

# **Epidemiology of adult Attention Deficit Hyperactivity Disorder (ADHD)**

**Thesis**

**Dr. Viktória Simon**

**Semmelweis University**

**Mental Health Sciences Doctoral School**



**Supervisor: Dr. István Bitter, MD, Ph.D.**

**Opponents: Dr. Gábor Gazdag, MD, Ph.D**

**Dr. Oguz Kelemen, MD, Ph.D**

**President of examination committee: Dr. Zoltán Nagy, MD, DSc.**

**Members of examination committee: Dr. Attila Oláh, MD, DSc.**

**Dr. György Purebl, MD, Ph.D**

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## **Introduction**

ADHD is one of the most frequent psychiatric conditions in childhood. The main features – the so called „core symptoms” – of ADHD are inattention, hyperactivity and impulsivity. According to the estimations published in the literature, ADHD affects 3-9% of school age children. ADHD in adults became the focus of research in the past two decades. During this time, the results of follow-up studies proved that ADHD is not only a childhood condition, but persists into adulthood in a high proportion of cases. The validity of the diagnosis of ADHD in adults was further supported by findings of imaging studies, reporting on several structural and functional brain abnormalities similar to those found in children with ADHD; findings of neuropsychological studies showing congruent dysfunctions with the brain abnormalities reported in imaging studies and similar to those reported in children; as well as reports on the therapeutic efficiency of stimulants, specifically used for the pharmacotherapy of ADHD both in children and in adults.

The pertinent literature consistently supports the notion that ADHD in adults is associated with poor socioeconomical outcome and serious functional impairments. Moreover, ADHD was shown to be also a serious risk factor for psychiatric comorbidity. ADHD in adults, due to the high level of criminality and unemployment represents serious burden on the society with significant economical consequences, beyond its obvious effect on the health care system and the individual's life. Taking into consideration these broadly impairing effects, and the fact that effective treatment tools exist in the management of ADHD both in childhood and in adulthood, identifying and diagnosing ADHD is crucial. To date there are no validated, clear diagnostic criteria for adult ADHD. The reason for this scarcity can partially be explained by the fact that up till the early 80's ADHD was considered to be a disorder of childhood. The currently applied DSM-IV diagnostic criteria was originally created for and validated among children and adolescents. Many aspects of these criteria have been criticised by several authors in the literature. However, most of the epidemiological studies, assessing the prevalence of ADHD among adults in the community, applied the DSM-IV criteria, although almost all of them used alternative criteria as well. These community based epidemiologic studies estimated 1-7.3% prevalence of adult ADHD, based on DSM-IV criteria.

To date, in Hungary, no epidemiologic survey has been conducted for the estimation of the prevalence of adult ADHD. Furthermore, not only public, but professional awareness is also lacking about this disorder. Although ADHD in childhood is well known and treated condition in Hungary, the treatment of those individuals diagnosed with ADHD in childhood and continuously showing impairing symptoms in adulthood is not solved yet. In addition, outpatient services dedicated for the treatment and diagnosis of adult ADHD are completely missing.

### **Objectives**

- 1) To estimate the prevalence of adult ADHD for the first time, in a large (N=3529) Hungarian community sample, with the inclusion of 17 GP practices in Budapest.
- 2) To investigate how do different diagnostic criteria affect the prevalence estimates of adult ADHD, in the same Hungarian GP population.
- 3) To pool the prevalence estimates published in the literature and to identify correlates of the prevalence of adult ADHD by employing a meta-analytic approach.
- 4) To examine whether those correlates have a similar effect on the first Hungarian prevalence estimates.
- 5) Our fifth objective was rather speculative. Specifically, it implicates that Hungary is a country where public and professional awareness are both missing regarding adult ADHD. This means that case identification would not be biased by professional „attention preference”, or public „overcommunication of the disorder”. People of Hungary practically do not know and the majority of people have not even heard about this disorder. We assumed that if the results of our estimation will be comparable to those prevalence estimates reported in the literature, it might provide, although indirectly, additional support for the validity of the diagnosis.

## **Methods**

### **Methods of the meta-regression analysis**

#### *Study selection*

We used Medline, Psychlit and Embase databases, searching for publications dealing with the epidemiology of adult ADHD. Only publications in English were considered. As a first step, we used the following terms for our search: („adult” AND ”ADHD”) AND („prevalence” OR „epidemiology”). In addition to the above search procedure, we used the reference lists of the identified publications to find further relevant articles. After excluding follow-up and family studies – that do not provide prevalence data of adult ADHD -, those studies that were dealing with the prevalence of ADHD in special groups (patients with panic- or bipolar disorder, drug addicts, obese patients, prisoners) and those that did not provide raw data or did not apply DSM-IV criteria during the estimations at all, we included 6 studies in our meta-regression analysis.

#### *Statistical analyses*

The Statistical Analysis System for Windows (version 9.1; SAS Institute, Cary, NC) was used for statistical analyses. A mixed-effect (with fixed and random effects) meta-regression - a meta-analytic technique of multivariate linear regression across studies - was applied to estimate the prevalence of ADHD across various study samples and in order to evaluate the impact of potential demographic variables of interest including age and gender on the prevalence estimates.

### **Methods of the first Hungarian study estimating the prevalence of adult ADHD on a community sample**

This investigation was part of a larger study examining the epidemiology, neuropsychology, genetic background, psychopathology and clinical features of adult ADHD. The parent study was a multiphase, multicenter study including the Semmelweis University, Department of Psychiatry and Psychotherapy, and 17 general practitioners (GP) in Budapest.

### *Sample and data collection*

Between June 2006 and June 2007, 3529 patients of 17 GP practices entered the epidemiological study in the area of Budapest, Hungary. Data collection took place in the participating GP practices. Subjects between 18 and 60 years from both genders without major neurological disorder in their clinical history were included in the study. During the *screening phase*, consecutively arriving patients entered in the study every office day of the GPs. The assistant distributed the ADHD screener - the 6-item screener version of Adult ADHD Self-report Scale - to the subjects. Positively screened subjects (n=279) were asked by the GP to further participate in the *interview phase* of the study. From this sample of positively screened subjects 29.4% (n=82) refused participation in the interview phase and 12.9% (n=36) failed to show up.

In the *interview phase*, positively screened subjects enrolled for this phase (n=161) participated in a detailed semi-structured clinical interview, based on the DSM-IV criteria, and filled out a self-report questionnaire in order to confirm the diagnosis of adult ADHD.

### *Diagnosis of adult ADHD*

Based on the documentation of the interview and the DSM-IV diagnostic criteria the interviewer team decided whether the participant fulfilled the criteria for the clinical diagnosis of adult ADHD. However, similar to other adult ADHD prevalence studies, alternative groups were created next to DSM-IV diagnosis:

1. *'ADHD\_DSM-IV' diagnostic group*: based on full DSM-IV criteria for both childhood and adult ADHD with supporting background information based on the clinical interview.
2. *'ADHD\_No-onset' group*: based on DSM-IV criteria for both childhood and adult ADHD, excluding onset criterion.
3. *'ADHD\_full/Sx' group*: based on DSM-IV symptom criterion only (6 symptoms had to be present out of the 9 symptoms of either inattention or hyperactivity/impulsivity, or both) for both childhood and adult ADHD.
4. *'ADHD\_reduced/Sx' group*: based on a reduced number of symptoms present from DSM-IV symptoms (4 out of 9 symptoms of either inattention or hyperactivity/impulsivity, or both) in adulthood, while in childhood original DSM-IV symptom criterion had to be present.

## ***Statistical Analysis***

The Statistical Analysis System for Windows (version 9.1; SAS Institute, Cary, NC) was used for statistical analyses. All statistical analyses used the alpha error level of 0.05 (two-sided) and 95% confidence intervals. Demographic and basic background characteristics were summarized by descriptive statistics, for the purpose of inferential statistical analyses, the group comparisons were based on the General Linear Model (GLM) approach. Estimation of prevalence from the study sample was based on the binomial model using the proportion of the subjects who screened positive on the ADHD screener test. For the estimation of 95% confidence interval around the sample proportion of positive cases, the sample estimate of the standard error was adopted. For the computation of the standard error, the following formula was applied:

$SEp = \sqrt{p * (1 - p) / n}$ , where  $n$ ,  $p$  and  $SEp$  denote the sample size, the estimated proportion of cases (subjects with ADHD), and the standard error of the estimate, respectively.

Adjusting for the screening test's specificity and sensitivity, we applied the following formula, provided by Gart and Buck:

$PREVp = (POS + Sp - 1) / (Se + Sp - 1)$ , where  $PREVp$ ,  $POS$ ,  $Sp$  and  $Se$  denote, respectively, the true population prevalence, the proportion of positive cases in the sample, and the specificity and the sensitivity of the screening test.

## **Results**

### **Results of the meta-regression analysis**

Mixed-effect meta-regression analysis was applied to estimate the prevalence across samples and to investigate prevalence as a function of gender composition and mean age in the respective samples. Results of the meta-regression analysis indicated that the pooled prevalence of ADHD across samples was 2.5% (95% CI: 2.1-3.1;  $t=42.3$ ,  $p<0.0001$ ).

Heterogeneity among studies included in the meta-analysis was tested by the likelihood ratio statistic, by comparing the maximum log-likelihood (LL) of the random-effect with that of the fixed-effect model. Our results showed that the random and fixed-models yielded a maximum LL value of -9.9 and -42.5, respectively. This indicates a statistically significant heterogeneity across studies (Chi-square= 65.2,  $df=1$ ,  $p<0.0001$ ), which (as shown

by subsequent analyses) was due, at least in part, to principal demographic variables that we examined in our study.

In particular, our results showed that the prevalence of ADHD was significantly related to the gender composition in the sample ( $t=4.34$ ,  $p=0.012$ , standardized beta for log-odds of observed prevalence:  $15.19 \times 10^{-2}$ ) and to the mean age ( $t=3.03$ ,  $p=0.039$ , standardized beta for log-odds of observed prevalence:  $20.98 \times 10^{-2}$ ). Furthermore, the interaction between the two covariates also reached statistical significance ( $t=-3.42$ ,  $p=0.027$ , standardized beta for log-odds of observed prevalence:  $0.50 \times 10^{-2}$ ). In specific, our results indicated that for younger age groups the prevalence increases, whereas for the older age group prevalence decreases with higher proportion of males in the sample, or from the other aspect, prevalence decreases with age when males are represented at 50% or more in the sample, whereas the prevalence increases with age when females are predominantly represented in the sample (male percentage=33.3%).

### **Results of the Hungarian study estimating the prevalence of adult ADHD**

Crude prevalence estimates adjusted for the specificity and sensitivity data of the screener were 1.35% in the ‘DSM-IV’ group, 1.64% in the ‘No-onset’ group, 3.65% in the ‘Sx/full’ group and 4.16% in the ‘Sx/reduced’ group. Logistic regression analysis showed that ADHD was significantly more prevalent with younger age and male gender [ $\chi^2=14.46$ ;  $p=0.0007$ ], however there was no significant interaction between the effect of gender and age [Estimate: -0.031, Standard Error: 0.043,  $\chi^2=0.5124$ ;  $p=0.4741$ ].

A corrected estimate of prevalence of adult ADHD was also calculated by accounting for the ‘not-interviewed’ subsample. The sample was stratified by age and gender because of the previously described effect of these variables on ADHD diagnostic status. For the purpose of age stratification we applied the median age of the sample (40.5 years), thus two strata were described: subjects  $\leq 40$  years old and subjects  $>40$  years old. Prevalence estimates corrected for the ‘not-interviewed’ subsample and adjusted for specificity and sensitivity data of the screener was 2.3% in males, 0.91% in females; 2.02% in the  $\leq 40$  years age group and 0.70% in the  $> 40$  years age group, based on DSM-IV diagnostic criteria.

## **Conclusions**

One of our main objectives was to estimate the prevalence of adult ADHD for the first time, in a large Hungarian community sample. In summary, prevalence rates found in the Hungarian study population are somewhat more conservative, but still are in line with those reported previously in the literature. Notably, even when the most restrictive diagnostic criteria are applied ADHD is highly prevalent among Hungarian adults. In particular, prevalence rate of even 1.35% is similar to the prevalence of schizophrenia.

We assume that our reported prevalence rates indirectly support the validity of ADHD diagnosis in adults, taking into consideration the previously mentioned lack of both public and professional awareness of this disorder.

Another objective was to investigate how do different diagnostic criteria affect the prevalence estimates of adult ADHD, in the same Hungarian GP population. Relaxing DSM-IV diagnostic criteria with regard to the age-onset criterion as well as the symptom threshold increased the prevalence estimates. Although prevalence estimates increased substantially, they remained within the range of prevalence rates found in previous studies based on only DSM-IV criteria. This might be due to the rigorous data assessment and setting, especially with regard to retrospective childhood ADHD diagnosis. This latter observation suggest that next to diagnostic criteria, other factors, such as design, setting, assessment methods also play a key role in prevalence estimation and might have contributed to the high variability of reported prevalence estimates. Another factor, that needs further clarification is cultural and/or economical influence on the occurrence (or identification) of ADHD cases in adults, since we have found that our prevalence estimates are closer to estimates from lower income countries, which are significantly lower compared with estimates from higher income Western-European countries and the US. This notion, speculatively, might be linked with the previously mentioned effect of professional awareness and attention preference as well as public awareness of the disorder.

A further objective was to pool the prevalence estimates published in the literature and to identify correlates of the prevalence of adult ADHD by employing a meta-analytic approach. Based on our meta-regression analysis, the pooled prevalence of adult ADHD was 2.5% and we identified a complex effect of gender and age on the prevalence estimates. In particular, our finding is consistent with the suggestion that the prevalence of ADHD declines with age, however this association is mediated by gender. The background of this phenomenon remains unclear and a caveat is needed in this regard. Specifically, the lack of

validity of DSM-IV diagnostic criteria for diagnosing adult ADHD is an important issue, emerging both from the interpretation of our findings and also from the relevant literature. It seems that the DSM-IV criteria in the diagnosis of adult ADHD functions differently across age groups and gender and thus, may underestimate the prevalence of the disorder in adults.

We found the effect of gender and age on prevalence rates also in the epidemiologic study, however, the interaction between these two effects could not be detected most probably because of the small sample size.

Taking together our results and previously described findings in the literature it can be suggested that further investigations are necessary to find out in what proportion methodological issues or natural developmental features are responsible for the observed decline in the prevalence of ADHD with age. Future well-designed, community-based epidemiological studies critically depend on an improved understanding of the etiology and pathophysiology of the disorder, which in turn would help to improve the current diagnostic criteria and would thereby facilitate a more reliable identification of patients with ADHD.

## **List of publications**

### ***Publications linked to the topic of the dissertation***

Murai Z, Porkoláb N, Simon V, Telek T, Bitter I. (2005) Felnőttkori figyelemhiányos/hiperaktív zavar (Felnőttkori ADHD) - Irodalmi áttekintés. Orvostovábbképző Szemle, suppl 18-39.

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Mészáros Á, Czobor P, Bálint S, Simon V, Bitter I. (2007) A felnőttkori figyelemhiányos/hiperaktivitás zavar (ADHD) gyógyszeres kezelésének hatékonysága: irodalmi áttekintés. Psychiatr Hung, 22:259-70.

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Bitter I, Simon V, Bálint S, Mészáros Á, Czobor P. (2009) How do different diagnostic criteria, age and gender affect the prevalence of Attention Deficit Hyperactivity Disorder in adults? An epidemiological study in a Hungarian community sample. *Eur Arch Psychiatry Clin Neurosci*, DOI: 10.1007/s00406-009-0076-3.

#### ***Publications independent from the topic of the dissertation***

Simon V, Sik Lányi C, Simon L. (2004) Using virtual public transport for treating phobias. *Int J on Disability and Human Development*, 4:211-215.

Simon V, De Hert M, Wampers M, Peuskens J, Van Winkel R. (2009) The relation between neurocognitive dysfunction and impaired insight in patients with schizophrenia. *Eur Psychiatry*, 24:239-243.

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De Hert M, Simon V, Vidovic D, Franic T, Wampers M, Peuskens J, Van Winkel R. (2009) Evaluation of the association between insight and symptoms in a large sample of patients with schizophrenia. *Eur Psychiatry*, DOI: 10.106/j.eurpsy.2009.04.004.

#### **Book chapters:**

Sík Lányi C, Laky V, Tilinger Á, Pataky I, Simon L, Kiss B, Simon V, Szabó J, Páll A. *Developing Multimedia Software and Virtual Reality Worlds and their Use in Rehabilitation*

and Psychology, Transformation of Healthcare with Information Technologies, IOS Press, 2004, pp. 273-284.

Sik Lányi C, Simon V, Pataky I, Kosztyán Zs T, Mátrai R: Medical Applications of Virtual Reality Worlds and Multimedia, Overcoming the barriers to e-health growth in Enlarged Europe, Health and Management Press, Krakow, 2004, pp. 189-204.