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A Critical Appraisal of a Harm Study: Being Children of Immigrant Parents and Acquiring Attention-Deficit/Hyperactivity Disorder.

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Abstract:
Background and aims: *Mental health problems are not uncommon among children of the immigrants. Recently, the immigrants' toll has increased in most developed nations. The children of immigrant parents are frequently susceptible to mental illnesses like attention-deficit/hyperactivity disorder (ADHD). The association between being diagnosed with ADHD and being children of immigrant parents is poorly understood. A study by Lehti et al. (2016) has researched such association using data from a population-based register, the Finnish Hospital Discharge Register (FHDR). This study attempts to critically appraise and evaluate the validity of the evidence of Lehti et al. (2016) study. The validity of FHDR has also been discussed since multiple psychiatric research are based on FHDR.*
Methods and Material: *This critical appraisal was done using critical appraisal tool (CAT) mentioned in Glynn (2006) study which calculates overall and section validity of a research paper (by calculating validity scores).*
Statistical analysis: *Percentage calculation for validity was done.*
Results and Conclusions: *The study appraised here couldn't attain overall validity, therefore according to this appraisal, future studies are required to address the knowledge gap in this pertinent area of child psychiatry. In addition, to make FHDR a better tool for psychiatric research, incorporation of codes of Diagnostic and Statistical Manual of Mental Disorders along with codes of International Classification of Diseases is highly recommended.*
Keywords - *ADHD; immigrant; critical; appraisal; FHDR; validity*

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I. Introduction

Attention-deficit/hyperactivity disorder (ADHD) has a global prevalence of 5-10% among children.[1,2] It is characterized by inattention (manifests as daydreaming, easy distractibility, and inability to remain focused on a single task for a long duration) and hyperactivity (represents fidgeting, talkativeness, and restlessness).[3] Following are the risk factors of ADHD that have been proposed in the literature- adverse family environment, the role of certain genes, hyperactivity as a heritable trait, perinatal factors etc.[4-7] However, despite mental health problems being common among children of immigrants [8–11] their predisposition to ADHD has not been studied in detail.

Childhood ADHD can disrupt the social and academic life of the children and make them skill deficient.[3] Moreover, Immigrant children with ADHD are often vulnerable to post-traumatic stress disorder (PTSD) and when both of these conditions occur together the treatment of ADHD has been found to beneficial in ameliorating the PTSD symptoms.[12-14] Therefore, an understanding of the association between being diagnosed with ADHD and being children of immigrant parents can be helpful to establish an early diagnosis of ADHD and initiate a timely treatment. The study by Lehti et al. (2016) titled "Association between immigrant background and ADHD: a nationwide population-based case-control study", based on a population register of Finland, the Finnish Hospital Discharge Register (FHDR) [15] is an appreciable attempt to address this knowledge gap in this area of child psychiatry. The FHDR is maintained by National Institute for Health and Welfare.[16] It collects data on all medical diagnosis (physical and psychiatric) from psychiatric, prison and private hospitals, inpatient wards of local health centers, military wards, and all outpatient services of public hospitals.[16]

This study was published at a time when high immigration trends were observed in most developed nations like North America, Oceania, and Europe.[17] A similar trend was observed in Finland too where the Lehti et al. (2016) study [15] was conducted. The number of asylum applications increased by 890% between 2014 and 2015 in Finland.[18]

Since the raw evidence that contributes to medical sciences are comes from research papers it's important that the latter undergo a critical analysis of its quality and reproducibility.[19] Therefore, a critical appraisal of the Lehti et al. (2016) study [15] is presented here to assess the validity of its evidence.

Critical appraisal is a key skill necessary for both policymakers and health professionals [20] to understand research methods and draw conclusions from a research paper.[21] Researchers have persistently tried to develop critical appraisal tools (CAT) to appraise research papers published in various fields like public health, qualitative research etc.[20,22] Studies assessing harm, as done in this study, are generally assessed by answering a set of questions.[23,24] Then a scoring for each component is analyzed and a summary score is obtained for the entire study.[25]

The CAT mentioned in Glynn (2006) [19] was chosen for this critical appraisal because it assesses the validity of individual sections of a study along with the overall validity.[19,25]

A study is said to achieve its validity when it measures what it should measure.[21] Whereas reliability is assured when independent researchers get similar results by doing a test, however, a research can't achieve reliability if it hasn't achieved validity.[21,26]

II. Material and Methods

Using the questions in each of the 4 sections (named A, B, C and D which evaluates the study population, data collection, study design, and results respectively) of the CAT mentioned in 'Glynn (2006) study [19] the validity of each of these sections and an overall validity has been calculated for the Lehti et al 2016 study.[15] Each of the questions in the CAT proposed in the Glynn (2006) study could have any one of the four answer choices - 'Yes', 'No', 'Unclear' and 'Not applicable'.[19] Based on the score obtained using Glynn (2006) CAT a score of 75% or more (obtained by dividing total 'Yes' answers divided by the total of 'Yes', 'No' and 'Unclear' answers) is considered sufficient to conclude a study as valid.[19] Alternatively, a CAT analysis score of 25 or less obtained by dividing the total number of 'No' and 'Unclear' answers by the total of 'Yes', 'No' and 'Unclear' answers is also considered valid.[19] The validity of each of its 4 sections and the overall validity is then calculated.[19] The CAT along with the description of each of the questions under each section (A, B, C, and D) and detailed methods of validity calculation can be found elsewhere.[19]

III. Results

The responses to the questions and the calculation of (section and overall) validity as per the CAT of Glynn (2006) study [19] is depicted for Lehti et al. (2016) study [15] in Table 1 and Table 2 respectively. The overall score for Lehti et al. (2016) study [15] was 64% when the numerator was the sum of 'Yes' answers and 36% when the numerator consisted of the combination of total 'No' and 'Unclear' answers (Table 2). Therefore, based on the cut-offs of validity calculation of CAT of Glynn (2006) study [19] based on this author's marking an appraisal the Lehti et al. (2016) study [15] couldn't attain an overall validation score although it could achieve section validity for section B and C (i.e. for data collection, study design respectively) (Table 1).

IV. Discussion

Various components of the CAT provided in Glynn (2006) study [19] were assessed for the Lehti et al. (2016) study.[15]

Study population and inclusion criteria:

Regarding representativeness of the study population and the inclusion criteria, it is not clear if the study population of Lehti et al. (2016) study [15] is representative of all eligible participants because it is unclear if the outcome being studied were ADHD cases without co-morbidities or ADHD cases with co-morbidities. The term 'co-morbid' refers to two or more mental disorders occurring in an individual.[27] The perplexity in this regard worsens further due to the International Classification of Diseases (ICD) codes which were used in the Lehti et al. (2016) study.[15] The Lehti et al. (2016) study used ICD-9 and ICD-10 codes which don't include conduct disorders (CD) (314.0 and F90.0 respectively) and also codes that include CD (314.2 and F90.1 respectively).[15,28–30] Therefore, it is not apparent if the authors of Lehti et al. (2016) study wanted the co-morbidity 'CD' to be included or excluded.

ADHD may be of a pure variety without any comorbidity or may be associated with various co-morbidities like anxiety disorder, oppositional defiant disorder (ODD) or CD.[31] In addition, only ADHD (i.e.

without any co-morbidities) and ADHD with CD are two distinct types of disorders with different possible aetiologies.[28,31,32] Furthermore, when ADHD and CD occur together as a co-morbid condition it is much more severe than when ADHD occurs independently.[27,33] ADHD and CD have about 20-35% chance to occur as a co-morbid condition.[34–36]

Moreover, it was not clear why CD was considered as the only co-morbid condition to be studied along with ADHD (if the authors of Lehti et al. (2016) study really wanted to study it), because PTSD, another condition co-morbid with ADHD is also important from the immigrants' perspective [12] and could have also been studied. The treatment of ADHD helps to control the symptoms of the PTSD and vice-versa.[12] Furthermore, the incorporation of the code 314.01 as ICD-9 code in the inclusion criteria by Lehti et al. (2016) study is probably not totally agreeable, since the code 314.01 is a coding used in International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-CM-9) system and not ICD-9.[29,37] ICD-9-CM is a US version of the World Health Organization's Ninth Revision of International Classification of Diseases.[38]

The Exclusion criteria:

Regarding the exclusion criteria of the Lehti et al. (2016) study, [15] the rationale for the exclusion of severe/profound mental retardation cases was not clearly depicted. Despite mental retardation being associated with ADHD in children [39–41] research studies done in relation to childhood and adolescent ADHD [15,42,43] often exclude intellectually disabled patients (sometimes the more severe cases) without mentioning proper rational of such exclusion. Moreover, depiction of the exclusion criteria, possibly, would have been more rationalised if the ICD codes (or any other disease classification system) that were used in Lehti et al. (2016) study [15] for excluding the controls with ADHD, CD, and severe/profound mental retardation were mentioned, as was done for the cases.

Sample size:

Although in Lehti et al. (2016) study [15] any mention of power or how the desired sample size was calculated couldn't be found, the sample size was alike two other studies that dealt with ADHD [42,44] hence it may be considered as an appropriate estimate of sample size.[19]

Selection bias:

After sample size, the selection bias was assessed. Selection bias is a systemic error that can happen in any epidemiological study, due to an error in identification of the study population correctly.[45] Selection bias is a possibility in the Lehti et al. (2016) study [15] because the sample population of Lehti et al. (2016) [15] study did not recruit other children with ADHD diagnosis (if any) who were not registered in the FHDR like asylum seekers and recent immigrants (who might also have affected the sample size).[15]

Randomization:

In an ideal case-control study the sample should be chosen by randomization, since studying the entire population may not be feasible.[46] Randomization eliminates the risk of systemic bias,[46] henceforth recommended for case-control studies.[47] Any mention about utilizing of any randomization method in Lehti et al. (2016) study [15] to choose the study population couldn't be found. Neither such is mentioned to the study to which Lehti et al. (2016) study [15] referred to, for in its study description (i.e. the Joelsson et al. (2015) study). [42]

Subjectivity in the collected statistics:

Despite the fact that ADHD cases included in Lehti et al. (2016) study [15] were primarily diagnosed by a psychiatrist or a neurologist, it wasn't clear from Lehti et al. (2016) study [15] how many cases of ADHD were diagnosed by such specialist physicians (like psychiatrist or neurologist) and how many by other non-specialist health professionals. ADHD diagnosis is not straightforward due to its non-specific nature of symptoms and the likelihood of its co-occurring with other co-morbidities, hence establishing a definitive diagnosis of ADHD is quite intricate for physicians not having any specialized training in child psychiatry.[48] While diagnostic criteria (like Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) makes the diagnostic process of ADHD systematic, subjective role of diagnosing physician prevails due to the nature of the

disease.[48] The issue of subjectivity could have been addressed better if the authors of Lehti et al. (2016) study [15] could have contacted the psychiatrists who made the diagnoses.

Study type (case-control):

The Lehti et al. (2016) study is a nested case-control study.[15] Case-control studies are generally ideal for rare diseases.[49] In Europe, a disease is considered as rare if it affects 1 in 2000 individual.[50] To search if ADHD is a rare disease a search in rare disease database of Europe 'Orphanet' [50,51] was done using this website's inbuilt search system and also by manually searching through the list of rare diseases (http://www.orpha.net/consor4.01/www/cgi-bin/Disease_Search.php?lng=EN&search=Disease_Search_List). Following search terms were used for the search- 'ADHD', 'Hyperkinetic disorders', Attention-deficit hyperactivity disorder', 'Disturbance of activity and attention', 'Hyperkinetic conduct disorder', 'Other hyperkinetic disorders' (most of these search terms were those used in ICD-9 and ICD-10).[28,29] This search was also extended to the US-based rare disease database - 'Genetic and Rare Diseases Information Center (GARD)' (https://rarediseases.info.nih.gov).[52] However, ADHD couldn't be retrieved in these rare disease databases. Moreover, the Northern Finland Birth Cohort (NFBC) Study revealed a 12.6% prevalence of retrospective childhood ADHD in Finland.[43] Therefore, it's probably safe to conclude (as of the current time) ADHD isn't a rare disease, hence case-control study design is less likely the best study design for studying ADHD.

Face validity:

Face validity is the common-sense-based assessment of the appropriateness of methodology used in a research.[19] The method of doing the nested case-control study by Lehti et al. (2016) appears appropriate since authors of Lehti et al. (2016) study chose 4 matched controls for each case and both cases and controls were representatives of the same population.[15]

Subset analysis:

In Lehti et al. (2016) study [15] Sub-Saharan Africa was a subset that probably received a substantial amount of focus. The possible cause might be the fact that, Sub-Saharan Africa achieved the highest odds ratio even after adjustment for confounders.[15] The authors of Lehti et al. (2016) study made additional regional analysis using the same covariates used for other calculations in their paper (where sub-Saharan Africa was used as a reference); the calculations of which are available online.[15]

External validity:

Throughout the discussion above this author argued of various weak points of the Lehti et al. (2016) study. These are – haze about what outcome was studied in the Lehti et al. (2016) study [15] (pure ADHD or ADHD with comorbidity), unclear ADHD co-morbidity criteria (due to some of the ICD codes used in the inclusion criteria), possibility of selection bias, non-mention of any randomisation method for sample selection, possible role of subjectivity in the secondary data used for the study, the study type (case-control), and no power calculation for determining the sample size. In addition, this author is not in accord with the trust the authors of Lehti et al. (2016) study [15] has shown for the Joelsson et al. (2015) study's [42] validity estimation of the FHDR for ADHD diagnosis (discussed below). Based on most of these parameters this author finds it difficult to agree that Lehti et al. (2016) study [15] is externally valid.

FHDR's validity:

Similar to the Lehti et al. (2016) study, several other studies were done based on FHDR,[15,16,42,53,54] hence validity of the FHDR for its use in research needs special mention. According to a systemic review done by Sund (2012), the positive predictive value of FHDR for common diagnoses is quite varied ranging from 75% to 99%.[53] Most studies that assessed FHDR's validity didn't calculate the sensitivity (i.e. the power of diagnosing a disease correctly in a diseased individual) of the diagnoses entered in the register.[53] Therefore, it appears to be difficult to make a precise estimate about the certainty of a diagnosis in FHDR. Said so, the importance of FHDR remains high for research purposes where secondary data is the only better option.

To highlight the validity of the ADHD diagnosis entered in FHDR the authors of Lehti et al. (2016) study have cited the study by Joelsson et al. (2015).[15,42] However, this author expresses doubt about the validity of the validity assessment of FHDR depicted in Joelsson et al. (2015).[42] Despite best efforts by the authors of Joelsson et al. (2015) study [42] the following points probably compromises its validity estimation of the FHDR. The Joelsson et al. (2015) study [42] study was not blinded, was at risk of recall bias (as it was conducted by telephone interviews), was based on a relatively small sample size, had chances to miss less severe ADHD cases (as it utilised services of specialised mental health clinics), was a nested case-control study (not a higher level of epidemiologic evidence like a randomised control trial) and there were no other similar studies this author could find, to reinforce its findings. Moreover, the Development and Well-Being Assessment (DAWBA) tool which was utilized by Joelsson et al. (2015) study [42] have a positive predictive value of 40 to 80 percent, making it a less reliable test for making a definitive diagnosis of ADHD. Instead, the DAWBA tool may be useful as a low-cost screening tool to identify children who require further clinical assessment of mental health problems.[55] The study done by Joelsson et al. (2015) could achieve only 88% percent validation for ADHD diagnosis, i.e. the FHDR database misses about 12% of the cases.[42]

Another interesting point to note here is that in contrast to the FHDR where diagnoses entries are based on ICD codes [42,44] the FHDR's validity assessment done by Joelsson et al. (2015) was performed using the DSM-IV codes as a standard criterion.[42] Worldwide most psychiatrists prefer to use DSM-IV for research purposes and ICD-10 for clinical diagnosis and training.[56] Therefore, DSM-IV could have been a better diagnostic tool for selecting ADHD cases and excluding controls (who don't meet the criteria to be in the control group) in Lehti et al. (2016) study.[15] However, even if the authors of Lehti et al. (2016) study would have thought of using DSM-IV criteria, it wouldn't have been feasible to do so using the FHDR data directly, because ICD system is used in Finland to diagnose mental illnesses since 1969.[44] Till 1986, ICD-8 was used for diagnosing disease, then between 1987 and 1995 ICD-9 came into action and from 1996 onwards ICD-10 is in use.[42,44] Therefore, incorporation of DSM-IV based diagnoses in FHDR may be considered by the Finnish authorities for better research related use of the FHDR.

Strength and weakness of this critical appraisal:

Nevertheless, it is possible that this critical appraisal is biased by the subjectivity of this author. Heller et al. (2008) found that if multiple health professionals are asked to answer a set of queries relating to the validity, transferability, methodology etc. of a critical appraisal checklist the variability of correct answers among the respondents can be between 65% to 96%.[20]

Using the same Glynn (2006) study's [19] CAT other authors can test if similar validity score like this study is reproducible or not for the Lehti et al. (2016) study.[15] For this reason, the scoring based CAT by Glynn (2006) [19] was used in this appraisal. If non-scoring-based appraisal techniques [23,57] were chosen it could have been difficult to test the reliability of this appraisal in future.

Last but not the least, this critical appraisal paper is not meant to undermine the effort of the authors of any study discussed here including the Lehti et al. (2016) study.[15] Rather this study may be considered as an endeavor to aid in the process of deciding about the quality of evidence that is available in the medical literature. This critical appraisal would hopefully contribute to future systemic reviews, meta-analysis or other similar types of research, by aiding the researchers to decide about the strength of evidence they are considering to include or exclude from their research. Possibly, no research is hundred percent error-free or perfect, and hence critical appraisal is necessary for evaluating every piece of evidence that is added to the medical literature.

V. TABLES

Table 1: Answer to CAT questions of Glynn (2006) study [19] for the Lehti et al. (2016) study[15]:

Questions	Answers*
SECTION A (population)	
Is the study population representative of all users, actual and eligible, who might be included in the study?	U
Are inclusion and exclusion criteria definitively outlined?	N
Is the sample size large enough for sufficiently precise estimates?	Y
Is the response rate large enough for sufficiently precise estimates?	N/A
Is the choice of population bias-free?	N
If a comparative study: Were participants randomized into groups?	N
If a comparative study: Were the groups comparable at baseline?	Y
If a comparative study: If groups were not comparable at baseline, was incomparability addressed by the authors in the analysis?	N/A
Was informed consent obtained?	N/A
SECTION B (data collection)	
Are data collection methods clearly described?	Y
If a face-to-face survey, were inter-observer and intra-observer bias reduced?	N/A
Is the data collection instrument validated?	Y
If based on regularly collected statistics, are the statistics free from subjectivity?	N
Does the study measure the outcome at a time appropriate for capturing the intervention's effect?	N/A
Is the instrument included in the publication?	Y
Are questions posed clearly enough to be able to elicit precise answers?	Y
Were those involved in data collection not involved in delivering a service to the target population?	N/A
SECTION C (study design)	
Is the study type / methodology utilized appropriate?	N
Is there face validity?	Y
Is the research methodology clearly stated at a level of detail that would allow its replication?	Y
Was ethics approval obtained?	Y
Are the outcomes clearly stated and discussed in relation to the data collection?	Y
SECTION D (results)	
Are all the results clearly outlined?	Y
Are confounding variables accounted for?	Y
Do the conclusions accurately reflect the analysis?	Y
Is subset analysis a minor, rather than a major, focus of the article?	N
Are suggestions provided for further areas to research?	Y
Is there external validity?	N

*Yes (Y), No (N), Unclear (U) or Not applicable (N/A)

Table 2: Validity calculation for Lehti et al. (2016) study[15] based on CAT by Glynn (2006) study[19]*:

Section A	Y-2, N-3,U-1; T=6 Y/T = 2/6= 33% (N+U)/T = 4/6 = 67%	Overall validity: Y = 2+4+4+4 = 14 N= 3+1+1+2 = 7 U= 1+0+0+0 = 1 T = Y+N+U = 22 Y/T = 14/22 = 64% (N+U)/T = 8/22= 36%
Section B	Y=4, N=1, U=0, T=5 Y/T = 4/5 = 80% (N+U)/T = 1/5 = 20%	
Section C	Y=4, N=1, U=0, T=5 Y/T = 4/5 = 80% (N+U)/T = 1/5 = 20%	
Section D	Y=4,N=2,U=0, T=6 Y/T = 4/6 = 67% (N+U)/T = 2/6 = 33%	

*Yes (Y), No (N), Unclear (U) or Not applicable (N/A)

VI. CONCLUSION

Based on this critical appraisal performed using the CAT mentioned in Glynn (2006) study [19] the Lehti et al. (2016) study [15] couldn't achieve overall validity. Some of the important reasons were confusing case definition of ADHD, selection bias, no randomization, the possibility of subjectivity in collected statistical data, the type of study (case-control), and lack of power calculation in sample size determination. Further research is needed to assess the association between ADHD (pure form) or ADHD with co-morbidity and being children of immigrant parents.

However, this critical analysis has the potential risk of being biased by the subjectivity of the author and therefore, a further appraisal is recommended for the Lehti et al. (2016) study to test if validity analysis of this study is reliable or not.

Finally, to make FHDR a better research tool for psychiatric illnesses the Finland government may consider scopes of including DSM-IV based diagnoses too alongside the ICD based diagnoses.

VII. CONFLICT OF INTEREST

There is no conflict of interest.

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