



Early-onset major depressive disorder

Principal investigator

Daphne Korczak, MD, FAAP, FRCPC (paediatrics), FRCPC (psychiatry),
The Hospital for Sick Children, University of Toronto, Room 35A, 1145 Burton Wing,
555 University Ave., Toronto ON M5G 1X8; tel.: 416-813-6510; fax: 416-813-5326;
daphne.korczak@sickkids.ca

Co-investigators

Mark Feldman, MD, University of Toronto
John LeBlanc, MD, Dalhousie University
Mariana Ofner, PhD, University of Toronto (PHAC Representative)
Patricia Parkin, MD, University of Toronto
Sam Wong, MD, University of Alberta

Background

Major depressive disorder (MDD) is a significant public health problem. Data suggest that there has been an increase in the prevalence of pre-adult onset MDD, with 37% of subjects reporting a pre-adult onset.¹

There is now compelling evidence that early-onset MDD comprises a particularly severe form of illness, as it has been associated with a host of proxies for illness severity, including comorbid substance use disorders, psychiatric hospitalizations, greater functional impairment, increased episodicity, and suicidality in clinical studies.² Multiple family studies indicate that child and adolescent offspring of a parent with MDD are at high risk for development of the disorder, particularly when parental depression is severe and/or complicated by psychiatric comorbidity.^{3,4}

Despite the literature regarding pre-adult or youth-onset MDD, data regarding childhood-onset illness remain scant, as the definition of “early-onset” disease varies considerably in the literature. Epidemiological evidence suggests that childhood-onset MDD is associated with a more than fourfold increased risk of suicide attempts compared with adult-onset disease.⁵

The atypicality of childhood-onset MDD means that in Canada, a national approach to case ascertainment is required to generate meaningful study sample sizes. Increased knowledge regarding the incidence and presentation of these children is of critical importance in designing effective diagnostic and management approaches for children with this treatable illness.

PROTOCOLS



PROTOCOLS

Methods

Through the established methodology of the CPSP, over 2,500 paediatricians and paediatric subspecialists will be actively surveyed on a monthly basis for new cases of early-onset major depressive disorder (EOMD). For each reported case, participants will be asked to complete a detailed clinical questionnaire to ensure that the case definition is met.

Case definition

Report any child aged 5 to 12 years of age inclusively, seen in the previous month, with newly diagnosed early-onset major depressive episode, including children with unipolar mood disturbances sufficient to cause a disruption to social, family and/or academic functioning.

“Major depressive episode” is defined in DSM-IV-TR⁶ as:

- 1) Depressed or irritable mood, most of the day, nearly every day,
OR
- 2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day,

which is either newly present or has clearly worsened compared with the child’s pre-episode status.

AND

At least **four** of the following seven symptoms present during the same two-week period as either (1) **or** (2) above. These symptoms occur daily or near daily and represent a distinct change from previous functioning.

- 1) Significant weight change, failure to make expected weight gains, **or** significant appetite change.
- 2) Insomnia (difficulty falling asleep, night-waking or waking too early) **or** hypersomnia.
- 3) Psychomotor agitation **or** retardation: observable by others and does not represent subjective feelings.
- 4) Fatigue **or** loss of energy.
- 5) Feelings of worthlessness **or** excessive or inappropriate guilt (not merely guilt about being sick).
- 6) Diminished ability to think or concentrate, **or** indecisiveness.
- 7) Recurrent thoughts of death, recurrent suicidal ideation, **or** a suicide attempt.

AND

Impairment in social functioning (social withdrawal, family or peer conflicts) or academic functioning (school refusal, decreased school performance), which is either *newly present or worsened* compared with pre-episode status.

Exclusion criteria

- 1) Symptoms due to the direct physiological effects of a substance or a general medical condition.
- 2) Symptoms occurring exclusively during acute bereavement period (within two months after the loss of a loved one). Note: this exclusion does not apply to palliative care patients.
- 3) A previous diagnosis of a manic episode or bipolar disorder.



Early-onset major depressive disorder (continued)

Objectives

Primary objective

Determine a conservative incidence of early-onset major depressive disorder (EOMD) in Canadian children as reported by paediatricians and child and adolescent psychiatrists.

Secondary objectives

- 1) Describe the patterns of presentation and clinical features of children presenting to paediatricians and child psychiatrists with EOMD.
- 2) Examine pathways of referral of EOMD cases.
- 3) Examine duration of symptom onset prior to (a) initial medical presentation and (b) treatment initiation.
- 4) Examine seasonal and geographical differences in patterns of presentation and incidence rates in Canada.
- 5) Describe current treatment planned and/or offered to these children, including regional differences in management.
- 6) Compare Canadian data with non-Canadian epidemiological surveys to increase knowledge of EOMD.

Duration

January 2012 to December 2014

Expected number of cases

A lack of prospective, longitudinal studies of MDD onset in children less than 13 years of age makes estimating the number of expected new cases per year (incidence rate) in Canada challenging. Based on available literature, we estimate there will be approximately 75-100 newly reported cases per year in Canada.

Ethical approval

Research Ethics Board, The Hospital for Sick Children, Toronto

Analysis and publication

Data will be analyzed using descriptive statistics. Time from onset of symptoms to presentation to a physician will be modeled using survival analysis to assess the impact of geographic location, family structure, age and sex of the child, presence of comorbid conditions, ease of access to services, and referral source. If appropriate, a Cox proportional model will be applied to assess the relative impact of these factors on time to diagnosis.

Completed study results will be presented at national and international scientific meetings and submitted for publication in scientific peer-reviewed journals.

PROTOCOLS



References

1. Zisook S, Lesser I, Stewart JW, Wisniewski SR, Balasubramani GK, Fava M, et al. Effect of age at onset on the course of major depressive disorder. *Am J Psychiatry* 2007 Oct;164(10):1539-46.
2. Klein DN, Schatzberg AF, McCullough JP, Dowling F, Goodman D, Howland RH, et al. Age of onset in chronic major depression: relation to demographic and clinical variables, family history, and treatment response. *J Affect Disord* 1999 Oct;55(2-3):149-57.
3. Hammen C, Brennan PA. Severity, chronicity, and timing of maternal depression and risk for adolescent offspring diagnoses in a community sample. *Arch Gen Psychiatry* 2003 Mar;60(3):253-8.
4. Williamson DE, Birmaher B, Axelson DA, Ryan ND, Dahl RE. First episode of depression in children at low and high familial risk for depression. *J Am Acad Child Adolesc Psychiatry* 2004 Mar;43(3):291-7.
5. Korczak DJ, Goldstein BI. Childhood onset major depressive disorder: Course of illness and psychiatric comorbidity in a community sample. *J Pediatr* 2009 Jul;155(1):118-23.
6. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, text revision. Washington, DC: American Psychiatric Association; 2000.