Prevalence of and Associated Factors for Adult Attention Deficit Hyperactivity Disorder in Young Swiss Men

Natalia Estévez1,2*, Dominique Eich-Höchli3, Michelle Dey1, Gerhard Gmel4, Joseph Studer4, Meichun Mohler-Kuo1

1 Institute of Social and Preventive Medicine, Zurich, Switzerland, 2 Department of Neuroradiology, University Hospital Zurich, Zurich, Switzerland, 3 Psychiatric University Hospital Zurich, Zurich, Switzerland, 4 Alcohol Treatment Centre, Lausanne University Hospital CHUV, Lausanne, Switzerland

Abstract

Objective: The present study aimed to measure the prevalence of adult attention deficit hyperactivity disorder (ADHD) in a large, representative sample of young Swiss men and to assess factors associated with this disorder.

Methods: Our sample consisted of 5656 Swiss men (mean age 20 years) who participated in the Cohort Study on Substance Use Risk Factors (C-SURF). ADHD was assessed with the World Health Organization (WHO) adult ADHD Self Report Screener (ASRS). Logistic regression analyses were conducted to assess the association between ADHD and several sociodemographic, clinical and familial factors.

Results: The prevalence of ADHD was 4.0%, being higher in older and French-speaking conscripts. A higher prevalence also was identified among men whose mothers had completed primary or high school/university and those with a family history of alcohol or psychiatric problems. Additionally, adults with ADHD demonstrated impairment in their professional life, as well as considerable mental health impairment.

Conclusion: Our results demonstrate that ADHD is common among young Swiss men. The impairments in function and mental health we observed highlight the need for further support and interventions to reduce burden in affected individuals. Interventions that incorporate the whole family also seem crucial.

Citation: Estévez N, Eich-Höchli D, Dey M, Gmel G, Studer J, et al. (2014) Prevalence of and Associated Factors for Adult Attention Deficit Hyperactivity Disorder in Young Swiss Men. PLoS ONE 9(2): e89298. doi:10.1371/journal.pone.0089298

Introduction

According to the DSM-IV-TR [1], Attention Deficit Hyperactivity Disorder (ADHD) is characterized by inattention and/or hyperactivity-impulsivity symptoms, which affect functioning considerably in several life domains. In contrast to an earlier assumption that ADHD only occurs during childhood and adolescence, more recent research has demonstrated that ADHD often persists into adulthood [2,3]. Adult ADHD is associated with functional impairment relating to professional achievements (e.g., lower levels of education; poorer socioeconomic outcomes) [3–9] as well as with more difficulties in relationships (e.g., higher rates of unsuccessful marriage; more family conflicts; more problems with peers) [3,5,6,10,11]. Moreover, in adults with ADHD, comorbidities with other psychiatric disorders - particularly with mood disorders, anxiety disorders, antisocial personality disorder and substance use disorder [2,6,8,9,12] - are common and can lead to further impairment.

The functional impairment and poor mental health that many experience can have a cumulative effect over the course of one’s life [13], even in those who only exhibit a few ADHD symptoms and thereby fail to meet enough criteria for a clinical diagnosis [8,14]. Thus, achieving better insights into the prevalence of ADHD and its associated factors in young adults may be crucial to preventing negative consequences and reducing illness burdens during later phases of life.

To date, the prevalence of ADHD has mainly been investigated in children and adolescents. In the limited number of studies that have focused on adults, prevalence estimates for ADHD have varied considerably, ranging from 1.0 to 7.5% (For a review, see [15,16]), though even higher rates have been uncovered when more liberal diagnostic criteria were applied [4,14,16,17]. Most of these studies were potentially biased, however, due to their use of convenience samples, drawing from particular communities, families, or from student or patient populations [3,14,16–20] rather than enrolling samples more representative of the community [16]. Only a few studies have assessed prevalence within more representative samples [6,10,21]. However, some of these studies [6,10,21] utilized indirect methods (e.g., multiple imputation) by which prevalence was estimated only in a small subset of participants, and the attained estimates were extrapolated to the entire sample [16].

To date, no published epidemiological data on adult ADHD in Switzerland exist. In this country, prevalence estimates have been...
limited to children within the age range of 7 to 17 years. In that group, the prevalence was 5.2% (6.1% boys, 3.3% girls), meaning that it is one of the most common psychiatric disorders observed in this age group [23].

The aims of the present study were (1) to measure the prevalence of adult ADHD within a large, representative sample of young Swiss men; and (2) to identify factors associated with this disorder in this age-group. To our knowledge, this is the largest sample of young men used in a population-based study in Europe to estimate the prevalence of adult ADHD.

Materials and Methods

Study Design

The present study used data drawn from the ‘Cohort Study on Substance Use Risk Factors’ (C-SURF), a longitudinal study designed to assess substance use patterns within a cohort of young Swiss men. The study was approved by the Ethics Committee for Clinical Research at Lausanne University Medical School (protocol number 15/07) and informed written consent was obtained from the participants.

The sample was recruited between August 2010 and November 2011 at three of a total of six centres that recruit men for military service, covering 21 of 26 Swiss cantons (including all French-speaking cantons). Switzerland has a mandatory army recruitment process, such that all Swiss men must submit to a formal evaluation to determine their eligibility for military service, civil service, or no service at approximately age 19. Both those who were deemed eligible to serve in the army and those deemed ineligible for military service were eligible for enrolment in our study. As there is no pre-selection to army conscription, a representative sample of young Swiss men was thereby provided for the study. It is important to note that the army centres were used only to enrol participants into the study. Both the study itself and the men’s decision to participate were entirely independent of the army. The present study used data collected during the baseline assessment only.

Participants

A total of 7,563 conscripts gave informed consent to participate in the study. Among them, 5,990 (79.2%) completed the baseline questionnaire. A further 334 conscripts were excluded from the analysis due to missing data, so that the final sample consisted of 5,656 (74.8%) subjects.

Assessment of ADHD

Adult ADHD was assessed using the Adult ADHD Self-Report Scale Screener (ASRS-v1.1), developed by the World Health Organization (WHO) [24,25]. This instrument includes six questions about ADHD symptoms, which are based upon DSM-IV diagnostic criteria for ADHD. For this study, all questions referred to the last 12 months. Each item was rated on a five-point scale, from “never” (0) to “very often” (4), with responses summed up to generate a summary score ranging from 0 to 24. The answers then were dichotomized into the variable “no ADHD” (scores 0–13) and “ADHD” (scores 14–24). In order to distinguish those with borderline scores from those with more extreme scores, a four-strata classification system [25] also was utilized, with subjects assigned to the four strata as follows: 0–9 “stratum I”, 10–15 “stratum II”, 14–17 “stratum III”, and 18–24 “stratum IV”.

Participants who failed to answer at least three questions from the ASRS Screener were excluded (n = 20, 0.4%). In contrast, when participants failed to answer only one or two questions, these missing responses were replaced by means of nearest-neighbour hot-deck imputation, using a random recursive partitioning (RRP) dissimilarity matrix. This method was implemented within the RRP package [26] running in version 2.15 of the R statistical environment (R Team Core Development, 17).

Assessment of Co-morbidity

Major depression. Major Depression (MD) was assessed using the Major Depressive Inventory (ICD-10) – WHO-MDI [28,29], which is a 10-item screening instrument that uses a 6-point scale for responses that range from “never” (1) to “all the time” (6). MDI items were first dichotomised to indicate the absence (0) or presence (1) of each symptom, and afterwards coded according to the DSM-IV criteria to generate a binary variable: “no MD” vs. “MD”. In accordance with the DSM-IV, MD was defined as the presence of at least five MDI items, with either item 1 or item 2 required to be among those five items [28].

Anti-Social Personality Disorder (ASPD). Symptomatology of anti-social personality disorder was measured via the Mini International Neuropsychiatric Interview (MINI plus, [30]). Responses were recorded using a 6-point scale, ranging from “never” (1) to “20 times or more” (6). Afterwards, answers were dichotomised to indicate the absence (0) or presence (1) of each symptom and further coded to generate a binary variable: “no ASPD” vs. “ASPD”. In accordance with the MINI plus, ASPD was defined as the presence of two symptoms, both before and after the age of 15. Cases were excluded when more than half of the questions were not answered for before and/or after the age of 15.

Alcohol abuse and dependence. Twelve-month diagnoses of alcohol abuse and dependence were assessed by questionnaires [31] based on DSM-IV diagnostic criteria. The questions were originally adapted from the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) [32,33]. The presence of alcohol abuse and dependence was assessed as “yes” or “no” for alcohol and for psychiatric problems. The presence of substance dependence was assessed as “yes” or “no” for alcohol and for psychiatric problems. In order to reduce the number of predictors for logistic regression, answers for all family members were combined to generate two dichotomous variables for the whole family, one for alcohol abuse and one for psychiatric problems. The assessment was based on questions adapted from the Addiction Severity Index (ASI) [27]. Answers for family members on the mother’s side were combined to generate two dichotomous variables, one for alcohol abuse and one for psychiatric problems. The assessment was based on questions adapted from the Addiction Severity Index (ASI) [27]. Answers for family members on the mother’s side were combined to generate two dichotomous variables, one for alcohol abuse and one for psychiatric problems. The assessment was based on questions adapted from the Addiction Severity Index (ASI) [27]. Answers for family members on the mother’s side were combined to generate two dichotomous variables, one for alcohol abuse and one for psychiatric problems.
Results

Prevalence of ADHD

The socio-demographic characteristics of the study sample are summarized in Table 1 (columns 1 and 2). The 12-month prevalence of ADHD was 4.0% (n = 226). Using the four-strata classification system, no ADHD was reported in 81.3% of participants, while 14.7%, 3.4%, and 0.6% of the participants were classified within strata II, III, and IV, respectively, representing possible through definite cases of ADHD (Table 2).

More than half (50.8 to 65.3%) of the sample reported at least one ADHD symptom “rarely”, “sometimes”, “often” or “very often”. Symptoms of hyperactivity were reported slightly more frequently than the majority of inattention symptoms (56.0 to 65.3% and 50.8 to 61.4%, respectively). Symptoms of inattention were reported as occurring “often” or “very often” in 0.7 to 9.0% men and hyperactivity symptoms in 1.9 to 13.6%. The frequencies of each symptom are shown in Table 3.

Socio-demographic Variables and Childhood Factors

A positive association with ADHD was found for subject age, linguistic region, education level, and degree of financial autonomy. Older subjects and those from French-speaking regions were more likely to report ADHD symptoms than those who were younger or from German-speaking regions. For education, a trend (p<0.10) was observed, with a high school/university level education associated with a higher prevalence of ADHD than having completed primary school only; however, this association failed to achieve statistical significance after adjusting for all other variables. Additionally, compared to financial autonomy, ADHD was positively related to partial or complete financial dependency. However, when adjusting for all other variables, only complete financial dependency was significant. No significant difference between participants with and without ADHD was identified for residence or marital status.

For childhood factors, logistic regression analysis revealed that subjects whose mothers had completed high school/university or just primary school were more likely to report ADHD than those whose mothers completed secondary school. Frequencies for these two former education levels were similar. Reporting a family history of alcohol or psychiatric problems was significantly associated with a higher prevalence of ADHD than not having such a history. Family affluence, living arrangement before the age of 10, and separation of parents before 10 years of age did not differ between those with and without ADHD. Table 1 presents unadjusted and adjusted ORs and 95% CI for correlates of adult ADHD.

Co-morbid Conditions

Using the dichotomous classification (“no ADHD” vs. “ADHD”) 13.7% of our subjects with ADHD reported MD, 36.3% ASPD, 38.9% alcohol abuse, and 20.8% alcohol dependence. Rates for all these disorders were significantly higher among those with than those without ADHD (MD: X^2 = 114.94, p<.001; ASPD: X^2 = 67.99, p<.001; alcohol abuse and dependence X^2 = 58.90, p<.001). Similarly, a higher percentage of men in strata II, III and IV reported the presence of MD, ASPD, alcohol abuse and dependence than men allocated to stratum I. The rate of having at least one of these psychiatric disorders systematically increased from strata I to IV (Figure 1), indicating that men with more ADHD symptoms are more likely to suffer from other psychiatric disorders as well. Rates for these co-morbid disorders, per stratum, are presented in Table 4.

Discussion

Prevalence of ADHD

The present study aimed to assess the prevalence of adult ADHD in a large, representative sample of young men living in Switzerland, and to examine factors associated with ADHD. In our sample, the prevalence of adult ADHD was 4.0%. This rate is midway between the rates of 1.0 to 7.5% reported in previous studies [15,16]. Although we assessed prevalence only by applying a self-report screening questionnaire, our rate was similar to the average rate of 4.2% that was reported for higher income countries in a WHO-orchestrated international survey [6]. In the WHO study, more accurate diagnostic assessments were performed at least for a small portion of the recruited US sample, and multiple imputations were applied to estimate prevalence across all other participating countries. Our results are also in line with the crude prevalence estimate of 4.7% reported recently for a representative sample of the German population [9], in a study in which a variety of self-report instruments were used. Relative to the only pre-existent prevalence estimates for Switzerland, specifically for youths between the ages of 7 and 17 (6.2%) [23], our rates are somewhat lower. However, the previous estimate only incorporated the city of Zurich.

Socio-demographic Variables

Contradicting earlier findings [6,9,16,20], the prevalence of ADHD increased with age in our sample. By analysing the rates of adult ADHD for each age separately, we noticed that they fluctuated from age to age among older subjects (≥20 years) (data not shown). For example, a higher rate of adult ADHD was found among those who were 20 years old (5.4%) than those who were 21 (3.7%). The latter rate was similar to the rates obtained for subjects aged 18 (3.1%) and 19 (3.8), who were assigned to the younger of our two dichotomized age groups (<20 years). One possible explanation for this result may be our use of self-reports to diagnose ADHD, as self-reports may be less reliable than informant/proxy reports (e.g. parents, teachers) because people with ADHD exhibit diminished self-appraisal/awareness and thereby tend to underreport their own symptoms [34,35]. Nevertheless, it is also possible that critical life periods may lead people with ADHD to increasingly having to confront their difficulties and, hence, be more likely to self-report symptoms. For
Table 1. Description of the study sample and correlates of adult ADHD; logistic regression analyses with ADHD as the outcome variable.

| Characteristics | Participants with characteristic | Prevalence of ADHD within characteristic | Unadjusted | Adjusted* |
|-----------------|---------------------------------|-----------------------------------------|------------|-----------|
| Ageb            |                                 | % (n = 5656)                           | % (n = 226) | Odds ratio [95% CI] | Odds ratio [95% CI] |
| <20             | 60.0                             | 3.4                                     | 1.00       |           |
| ≥20             | 40.0                             | 4.9                                     | 1.45 [1.11, 1.89]* | 1.35 [1.02, 1.80]* |
| Linguistic region |                                |                                        |            |           |
| German          | 45.2                             | 2.7                                     | 1.00       |           |
| French          | 54.8                             | 5.1                                     | 1.96 [1.47, 2.62]** | 1.75 [1.27, 2.40]** |
| Residence       |                                 |                                        |            |           |
| rural           | 33.0                             | 3.4                                     | 1.00       |           |
| urban           | 67.0                             | 4.3                                     | 1.26 [0.94, 1.69] | 1.00 [0.74, 1.36] |
| Marital statusc |                                |                                        |            |           |
| in relationship | 5.1                              | 2.8                                     |           |           |
| single          | 94.9                             | 4.1                                     |           |           |
| Education       |                                 |                                        |            |           |
| primary school  | 50.0                             | 3.9                                     | 1.00       |           |
| secondary vocational school | 28.5 | 3.2 | 0.82 [0.58, 1.14] | 0.80 [0.56, 1.15] |
| high school/university | 21.5 | 5.2 | 1.34 [0.98, 1.84] | 0.97 [0.69, 1.37] |
| Financial autonomy |                              |                                        |            |           |
| financial autonomy | 23.5 | 2.7 | 1.00       |           |
| partial financial dependency | 42.7 | 4.0 | 1.49 [1.01, 2.20]* | 1.36 [0.91, 2.04] |
| financial dependency | 33.8 | 4.9 | 1.86 [1.26, 2.75]* | 1.78 [1.16, 2.72]* |
| Living arrangementd |                            |                                        |            |           |
| biological parents | 78.1 | 3.8 | 1.00       |           |
| others           | 21.9                             | 4.7                                     | 1.24 [0.91, 1.68] | 1.02 [0.74, 1.41] |
| Separation of parentsd |                              |                                        |            |           |
| no               | 74.5                             | 3.8                                     | 1.00       |           |
| before birth     | 1.5                              | 5.8                                     | 1.55 [0.62, 3.89] |           |
| after birth      | 24.0                             | 4.4                                     | 1.16 [0.86, 1.58] |           |
| Mother’s education |                              |                                        |            |           |
| primary school  | 13.5                             | 5.4                                     | 1.00       |           |
| secondary vocational school | 62.2 | 3.2 | 0.59 [0.41, 0.84] | 0.64 [0.44, 0.94] |
| high school/university | 24.3 | 5.2 | 0.98 [0.66, 1.45] | 0.94 [0.61, 1.43] |
| Family affluence |                                |                                        |            |           |
| above average   | 44.5                             | 3.7                                     | 1.00       |           |
| average          | 41.1                             | 4.0                                     | 1.09 [0.81, 1.46] | 1.06 [0.78, 1.45] |
| below average   | 14.4                             | 4.7                                     | 1.26 [0.86, 1.85] | 1.13 [0.75, 1.72] |
| Family history  |                                |                                        |            |           |
| Problems with alcohol |                              |                                        |            |           |
| no               | 76.2                             | 3.4                                     | 1.00       |           |
| yes              | 23.8                             | 6.0                                     | 1.84 [1.39, 2.44]** | 1.46 [1.09, 1.96]* |
| Psychiatric disease |                              |                                        |            |           |
| no               | 85.0                             | 3.4                                     | 1.00       |           |
| yes              | 15.0                             | 7.6                                     | 2.39 [1.77, 3.21]** | 2.13 [1.56, 2.92]** |

*p<.10,
*p<.05,
**p<.001;
*adjusted for all variables;
1age range: 17–28;
no logistic regression analyses were performed due to the small number of participants in one of the variable’s categories;
*before 18 years of age.

doi:10.1371/journal.pone.0089298.t001
instance, at the age of 20 years, most Swiss people start university or their first job after training, which may be experienced as rather challenging, potentially contributing to the higher prevalence rates that we observed.

We noted no significant differences in the prevalence of ADHD between those with a rural versus urban residence. This result is consistent with some previous findings [10], but stands in contrast with other prior studies identifying higher rates in urban [4] or rural areas [9]. This inconsistency might be due to differences in how rural and urban were defined in the different studies, as well as to differences in the nature of the rural and urban areas themselves [36].

Linguistic region was associated with adult ADHD, in that a higher prevalence was discovered among French-speaking versus German-speaking conscripts. Differences in prevalence between countries with different cultures have already been reported [6,18], as well as between culturally-diverse populations within the same country [37]. These differences could be explained by differences in knowledge, understanding, and the assessment and management of ADHD symptoms between different countries and cultures. For example, a given symptom might be considered deviant in some cultures, while more accepted in others. This could affect the reports of informants [18,37,38]. Since how ADHD is understood, diagnosed and managed is similar throughout Switzerland, at least among health professionals and in schools, we suspect that cultural differences in response behaviours were primarily responsible for the linguistic effect we observed. French-speaking conscripts, for instance, seem to give more extreme responses than those who speak German, a pattern that was observed for every ADHD item (data not shown) as well as for other variables [39].

For our analysis, highest achieved education and financial autonomy were used as markers of professional achievement. Men with adult ADHD were more likely to have completed high school or attended university (p<0.10), although this association failed to achieve statistical significance after adjusting for all other variables. Our results are clearly contrary to most previous reports, which constantly revealed a positive association between ADHD and lower education level [3,6,7,9]. It is possible that enhanced identification and referral of cases with ADHD in Switzerland, as well as more accessible and effective treatment during childhood and adolescence, might have allowed affected individuals to achieve higher levels of education than in other countries. However, it must be emphasized that, consistent with the findings of others [7], in our sample adult ADHD was positively related to partial and, even more so, to complete financial dependency. The observed positive relationship between adult ADHD and financial dependency may suggest that adults with ADHD still are impaired in some aspects of their professional life, despite having achieved a similar education level as those without ADHD. Thus, they may need more support to manage tasks at work.

In contrast to previous studies, in which problems with personal relationships were reported [3,6,10], in our sample no significant difference was found in marital status between those with and without ADHD. This failure to identify any significant marital difficulties could be due to the definition of marital status we used: being in a relationship was defined as being married or living with a partner, and not just having a girlfriend. Due to the young age of our participants, only a small number of subjects fulfilled our requirements for ‘marriage’ (286/5656), meaning that the number of partnered subjects with ADHD (8/226) was too small to allow for meaningful analysis.
Childhood Factors

We did find that both a subject’s mother’s level of education and a family history of alcohol or psychiatric problems differed between those with and without adult ADHD. Mothers of participants with adult ADHD were more likely to have either a primary school or high school/university level education, while those without ADHD more often had mothers who had completed secondary school but not beyond. The finding that a low level of maternal education was associated with a greater prevalence of adult ADHD is consistent with the results of other studies, in which a higher risk for ADHD in children was observed in those with less-educated parents [40,41]. In this context, it has been claimed that, due to its strong genetic component, parents of affected children may be more likely to have had ADHD themselves and, as a consequence, to have not been able to achieve higher education levels [41]. In contrast, the observation that a higher level of maternal education was associated with a greater prevalence of ADHD in offspring has not been reported before; but it is consistent with what Gau et al. [42] have found: a positive association between the number of psychiatric referrals and higher maternal education levels in children with ADHD. This, in turn, suggests that mothers of higher education may be more likely to be aware of their children’s problematic behaviours and have more knowledge about ADHD. One could speculate that higher parental awareness of ADHD might help their offspring to better identify and report their own symptoms.

Family history of either alcohol or psychiatric problems also was positively associated with adult ADHD. In fact, a family history of psychiatric problems exhibited the highest odds ratio for ADHD of any variable, on logistic regression analysis. Once again, the strong genetic component of ADHD and the high comorbidity of ADHD with alcohol use disorders and other mental disorders could explain this association [2]. Additionally, the difficulties and stress inherent to raising a child with ADHD could affect family functioning and the well-being of family members (for a Review, see [43]). For instance, ADHD in adolescents is linked to more depressive symptoms in mothers [44] and to more alcohol use disorders in parents [44–46]. These findings are even stronger when parents of affected children have ADHD themselves [44,45]. Thus, a higher rate of family alcohol abuse and psychiatric problems may be induced by both genetic factors and challenges in the interactions of family members with the ADHD-affected individual. As such, further efforts should be undertaken to include all family members in the treatment of ADHD, and to provide special interventions for families with more than one ADHD-affected individual.

Co-morbid Conditions

Consistent with previously-published findings [2,6,8–10,12], a considerable proportion of our men with ADHD appeared to suffer from major depression, anti-social personality disorder, and either alcohol abuse or dependence. Additionally, men with more ADHD symptoms appear to be more likely to suffer from one of these psychiatric disorders [8]. In our sample, among those with the highest number of ADHD symptoms, the probability of having MD was nine times greater than among those in the lowest strata, in which any ADHD cases are expected. For ASPD, alcohol abuse and dependence, the rates were approximately four, two, and three times greater in the highest vs. lowest stratum, respectively. For all these psychiatric disorders, an elevated rate also was identified in those with few ADHD symptoms [8,14]. Our results, combined with previous findings, highlight the considerable impairments in mental health that young men with ADHD can experience, as well as the need for health care providers to offer appropriate interventions for this population to reduce further illness burdens.

Study Limitations

The following limitations must be considered relating to the currently-presented study. First, women were not included in our sample. Although some study results suggest that men and women...
experience ADHD in a similar way [8], inconsistent results in ADHD prevalence estimates have been reported comparing adult males and females. The reasons behind these inconsistent results remain unclear and must be clarified in future studies.

Second, the prevalence of ADHD was assessed in the context of a population-based study that was not initially intended or designed to address ADHD-related questions. Therefore, prevalence only was assessed by means of self-report using the ASRS Screener and did not further include any confirmatory diagnostic assessment. This also was true for the assessment of MD, ASPD, alcohol abuse and alcohol dependence, as well as for family histories of alcohol and psychiatric problems. However, the assessment instruments we used are all well validated. Thus, we feel that our study provides a reasonable approximation of the prevalence of ADHD among young Swiss men. Nevertheless, it is important to note that, despite excellent concordance between the ASRS Screener and a clinical diagnosis of ADHD [24,25], the ASRS is based upon the DSM-IV criteria originally developed for children and might not provide appropriate information for the diagnosis of adult ADHD. Indeed, some study results suggest that these criteria are too conservative for adults [4,20]. As a consequence, the true prevalence of ADHD might be slightly underestimated in our study.

Third, the medical history for ADHD, mental disorders and family histories of alcohol and psychiatric problems, was not assessed; consequently, we do not know the clinical status of our study participants or whether they had received or continued to receive any treatment.

Finally, since our data were collected at a single time point and not longitudinally, we cannot draw causal inferences. In summary, we found that roughly 4.0% of young Swiss men have ADHD, and that associations exist with other mental disorders, like major depression and alcohol abuse, as well as with family histories of alcohol and psychiatric problems. ADHD adversely affects work, health and interpersonal relationships. As such, clinicians and school professionals should remain alert to its existence and consequences in young males.

Acknowledgments We are grateful to Dr. Alois Tschopp and Prof. Alex Gamma for their methodological advice and to Charlotte Eidenbenz and Petra Dermota for their valuable input.

Author Contributions
Conceived and designed the experiments: MMK GG. Performed the experiments: MMK GG JS. Analyzed the data: NE MD JS. Contributed reagents/materials/analysis tools: MMK GG. Wrote the paper: NE. Interpretation of data: NE DEH. Revising manuscript: NE DEH MD JS GG MMK.

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Author/s:
Estévez, N; Eich-Höchli, D; Dey, M; Gmel, G; Studer, J; Mohler-Kuo, M

Title:
Prevalence of and associated factors for adult attention deficit hyperactivity disorder in young Swiss men.

Date:
2014

Citation:
Estévez, N., Eich-Höchli, D., Dey, M., Gmel, G., Studer, J. & Mohler-Kuo, M. (2014). Prevalence of and associated factors for adult attention deficit hyperactivity disorder in young Swiss men.. PLoS One, 9 (2), pp.e89298-. https://doi.org/10.1371/journal.pone.0089298.

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