

**Self-reported and proxy-reported depressive symptoms in adolescents with
Type 1 Diabetes:**

**The agreement between the reports and the moderation of age in the relation
between the reports and HbA1c**

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Abstract

Aims To examine the agreement between self-reported and proxy-reported depressive symptoms in adolescents with Type 1 Diabetes Mellitus (T1DM), and to examine if adolescents' age moderated the relation between depressive symptoms and HbA1c.

Methods Data were obtained from the longitudinal study of emotional problems in adolescents with T1DM between 12-18 years old and their parents. The intra-class correlation (ICC) examined the agreement between the Children's Depression Inventory-II (CDI-II; cut-off for self-report ≥ 14 , cut-off for proxy-report ≥ 17 ; higher scores indicating more depressive symptoms) by adolescents ($n=115$) and their parents ($n=115$). The moderation of age in both reports is assessed by hierarchical linear regression analyses, including the covariates adolescents' gender, T1DM-duration, and method of insulin delivery in the first step, adolescents' age and depressive symptoms in the second step, and interaction between depressive symptoms and age in the third step.

Results Of the adolescents, 53.0% was male, average age was 15.0 ± 1.8 years. Of the parents, 87.7% were women, average age was 46.0 ± 4.7 years. Clinically significant depressive scores were found in 9.6% of self-reports, and in 17.4% of proxy-reports. The ICC between self-report and proxy-report was moderate ($ICC=.66$). In the final model, no significant moderation of age in the relation between depressive symptoms and HbA1c was found in self-report ($p=.33$) and proxy-report ($p=.91$). Age was not significantly related to HbA1c in self-report ($p=1.00$) and proxy-report ($p=.92$). However, higher depressive symptoms score was significantly related to higher HbA1c in self-report ($\beta=.18$, $p=.036$) and proxy-report ($\beta=.20$, $p=.019$).

Conclusions A moderate agreement between self-reported and proxy-reported depressive symptoms in adolescents with T1DM was found. Age was not a significant moderator in the relation between the reports and HbA1c. Health-care professionals should take both reports into account, and should be aware of the relation between depressive symptoms and HbA1c.

Key words: self-report, proxy-report, depression, T1DM, HbA1c, adolescents

1. Introduction

As of 2014, an estimated 387 million people have diabetes worldwide, of which Type 1 Diabetes Mellitus (T1DM) accounts for between 5% and 10% (1). The overall prevalence of T1DM in The Netherlands during 2009-2011 was 143.6 per 100.000 children (2). Specific incidence in adolescents with T1DM is unknown, but the incidence is rising in the last few years in adolescents with T1DM in The Netherlands (1-3). In people with T1DM, the body's immune system attacks beta-cells of the pancreas. Probably because the immune system mistakenly sees the insulin-producing cells in the pancreas as foreign and destroys or inactivate them (4). Without insulin, it is difficult for the body to transport the glucose into the body cells, most of the glucose stays in the bloodstream (4). Body cells starve due to the lack of glucose (4).

Long term excess of blood glucose or hyperglycemia damage the blood vessels (5). Hyperglycemia results from defects in insulin secretion, insulin action, or both. In that case, the blood glucose level raises above 7 mmol/liter fasting or before a meal and can lead to polyuria, polydipsia, polyphagia and blurred vision (6-8). Chronic hyperglycemia in diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels (8). Besides hyperglycemia, hypoglycemia is a common side-effect of the external supply of insulin in patients with T1DM which occur frequently. Hypoglycemia is the result of the interplay of insulin excess and physiological activities, such as physical activity, vomiting and hormones (9). In case of hypoglycemia, the blood glucose level is below 3.9 mmol/liter and can lead to neurogenic symptoms (palpitations, tremor, hunger and sweating), neuroglycopenic symptoms (behavior changes, difficulty thinking and frank confusion) which can lead to seizure, coma and even death (9, 10). Mild hypoglycemia occurs about once or twice a week (11). Severe hypoglycemia, defined as any episode requiring external help, affects up to 30% of people with T1DM annually (11). If blood glucose values fall below an individual threshold in patients with T1DM, epileptic seizures or hypoglycemic coma may occur (12).

To maintain a blood glucose level between the ranges, consequent self-care is needed (13). Diabetes self-care includes a range of activities, such as self-monitoring of blood glucose, counting carbohydrates, preparing injections and blood glucose meter and deciding if it is possible to eat something based on the blood glucose (14). It can be difficult to control the blood glucose level, hypoglycemia and hyperglycemia may be present unexpectedly (15).

To obtain an overview of the average blood glucose levels over the past eight weeks, glycated hemoglobin (HbA1c) could be measured and gives an impression of successfulness in self-care treatment

in patients (16). HbA1c is an element that is involved in the metabolic control in T1DM (17). One of the important aims in patients with T1DM is to achieve the age appropriate HbA1c-levels (18). The higher the HbA1c, the greater the risk of developing diabetes-related complications (13).

Adolescents with T1DM as a group displays the highest HbA1c compared to other age-groups, in which the risk to develop complications is increased (19-22). For example, earlier literature showed that the HbA1c of pre-schoolers was 7.1%, the HbA1c of school-agers was 7.8% and the HbA1c of adolescents was 8.1% (23). For youth with T1DM, the transition into adolescence often results in poorer adherence to treatment and deteriorating metabolic control (24, 25). These results from earlier studies showed that the transition into adolescence for youth with T1DM is harder compared to healthy peers.

Adolescence is the transitional period between childhood and adulthood that begins at 13 years till 18 years, which starts with puberty and ends when the individual has acquired adult competencies and responsibilities (26). The Dutch Health System anticipates on the acquirement of competencies and responsibilities: from 12 years onwards, both patient and parent receive information about treatment and decide together about the probabilities (27). From 16 years onwards, the patient has the possibility to make decisions about health care by his- or herself, the patient is more autonomous and has more responsibility. Also in diabetes self-care is this transition noticeable. Over time, adolescents increasingly take over self-care activities from their parents (28).

While adolescents develop independence, they experience rapid biological and hormonal changes (26). The period is marked by physical growth and attainment of puberty or sexual maturity. A combination of genes, hormones and environmental factors determine the timing and rate of growth and puberty (29). The physical changes during the adolescence have significant psychological implications (26).

Further explained, the general health of an adolescent depends on both physical well-being and psychosocial well-being (30). Psychosocial well-being is a general construct, with a clear distinction between two different types of psychosocial problems: externalizing and internalizing. Internalizing psychosocial problem behavior encompasses anxiety and depression (31). Depression is a state of low mood and aversion to activity or apathy that affect a person's thoughts, behavior, feelings, and sense of well-being (32). It is important to take internalizing psychosocial well-being into account. Worrying about the complications that could establish due to the increased HbA1c in adolescents, could have an impact on internalizing psychosocial well-being (33). Depression in adolescents with T1DM appears in approximately two- to threefold higher incidence with a medium effect size compared to a healthy control group, even though the diverse results in the literature (34-37). Depressive symptoms are

significantly associated with higher HbA1c (36, 38, 39).

Earlier studies showed that it is important to take the person who completed the questionnaires about internalizing psychosocial well-being into account because the appreciation of internalizing psychosocial well-being depends on who reported the depressive symptoms (40). Adolescents with T1DM reported poorer emotional and mental health, including depression scores, compared to parents' report (34, 40, 41). These results can occur due to the reduction in parental involvement in T1DM-care (18). Besides, adolescents become more independent and extend the activities about self-care in T1DM (42). Contradictory, creating independence is associated with cognitive and psychosocial development in the adolescence what may limit the adolescents' ability to perceive and judge effectively about emotional well-being (43).

Based on abovementioned information, firstly, this study aims to examine what the agreement is between adolescents' self-reported and proxy-reported depressive symptoms in adolescents with T1DM. According to the earlier literature, a poor positive agreement between self- and proxy-reported depressive symptoms in adolescents is hypothesized. Secondly, the study aims to examine if the age of the adolescent is a moderator in the relation between self-reported and proxy-reported depressive symptoms and HbA1c. It is hypothesized that the relation between both reports and HbA1c, significantly are moderated by age due to the earlier mentioned mental and physical growth during the adolescence. Further explained, the hypothesis is based on the fact that adolescents develop more independence over time and self-care activities in T1DM. Parents generally expect that adolescents develop independence in T1DM self-care, what can cause pressure in the adolescents to perform independent (44). This could lead to a strong relation between depressive symptoms and HbA1c in adolescents (42). Besides, when adolescents get older, the involvement of parents in diabetes care decrease. This could also mean that parents are less apprised of the depressive symptoms in the adolescents (42).

Based on earlier research, several covariates will be taken into account. Firstly, duration of T1DM because of the strong effect to HbA1c over the years after the onset of T1DM(45). Secondly, the gender of the adolescent because of the higher HbA1c in girls/women over all age groups compared to boys/men (45, 46). And thirdly, the method of insulin delivery (Multiple daily insulin injections (MDII) or continuous subcutaneous insulin infusion (CSII)) because the HbA1c is lower in people who use CSII (47).

2. Subjects, materials, and methods

2.1 Participants and procedure

2.1.1 Ethical consideration

The present study is part of the baseline data of the Longitudinal study about Emotional problems in Adolescents with Type 1 diabetes and their Parents (Diabetes LEAP study). For three years, data were obtained in a cooperation between Tilburg University and locations of Diabeter, which are research- and treatment centers for T1DM in The Netherlands. The study is approved by the Medical Ethics Committee of Máxima Medisch Centrum. Permission of both parents and the adolescent was required when an adolescent wanted to participate. Parents were only allowed to participate if their adolescent also signed the inform consent to participate.

2.1.2 Study population

Youth between 12 and 18 years old with T1DM were eligible to approach. Before approaching, exclusion criteria were checked which were < 6 months duration of T1DM, mild or severe mental disability, insufficient understanding of spoken and written Dutch language and severe circumstances which obstructed participation.

In total, there were 528 adolescents between 12 and 18 years with T1DM at Diabeter. Based on the criteria, 461 adolescents were eligible to approach. The inform consent was signed by 154 adolescents and 141 parents. However, only 134 parents fulfilled the questionnaires. The total sample size for both adolescents and parents after listwise deletion for missing data and checking the assumptions was $n = 115$. See Figure 1 for the flow diagram in the appendix. Information about the adolescents and parents who did not wish to participate was not available for Diabetes LEAP study. Physicians of Diabeter assessed the reasons for rejection which were often 'no time' or 'tired of participation in research studies'.

2.1.3 Procedure

The approachable adolescents received a letter and an invitation to participate during the appointment with the physician of Diabeter. Adolescents and parents were further informed by the physicians about the aim, scope, and effort of the study. The effort for adolescents was to participate in an interview and to complete questionnaires during, 90 minutes, once a year for three years in a row at Diabeter, and for parents was the effort to complete questionnaires during 30 minutes, once a year for three years in a row at home. Questionnaires for parents were sent and returned by postal mail. For traveling was travel' allowance offered.

After signing the informed consent, an appointment for the interview was made. The structured interviews were conducted by members of the LEAP-research team. Before the interview started, it was stated that information was anonymized and that information should be transferred to the physician in case of clinical cut-off scores. Adolescents were requested to measure the blood glucose level and had the opportunity to optimize it before the interview started and questionnaires were completed. The strive was no hypoglycemia (≤ 3.9 mmol/l, 60 mg/dl) or hyperglycemia (≥ 15.0 mmol/l, 300 mg/dl) (48).

2.2 Measurements

2.2.1 Sociodemographic characteristics

By obtaining the introduction module of the Diagnostic Interview Schedule for Children (DISC-IV), the covariate gender of the adolescents was taken into account. The DISC-IV, which is designed by Schaffer et al. (2000), is a screener for over 30 psychiatric disorders in children between 9 and 17 years (49). Reliability, validity and criteria validity of the COTAN were not available.

The sociodemographic characteristics of the adolescents (educational level, primary caregiver, siblings, and age of the adolescent) were also obtained by the DISC-IV (50, 51). Age was computed by subtracting the completion date from the birthdate of the adolescents.

The social demographic characteristics of the parents (gender, age, ethnical background, financial difficulties, work status, educational level) were obtained by the self-reported general questionnaire.

2.2.2 Clinical characteristics

Clinical covariates which were extracted from medical charts of Diabeter. Covariates were the duration of T1DM (in years), and method of insulin delivery (multiple daily insulin injections (MDII) versus continuous subcutaneous insulin infusion (CSII)) (50, 51).

Information about clinical characteristics, from medical charts, were mean HbA1c (mmol/mol), and the percentage above the recommended cut-off score of HbA1c ($> 7.5\%$) which was based on to the American Diabetes Association guidelines and International Society for Paediatric and Adolescent Diabetes (18, 45, 52). The HbA1c which was the closest measured by the date of the interview and questionnaires, via a fingerstick during the standard control appointment once in three months, was taken into account in this study. Another characteristic was the mean blood glucose level of this sample because an earlier study showed that the performance was poorer during hyperglycemia and the rate of responding was slowed during hypoglycemia (48). Due to few investigation in the literature about this relation, blood glucose level of the adolescent was not taken into account as a covariate. Also,

adolescents' self-reported physical and psychological comorbid conditions via the general questionnaire were included (51).

2.2.3 Depressive symptoms

To examine self-reported and proxy-reported depressive symptoms, the Children's Depression Inventory 2 (CDI-II) was used, which is authored by Dr. Maria Kovacs (53). CDI-II can be used in educational and clinical settings to evaluate depressive symptoms in the last two weeks in children and adolescents between 7 and 17 years (53). Time to administer is five till ten minutes (53). Reliability, validity and criteria validity of the COTAN were not available (54). Based on standardized items was the Cronbach's Alpha in this study for self-report (CDI-II) $r = .82$, for proxy-report (P-CDI-II) $r = .83$. The clinical cut-off score for the self-reported depressive symptoms is ≥ 14 , for the proxy-reported depressive symptoms is ≥ 17 (53).

2.3 Statistical analyses

Data were analyzed by using SPSS version 22 (IBM SPSS statistics, Somers, New York). GPower 3.1 was used to calculate the sample size. Before exploring the social demographic characteristics, clinical self-care and psychological characteristics of the adolescents and parents, missings were listwise deleted to represent the same sample size as in the analyses of this study.

Agreement between variables was examined with the consistency definition of intra-class correlation (ICC). Before examining the agreement between self-reported and proxy-reported depressive symptoms in adolescents with T1DM, assumptions (level of measurement, related pairs, independency of observations, normality, outliers, linearity, and homoscedasticity) were checked (55). Respectively in an earlier study, based on a 95% confidence interval of the ICC, a value of $ICC < 0.50$ was indicated as a poor agreement, ICC between 0.50-0.75 was moderate, ICC between 0.76-0.90 was good, $ICC > 0.90$ was excellent (56).

Two hierarchical linear regression analyses (one for self-report and one for proxy-report) were used to examine the moderation of the age of the adolescent in the relation between depressive symptoms and HbA1c. Before examining, assumptions (number of cases, normality, outliers, linearity, homoscedasticity, and multicollinearity) were checked. Based on violation of assumptions, five participants were not taken into account. In step one, the covariates duration of T1DM, gender of adolescent (whereby females were compared to males) and method of insulin delivery (whereby insulin pump was compared to insulin pen) were taken into account. In step two, the centered variables age of the adolescent and reported depressive symptoms were added. In step three, the interaction between

the centered variables age of the adolescent and reported depressive symptoms through product terms was added.

Listwise deletion for missing data in both ICC and hierarchical linear regression, were not taken into account. Alpha level of 0.05 was considered to be statistically significant.

3. Results

3.1 Sample characteristics

3.1.1 Characteristics of the adolescents

The characteristics of the total sample of adolescents' self-report ($n = 115$), which are displayed in Table 1, shows that 53% was male, the average age was 15.0 years ($SD = 1.8$), and 84.3% of the adolescents had siblings.

The mean duration of T1DM was 7.1 years ($SD = 4.1$). Most adolescents used CSII (78.3%) to deliver insulin instead of MDII. While an $HbA1c \leq 7.5\%$ is desired, the mean $HbA1c$ of this sample was 7.8 ($SD = 1.1$), and 59.1% had an $HbA1c$ above the desirable percentage (18). Before starting the interview, the mean level of blood glucose in adolescents was 11.1 ($SD = 4.6$). The mean blood glucose level before starting answering the questionnaires was 10.1 ($SD = 4.4$).

Most common physical and psychical co-morbid chronic conditions were allergies (12.2%), ADHD/ADD (7.8%) and thyroid disease (7.0%). The mean CDI-II score in this sample was 6.2 ($SD = 4.9$). In 9.6% of the self-reports, a clinical cut-off score for depressive symptoms was found.

3.1.2 Characteristics of the parents

Table 2 shows that mothers mostly fulfilled the questionnaires (87.7%). The average age of the parents was 46.0 years ($SD = 4.7$) and most parents were identified with Dutch as their ethnical background (96.5%). Only 2.6% experienced financial difficulties. Most parents (83.2%) had a paid job, the second biggest work status was being homemaker (24.8%). The educational level was very varied distributed.

The mean proxy-reported CDI-II score in this sample was 10.9 ($SD = 6.1$). In 17.4% of the proxy-reports, a clinical cut-off score for depressive symptoms was found.

3.2 Assumptions

Prior to interpreting the results of the intra-class correlation, the assumptions were checked. The assumption met the level of measurements. Due to the dismissal of missings, the assumption for related pairs was not violated. The observations were independent, so this assumption was also met. The stem-

and-leaf and P-P plots and scatterplots showed that the assumptions normality, outliers, linearity, and homoscedasticity were not violated.

Before examining the hierarchical linear analyses, the assumptions were checked, leaving a total sample of 115 adolescents and 115 parents. In both analyses, the assumptions of the number of cases were met according to the 'rules of thumb' (57). According to the stem-and-leaf, the assumptions for normality and univariate outliers in both analyses were violated, whereby extreme values were deleted. In the coefficients in both reports, values for tolerance (> 0.20) and the variance inflation factor ($VIF < 4$) did not indicate multicollinearity for any of the measures (58). According to the Mahalanobis distance in the residuals statistics in the model of proxy-report, the assumption for multivariate outliers was violated, whereby the participant with a score above the cut-off score of the critical χ^2 -values for the degrees of freedom, was deleted. In the model with self-report, the assumption for multivariate outliers was met. The histogram showed a normal distribution, the normal P-P plot of regression standardized residuals showed no big deviations from normality and the scatterplot showed no big deviations. The plots and histogram indicated that the assumptions of normality, linearity, and homoscedasticity of the residuals were not violated. After deleting five participants, the assumptions before examining the hierarchical linear regression analyses were met.

3.3 Agreement between proxy- and adolescents' self-report about depressive symptoms in adolescents with T1DM

A questionable reliability ($\alpha = .66$) was found between adolescents' self-report and proxy-report. By using the consistency definition, the average measures intra-class correlation (ICC) was .66, which is a moderate agreement, with a 95% confidence interval from .50 to .76 ($F(114, 114) = 2.915, p < .001$).

3.4 Moderation of age in the relation between adolescents' self-reported depressive symptoms and HbA1c

As displayed in Table 3, in the first regression model, which included the duration of T1DM, the gender of the adolescent and method of insulin delivery, was statistically significant ($F(3,111) = 7.448, p < 0.01$). Longer duration of T1DM ($\beta = .32, p < 0.01$) and MDII ($\beta = -.29, p < 0.01$) were significantly related to higher HbA1c. This model accounted for 17% of the variance in HbA1c ($R^2 = .17$).

In the second regression model the centered variables age of the adolescent and self-reported depressive symptoms were added. This resulted in a non-significant improvement of the model ($\Delta R^2 = .03, F\text{-change}(2, 109) = 2.265$). However, a higher depressive symptoms score was significantly related

to higher HbA1c ($\beta = .19, p < 0.05$). Also in the second model, the longer duration of T1DM ($\beta = .31, p < 0.01$) and MDII ($\beta = -.29, p < 0.01$) were still significantly related to HbA1c. This model accounted for 20% of the variance in HbA1c ($R^2 = .20, \text{adjusted } R^2 = .16$).

In step 3 the interaction between the centered variables the age of adolescent * self-reported depressive symptoms was added. This also resulted in a non-significant improvement of the model ($\Delta R^2 = 0.007, F\text{-change } (1, 108) = .972$). Age was not significant related to HbA1c ($p = 1.00$). However, a higher depressive symptoms score was significantly related to higher HbA1c ($p = .036$). Furthermore, longer duration of T1DM ($\beta = .31, p < 0.01$) and MDII-therapy ($\beta = -.29, p < 0.01$) were still significantly related to HbA1c. The model accounted for 21% of the variance in HbA1c ($R^2 = .21, \text{adjusted } R^2 = .16$).

3.5 Moderation of age in the relation between proxy-reported depressive symptoms and HbA1c

As displayed in Table 4, in the first regression model, which included duration of T1DM, gender of the adolescent and method of insulin delivery, was statistically significant ($F (3, 111) = 7.448, p < 0.01$). Longer duration of T1DM ($\beta = .32, p < 0.01$) and MDII ($\beta = -.29, p < 0.01$) were significantly related to higher HbA1c. This model accounted for 17% of the variance in HbA1c ($R^2 = .17, \text{adjusted } R^2 = .15$).

In the second regression model, the centered variables age of the adolescent and proxy-reported depressive symptoms were added. This resulted in a non-significant improvement of the model ($\Delta R^2 = .209, F\text{-change } (2, 109) = 2.823$). A higher depressive symptoms score was significantly related to higher HbA1c ($\beta = .20, p < 0.05$). Also in the second model, the longer the duration of T1DM ($\beta = .31, p < .01$) and MDII-therapy ($\beta = -.28, p < .01$) were significantly related to HbA1c. This model accounted for 21% of the variance in HbA1c ($R^2 = .21, \text{adjusted } R^2 = .17$).

In step 3, the interaction between the centered variables the age of adolescent * proxy-reported depressive symptoms was added. This also resulted in a non-significant improvement of the model ($\Delta R^2 = 0.000, F\text{-change } (1, 108) = .013$). Age was not significant related to HbA1c. However, a higher proxy-reported depressive symptoms score was significantly related to higher HbA1c ($\beta = .20, p < .05$). Furthermore, longer duration of T1DM ($\beta = .30, p < 0.01$) and MDII-therapy ($\beta = -.28, p < 0.01$) were still significantly related to HbA1c. The model accounted for 21% of the variance in HbA1c ($R^2 = .21, \text{adjusted } R^2 = .17$).

4. Discussion

The first aim of the study was to examine the agreement between self-reported and proxy-reported depressive symptoms in adolescents with T1DM. Secondly, the study aimed to examine if the age of the adolescent moderated the relation between adolescents' self-report and proxy-report and HbA1c.

4.1 The agreement between self-report and proxy-report

In this study, the agreement, measured with intra-class correlation, was moderate between adolescents' self-report and proxy-report. This result is not in accordance with the hypothesized poor significant agreement, which was based on results of earlier studies that investigated the agreement between self-report and proxy-report in adolescents with other chronic diseases (41, 59).

In the literature, a few studies investigated the agreement between proxy- and self-reported depressive symptoms in adolescents with T1DM. An earlier study showed a high correlation between parent and youth reports ($r=.61$) (60). With a critical view to the guidelines, it should be a moderate correlation (61). Nonetheless, the agreement in that study is comparable to the agreement of this study and both agreements were higher than expected. Another study, in which the characteristics of that sample were mostly concordant to the sample of this study (distribution of gender, mean age), was also surprised by the results that showed a higher agreement than expected (34).

Both previous studies had an explanation for this discrepancy, namely the 'depression-distortion hypothesis' that suggests that the proxy-reported depressive symptoms are influenced by the level of depressive symptoms in the parents themselves (34, 50). In contrast, the agreement between proxy-reported and self-reported depressive symptoms was higher when parents self-reported less depressive symptoms (50). In the current study, the self-reported depressive symptoms of the parents were not taken into account. However, it could explain the agreement between self-report and proxy-report in the current study. Another reason for the incongruence between the hypothesis and the results could be the level of effective involvement in diabetes management, in which a high level of effectiveness was presented in consistent proxy-reported and self-reported depressive symptoms (60). The effectiveness of involvement in diabetes management was not taken into account but could also be an explanation for the agreement between proxy- and self-report in the current study.

4.2 The moderation of age between depressive symptoms and HbA1c

A significant moderation of age between self- and proxy-reported depressive symptoms and HbA1c was expected but not found. Furthermore, age was not significantly related to HbA1c. As earlier is stated, the transition into adulthood acquires competencies and responsibilities, leads to autonomous and responsibility for own decisions (26). This suggests that probably other, more specific, moderating variables instead of age, should be taken into account in the relation between self- and proxy-reported depressive symptoms and HbA1c.

For example, earlier research in adults with type 1 or type 2 diabetes, showed that distress about diabetes self-care as a mediator explained a lot of variance in the relation between depressive

symptoms and HbA1c (62). That article used a sample with adults instead of adolescents but could still be relevant in the current sample because of the increased number of self-care activities in diabetes during the adolescence, what could cause more distress about diabetes self-care (62). Another study found that coping was a better predictor for metabolic control and a decrease in HbA1c, compared to general emotional adaptation what is related to depression (63, 64). Coping could also be a moderating variable that should be taken into account in the relation between depressive symptoms and HbA1c (65). A third moderator could be gender because of an earlier study that found that the girls between 10 and 15 years had more depressive symptoms which predicted poorer adherence in T1DM. Boys were less likely to reveal both depression and poor adherence across age (66).

4.3 The relation between depressive symptoms and HbA1c

Regarding the significant relation between depressive symptoms and HbA1c, the results of the current study were according to earlier meta-analyses (36, 38, 39). The current study was the first study in which distinguish between self-reported depressive symptoms and proxy-reported depressive symptoms in the relation with HbA1c was made.

The current study found in 9.6% of the adolescents' self-reports and in 17.4% of the proxy-reports a cut-off score for clinical depressive symptoms. Without the relation to HbA1c, a previous study distinguished between self-reported and proxy-reported depressive symptoms in adolescents with T1DM. That study found that the adolescents experienced a better emotional well-being according to self-report, compared to the proxy-reported emotional well-being (67). Regarding depressive symptoms, the result of that study is comparable to the current study. Another study found that, in a population of youth between 14 and 18 years with T1DM, parents proxy-reported significant depression and internalizing problems, while the self-reports of the adolescents were not significant in these two domains (68).

Notable are the low percentages that were found in this study compared to the percentages that were mentioned in the introduction, in which the percentage could reach till 33% depressive symptoms in adolescents compared to 10% in the healthy control group (69). However, recent studies which investigated reported depressive symptoms, found a percentage of cut-off scores for clinical depressive symptoms comparable to the results of this study (34, 50). Despite the unexpected lower percentages, a significant relation between the reported depressive symptoms and HbA1c is found in both reports.

4.4 Covariates

Regarding the including covariates in this study (duration of T1DM (45), gender of the adolescent (45, 46), method of insulin delivery(47)), the results showed that a longer diabetes duration and MDII-therapy were related to higher HbA1c.

4.5 Limitations of the present study

There are some general limitations that need to be taken into account to interpret the findings of this study. Firstly, the center of inclusion could give a biased view of the (inter)national T1DM-regulation in adolescents. Diabeter found that approximately 55% of their patients had an HbA1c < 7.5 %, which makes Diabeter the best performing clinic in the Netherlands (70). This recommended HbA1c is found in 18% of the patients with T1DM in the USA, and in 11 till 15% in the UK (70). It is possible that the sample of this study is not representative in comparison with other samples of Dutch and international adolescents with T1DM. Reasons for this supposition are based on the mean HbA1c of 7.8 in this sample, which is much lower than the general HbA1c in earlier research that showed that less than 15% of the young patients reached HbA1c levels below 8% from pre-puberty to young adulthood (71-73).

Secondly, in this study, the frequency of blood glucose measuring (BGM) was not taken into account while that is important because of the probable moderating effect in the relation between the proxy- and self-report and HbA1c (74). Earlier studies showed that a higher frequency of blood glucose monitoring could lead to a significant decreased HbA1c (74). Also, the literature showed that less frequent BGM was associated with higher levels of depressive symptoms (60).

Thirdly, the CDI-II is a questionnaire in which the items are concerned about the occurrence of depressive symptoms in the last two weeks (53). HbA1c is a measurement over eight weeks because of the life span of red blood cells (17). Both measurements are indicators over different periods, what raises the concern about the possibility to use them together in assessing the research aims of this study. Until now, the literature never investigated the influence of these time span differences.

Fourthly, as shown in Figure 1, 307 adolescents were not interested in participating in the LEAP study. Information about the adolescents who rejected participation was not available. It could be possible, but could not be proven that those adolescents would have reported more depressive symptoms or had a higher HbA1c compared to this sample – it is all conjecture.

Fifthly, this study is a cross-sectional study in which only correlations are examined what ascertains that causal relations cannot be inferred.

4.6 Strengths of the present study

One of the strengths of the study is the distribution of adolescents in the sample. For example, men and women (53% versus 47%) were rather well equally distributed. Also, the age of adolescents was well distributed in this sample. The mean age of the adolescents (15 years) was the middle of the range, because the allowed range was 12 until 18 years.

Diabeter is an institute with treatment centers in different places in The Netherlands (data were obtained from Veldhoven, Schiphol, Deventer, and Rotterdam) (70), what makes that the population of the sample in this study is generalizable to Dutch adolescents with T1DM. Herewith, it should be taken into account that the mean HbA1c of Diabeter was lower than other treatment centers in The Netherlands what reduces the generalizability.

As mentioned in the method section, the HbA1c was obtained via medical charts in the electronic patient files of Diabeter while earlier studies often used self-reported HbA1c-levels, which could deviate from the accurate HbA1c due to e.g. social desirability (75).

It attracted attention how scarcely the blood glucose levels of the participants were taken into account in recent studies. The mean blood glucose levels before the interviews and questionnaires, were classified as euglycemia, what helped to maintain the reliability of the results because the cognitive functioning in euglycemia is more stable in comparison with hyperglycemia or hypoglycemia (48).

4.7 Recommendations for future research

Future research is needed to specify the moderate agreement between self-reported and proxy-reported depressive symptoms. This should be done by examining which report (proxy-report or self-report) is more appropriate and a rendition of the real depressive symptoms in adolescents with T1DM (e.g. qualitative study, an interview between the psychiatrist and adolescents, observational study in different environments, causality studies). The given limitations of this study should be taken into account in future research. In this manner, deliberate considerations about health care for depressive symptoms in adolescents with T1DM can be made, during the development of being more independent from parents and having more responsibilities.

The results of the present study did not provide evidence for age as moderator in the relation between depressive symptoms and HbA1c. Future research should investigate the probable moderators in the relation between depressive symptoms and HbA1c in which the earlier limitations and recommendations should be taken into account.

A higher depressive symptoms score was significantly related to a higher HbA1c. Future research should investigate what factors influence the decrease in depressive symptoms in adolescents with T1DM, because of the significant positive relation with HbA1c.

4.8 Clinical implications

As mentioned in the introduction, from 12 years on, Dutch adolescents decide together with their parents about their care instead of full decision-making by the parents (27). The moderate agreement between parent and adolescents could carefully confirm that it is important to take both opinions (of the adolescent and the parent) about depressive symptoms in adolescents with T1DM into account. In spite of the moderate agreement, this suggestion is supported by the significant relation between depressive symptoms and HbA1c in both reports.

For health professionals, it is important to be alert of the influence of depressive symptoms in the treatment by T1DM because of a higher depressive symptoms score was significantly related to a higher HbA1c. Otherwise, for psychologists, it is important to take the level of HbA1c into account because a higher HbA1c is related to a higher depressive symptoms score. An integral approach in a multidisciplinary team in the treatment of adolescents with T1DM is recommended.

4.9 Conclusion

This study investigated the agreement between self- and proxy-reported depressive symptoms in adolescents with T1DM. A moderate agreement was found, which was higher than the hypothesized poor agreement based on other chronic diseases.

Besides, this study investigated the moderation of adolescents' age in the relation between depressive symptoms and HbA1c. A significant moderation of age was expected in the relation between self- and proxy-reported depressive symptoms and HbA1c. This hypothesis was based on the transition in responsibility for self-care activities between parents and adolescents during the adolescence. The moderation of age was not found in the relation between self-reported and proxy-reported depressive symptoms and HbA1c in adolescents with T1DM. Age was not significantly related to HbA1c. However, in both reports, a higher depressive symptoms score was significantly related to a higher HbA1c.

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Table 1.

Social Demographic Characteristics, Clinical Self-care and Psychological Characteristics of the Adolescents

	<i>All (n=115)</i>	<i>N Missing</i>
<i>Demographic characteristics</i>		
Gender (% male)	53.0	
Age, years	15.0 (\pm 1.8)	
Educational level, %		1
Primary school	10.5	
Secondary school	77.2	
After secondary school	12.4	
Primary caregiver, % ((biological) mother)	83.5	
Siblings, %	84.3	
<i>Clinical characteristics</i>		
Diabetes duration, years	7.1 (\pm 4.1)	
Method of insulin delivery		
Insulin injections, %	21.7	
Insulin pump, %	78.3	
HbA1c \geq 7.5% or \geq 58 mmol/mol	59.1	
Mean HbA1c, %	7.8 (\pm 1.1)	
Mean Blood glucose level at the start of interview	11.1 (\pm 4.6)	
Mean Blood glucose level at the start of questionnaires	10.1 (\pm 4.4)	
Co-morbid chronic conditions, %		
Chronic heart failure/heart disease	1.7	
Thyroid disease	7.0	
Asthma	4.3	
Eczema	2.6	
Coeliac disease	2.6	
Allergies	12.2	
Autism	2.6	
ADHD/ADD	7.8	
Others	10.5	1
<i>Psychological characteristics</i>		
Self-reported CDI-II score	6.2 (\pm 4.9)	
Self-reported clinically depressive score ^a , %	9.6	
<i>Note. Values are mean \pm SD or valid percentage (%) (n/N); ^acut-off score of CDI-2 \geq 14</i>		

Table 2.

Social Demographic Characteristics and Proxy-reported Psychological Characteristics of the Parents

	<i>All (n= 115)</i>	<i>N missing</i>
<i>Demographic characteristics</i>		
Male sex (% male)	12.3	1
Age, years	46.0 (\pm 4.7)	
Dutch ethnical background, %	96.5	1
Financial difficulties, %	2.6	1
Work status, %		2
Paid job	83.2	
No job	4.4	
Unfit to work	5.3	
Homemaker	24.8	
Volunteer	9.7	
Student	2.7	
Educational level, %		2
Lower or vocational education	6.2	
General secondary education	6.2	
Secondary vocational education	28.3	
Higher general and pre-university education	16.8	
Higher professional education	23.9	
University	15.9	
Others	2.7	
<i>Psychological characteristics</i>		
Proxy-reported CDI-II score	10.9 (\pm 6.1)	
Proxy-reported clinically depressive score ^a , %	17.4	
<i>Note: Values are mean \pm SD or valid percentage (%) (n/N); ^acut-off score of CDI-2 \geq 17 (41)</i>		

SELF- AND PROXY-REPORTED DEPRESSIVE SYMPTOMS IN ADOLESCENTS WITH T1DM

Table 3.

Hierarchical Multiple Regression Analyses Examining the Relation Between Age of Adolescent, Self-reported Depressive Symptoms and Moderation of Age and Depressive Symptoms, and HbA1c

Variable	Model 1			Model 2			Model 3		
	<i>B</i>	<i>SE B</i>	β	<i>B</i>	<i>SE B</i>	β	<i>B</i>	<i>SE B</i>	β
Duration of T1DM	.08	.02	.32**	.08	.02	.31**	.08	.02	.31**
Gender of adolescent ^a	.03	.19	.01	-.09	.20	-.04	-.09	.20	-.04
Method of insulin delivery ^b	-.78	.23	-.29**	-.75	.23	-.29**	-.77	.23	-.29**
Age of adolescent				.00	.06	.00	.02	.06	.03
Depressive symptoms self-report				.04	.02	.19*	.04	.02	.18*
Depressive symptoms self-report * age							.02	.02	.09
R^2		.17			.20			.21	
ΔR^2		.17			.03			.01	
ΔF		7.448**			2.265			.972	

Note. *N* = 115. ^a0 = male, 1 = female; ^b0 = MDII, 1 = CSII

* $p < 0.05$, ** $p < 0.01$.

SELF- AND PROXY-REPORTED DEPRESSIVE SYMPTOMS IN ADOLESCENTS WITH T1DM

Table 4.

Hierarchical Multiple Regression Analyses Examining the Relation Between Age of Adolescent, Proxy-reported Depressive Symptoms and Moderation of Age and Depressive Symptoms, and HbA1c

Variable	Model 1			Model 2			Model 3		
	<i>B</i>	<i>SE B</i>	β	<i>B</i>	<i>SE B</i>	β	<i>B</i>	<i>SE B</i>	β
Duration of T1DM	.08	.02	.32**	.08	.02	.31**	.08	.02	.30**
Gender of adolescent ^a	.03	.19	.01	.04	.19	.02	.04	.19	.02
Method of insulin delivery ^b	-.78	.23	-.29**	-.74	.23	-.28**	-.74	.23	-.28**
Age of adolescent				.01	.06	.01		.06	.01
Depressive symptoms proxy-report				.04	.02	.20*		.02	.20*
Depressive symptoms proxy-report * age								.01	.01
R^2		.17			.21			.21	
ΔR^2		.17			.04			.00	
ΔF		7.448**			2.823			.013	

Note. *N* = 115. ^a0 = male, 1 = female; ^b0 = MDII, 1 = CSII

* $p < 0.05$, ** $p < 0.01$.

Figure 1.

Flow Diagram of Inclusion and Exclusion Process

