



## Invited review

## Symptoms of depression and anxiety in youth with type 1 diabetes: A systematic review and meta-analysis



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## ABSTRACT

**Introduction:** The interaction between psychosocial factors and type 1 diabetes is complex and screening for psychosocial risk factors from diagnosis of type 1 diabetes has been recommended. This is a systematic review and meta-analysis to address the following questions: (1) How prevalent are symptoms of depression and anxiety in children and adolescents with type 1 diabetes? (2) Is there an association of symptoms of depression and anxiety with diabetes management and glycemic control?

**Material and methods:** We searched EMBASE, MEDLINE, The Cochrane Library, and PsycINFO in April 2014 with an update in May 2015. When possible, data were pooled to estimate summary effects.

**Results:** 14 studies investigated symptoms of depression and anxiety in children and adolescents with type 1 diabetes. The pooled prevalence of depressive symptoms was 30.04%, 95% CI [16.33; 43.74]. There were correlations between symptom levels and glycemic control as well as three-way interactions between HbA1c, blood glucose monitoring frequency or diabetes-specific stress and depression. Symptoms of anxiety were reported for up to 32% of patients. A negative impact on glycemic control was demonstrated.

**Conclusions:** Our analyses confirmed a high prevalence of symptoms of depression and anxiety in youth with type 1 diabetes that potentially compromise diabetes management and glycemic control. In our opinion these findings support recommendations for early screening for psychological comorbidity and regular psychosocial assessment from diagnosis. Future prospective studies are warranted to further explore the interaction of symptoms of depression and anxiety with type 1 diabetes and develop evidence-based treatment models.

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## 1. Introduction

Living with type 1 diabetes interferes with normal childhood activities and can lead to psychological distress (Reynolds and Helgeson, 2011). The estimated prevalence of psychiatric disorders in children and adolescents with type 1 diabetes varies by study design, the screening or diagnostic tool, diagnostic criteria and training of the interviewers. A ten year longitudinal analysis identified depression as the most common psychiatric comorbidity, followed by anxiety and behavior disorders (Kovacs et al., 1997). Main risk factors for depression in youth are female sex, family dysfunction, low socioeconomic status, and stressful experiences, which include being diagnosed with type 1 diabetes (Garrison et al., 1992; Grey et al., 2002; Hood et al., 2006). Individuals with type 1 diabetes and concomitant psychiatric disorders were found to be less able to psychologically adapt to diabetes (Lernmark et al., 1999). This negatively affects glycemic control and adherence to treatment (Ducat et al., 2015). Long-term glycemic control is reflected by the hemoglobin A1c (HbA1c). This refers to “glycated hemoglobin” and identifies the average plasma glucose concentration over 120 days (the average life span of an erythrocyte) (Braun et al., 2016; Diabetes.co.uk, 2016). Non-adherence to treatment includes omitting insulin doses and reduced blood glucose monitoring frequency (BGMF) and has been proposed as the link between psychological symptoms and glycemic control (Herzer and Hood, 2010; Hood et al., 2006). Depression associated with poorly managed diabetes leads to a higher risk of severe hypoglycemia (Rewers et al., 2002), hospitalization due to complications like diabetic ketoacidosis, negative health outcomes (Stewart et al., 2005) and reduced quality of life (QoL) in adolescents (Grey et al., 2002). Furthermore, suicidal ideation is more common in youth with type 1 diabetes than in the general population (Grey et al., 2002). There is a strong association between suicidal thoughts, psychiatric disorders and non-adherence to the treatment regimen (Goldston et al., 1997). Fluctuating blood glucose levels seem to aggravate symptoms in depressive children and can eventually have adverse effects on their neurocognitive development (Johnson et al., 2013).

A biological link between diabetes and depression has been proposed: compensatory metabolic and inflammatory alterations to the autoimmune-mediated destruction of beta-cells are thought to aggravate depression (Kongkaew et al., 2014). Dyslipidemia appears to be a biological correlate of depression in youth with diabetes (Hood et al., 2012).

This knowledge about the complex interaction between psychosocial factors and type 1 diabetes is reflected in international guidelines. Recommendations include screening for psychosocial risk factors and psychological comorbidities from diagnosis of type 1 diabetes and integrated care by a multidisciplinary team that includes a diabetes educator, psychologist, psychiatrist, social worker, dietitian and endocrinologist (American Diabetes Association, 2014; Delamater et al., 2014). Comprehensive background knowledge is needed to improve evidence-based management.

Reynolds and Helgeson (2011) suggested that more recently youth with diabetes are likely to experience less depressive symptoms than comparison groups. The aim of this article is to update the current knowledge base in this area. We systematically searched for high level evidence to address the following questions: (1) How prevalent are symptoms of depression and anxiety in children and adolescents with type 1 diabetes? (2) Is there an association of symptoms of depression and anxiety with diabetes management and glycemic control?

## 2. Material and methods

This report follows the guidelines for Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) where applicable (Moher et al., 2009; Stroup et al., 2000). It was prepared by the research unit “Health Technology Assessment (HTA) and Systematic Reviews”, Institute for Health Care Management and Research, University of Duisburg-Essen, Germany, working regularly in cooperation with German HTA agencies, and a clinical specialist in pediatrics and endocrinology.

### 2.1. Data sources and searches

We searched MEDLINE and EMBASE via Elsevier, PsycINFO via Ovid, and The Cochrane Library in April 2014 and updated our searches in May 2015. A highly sensitive search strategy was used that included both medical subject headings and free-text terms (e.g. “diabetes mellitus”, “child”, “adolescent”, “mood disorders”, “comorbidity”) (see Appendix Table A1 for complete search strategy). This search was initiated to provide an update for the 2009 German clinical guideline “Diagnosis, therapy and control of diabetes mellitus in children and adolescents” (Deutsche Diabetes Gesellschaft 2009; Deutsche Diabetes Gesellschaft, 2015). This evidence-based guideline is part of the AWMF framework (German working group of the scientific medical societies, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften), based on a systematic literature search. The previous guideline included literature until December 2007. Following upon this we run our searches from 2008 until today, limited to publications in German and English. In addition, we searched reference lists of obtained articles.

### 2.2. Study selection

Two reviewers independently screened titles, abstracts, and full-texts and decided about the eligibility of articles. Any disagreements were resolved by discussion. We considered randomized and non-randomized controlled trials, cohort studies, case-control studies and cross-sectional studies reporting on children and adolescents up to 19 years diagnosed with type 1 diabetes as being appropriate for our investigation. Case reports, case series, abstract publications and unpublished studies were excluded. The main

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