Journal of Affective Disorders 210 (2017) 166–173

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Review article

How prevalent and morbid are subthreshold manifestations of major depression in adolescents? A literature review

Nicholas W. Carrellas[a], Joseph Biederman[a,b], Mai Uchida[a,b,*]

[a] Pediatric Psychopharmacology Program, Division of Child Psychiatry, Massachusetts General Hospital, Boston, MA 02114, USA
[b] Department of Psychiatry, Massachusetts General Hospital, and Harvard Medical School, Boston, MA 02114, USA

ARTICLE INFO

Keywords:
Subthreshold
Subsyndromal
Minor
Depression
Impairment
Adolescent

ABSTRACT

Introduction: Major Depressive Disorder (MDD) among youth is a public health concern. Our aim was to examine the current body of knowledge to better characterize the prevalence and morbidity associated with subthreshold forms of MDD among youth. Given that MDD tends to develop gradually over time, we hypothesized a high prevalence and considerable impairment associated with youth suffering from depressive symptoms that fall short of full, syndromic status.

Methods: A literature search was conducted using PubMed exclusively to identify studies assessing the prevalence and clinical characteristics of subthreshold MDD in adolescents.

Results: Six scientific papers that met our priori inclusion and exclusion criteria were identified. All papers sampled adolescents. The prevalence of subthreshold MDD ranged from 5% over the past year, to 29% over the two weeks prior to screening. These papers reported clinically significant morbidity associated with subthreshold MDD among adolescents, with evidence for elevated rates of psychiatric comorbidities, impaired functioning in social and familial domains, increased suicidality, and frequent mental health service utilization.

Limitations: Though we examined a sizeable and diverse sample, we only identified six cross-sectional informative studies for this review. Variability of subthreshold MDD and major outcome definitions across studies, likely limits the specificity of findings.

Conclusions: Subthreshold MDD is prevalent among youth, and is associated with emotional and social impairments that reach the level of obtaining clinical care. These findings could lead to early intervention efforts aimed at mitigating the adverse outcomes associated with subthreshold MDD as well as the progression to full syndrome MDD. Our review documents that regardless of whether progression to full diagnostic status occurs, this condition is morbid.

1. Introduction

Major Depressive Disorder (MDD) is among the most common manifestations of psychopathology in youth. In the United States, depression among young people is associated with a wide range of adverse consequences that have resulted in the Center for Disease Control (CDC) labeling MDD as a major, public health concern (Perou et al., 2013). In 2014, an estimated 2.8 million adolescents aged 12–17 had at least one major depressive episode in the past year, equating to roughly 11.4% of the population in that age range (Center for Behavioral Health Statistics and Quality, 2015). MDD is a major risk factor for suicide, and suicide is second only to accidents as the most common cause of death in adolescents. Additionally, significant social, familial, and academic impairment (Jaycox et al., 2009; Keenan-Miller et al., 2007), as well as recurrent illness though adulthood (Birmaher et al., 2007), are associated with the disorder.

Considering that MDD tends to evolve slowly over time, there is often a delay between the initial onset of symptoms and their conversion to the full syndromic state (Bertha and Balazs, 2013). Given the high prevalence of pediatric MDD, it is very likely that a sizeable number of children and adolescents are affected with subthreshold manifestations of MDD before they reach full syndromic status. However, little is known about the prevalence and morbidity of subthreshold forms of MDD.

Better insight into the prevalence and morbidity of subthreshold forms of MDD is a subject of high clinical, scientific and public health relevance. Clinically, if subthreshold forms of MDD are morbid, they should be targeted for intervention to prevent their progression to full diagnostic status. From the scientific perspective, subthreshold forms

* Correspondence to: Department of Pediatric Psychopharmacology, Massachusetts General Hospital, 55 Fruit Street, Warren Building 6th Floor, Boston, MA 02114, USA.
E-mail address: muchida@partners.org (M. Uchida).

http://dx.doi.org/10.1016/j.jad.2016.12.037
Received 7 September 2016; Received in revised form 21 November 2016; Accepted 22 December 2016
Available online 27 December 2016
0165-0327/

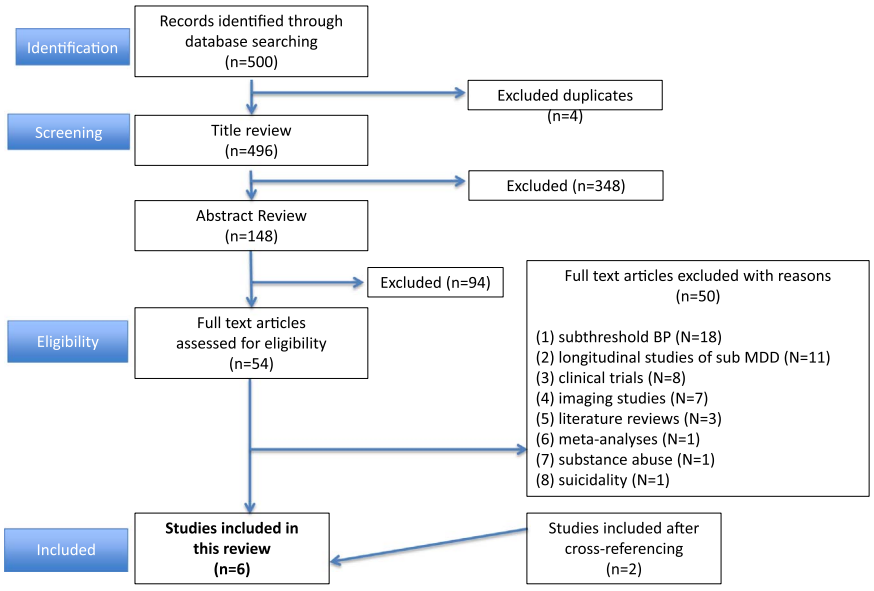

Fig. 1. Prisma Flow Diagram.

of MDD can provide unique insights into the neurobiology of pediatric MDD.

The main aim of the present study was to assess what is known about the prevalence and morbidity of pediatric MDD. To this end, we conducted a systematic review of the extant literature focused on this topic. We hypothesized that subthreshold forms of MDD would be both prevalent and morbid.

2. Methods

2.1. Literature review

We performed a systematic literature search through **PubMed exclusively in November 2015,** utilizing the following search algorithm: (sub threshold or subthreshold or subsyndromal) AND (depression or mania or mood or mood disorder or bipolar disorder or bipolar or depressive or hypomania or cyclothymia) AND (child or children or youth or adolescent or teen or pediatric). Reference lists of retrieved papers were further screened, and papers that possibly met inclusion criteria were retrieved and assessed for inclusion.

2.2. Selection criteria

We included only original studies that specifically evaluated subthreshold depressive symptoms. Of note, the above algorithm was used as part of a more expansive search than is reported on here; for this particular report, we only included studies that examined the cross-sectional morbidity associated with subthreshold depressive symptoms. We implemented the following inclusion criteria: (1) original research, (2) includes clear definition of subthreshold MDD that is mutually exclusive from MDD (3) documents rates of subthreshold MDD and associated levels of impairment (4) subjects are limited to adolescent/youth samples with a mean age ≤18, and (4) cross-sectional examination. Articles were excluded if (1) they did not clearly define subthreshold MDD (2) the subthreshold MDD group was not mutually exclusive from MDD (3) the study had a prospective design examining the risk factors of conversion from subthreshold MDD to full syndrome MDD, (3) the study was a meta-analysis, psychosocial intervention, clinical trial, imaging protocol, or literature review, or (4) not available in English or accessible through PubMed.

Of importance, we did not exclude studies based on the type of criteria they used to define subthreshold MDD, provided that definition for subthreshold MDD was clearly distinguished from MDD. Additionally, we included studies that documented prevalence rates without restriction to the time duration across which prevalence was investigated (e.g. 1 week vs. lifetime).

Two psychiatrists and a research assistant screened the articles for relevance by examining the abstracts, and two psychiatrists and a research assistant reviewed the identified relevant articles in full text to evaluate their eligibility.

2.3. Data extraction

The following variables were extracted: study sample size, proband age range, and characteristics that differentiated subjects with subthreshold MDD from those with full syndrome MDD or those unaffected by depressive symptomatology.

2.4. Qualitative analysis

We reviewed the included articles, extracting the relevant details. We also performed a qualitative analysis of the methods and results with particular note of the prevalence of subthreshold MDD, in addition to rates of the following: psychiatric comorbidities, functional and school impairment, suicidal ideation, and mental health service utilization. Our analysis was centered on the identification and extraction of working definitions and rates for the above variables. If no working definition was present, or a variable was not sufficiently investigated, it was dropped from the analysis.

3. Results

Fig. 1 provides the results of the identification of the articles using the aforementioned algorithm. From the initial database search using **PubMed only**, a total of 500 papers were identified and screened by 3 of the authors (JB, MU and NC). After the initial screening, 54 articles were deemed to be of potential interest. Upon closer consideration, 50 of these articles were excluded due to (1) results reporting on subthreshold BP instead of subthreshold MDD (N=18), (2) longitudinal studies reporting on the predictive nature of subthreshold MDD to full MDD (N=11), (3) clinical trials (N=8), (4) imaging studies (N=7), literature reviews (N=3), meta-analyses (N=1), confounding substance abuse (N=1) and a focus on suicidality (N=1). Additionally, 2 papers were included after cross-referencing. Thus, 6 studies met all our