, Bartoli C, Sastre C, Leonetti G, Pelissier-Alicot AI. Medication misuse and abuse: duties and responsibilities of dispensing pharmacists. Med Sci Law 2011;51 (1):49-55
19. Holstein BE, Hansen EH, Andersen A, Due P. Self-rated health as predictor of medicine use in adolescence. Pharmacoepidemiology and drug safety. 2008;17(2):186-92. doi:10.1002/pds.1529
20. Stogner J, Gibson CL. The influence of health strain on the initiation and frequency of substance use in a national sample of adolescents. Journal of Drug Issues. 2011;41(1):69-93.
21. Falck RS, Wang J, Carlson RG. Health status of illicit stimulant drug users in rural Ohio. J Psychoactive Drugs. 2007;Suppl 4:401-5.
22. Falck RS, Wang J, Siegal HA, Carlson RG. Longitudinal application of the medical outcomes study 36-item short-form health survey with not-in-treatment crack-cocaine users. Medical care. 2000;38(9):902-10.
23. Novak SP, Herman-Stahl M, Flannery B, Zimmerman M. Physical pain, common psychiatric and substance use disorders, and the non-medical use of prescription analgesics in the United States. Drug Alcohol Depend. 2009;100(1-2):63–70.
24. Viana A, Trent L, Tull M, et al. Non-medical use of prescription drugs among Mississippi youth: constitutional, psychological, and family factors. Addict Behav. 2012;37(12):1382-8. doi:10.1016/j.addbeh.2012.06.017
25. Fitch K. Proscribed drugs at the Olympic Games: permitted use and misuse (doping) by athletes. Clin Med. 2012;12(3):257–60.
26. Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based guidelines for the pharmacological treatment of anxiety disorders: recommendations from the British Association for Psychopharmacology. J Psychopharmacol. 2005;19(6):567-96.
27. Maher B. Poll results: look who's doping. Nature. 2008;452(7188):674-5. doi:10.1038/452674a
28. Studer J, Baggio S, Mohler-Kuo M, et al. Examining non-response bias in substance use research: Are late respondents proxies for non-respondents. Drug Alcohol Depend. 2013;132(1-2):316-23.
29. Studer J, Mohler-Kuo M, Dermota P, et al. Need for Informed Consent in Substance Use Studies – Harm of Bias? J Stud Alcohol Drugs 2013; 74(6):931-40.
30. Ware J, Kosinski M, Turner-Bowker D, Gandek B. How to score version 2 of the SF-12 health survey (with a supplement documenting version 1): QualityMetric Incorporated; 2002.
31. Ware J, Kosinski M, Keller S. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Medical care. 1996;34(3):220-33.
32. Dey M, Gmel G, Studer J, Mohler-Kuo M. Health-risk behaviors and quality of life among young men. Qual Life Res (in press).
33. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Medical care. 2003;41(5):582-92.
34. Borders TF, Booth BM, Falck RS, Leukefeld C, Wang J, Carlson RG. Longitudinal changes in drug use severity and physical health-related quality of life among untreated stimulant users. Addict Behav. 2009;34(11):959-64. doi:10.1016/j.addbeh.2009.06.002
35. Becker WC, Fiellin DA, Desai RA. Non-medical use, abuse and dependence on sedatives and tranquilizers among US adults: psychiatric and socio-demographic correlates. Drug Alcohol Depend. 2007;90(2):280-7.
36. Becker WC, Sullivan LE, Tetrault JM, Desai RA, Fiellin DA. Non-medical use, abuse and dependence on prescription opioids among U.S. adults: psychiatric, medical and substance use correlates. Drug Alcohol Depend. 2008;94(1-3):38-47.
37. Simoni-Wastila L, Strickler G. Risk factors associated with problem use of prescription drugs. Am J Public Health. 2004;94(2):266-8.
38. Simoni-Wastila L, Ritter G, Strickler G. Gender and other factors associated with the nonmedical use of abusable prescription drugs. Subst use misuse. 2004;39(1):1-23.

39. Ford T. Practitioner review: How can epidemiology help us plan and deliver effective child and adolescent mental health services. J Child Psychol Psychiatry. 2008 49(9):900-14.

Table 1: Descriptive data of independent and dependent variables (N = 4,958)

Baseline variables	n (%)
Educational level	
Primary (<10 years)	2,421 (48.83)
Secondary (10–12 years)	1,224 (24.69)
Tertiary (13 years or more)	1,313 (26.48)
Relationship status	
Single/divorced	4,720 (95.20)
Married/couple	238 (4.80)
Current living arrangements	
Family/couple	4,793(96.67)
Other (alone/orphanage/foster home/homeless)	167 (3.33)
Physical health	
Poor	247 (4.98)
Good	4,711 (95.02)
Mental health	
Poor	1,265 (25.51)
Good	3,693 (74.49)
Non-medical prescription drugs use	
Yes	521 (10.51)
No	4,437 (89.51)
Class of drugs	
Opioid analgesics	324 (6.53)
Sedatives/sleeping pills	143 (2.88)
Anxiolytics	127 (2.56)
Stimulants	93 (1.88)
Antidepressants	43 (0.87)
Beta blockers	24 (0.48)

Table 2: Multiple logistic regression using NMPDU at baseline to predict mental and physical health at follow-up.

PREDICTOR ***NMPDU Baseline***	DEPENDENT ***Mental Health Follow-up***		***Physical Health Follow-up***	
	AOR[1](N=4,958)	**AOR[2](excluding participants in poor mental health at BS) N=3,693**	**AOR[1](N=4,958)**	**AOR[2](excluding participants in poor physical health at BS) N=4,711**
Any NMPDU	1.26 (1.03-1.54)*	1.26 (0.98-1.64)	1.36 (0.93-2.00)	1.29 (0.83-2.00)
Opioid analgesics	1.07 (0.84-1.38)	1.06 (0.77-1.47)	1.55 (1.00-2.42)*	1.62 (0.99-2.66)
Sedatives/sleeping pills	1.45 (1.01-2.08)*	1.51 (0.91-2.50)	1.57 (0.83-2.97)	1.75 (0.87-3.53)
Anxiolytics	1.52 (1.04-2.24)*	2.11 (1.25-3.56)*	1.34 (0.67-2.71)	0.90 (0.32-2.49)
Stimulants	1.18 (0.75-1.84)	1.16 (0.62-2.15)	1.18 (0.52-2.69)	1.11 (0.40-3.12)
Antidepressants	1.56 (0.81-3.01)	2.53 (0.87-7.38)	0.24 (0.03-1.85)	0.58 (0.08-4.31)
Beta blockers	1.93 (0.82-4.57)	2.97 (1.04-8.51)*	0.61 (0.07-4.71)	1.40 (0.18-10.68)

1: adjusted for poor mental or physical health at baseline, age, alcohol, tobacco, cannabis, relationship status, educational level, current living arrangements and financial independence, *p < .05.

2: adjusted for age, alcohol, tobacco, cannabis, relationship status, educational level, current living arrangements and financial independence,

*p < .05.

BS, baseline study; NMPDU, non-medical prescription drug use; AOR, adjusted OR

Table 3: Multiple logistic regression using mental and physical Health at baseline to predict NMPDU at follow up.

		DEPENDENT **NMPDU** ***Follow-up***						
PREDICTOR		Any NMPDU	Opioid analgesics	Sedatives/ sleeping pills	Anxiolytics	Stimulants	Antidepressants	Beta blockers
Mental Heath Baseline	**AOR[1] (N=4,958)**	1.88 (1.53-2.31)**	1.82 (1.42-2.35)**	2.02 (1.41-2.91)**	2.25 (1.53-3.33)**	1.37 (0.84-2.24)	3.73 (2.13-6.52)**	2.06 (0.95-4.45)
	AOR[2] (excluding participants using NMPD at BS)	**n=4,437** 1.79 (1.39-2.30)**	**n=4,634** 1.69 (1.26-2.27)**	**n=4,815** 1.97 (1.30-2.97)**	**n=4,831** 2.63 (1.71-4.05)**	**n=4,865** 1.10 (0.60-2.01)	**n=4,915** 3.74 (2.07-6.77)**	**n=4,769** 2.02 (0.88-4.61
		NMPDU ***Follow-up***						
		Any NMPDU	Opioid analgesics	Sedatives/ sleeping pills	Anxiolytics	Stimulants	Antidepressants	Beta blockers
Physical health Baseline	**AOR[1] (N=4,958)**	1.32 (0.88-1.97)	1.82 (1.18-2.81)**	1.33 (0.69-2.59)	2.01 (1.07-3.77)*	0.86 (0.33-2.24)	1.95 (0.84-4.54)	2.12 (0.69-6.54)
	AOR[2] (excluding participants using NMPD at BS)	**n=4,437** 1.50 (0.93-2.40)	**n=4,634** 2.10 (1.29-3.41)**	**n=4,815** 2.01 (1.03-3.95)*	**n=4,831** 2.54 (1.28-5.01)**	**n=4,865** 1.10 (0.33-3.59)	**n=4,915** 3.25 (1.42-7.41)**	**n=4,769** 3.48 (1.16-10.43)*

1: adjusted for poor mental or physical health at baseline, age, alcohol, tobacco, cannabis, relationship status, educational level, current living arrangement and financial independence, *p < .05, **p ≤ .001

2: adjusted for age, alcohol, tobacco, cannabis, relationship status, educational level, current living arrangement and financial independence,

*p < .05, **p ≤ .001

BS, baseline study; NMPDU, non-medical prescription drug use; AOR, adjusted OR