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Hospital de Clínicas de Porto Alegre

How to write a paper: Experience across the years”

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Porto Alegre, Brazil
June, 2007**

Disclosure: Luis A Rohde, MD

Source	Consultant	Advisory Board	Stock Equity	Speaker's Bureau	Research Contract
Novartis		X		X	X
Janssen-Cilag	X	X		X	X
Lilly	X	X		X	X
Shire	X			X	
Bristol					X

Why Does the Worldwide Prevalence of Childhood Attention Deficit Hyperactivity Disorder Matter?

How many children around the world have attention deficit hyperactivity disorder (ADHD)? Is ADHD a creation of permissive Western culture rarely seen outside North America? Do world regions with elevated ADHD rates hold the key to causation? Childhood ADHD is diagnosed when a child exhibits a persistent syndrome of inattention, hyperactivity, and impulsivity that impairs functioning both at home and at school before the child is 7 years old. The worldwide prevalence of this disorder is 5.2%, as uncovered in this issue by a Brazilian research team led by Polanczyk and Rohde. Their elegant research synthesized studies of ADHD from around the world in the most comprehensive

"Becoming an identified ADHD patient is partly a function of the gap between a child's behavior and the expectations of the adults in his or her world about how children ought to behave."

literature search undertaken to date. A method called meta-analysis was applied to the resulting database to investigate why studies in some world regions report estimates that deviate from the worldwide rate.

At stake is ADHD's identity as a bona fide mental disorder (as opposed to a social construction). When initial reports of ADHD prevalence emerged, higher prevalence in North American than European samples was remarked upon. This observation spawned a 10-year debate, exemplified by articles with titles such as "Is Childhood Hyperactivity the Product of Western Culture?" (1) and, more recently, "ADHD Is Best Understood as a Cultural Construct" (2). Having an explanation for inconsistencies in the cross-national prevalence of ADHD is important because such inconsistencies fuel assertions that ADHD is a fraud propagated by the "profit-dependent pharmaceutical industry and a high-status profession [psychiatry] looking for new roles" (2). Also at stake is the potential for scientists to exploit geographic variation in ADHD's prevalence to yield new information concerning its causes, which currently remain frustratingly unknown. Geographic comparisons are a powerful tool for investigating the etiology of disorders. In the first epidemiological study ever conducted, John Snow compared rates of cholera across areas of London during the 1854 cholera epidemic. Going against the then-prevalent "miasma" theory, which stipulated that diseases are carried by foul air, Snow surveyed residents about their source of drinking water and, using simple statistics, discovered that cholera cases were clustered around one particular water pump. This discovery led to the closing of the infected pump and prevented new cases. Moreover, although Snow was unable to identify the water-borne particles that cause cholera, his finding advanced the germ theory of disease (3). Contemporary examples show that when populations vary on their exposure to risk factors, geographic comparisons of disorder rates can generate new hypotheses about etiology. High rates of asthma and allergy in developed Western countries, compared to developing countries, generated new hypotheses about the etiology of respiratory disorders (e.g., childhood exposure to antibiotics, exposure to dust mite allergens, overly hygienic life styles) (4). In psychiatry, geographic comparisons reveal that the prevalence of schizophrenia in urban locations is more than double that in rural locations (5). This observation generated new hypotheses now subject to intense research (e.g., urban social isolation, infectious exposure exacerbated by urban crowding). In child psychiatry, geographic

tic Review

One hundred and twenty-eight studies including 171,756 subjects from 15 countries were included. The wide-pooled prevalence estimate was associated with variability. In the multilevel model, diagnostic information, requirement for diagnosis, and prevalence of the studies were significant with ADHD/HD prevalence. Geographic location was a significant variability only for studies from North America and the Middle East. No differences were found between studies from North America.

Our findings suggest that geographic location plays a limited role in explaining the large variability of prevalence estimates worldwide. This variability seems to be primarily by the methodological characteristics of studies.

Watry 2007; 16:439-42-948

The Worldwide

Guilherme Polanczyk, M.D.

Maurício Silva de Lima, M.D., Ph.D.

Bernardo Lessa Horta, M.D., Ph.D.

Joseph Biederman, M.D.

Luis Augusto Rohde, M.D.,

Why select this paper?

- The core feature of this paper is a systematic review.
- Having access to the web, virtually anyone may conduct a systematic review of the literature.
- Through the web is possible to learn how to perform an adequate systematic review and even a meta-analyses (e.g., Cochrane).

An important issue...

- We are not discussing on how to conduct a research.
- Our departing point is how to write a paper considering that you already finished data collection and analyses.
- Hard task: Abstract in medical meetings versus papers in the medical literature.

The starting point...

- Find a mentor (Ellen's presentation) .
- However, this is “a rare bird” in LA, at least for the child mental health field.
- Decide where to publish:
- Always one level above your work:

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RE: The worldwide prevalence of Attention-Deficit Hyperactivity Disorder;
Do geographic location and income of countries have an impact on variability
of estimates? A Systematic Review and Meta-Regression Analysis

Dear Prof. Rohde;

Thank you for submitting your manuscript to JAMA. Only about half of the
more than 5,000 manuscripts submitted to us annually are sent for external
peer review and less than 7% are accepted for publication in JAMA.

Based on our editorial evaluation and the comments of our peer reviewers,
I regret to inform you that we will not pursue your manuscript for
publication. Your manuscript may be suitable for a more specialized
journal. I am enclosing the reviewers' comments, which I hope you will find
helpful.

Thank you for the privilege of reviewing your work.

Sincerely yours,

Jody W Zylke, MD
Contributing Editor, JAMA
E-mail: Jody.Zylke@jama-archives.org

The starting point...

- **Decide where to publish:**
 - **Always one level above your work*:**
 - **When reviewed , it always help to prepare a better submission for your target.**
 - **Preference: journals with international visibility: PUBMED and ISI.**
- * Exception: need to publish quickly – fast track journals**

Make a timetable

- Session 1: Make notes on the literature, outline template papers, set provisional date for completion.
- Session 2: Devise an outline and title for your paper.
- Session 3: Create a rough first draft.
- Sessions 4 and 5: Write revisions one and two.
- Session 6: Write third revision, prepare tables and graphs, then give to coauthors.
- Session 7: Incorporate suggestions from coauthors into the text.
- Session 8: Prepare all figures and abstract.
- Session 9: Proof all changes, check all numbers and units, and review the final product with mentor.
- Session 10: Read one last time and send out.

Just a remark

- **Independently how good you think you are in English, find someone better (preferentially a native speaker) to review your final manuscript (last person to review).**

The next step...

- Find a template in the journal that you want to submit. Follow it strictly, avoiding plagiarism.
- Prepare an outline
- Find the sequence that you feel more comfortable: methods, introduction, results discussion, title, abstract.

Material e Methods: Sample

Key-elements:

- **1° paragraph:** - Study design (might be a separate subheading).
- - Origin of the sample (decision on breaking the blindness of the review process) + period of data collection).
- **Optional:** describe the environment :
- *Porto Alegre is the capital of Brazil's southernmost state with a population of 1,800.000 inhabitants.*
- **2° paragraph:** - inclusion and exclusion criterion (clinical trials).

Material e Methods: Sample

Key-elements:

- **3^o paragraph:** ethics:
- - *This investigation was approved by the Ethical Committee of our University Hospital. **Written informed consent** was obtained from parents and **verbal assent** was requested from children and adolescents to participate.*

Material e Methods: screening and diagnostic procedures

Key - elements:

- If there are screening procedures = describe them;
- Diagnostic procedures:
 - Describe which screening scale and which diagnostic instrument were used : SNAP-IV, DYBOCS, KSADS-E, SCID-R, MINI...
 - Describe the psychometrics of the instruments: internal consistency, predictive validity, face, content validity and/or concurrent validity.

Material e Methods: screening and diagnostic procedures

Key - elements:

- Translation process
 - If you do not have enough data: “*This instrument has been widely used in similar investigations (ref1, ref2, ref3)*”, or “*This measure has been frequently used in ADHD investigations, including those designed to assess clinical interventions (ref)*”.

Material e Methods: screening and diagnostic procedures

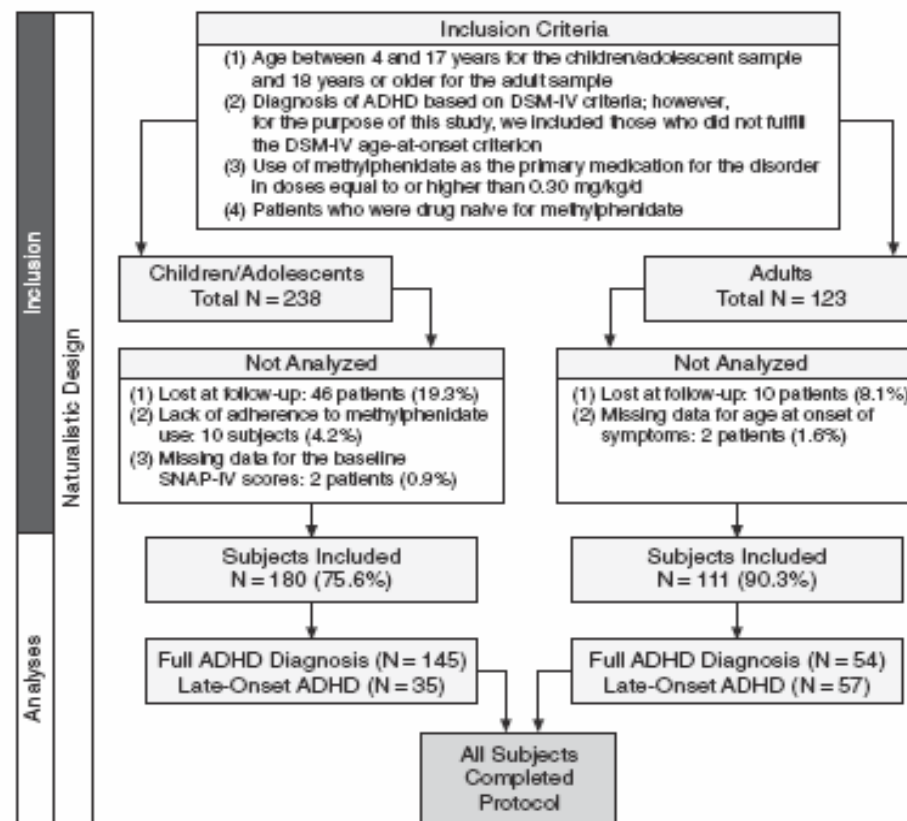
Key-elements:

- Internal consistency (α de cronbach) of the scale
- Inter-rater reliability: if more than 1 interviewer
- Figure describing the data collection process

Is Age-at-Onset Criterion Relevant for the Response to Methylphenidate in Attention-Deficit/Hyperactivity Disorder?

Marcelo C. Reinhardt, M.D.; Lucia Benetti; Marcelo M. Victor, M.D.; Eugenio H. Grevet, M.D.; Paulo Belmonte-de-Abreu, M.D.; Stephen V. Faraone, Ph.D.; and Luis A. Rohde, M.D.

Figure 1. Flow Chart Showing Criteria Used for Inclusion in the Samples of Children/Adolescents and Adults in This Naturalistic Study



Abbreviations: ADHD = attention-deficit/hyperactivity disorder, SNAP-IV = Swanson,

Material e Methods: screening and diagnostic procedures

a. Who translated and validated the SNAP-IV?

- The SNAP-IV was translated in our country under the coordination of Prof. Paulo Mattos from the Federal University of Rio de Janeiro. The paper describing the process is under revision in a national journal. It is important to note that, as described in the previous version of the paper, this measure has been frequently used in ADHD investigations. The internal consistency of the SNAP-IV varies from good to excellent (Stevens et al., 1998). In a previous study, we obtained a Cronbach's alpha coefficient of 0.74 for the complete scale (26 items) in a different sample from Brazil (Correa-Filho et al., 2005).

Correia-Filho A, Bodanese R, Silva T, Alvares J, Aman M, Rohde LA (2005), Comparison of risperidone and methylphenidate for reducing ADHD symptoms in children and adolescents with moderate mental retardation. *J Am Acad Child Adolesc Psychiatry* 44:748-55

Mattos P, Pinheiro MA, Rohde LA et al (submitted), Transcultural adaptation for the Portuguese of the SNAP-IV.

Stevens J, Quittner AL, Abikoff H (1998), Factors influencing elementary school teachers' ratings of ADHD and ODD behaviors. *J Clin Child Psychol* 27:406-14

Material e Methods: screening and diagnostic procedures

10) Page 6 - Please include a reference for the DSM IV version of the KSADS -E. Please specify the training of the research assistants who administered it. The KSADS is intended for use by trained clinicians, with additional training in the KSADS. Reliability and validity data based on clinically trained interviewers can not be assumed to apply to non-clinician interviewers. Was there any measure of reliability of interviewers in this study, not just by extension from Polanczyk et al.? Interviewers should be trained to a standard of reliability.

Several previous studies from other groups used the same version of the KSADS-E with modifications to allow DSM-IV diagnoses including one recently published in the JAACAP (see Wilens et al., 2006).

The inter-rater reliability for diagnoses included in this version of the KSADS-E was previously checked among all research assistants involved in this project and published in the mentioned paper by Polanczyk et al. (2003). If you check, you will find that name of the three research assistants involved in this project listed as co-authors in both papers (see below). Thus, data presented in that paper is related to training and inter-rater reliability for research assistants involved in this project. We are not presenting just an inferring reliability based on other investigators.

The training process is described in detail in that paper. In short, seminars on child psychopathology and principles of interviewing children are provided by child psychiatrists to them. Each research assistant attends applications of the KSADS -E for 4 months. Afterwards, they interview 5-10 patients using the KSADS-E with the participation of senior research assistants during all interviews. During this 6-month process, they take part of weekly clinical discussions on findings from applications of the KSADS -E by senior research assistants. Finally, inter-rater reliability is checked among them through videos of around 40 patients interviewed using the KSADS-E.

Material e Methods: screening and diagnostic procedures

We think that we can not miss the relevant point here: The diagnostic process used in this study is a strength not a weakness of the study. All diagnoses generated by the application of the KSADS-E by extensively trained research assistants (with their reliability previously checked) were re-checked by a senior child psychiatrist in a clinical committee and all patients were re-interviewed by an experienced child psychiatrist. In other words, differently from what has been done by others, findings generated by the KSADS-E applied by research assistants are not used as a final diagnosis, they are integrated with diagnoses provided by an experienced child psychiatrist using DSM-IV criteria.

Polanzyk G, Eizirik M, Aranovich V, Denardin D, Silva TL, Conceição TV, Pianca TG, Rohde LA. Interrater agreement for the Schedule for Affective Disorders and Schizophrenia, Epidemiological Version for school age children (K-SADS-E). *Rev Bras Psiquiatr* 2003; 87-90.

\ Wilens TE, et al, Characteristics of Adolescents and Young Adults With ADHD Who Divert or Misuse Their Prescribed Medications . *Journal of the American Academy of Child and Adolescent Psychiatry* v. 45 no. 4 (April 2006) p. 408-14.

Material e Methods: screening and diagnostic procedures

11) Page 7 - Is there a more recent reference for the psychometric performance of the CGAS?

Unfortunately, we are not aware of a more recent reference. As a quick note, a study published in the JAACAP two months ago (Wagner et al, 2006) used the same reference for describing psychometric properties of the CGAS.

Wagner, K. D., et. al., A Double-Blind, Randomized, Placebo-Controlled Trial of Escitalopram in the Treatment of Pediatric Depression . *Journal of the American Academy of Child and Adolescent Psychiatry* v. 45 no. 3 (March 2006) p. 280-8

12) Page 8 - the internal consistency of the SNAP complete scale is irrelevant, since it presumes to assess two different disorders - inattentive type and combined type.

The sentence about this issue was deleted, as suggested.

Material e Methods: study factor, outcome, and confounding variables

Key-elements:

- Description of the study factor: applies all previous discussion on psychometric properties of the instruments.
 - *The study factor (smoking during pregnancy) and possible confounding factors were assessed by direct interview with the biological mother.*
 - *Parental ADHD was assessed by a child and adolescent psychiatrist using the ADHD module of the K-SADS-E, modified to assess DSM-IV criteria. This strategy has been used in several previous studies (Biederman et al 2004; Roman et al 2003).*

Material e Methods: study factor, outcome, and confounding variables

Key-elements:

- Description of the study factor (independent variable):
- In studies of pharmacological intervention like RCT it might be de description of the pharmacological intervention.
- In studies of molecular genetics, it might be the description of the polymorphism and genotyping. In these cases, the description of the outcome might comes first.

Material e Methods: study factor, outcome, and confounding variables

Key-elements:

- Description of the study factor: applies all previous discussion on psychometric properties of the instruments.
- Make it explicit which are primary and secondary outcomes.

Material e Methods: study factor, outcome, and confounding variables

Key-elements:

- *Based on previous investigations in our population showing an association between ADRA2A and inattentive scores,^{15,18} we selected the parent-rated inattentive subscale of the Swanson, Nolan, and Pelham scale - version IV (SNAP-IV) as the primary outcome measure. The SNAP-IV scale is a revision ...*

Material e Methods: study factor, outcome, and confounding variables

Key -elements:

- Description of the outcome variable:
 - *The Family System Test (FAST): The FAST (Gehring, 1998) is a standardized figure placement technique which assesses family cohesion and hierarchy through the inside perspective of family members. The test consists of a square board divided into 81 squares, male and female figures for the representation of the family members and cylindrical blocks of three different heights for the elevation of the figures. The subject is asked to portray the family on the board in a typical situation as has been done by others.*

Material e Methods: study factor, outcome, and confounding variables

Key -elements:

- Description of the outcome variable:

Cohesion is measured through the distance between the figures using the Theorem of Pythagoras. Hierarchy is evaluated through the differences in height of the figures. Previous investigations documented acceptable test-retest reliability and convergent, discriminate and construct validity for the FAST (Gehring, 1998). In addition, this measure was already used in previous studies on ADHD (Saile et al., 1999) and in Brazilian samples (Graeff-Martins et al., in press; Marti, Käppler, Eryksel & Gehring, 2004; Oswald, 2002).

Material e Methods: study factor, outcome, and confounding variables

Key-elements:

- Description of potential confounders:
 - *Demographic characteristics (gender, ethnic background, and age) were collected by direct interview. Intellectual functioning was measured in children and adolescents by the Wechsler Intelligence Scale – Third edition (WISC – III)²⁶ administered by a trained psychologist to assess full-scale IQ score. In adults, the intellectual functioning was estimated by vocabulary and block design subtests of the Wechsler Adult Intelligence Scale – Revised (WAIS-R)²⁷, also applied by a trained psychologist.*

Material e Methods: Data analyses

Key-elements:

- In general, there is a comparison between two groups (cases and controls; treated and non -treated/placebo).
- **Initially, state** how potential confounders were treated.
 - *Patients were compared regarding demographic characteristics, IQ, ADHD subtype, comorbid conditions, previous use of medication, baseline scores in measures assessed, and MPH dose using the χ^2 test or Fisher's Exact Test (categorical variables), and the Student t test (continuous variables with normal distribution)*

Material e Methods: Data analyses

The issue of normality of data

RESULTS

Tests of the Validity of Executive Functions as Putative Endophenotype Measures

Tests of distributional normality. Although not a prerequisite for validity or utility, endophenotype measures will be more tractable for subsequent analyses if they exhibit good psychometric properties, including normal distributions with the absence of skewness and kurtosis. Unfortunately, none of the EF measures examined as putative endophenotypes in this study were normally distributed, as indicated by the Shapiro–Wilk test of normality, which was significant (i.e., $p < .05$) for all of the EF measures. In addition, with the lone exception of the Stroop word condition, all of the EF measures exhibited significant skewness and kurtosis (i.e., $p < .05$), as indicated by the skewness and kurtosis values exceeding twice their standard errors. Although these findings do not prevent meaningful analyses of endophenotype measures, they suggest caution in their interpretation.

Material e Methods: Data analyses

Key-elements:

- In general, there are sample losses. How were they treated to assess selection bias?
- State that comparisons that were made between cases and controls regarding potential confounders were also performed between those included and excluded from analyses. This might be mentioned in the results.

Is Age-at-Onset Criterion Relevant for the Response to Methylphenidate in Attention-Deficit/Hyperactivity Disorder?

Marcelo C. Reinhardt, M.D.; Lucia Benetti; Marcelo M. Victor, M.D.; Eugenio H. Grevet, M.D.; Paulo Belmonte-de-Abreu, M.D.; Stephen V. Faraone, Ph.D.; and Luis A. Rohde, M.D.

From a total sample of 238 children and adolescents with ADHD fulfilling our inclusion/exclusion criteria, we were able to include 180 subjects (75.6%). Reasons for exclusion were (1) lost at follow-up: 46 patients (19.3%); (2) lack of adherence to methylphenidate use: 10 subjects (4.2%); and (3) missing data for the baseline SNAP-IV scores: 2 patients (0.9%). From a total sample of 123 adults with ADHD fulfilling our inclusion/exclusion criteria, we were able to include 111 subjects (90.3%). Reasons for exclusion were (1) lost at follow-up: 10 patients (8.1%) and (2) missing data for age at onset of symptoms: 2 patients (1.6%) (Figure 1).

We compared patients included in and excluded from analyses in both samples on demographic characteristics, IQ scores, ADHD subtype, comorbid conditions (current disruptive behavior disorders, anxiety and mood disorders), SNAP-IV scores at baseline, doses of methylphenidate, and use of a second medication. There was no significant difference between children and adolescents with ADHD included in the study compared with those excluded on any assessed variable. Regarding the adult

Review Only

For Review Only

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Material e Methods: Data analyses

Key-elements:

- Definition of a confounder:
 - *We also determined the association between all the above mentioned variables and response to MPH (dependent variable).*



Material e Methods: Data analyses

Key-elements:

- Definition of a confounder:
- - *First, we defined potential confounders. They were defined based on conceptual analyses of the literature and/or using a broad statistical definition (association with both the independent and dependent variables at a $p < 0.20$). This approach assured very conservative analyses.*

Material e Methods: Data analyses

Key-elements:

- Since this point, you need to describe the main data analyses approaches which might be extremely variable:
 - Qui-square; Test t;
 - ANOVA / ANCOVA for repeated measures
 - Factorial Analyses / SEM...

Well-established statistical approaches do not need to be described or referenced.

Material e Methods: Data analyses

Key-elements:

- Statistical package:
 - All analyses were conducted using SPSS version 13.0.
- Level of significance accepted:
 - A significance level of 5% was accepted in all analyses (except for confounders, see above).
- Bi or uni-tailed:
 - Tests were two-tailed.

Introduction

Key - elements:

- **1o paragraph : Clinical relevance of the research question – epidemiological or biological data**
- **2o e 3o paragraph: literature review about the topic**
- **Frequent mistakes:**
 - **too extensive review (original papers) (editorial space = money);**
 - **left the reviewer that the research issue is already esgotada in the literature (leave an atmosphere of controversy, or that something is lacking, or that previous studies have methodological problems – point them);**

Introduction

Key - elements:

- **Frequent mistakes:**
 - **not mention of the work of potential reviewers (PUBMED potential reviewers – some journal will even request a list of them);**

Introduction

Key- elements:

- **4o paragraph: objectives e hipoteses**
- **Frequent mistakes:**
 - **Not explicit the hypotheses;**
- **- Not differentiate primary from secondary objectives**

Article

The Worldwide Prevalence of ADHD: A Systematic Review and Metaregression Analysis

Guilherme Polanczyk, M.D.

Maurício Silva de Lima, M.D.,
Ph.D.

Bernardo Lessa Horta, M.D.,
Ph.D.

Joseph Biederman, M.D.

Luis Augusto Rohde, M.D., Ph.D.

Objective: The worldwide prevalence estimates of attention deficit hyperactivity disorder (ADHD)/hyperkinetic disorder (HD) are highly heterogeneous. Presently, the reasons for this discrepancy remain poorly understood. The purpose of this study was to determine the possible causes of the varied worldwide estimates of the disorder and to compute its worldwide pooled prevalence.

Method: The authors searched MEDLINE and PsycINFO databases from January 1978 to December 2005 and reviewed textbooks and reference lists of the studies selected. Authors of relevant articles from North America, South America, Europe, Africa, Asia, Oceania, and the Middle East and ADHD/HD experts were contacted. Surveys were included if they reported point prevalence of ADHD/HD for subjects 18 years of age or younger from the general population or schools according to DSM or ICD criteria.

Results: The literature search generated 9,105 records, and 303 full-text articles

were reviewed. One hundred and two studies comprising 171,756 subjects from all world regions were included. The ADHD/HD worldwide-pooled prevalence was 5.29%. This estimate was associated with significant variability. In the multivariate metaregression model, diagnostic criteria, source of information, requirement of impairment for diagnosis, and geographic origin of the studies were significantly associated with ADHD/HD prevalence rates. Geographic location was associated with significant variability only between estimates from North America and both Africa and the Middle East. No significant differences were found between Europe and North America.

Conclusions: Our findings suggest that geographic location plays a limited role in the reasons for the large variability of ADHD/HD prevalence estimates worldwide. Instead, this variability seems to be explained primarily by the methodological characteristics of studies.

(Am J Psychiatry 2007; 164:942–948)