



Prevalence of depression among children and adolescents with type 2 diabetes: a systematic review and meta analysis

Lisha Luo, Jieyin Deng, Yejin Li, Yang Qin

Department of General Medicine, Western Theater Command General Hospital, Chengdu, China

Contributions: (I) Conception and design: L Luo; (II) Administrative support: All authors; (III) Provision of study material or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Yang Qin, Department of General Medicine, Western Theater Command General Hospital, Chengdu, China. Email: 1420157286@qq.com.

Background: The prevalence of depression in children and adolescents with type 2 diabetes (T2D) is a clinical, public and social problem. To evaluate the characteristic of depression in children and adolescents, a systematic review and meta-analysis was performed to investigate the association between T2D and prevalence of depression among children and adolescents.

Methods: Retrospective study and prospective study on the prevalence of depression in children with T2D were searched by computer from databases such as PubMed, EMBASE, the Cochrane Library, CNKI, VIP and Wanfang Data. The retrieval time was April 2022. According to inclusion and exclusion criteria, the literature was screened, and data were extracted. Stata 14 software was used, and meta-analysis was performed using double arcsine method to calculate the prevalence and the 95% confidence interval.

Results: A total of 4,039 children or adolescents with T2D were enrolled in the study. After retrieving the literature database, finally, 8 studies were included. Meta analysis showed that the overall prevalence of depression in T2D was 19.9% (95% CI: 14.3–26.2%), and there was significant heterogeneity ($I^2=94.056\%$, $P=0.000$).

Discussion: The results of this study indicate that children with T2D have higher prevalence of depression, which is of clinical significance for screening and prevention of disease.

Keywords: Type 2 diabetes mellitus (T2D mellitus); depression; meta-analysis; systematic review

Received: 01 May 2022; Accepted: 08 August 2022; Published: 30 September 2022.

doi: 10.21037/jxym-22-17

View this article at: <https://dx.doi.org/10.21037/jxym-22-17>

Introduction

The prevalence of depression in children and adolescents with type 2 diabetes (T2D) is a clinical, public and social problem. Research reports that the average annual prevalence rate of depression in children and adolescents with T2D is about 4.8% (1). Compared with T2D in adults, T2D in children and adolescents has significant pathophysiological characteristics, including β the rapid decline of cell function of β cell and the significant increase of insulin resistance (2). Besides, epidemiological report

and clinical studies have found that T2D in children and adolescents was significantly associated with age, weight status, family history of diabetes, diabetic ketoacidosis at presentation, ethnicity and diabetes-associated antibodies (3-6). Walders-Abramson *et al.* found that the failure to maintain a sufficiently normal blood glucose level may be related to the high depression rate of children and adolescents with T2D (7). Besides, Gulley *et al.* believed that failure to maintain adequate blood glucose control may also lead to various adverse effects on patients (such as changes in drug compliance, eating habits and psychological

disorders) (8). These depression of T2D in children and adolescents may lead to stress, sadness, and a reduction in quality of life, adding the burden of families and society. Therefore, focusing on the current prevalence of depression in children and adolescents with T2D, and investigating the relationship between depression and T2D is very important for clinical treatment and attention to T2D children and adolescents and their depression. Collecting the prevalence of depression of children and adolescents with T2D can help clinicians plan for diseases prevention and treatment, as to provide evidence-based medical evidence for future clinical practice. We present the following article in accordance with the PRISMA reporting checklist (available at <https://jxym.amegroups.com/article/view/10.21037/jxym-22-17/rc>).

Methods

Inclusion and exclusion criteria

- ❖ Study type: retrospective study and prospective study.
- ❖ Subjects: children and adolescents with T2D (age ≤ 18 years).
- ❖ Outcome measures prevalence of depression.
- ❖ Exclusion criteria: (I) non-English literature; (II) research with repeated publication or similar data; (III) there are no relevant outcome to be included; (IV) significant statistical error in article or cannot be extracted, and it is still unavailable after contacting the author; (V) the research design has obvious defects, inappropriate statistical methods and other obvious errors.

Literature retrieval strategy

We searched PubMed, EMBASE, the Cochrane Library, CNKI, VIP, Wanfang Data and other databases to collect observational studies and RCTs on the prevalence of depression in children or youth with T2D. The retrieval time limit was from the establishment of the database to April 2022. The computed search is carried out by combining MESH and free words, and adjusted according to the characteristics of each database. At the same time, the references included in the study were searched to supplement and obtain relevant materials. Search terms include: type 2 diabetes, depression, prevalence, epidemiology, randomized controlled trials, etc. Search terms see [Appendix 1](#).

Literature screening and data extraction

Two reviewers screened the literature by independently screening the literature and extracting the data. After excluding the obviously irrelevant literature, we read the abstract and full text again to determine whether the article meets the inclusion and exclusion criteria. We extract the following contents: (I) research title, first author and publication date; (II) baseline data included in the study; (III) outcome measurement data.

Risk assessment of bias included in the study

NOS score (9) was used for retrospective studies and Jadad's score (10) was used for randomized controlled studies.

Statistical analysis

All analyses were performed using Stata version 14.0 software. The original data in the study is first converted by the double arcsine method to make it conform to the normal distribution, and then analyzed in Stata to draw the final conclusion. Statistical heterogeneity between effective measurement studies will be assessed by mantel Haenzel χ^2 test and I^2 statistics. When there is no significant heterogeneity ($I^2 < 50\%$), we use the fixed effect model. In addition, if there is significant heterogeneity ($I^2 \geq 50\%$), the random effect model is adopted (11). Different effect models and sensitivity analysis were selected to explore the source of heterogeneity.

Results

Literature search results

A total of 571 literatures were obtained through the initial search. After initial screening, 8 (12-19) literatures, with a total of 5,948 patients (4,039 cases were included in the analysis) meeting the inclusion and exclusion criteria, were included in this study (*Figure 1*). The basic characteristics of the literature and the evaluation results of literature quality are shown in *Table 1*.

Overall prevalence of depression in children with T2D

All the included studies reported the overall prevalence of depression in patients with T2D. The prevalence was 19.9% (95% CI: 14.3–26.2%), and there was significant heterogeneity among the studies ($I^2=94.056\%$, $P=0.000$)

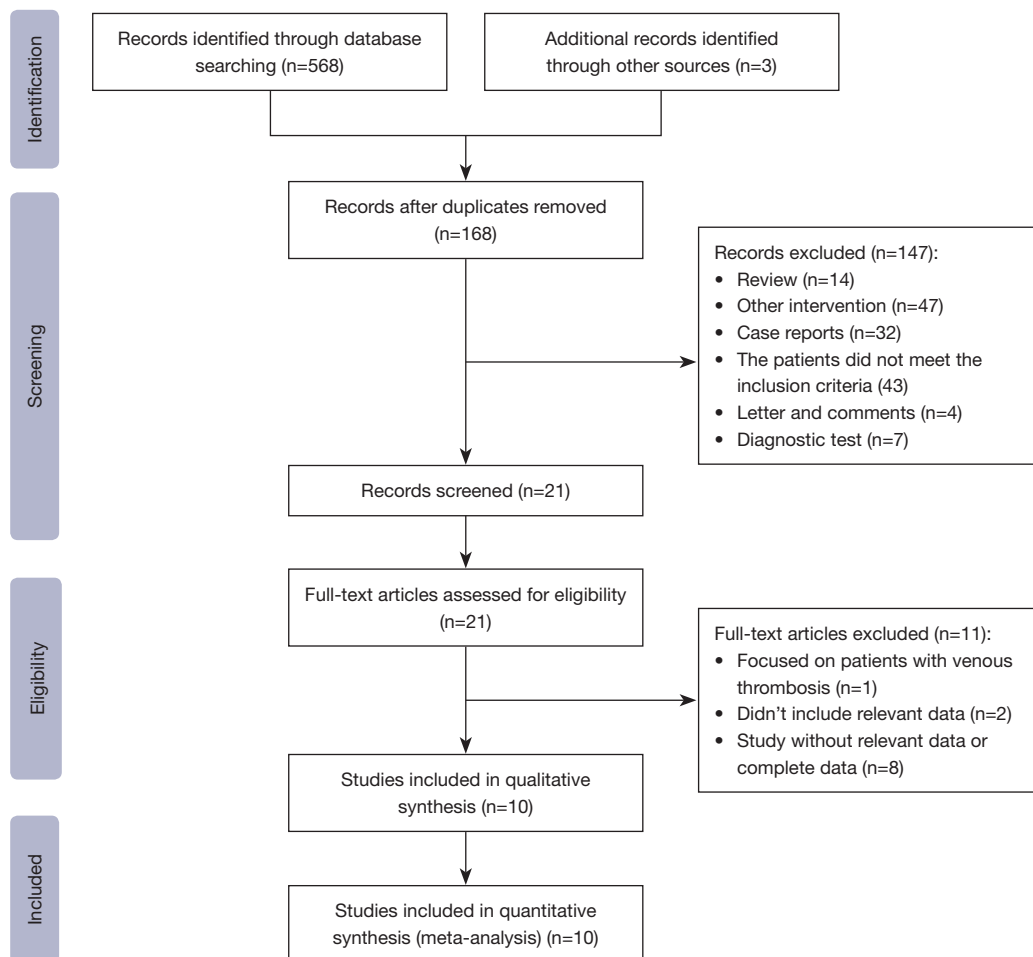


Figure 1 Flowchart of study inclusion.

(Figure 2). In addition, we conducted sensitivity analysis to explore potential sources of heterogeneity, but we did not find sources of heterogeneity.

Discussion

The pathogenesis of depression in T2D patients is complex and has not been fully clarified. The mechanism can be explained by fact that T2D may lead to the functional and structural problems of the peripheral nerves. Blood glucose level is significantly associated with the depression, as Picozzi *et al.* (19) reported that the use of insulin pump can not only control the blood glucose level of T2D children and adolescents, but also reduce the prevalence of depression (19,20). Based on the mentioned studies, we infer that the depression of T2D children and adolescents may be associated with the glucose level. Besides, the

racial differences, obesity and insurance status also have impact on the diabetes distress, depression and glycemic control (20). In addition, the depression of T2D children and adolescents is associated with many other factors such as age, glycosylated hemoglobin, gender, and heredity, suggesting that the depression of T2D children and adolescents is not caused by a single factor and it is associated with social, psychological and their own diseases (10,21), so further investigation is needed to explore the mechanism. Considering the complexity of the disease, the treatment of these patients can not only rely on drugs but need multidisciplinary treatment.

In this study, by collecting and sorting out the relevant studies on the prevalence of depression in T2D children and adolescents, and combining the relevant data, we finally found that the overall prevalence of this part of the population is about 19.9% (95% CI: 14.3–26.2%),

Table 1 Characteristics of studies and patient populations

Study	Year	Country	Design	Cases, n	Measuring tools	Age (years)	Sex ratio	Duration of diabetes	Jadad's score/ NOS score
Anderson <i>et al.</i> (16)	2011	USA	RCT	687 ^a	CDI/BDI-II	14	452/235	0.5	3
Cullum <i>et al.</i> (17)	2016	USA	Retrospective	31	CES-D	15.3	19/12	2.5	6
Lawrence <i>et al.</i> (18)	2006	USA	Retrospective	2,637 ^b	CES-D	15.3	1,376/1,261	NA	7
Picozzi <i>et al.</i> (19)	2019	USA	Retrospective	211 ^c	PHQ-9	15.8	117/94	6.3	7
Silverstein <i>et al.</i> (12)	2015	USA	Retrospective	600	CDI	14	347/253	NA	8
Van Buren <i>et al.</i> (13)	2018	USA	RCT	682	CDI/BDI-II	13.9	447/235	NA	3
Weinstock <i>et al.</i> (14)	2015	USA	RCT	623	CDI/BDI	13.9	395/228	NA	3
Zeitler <i>et al.</i> (15)	2015	USA	RCT	477	CDI/BDI	13.8	304/171	NA	4

a, in this study, only 513 cases received CDI; b, in this study, only 371 cases were diagnosed with type 2 diabetes; c, in this study, only 55 cases were diagnosed with type 2 diabetes. NOS, Newcastle-Ottawa scale; RCT, randomized control trial; CDI, Children's Depression Inventory; BDI-II, Beck Depression Inventory II; CES-D, Center for Epidemiological Studies Depression Scale for Children; PHQ-9, Patient Health Questionnaire-9; NA, not available.

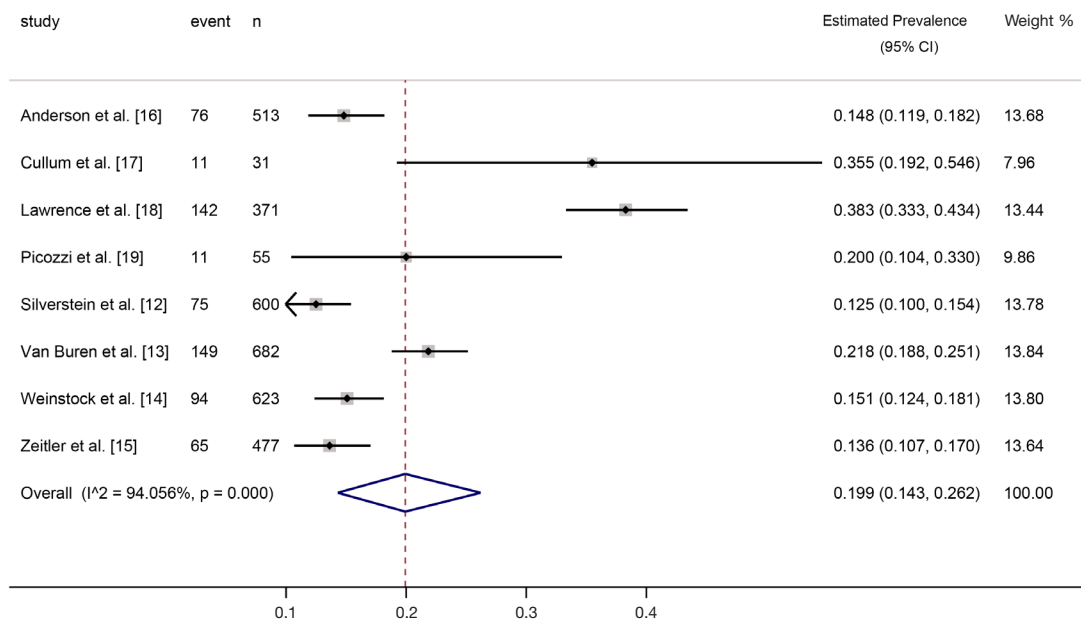


Figure 2 Forest of prevalence of depression in children and adolescents with type 2 diabetes.

indicating that the prevalence of depression in this part of the patients is worthy of attention. It is worth noting that Poulsen *et al.* (22) reported that 84% of T2D patients will be accompanied by depressive symptoms, while 19.9% of the population found in this study have depression, indicating that depressive symptoms and depression in T2D patients are high probability events. Besides, existing study has shown that the prevalence of depression in

T2D patients is associated with peripheral neuropathy and adverse events caused by peripheral neuropathy, such as pain and reduction of daily activities, may be the main factors leading to depression (23). Peripheral neuropathy related to T2D may lead to the irregularity of endocrine system and autoimmune system, which leads to the over stimulation of hypothalamic pituitary adrenal axis and the damage of glucocorticoid receptor, making the body enter

the state of high cortisol and leading to the abnormalities of hippocampus, amygdala and other areas associated with depression, this leads to an increase in the prevalence of depression (24-30). Unlike in children and adolescents, the prevalence of depression is 28% in T2D adults (31), which is higher than our results (19.9%). This difference can be explained by the fact that long-term high glucose level, peripheral neuropathy and high HbA1c is an important factor of depression.

There are still some limitations in this study: (I) only eight literatures with a total of 5,948 respondents (4,039 cases were included in the meta-analysis) were included in this study, and the sample size needs to be confirmed by larger sample studies in the future. (II) The included population is affected by the differences of living place and this series of interference factors cannot be analyzed. (III) The population included in this study are all from the United States, so they cannot fully represent the prevalence of the overall population. (IV) The authors included both RCT and retrospective studies. Based on the above limitations, future scholars need to carefully interpret the author's results.

In conclusion, based on the results of this study, it is suggested that children and adolescents with T2D have a high prevalence of depression, but the prevalence of depression in children and adolescents with T2D is the result of multiple factors. Therefore, future studies need to further verify the related factors of these diseases. We need to focus on prevention and treatment, reduce the burden of patients and improve the quality of life.

Acknowledgments

Funding: This work was supported by Sichuan cadre health care project (No. Sichuan Ganyan 2021-1302).

Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at <https://jxym.amegroups.com/article/view/10.21037/jxym-22-17/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jxym.amegroups.com/article/view/10.21037/jxym-22-17/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. van Sloten TT, Sedaghat S, Carnethon MR, et al. Cerebral microvascular complications of type 2 diabetes: stroke, cognitive dysfunction, and depression. *Lancet Diabetes Endocrinol* 2020;8:325-36.
2. Viner R, White B, Christie D. Type 2 diabetes in adolescents: a severe phenotype posing major clinical challenges and public health burden. *Lancet* 2017;389:2252-60.
3. Copeland KC, Zeitler P, Geffner M, et al. Characteristics of adolescents and youth with recent-onset type 2 diabetes: the TODAY cohort at baseline. *J Clin Endocrinol Metab* 2011;96:159-67.
4. Chernauek SD, Arslanian S, Caprio S, et al. Relationship Between Parental Diabetes and Presentation of Metabolic and Glycemic Function in Youth With Type 2 Diabetes: Baseline Findings From the TODAY Trial. *Diabetes Care* 2016;39:110-7.
5. Eriksson JG, Kajantie E, Lampl M, et al. Trajectories of body mass index amongst children who develop type 2 diabetes as adults. *J Intern Med* 2015;278:219-26.
6. Bhargava SK, Sachdev HS, Fall CH, et al. Relation of serial changes in childhood body-mass index to impaired glucose tolerance in young adulthood. *N Engl J Med* 2004;350:865-75.
7. Walders-Abramson N, Venditti EM, Ievers-Landis CE, et al. Relationships among stressful life events and physiological markers, treatment adherence, and psychosocial functioning among youth with type 2 diabetes. *J Pediatr* 2014;165:504-508.e1.
8. Gulley LD, Shomaker LB. Depression in Youth-Onset Type 2 Diabetes. *Curr Diab Rep* 2020;20:51.

9. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603-5.
10. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996;17:1-12.
11. Yan J, Deng M, Wang Y, et al. Transjugular intrahepatic portosystemic shunt for portal vein cavernous transformation: a systematic review and single-arm meta-analysis. *Dig Dis* 2022. [Epub ahead of print]. doi: 10.1159/000522313.
12. Silverstein J, Cheng P, Ruedy KJ, et al. Depressive Symptoms in Youth With Type 1 or Type 2 Diabetes: Results of the Pediatric Diabetes Consortium Screening Assessment of Depression in Diabetes Study. *Diabetes Care* 2015;38:2341-3.
13. Van Buren DJ, Wilfley DE, Marcus MD, et al. Depressive symptoms and glycemic control in youth with type 2 diabetes participating in the TODAY clinical trial. *Diabetes Res Clin Pract* 2018;135:85-7.
14. Weinstock RS, Trief PM, El Ghormli L, et al. Parental Characteristics Associated With Outcomes in Youth With Type 2 Diabetes: Results From the TODAY Clinical Trial. *Diabetes Care* 2015;38:784-92.
15. Zeitler P, Hirst K, Copeland KC, et al. HbA1c After a Short Period of Monotherapy With Metformin Identifies Durable Glycemic Control Among Adolescents With Type 2 Diabetes. *Diabetes Care* 2015;38:2285-92.
16. Anderson BJ, Edelstein S, Abramson NW, et al. Depressive symptoms and quality of life in adolescents with type 2 diabetes: baseline data from the TODAY study. *Diabetes Care* 2011;34:2205-7.
17. Cullum K, Howland LC, Instone S. Depressive Symptoms and Social Support in Adolescents With Type 2 Diabetes. *J Pediatr Health Care* 2016;30:57-64.
18. Lawrence JM, Standiford DA, Loots B, et al. Prevalence and correlates of depressed mood among youth with diabetes: the SEARCH for Diabetes in Youth study. *Pediatrics* 2006;117:1348-58.
19. Picozzi A, DeLuca F. Depression and glycemic control in adolescent diabetics: evaluating possible association between depression and hemoglobin A1c. *Public Health* 2019;170:32-37.
20. Hong KMC, Glick BA, Kamboj MK, et al. Glycemic control, depression, diabetes distress among adolescents with type 1 diabetes: effects of sex, race, insurance, and obesity. *Acta Diabetol* 2021;58:1627-35.
21. Jaser SS, Patel N, Xu M, et al. Stress and Coping Predicts Adjustment and Glycemic Control in Adolescents with Type 1 Diabetes. *Ann Behav Med* 2017;51:30-8.
22. Poulsen KM, Pachana NA, McDermott BM. Health professionals' detection of depression and anxiety in their patients with diabetes: The influence of patient, illness and psychological factors. *J Health Psychol* 2016;21:1566-75.
23. Jaiswal M, Divers J, Dabelea D, et al. Prevalence of and Risk Factors for Diabetic Peripheral Neuropathy in Youth With Type 1 and Type 2 Diabetes: SEARCH for Diabetes in Youth Study. *Diabetes Care* 2017;40:1226-32.
24. Champaneri S, Wand GS, Malhotra SS, et al. Biological basis of depression in adults with diabetes. *Curr Diab Rep* 2010;10:396-405.
25. Siddiqui S. Depression in type 2 diabetes mellitus--a brief review. *Diabetes Metab Syndr* 2014;8:62-5.
26. Pariante CM, Lightman SL. The HPA axis in major depression: classical theories and new developments. *Trends Neurosci* 2008;31:464-8.
27. Milanesechi Y, Simmons WK, van Rossum EFC, et al. Depression and obesity: evidence of shared biological mechanisms. *Mol Psychiatry* 2019;24:18-33.
28. Wittkamp KA, Naeije L, Schene AH, et al. Diagnostic accuracy of the mood module of the Patient Health Questionnaire: a systematic review. *Gen Hosp Psychiatry* 2007;29:388-95.
29. Carney CE, Ulmer C, Edinger JD, et al. Assessing depression symptoms in those with insomnia: an examination of the beck depression inventory second edition (BDI-II). *J Psychiatr Res* 2009;43:576-82.
30. Jokelainen J, Timonen M, Keinänen-Kiukaanniemi S, et al. Validation of the Zung self-rating depression scale (SDS) in older adults. *Scand J Prim Health Care* 2019;37:353-7.
31. Khaledi M, Haghghatdoost F, Feizi A, et al. The prevalence of comorbid depression in patients with type 2 diabetes: an updated systematic review and meta-analysis on huge number of observational studies. *Acta Diabetol* 2019;56:631-50.

doi: 10.21037/jxym-22-17

Cite this article as: Luo L, Deng J, Li Y, Qin Y. Prevalence of depression among children and adolescents with type 2 diabetes: a systematic review and meta analysis. *J Xiangya Med* 2022;7:22.

Appendix 1

- #1 type 2 diabetes [Mesh Terms]
- #2 diabetes [Title/Abstract]
- #3 #1 OR #2
- #4 depression [Title/Abstract]
- #5 depressive diseases [Title/Abstract]
- #6 #4 OR #5
- #7 randomized controlled trial [Mesh Terms]
- #8 controlled clinical trial [Title/Abstract]
- #9 randomized [Title/Abstract]
- #10 observational studies [Title/Abstract]
- #11 randomly [Title/Abstract]
- #12 trial [Title/Abstract]
- #13 #7 OR #8 OR #9 OR #10 OR #11 OR #12
- #14 humans [Mesh Terms]
- #15 child [Mesh Terms]
- #16 adolescents [Mesh Terms]
- #17 #14 OR #15 OR #16 OR
- #18 #3 AND #6 AND #13 AND #17