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Depression and anxiety in adolescents with type 1 diabetes and their parents

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BACKGROUND: Longitudinal studies including parental distress when examining adverse health outcomes in adolescents with type 1 diabetes are lacking. This study examined whether parental depression and anxiety predict adolescent emotional distress and glycated hemoglobin A_{1c} (HbA_{1c}) 1 year later and whether a relation between parental distress and HbA_{1c} is mediated by the level of parental involvement in diabetes care and by treatment behaviors.

METHODS: Longitudinal path modeling was applied to data from 154 adolescents and parents from diabetes centers participating in the Longitudinal study of Emotional problems in Adolescents with type 1 diabetes and their Parents/caregivers (Diabetes LEAP). At baseline and 1-year follow-up, participants completed measures of depression and anxiety. HbA_{1c} was extracted from medical charts. Responsibility and treatment behavior questionnaires were completed by adolescents at baseline.

RESULTS: Baseline parental depressive and anxiety symptoms were not associated with 1-year adolescent depressive symptoms, anxiety symptoms, and HbA_{1c}. Responsibility division and treatment behaviors did not mediate associations between parental emotional distress and 1-year HbA_{1c}.

CONCLUSIONS: Parental depressive and anxiety symptoms did not predict adolescent health outcomes 1 year later. Future studies may determine whether the link is present in case of mood/anxiety disorders or severe diabetes-specific distress, or whether adolescents are resilient in the face of parental distress.

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IMPACT:

- Adolescents with T1D are a vulnerable group in terms of psychological and health outcomes. Whether parental emotional distress (i.e., depressive and anxiety symptoms) is prospectively associated with adolescent emotional distress and/or HbA_{1c} has been understudied.
- Our results show that parental distress was not related to adolescent distress or HbA_{1c} 1 year later.
- Responsibility division and treatment behaviors did not mediate associations between parental emotional distress and 1-year HbA_{1c}.
- Future studies could determine whether these links are present in case of mood/anxiety disorders or severe diabetes-specific distress, or whether adolescents are resilient in the face of parental distress.

INTRODUCTION

Depression and anxiety are common during adolescence, with 20% of 12–16-year olds reporting emotional problems on self-report questionnaires.[1] For youth with type 1 diabetes mellitus the situation is even direr. Type 1 diabetes is a chronic condition requiring intensive daily self-care activities (such as, but not limited to, regular monitoring of blood glucose levels and administration of exogenous insulin).[2] A recent meta-analysis found a pooled prevalence of 30% for depression and 32% for anxiety among youth with type 1 diabetes, based on self-reported symptom severity.[3] Furthermore, emotional distress (a collective term used in clinical practice for depressive and anxiety symptoms) has been associated with suboptimal glycemic outcomes, such as glycated hemoglobin A_{1c}[3] (HbA_{1c}, which represents the mean blood glucose level over ~3 months).[4] This relationship may be explained by less optimal self-care behaviors.[5,6] With merely one-in-five adolescents with type 1 diabetes having HbA_{1c} values within target range,[7] more insight into factors contributing to their vulnerability is needed.

Emotional problems are also frequent among parents of adolescents with this chronic condition.[8,9] In the DAWN Youth Study, 4099 parents of youth with diabetes from eight nations were interviewed; suboptimal emotional well-being was reported

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by almost half of the parents.[10] Elevated parental anxiety symptoms seem to be particularly common, as they have been reported by 43–55%[11,12] of mothers and 23% of fathers.[11] Depressive symptoms were endorsed by 17–26% of mothers[11–13] and 19% of fathers.[11]

Research in the general population suggests that children of depressed parents are at 2–3-fold increased risk for the development of depression and anxiety themselves.[14,15] Despite the high prevalence of emotional distress in parents of youth with type 1 diabetes, possible prospective associations between parental and adolescent emotional problems are poorly studied in the context of type 1 diabetes mellitus. The few existing longitudinal studies show mixed results. One prospective cohort study suggested that children of mothers who were clinically distressed developed a psychiatric disorder at a doubled rate compared with children whose mothers were not clinically distressed.[16] More specifically, children of depressed mothers developed depressive disorders at a 2.63 higher rate than children whose mothers did not have depression.[16] However, another prospective study found that maternal and adolescent depressive symptoms were uncorrelated in both cross-sectional and longitudinal analyses.[17]

With respect to the relation between parental emotional problems and diabetes outcomes, maternal depression has been directly[18] and indirectly[19,20] linked to HbA_{1c}. However, these studies are limited by their cross-sectional design; hence, longitudinal research is needed for further insight into the nature of these associations.

Potential mediating mechanisms linking parental depression/anxiety and HbA_{1c} are also under-researched. Some studies suggest that the affected quantity and/or quality of parental involvement could be the explaining mechanism.[19–22] Furthermore, maternal involvement was associated with a better following of treatment recommendations when mothers had fewer depressive symptoms.[17]

To address the existing gaps in the literature, the present prospective observational study examines: (a) 1-year longitudinal associations between parental emotional distress (i.e., depressive and anxiety symptoms) and adolescent emotional distress (i.e., depressive and anxiety symptoms), (b) 1-year longitudinal associations between parental emotional distress and HbA_{1c}, and (c) whether such an association between parental emotional distress and HbA_{1c} is mediated by the division of diabetes management tasks and by the extent to which treatment recommendations are followed (treatment behaviors). We hypothesize that:

(1) Higher parental emotional distress at baseline is associated with higher symptoms of anxiety and depression in adolescents 1 year later.
(2) Higher parental emotional distress at baseline is associated with higher HbA_{1c} 1 year later.
(3) The longitudinal association between emotional distress and HbA_{1c} is mediated by both the division of diabetes management responsibilities and the level of following treatment recommendations.

Explorative analyses will assess whether the mediation can best be considered as (1) one sequential mediation pathway running to the division of diabetes management responsibilities and to the extent to which treatment recommendations are followed and (2) two simultaneous mediation pathways, one including the responsibility division and one including following of treatment recommendations. Figure 1 depicts the hypothesized model (a) without mediation, (b) with one, interconnected mediation pathway, and (c) with two separate mediation pathways.

METHODS

Study design and participants

For the purpose of this study, data were used from the baseline and 1-year follow-up waves in the first four Dutch pediatric diabetes clinics (Diabeter) included in the ongoing Longitudinal study of Emotional problems in Adolescents with type 1 diabetes and their Parents/caregivers (Diabetes LEAP). Families of adolescents (aged 12–18) with type 1 diabetes mellitus were eligible for participation unless the adolescent had (a) diabetes duration of <6 months (considered the first adjustment period following diagnosis), (b) an intellectual disability, (c) insufficient mastery of the Dutch language, or (d) other severe circumstances interfering with the ability to complete the assessment (as judged by their pediatrician). Eligible families ($n = 461$) were sent an invitation letter and study information. Written informed consent from adolescents and parents/caregivers were obtained at clinic visits. The primary caregiver, defined as the parent/caregiver most involved in diabetes management, was invited for the assessment. The baseline assessments were conducted in 2015–2016. After 1 year, participants were invited to take part in the second wave, which was concluded in 2017. For the present analyses, if the participating parent in the second wave was not the same parent as in the baseline assessment, the second wave was considered missing for the parent. The study protocol was approved by the Medical Research Ethics Committee of Máxima Medical Centre in Veldhoven (NL48232.015.14).

MEASURES

Demographic and clinical variables

Adolescent sex, date of birth, HbA_{1c} closest to both the baseline assessment and the 1-year follow-up interview date, date of diabetes diagnosis, and insulin treatment modality (multiple daily injections or continuous subcutaneous insulin infusion) were extracted from electronic medical charts. Age was determined by counting the number of years between the date of birth and the date of the baseline assessment; fractional parts were retained. Duration of diabetes was calculated by counting the years between the date of diagnosis and the date of the baseline assessment. HbA_{1c} <7.5% (58 mmol/mol) was considered indicative of optimal glycemic outcome, as advised by the International Society for Pediatric and Adolescent Diabetes at the time of the assessments.[23] In a separate, study-specific questionnaire, parents self-reported age and sex, and whether they were currently diagnosed with a mood and/or anxiety disorder by a physician, psychiatrist, or psychologist.

Depressive symptoms

Adolescents also completed the Children's Depression Inventory-2[24] at both time points. For each of the 28 items of this self-report questionnaire, participants choose the one statement out of three that best reflects their feelings in the past 2 weeks. After recoding the reversed items, a total score was computed (range 0–56) with higher scoring indicating more (severe) depressive symptoms. When three or less item scores were missing, they were imputed with the participant's mean score on the remaining items (person mean imputation).[23,24] If more than three item scores were missing, the participant's total score was considered missing. Scores ≥14 were indicative of elevated depressive symptoms. The estimated Cronbach's alpha was 0.83 at baseline and 0.79 at follow-up.

Parents were asked to complete the Patient Health Questionnaire-9 item scale (PHQ-9) at both time points, assessing the presence of nine symptoms of major depressive disorder in the past 2 weeks.[25] A sum score was computed (range 0–27) with higher scores indicating more depressive symptoms. A maximum of 20% missing items was allowed, in which cases person mean

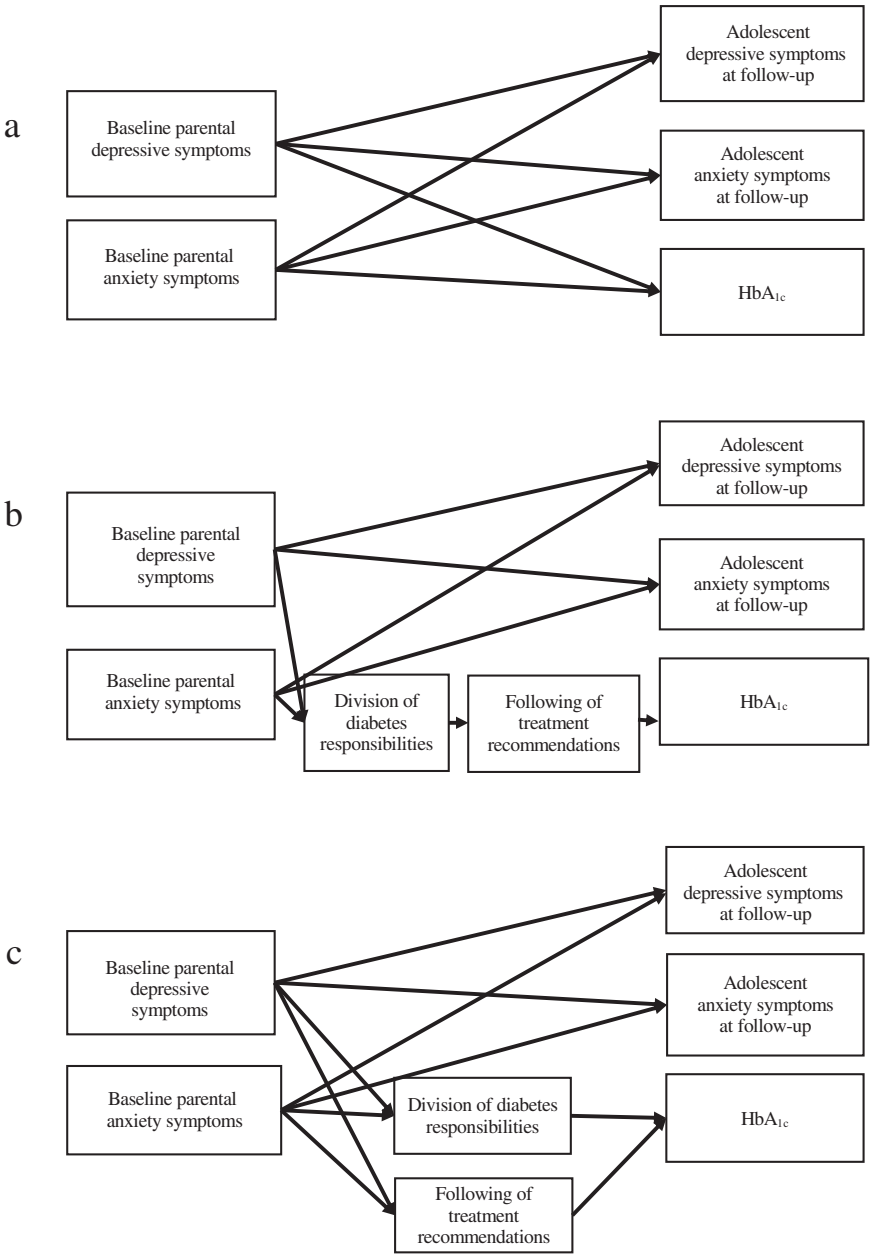

Fig. 1 Theoretical models of longitudinal associations between parental distress and adolescent health outcomes. a Hypothesized model in which parental emotional distress is longitudinally associated with adolescent health outcomes. **b** Hypothesized sequential model in which the association between parental distress and HbA_{1c} is mediated by the division of diabetes responsibilities and the extent to which treatment recommendations are followed. **c** Alternative model in which the association between parental distress and HbA_{1c} is mediated separately by the division of diabetes responsibilities and the extent to which treatment recommendations are followed. Note: for readability, covariates, correlations of exogenous variables, and correlations of error terms are not displayed in the theoretical models.

imputation was applied. If >20% was missing, the participant's total PHQ-9 score was considered missing. Scores ≥10 were considered indicative of elevated depressive symptoms. The estimated Cronbach's alpha was 0.80 at baseline and 0.83 at follow-up.

Anxiety symptoms

At both time points, adolescents and parents completed the Generalized Anxiety Disorder-7 item scale (GAD-7).[26] The GAD-7 assesses how often participants experienced anxiety symptoms over the past 2 weeks. For each participant, a total score (range 0–21) was computed by summing the seven item scores, with higher scores indicating more (severe) anxiety symptoms. Person mean imputation was used in cases of ≤20% missing item scores.[27] If more than one item score was missing, the participant's total GAD-7 score was considered missing. The GAD-7 was originally developed for adult populations,[26] but has recently been validated for use in adolescents.[28] Scores ≥10 were considered indicative of elevated anxiety symptoms.[26] Internal consistency at baseline was good: $\alpha = 0.71$ for adolescents and $\alpha = 0.86$ for parents. At follow-up, the estimated Cronbach's alpha's were 0.80 for adolescents and 0.85 for parents.

Division of diabetes management responsibilities

To assess how diabetes management responsibilities were shared or divided between parents and adolescents, the Diabetes Family

Responsibility Questionnaire (DFRQ)[29] was completed by adolescents at baseline. The DFRQ contains 17 items describing diabetes management tasks, each to be rated as 1 (parent[s] take or initiate responsibility for this almost all of the time), 2 (parent[s] and child share the responsibility for this about equally), or 3 (child takes or initiates responsibility for this almost all of the time). A total sum score was computed, ranging from 17 to 54, with higher scores indicating more child responsibility. Person mean imputation was used in cases of ≤20% missing item scores.[27] If more than three item scores were missing, the participant's total DFRQ score was considered missing. The estimated Cronbach's alpha was 0.71.

Following treatment recommendations

The extent to which treatment recommendations were followed (treatment behaviors) was assessed at baseline using the Adherence in Diabetes Questionnaire—version for conventional treatment (ADQ-C, 19 items) or the version for insulin pump treatment (ADQ-I, 17 items),[30] as applicable. Each item of the ADQ describes a diabetes management task and adolescents are asked how they handled this task in the preceding month (possibly with help from a parent), rated from 1 (Not at all) to 5 (Always). We updated the item concerning the recording of blood glucose levels in a chart or diabetes diary to contain "uploading the blood glucose values from the glucometer." A mean score was computed over item responses (range 1–5), with higher scores indicating greater following of treatment recommendations. Person mean imputation was used in cases of ≤20% missing item scores.[27] If >4 (ADQ-C) or 3 (ADQ-I) item scores were missing, the participant's total score was considered missing. The estimated Cronbach's alpha was 0.73 for the pen version, and 0.81 for the pump version.

Statistical analyses

First, IBM SPSS version 24.0 was used to describe the characteristics of the sample of adolescents and parents. Means and standard deviation, as well as median and interquartile range, were reported for continuous variables. Group differences between dyads with complete data and dyads with incomplete data were examined with *t* tests and Pearson's χ^2 tests. Normality of the distribution was tested using the Shapiro–Wilk test. Second, longitudinal path modeling using maximum-likelihood estimation in AMOS 23.0 was applied to test our hypotheses. Missing values were handled in AMOS using the Full Information Maximum Likelihood method.[31]

The actor–partner interdependence model[32] was used to take into account the dependency in the scores of adolescent–parent dyads. To evaluate model fit, we inspected the χ^2 test for exact model fit, the RMSEA (including 95% confidence interval (CI)), the NFI, the TLI, and the CFI. Based on criteria by Hu and Bentler,[33] we a priori planned to conclude good model fit in case of nonsignificant χ^2 tests, for RMSEA values <0.05 (and upper 95% CI bounds <0.10), and for NFI, TLI, and CFI values >0.95. In all models, we adjusted for the sex of the adolescent and the parent, and baseline adolescent depressive and anxiety symptoms, and HbA_{1c} value.

First, we fitted a reference model without mediators and hence only direct associations from parental depressive and anxiety symptoms to adolescent health outcomes (i.e., continuous total CDI-2 score, total GAD-7 score, and HbA_{1c}), adjusted for the division of diabetes management responsibilities [DFRQ total score] and the extent to which treatment recommendations were followed [ADQ total score]. Second, we fitted the hypothesized sequential model in which the association between parental distress and HbA_{1c} was mediated by the division of diabetes management responsibilities and the level of following treatment recommendations (and compared this to the reference model). Finally, we examined a model in which the division of diabetes responsibilities and the extent to which treatment recommendations are followed were fit as two separate parallel mediators between parental distress and HbA_{1c} (instead of sequentially); we compared this to the reference model. Sobel tests were conducted to test the statistical significance of these mediation pathways. If direct associations between baseline parental distress and adolescent outcomes at 1-year follow-up were not significant, mediation effects were examined nevertheless, as they were an integral part of the research question and to avoid overlooking possible suppression effects.[32,34] We determined the R^2 effect size for a predictor by computing the change in R^2 between a model where the predictor's regression coefficient was fixed to 0 and a model where the regression coefficient was freely estimated. Model fit comparisons were based mainly on the model fit indices, as the χ^2 difference test was not possible because the baseline model was not nested in the models including mediators. Statistical significance was tested against $\alpha = 0.05$.

RESULTS

Baseline characteristics of the 154 adolescents and 137 parents are presented in Table 1. Of these adolescents, 11% ($n = 16$) reported elevated depressive symptoms based on the CDI-2, while 5% ($n = 7$) reported elevated anxiety symptoms based on the GAD-7. Of the parents, 5% ($n = 6$) reported elevated depressive symptoms based on the PHQ-9, while 4% ($n = 5$) reported elevated anxiety symptoms based on the GAD-7.

At baseline, 150 adolescents and 133 parents provided complete data with respect to the variables used in the SEM models. At follow-up, 112 adolescents and 87 parents provided complete data. In total, 79 dyads provided complete data across the two time points and were suitable for longitudinal analysis. Dyads who provided complete data did not statistically differ from dyads who provided incomplete data on the variables included in the models (data not shown). Bivariate correlations between study variables are presented in Table 2.

Longitudinal associations between parental distress and adolescent health outcomes

The first a priori defined model, in which only direct associations between parental depressive and anxiety symptoms and adolescent outcomes were fitted (i.e., the baseline model), showed adequate exact model fit (χ^2 (14) = 12.26, $p = 0.59$), indicating that the estimated covariance matrix based on the model parameters closely resembled the observed covariance matrix. Fit indices further supported this finding (CFI = 1.00, NFI = 0.98, TLI = 1.00 RMSEA = 0.00; 95% CI: 0.00–0.07). However, when inspecting the path model estimates, it appeared that baseline parental depressive symptoms ($B = -0.12$, SE = 0.16, $p = 0.48$, R^2-change = 0.1%) and baseline parental anxiety symptoms ($B = 0.02$, SE = 0.16, $p = 0.91$, R^2-change = −0.1%) were not associated with adolescent depressive symptoms at follow-up. Similarly, baseline parental depressive symptoms ($B = -0.03$, SE = 0.13, $p = 0.81$, R^2-change = 0.0%) and baseline parental anxiety symptoms ($B = -0.03$, SE = 0.13, $p = 0.81$, R^2-change = 0.2%) were not significantly related to adolescent anxiety symptoms at follow-up. Furthermore, baseline parental depressive and anxiety symptoms were not significantly related to HbA_{1c} at follow-up ($B = -0.06$, SE = 0.04, $p = 0.13$, R^2-change = 0.9% and $B = 0.00$, SE = 0.04, $p = 0.99$, R^2-change = 0.0%). Standardized estimates are presented in Fig. 2.

The second model assessed whether the association between parental emotional distress and HbA_{1c} was mediated by the division of diabetes responsibilities and the extent to which treatment recommendations were followed. The exact model fit (χ^2 (27) = 41.37, $p = 0.04$) indicated that the model was rejected; the estimated covariance matrix based on the model parameters differed from the observed covariance matrix. NFI, TLI, and RMSEA also suggested suboptimal model fit (NFI = 0.94, TLI = 0.89;

Table 1. Baseline sample characteristics of the 154 adolescents with type 1 diabetes and 137 of their parents.

	% (*n*)	Mean ± SD	Median (IQR)	Range
Demographic characteristics				
Age adolescent (yr)		15.0 ± 1.9	15.0 (13.5–16.6)	12.0–18.7
Sex adolescent, women	49 (71)			
Age parent/caregiver (yr)		46.0 ± 4.6	46.0 (43.0–49.0)	34.0–59.0
Sex parent/caregiver, women	89 (121)			
Clinical characteristics				
Duration of diabetes (yr)		7.2 ± 4.2	7.2 (3.4–10.9)*	0.6–15.8
Insulin treatment modality (CSII)	77 (113)			
Most recent HbA_{1c} (%)		7.8 ± 1.1	7.8 (7.0–8.3)	5.4–11.5
Most recent HbA_{1c} (mmol/mol)		61 ± 12	62 (52–68)	36–102
Optimal HbA_{1c} (%, <7.5%/58 mmol/mol)	42 (65)			
Psychosocial characteristics				
Adolescent anxiety symptoms, GAD-7 total score		3.1 ± 2.7	3.0 (1.0–4.0)*	0.0–13.0
Adolescents depressive symptoms, CDI-2 total score		6.4 ± 5.1	5.0 (3.0–8.0)*	0.0–26.0
Division of diabetes management responsibilities, DFRQ total score		37.1 ± 4.2	37.0 (35.0–40.0)	25.0–50.0
Treatment behaviors, ADQ-C/ADQ-I mean score		3.9 ± 0.5	3.9 (3.6–4.3)*	2.4–4.9
Parent/caregiver anxiety symptoms, GAD-7 total score		2.4 ± 3.0	2 (0.0–4.0)*	0.0–14.0
Parent/caregiver depressive symptoms, PHQ-9 total score		2.3 ± 2.9	1 (0.0–3.0)*	0.0–16.0
Parent/caregiver self-reported anxiety disorder diagnosis	4 (5)			
Parent/caregiver self-reported mood disorder diagnosis	7 (9)			

Note: Reported are valid percentages.
yr Years, *CSII* continuous subcutaneous insulin infusion, *HbA_{1c}* hemoglobin A_{1c}, *GAD-7* generalized anxiety disorder-7, *CDI-2* Children's Depression Inventory-2, *DFRQ* Diabetes Family Responsibility Questionnaire, *ADQ-C* Adherence in Diabetes Questionnaire-Conventional treatment, *ADQ-I* Adherence in Diabetes Questionnaire-Insulin pump user, *PHQ-9* Patient Health Questionnaire- 9, *SD* standard deviation, *IQR* interquartile range.
*Shapiro–Wilk test: $p < 0.05$.

RMSEA = 0.06, 95% CI: 0.01–0.09), while the CFI statistic was good (CFI = 0.97). With respect to the path model estimates of the second model, baseline parental depressive and anxiety symptoms were not associated with 1-year adolescent depressive symptoms ($B = -0.11$, SE = 0.16, $p = 0.51$, R^2-change = 0.1% and $B = 0.02$, SE = 0.16, $p = 0.93$, R^2-change = 0.0%, respectively). Similarly, baseline parental depressive ($B = -0.02$, SE = 0.13, $p = 0.85$, R^2-change = 0.0%) and anxiety symptoms ($B = -0.03$, SE = 0.13, $p = 0.79$, R^2-change = 0.2%) were not associated with adolescent anxiety symptoms at follow-up. Baseline parental depressive and anxiety symptoms were also not directly related with HbA_{1c} at follow-up ($B = -0.06$, SE = 0.04, $p = 0.13$, R^2-change = 0.9% and $B = -0.00$, SE = 0.04, $p = 0.94$, R^2-change = 0.0%). The standardized estimates of the mediated pathways from parental depressive or anxiety symptoms to HbA_{1c} at follow-up were both 0.00.

As the reference model is not nested in the sequential mediation model, we compared the model fit of both models based on their χ^2, NFI, TLI, RMSEA, and CFI statistics and concluded that the reference model showed superior fit. Thus, the results of our analysis rejected the hypothesis that the division of diabetes responsibilities and treatment behaviors sequentially mediate an association between parental distress and HbA_{1c}.

The third model assessing two separate and simultaneous mediation pathways (division of diabetes tasks, following of treatment recommendations) between parental depressive and anxiety symptoms and adolescent HbA_{1c} also showed suboptimal exact model fit (χ^2 (25) = 40.59, $p = 0.03$). This finding was supported by most other fit indices (NFI = 0.94, TLI = 0.88; RMSEA = 0.06, 95% CI: 0.02–0.10), except CFI (CFI = 0.97). With respect to the path model estimates, baseline parental depressive and anxiety symptoms were not associated with adolescent 1-year depressive symptoms ($B = -0.11$, SE = 0.16, $p = 0.51$, R^2-change = 0.1% and $B = 0.01$, SE = 0.16, $p = 0.94$, R^2-change = 0.0% respectively). Baseline parental depressive and anxiety symptoms were also not associated with adolescent anxiety symptoms at 1-year follow-up ($B = -0.02$, SE = 0.13, $p = 0.85$, R^2-change = 0.0% and $B = -0.04$, SE = 0.13, $p = 0.78$, R^2-change = 0.2%). Finally, baseline parental depressive and anxiety symptoms were not directly related with HbA_{1c} at 1-year follow-up ($B = -0.06$, SE = 0.04, $p = 0.12$, R^2-change = 1.1% and $B = 0.00$, SE = 0.04, $p = 0.96$, R^2-change = 0.0%). The standardized mediated effect of parental depressive symptoms on HbA_{1c} at follow-up was 0.008, while the standardized mediated effect of anxiety symptoms was −0.005. The Sobel tests confirmed that there were no mediation effects of the division of diabetes tasks ($p = 0.47$) or following treatment recommendations ($p = 0.93$) in the association between parental depressive symptoms and HbA_{1c}. Similarly, the association between parental anxiety symptoms and HbA_{1c} at follow-up was not mediated by the division of diabetes tasks and the level of following treatment recommendations (Sobel tests $p = 0.59$ and $p = 0.85$, respectively).

Comparing the model fit of the simultaneous mediation model with the reference model based on χ^2, NFI, TLI, RMSEA, and CFI statistics, we concluded that the reference model showed superior fit. The results of our analysis did not support the hypothesis that the division of diabetes responsibilities and treatment behaviors acted as two separate mediators between parental distress and HbA_{1c}.

DISCUSSION

In this sample of 154 adolescents, baseline parental emotional distress (i.e., depressive and anxiety symptoms) was not significantly associated with 1-year adolescent depressive symptoms, anxiety symptoms, or HbA_{1c}. In line with these results, further analyses showed that the division of diabetes responsibilities and

Table 2. Bivariate correlations between study variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age adolescent	—												
2. Age parent	0.296**	—											
3. Duration of diabetes	0.331**	0.016	—										
4. Adolescent depressive symptoms at baseline	0.166*	0.124	0.051	—									
5. Adolescent anxiety symptoms at baseline	0.187*	0.091	−0.015	0.612**	—								
5. Adolescent HbA_{1c} at baseline	0.204*	−0.104	0.310**	0.202*	0.094	—							
7. Adolescents depressive symptoms at follow-up	0.093	−0.137	0.030	0.699**	0.436**	0.153	—						
8. Adolescent anxiety symptoms at follow-up	0.109	−0.090	−0.106	0.461**	0.419**	0.017	0.622**	—					
9. Adolescents HbA_{1c} at follow-up	0.078	−0.113	0.166	0.070	−0.063	0.695**	0.123	0.090	—				
10. Division of diabetes care responsibilities	0.493**	0.416**	−0.048	0.026	0.033	0.040	0.019	−0.037	0.040	—			
11. Following of treatment at recommendations	−0.358**	0.000	−0.106	−0.329**	−0.225**	−0.264**	−0.244**	−0.197*	−0.166	−0.010	—		
12. Parent depressive symptoms at baseline	−0.043*	0.008	−0.053	0.105	0.039	0.051	−0.007	0.005	−0.099	0.096	0.053	—	
13. Parent anxiety symptoms at baseline	−0.062	−0.085	−0.019	−0.013	−0.035	0.078	0.006	−0.017	0.017	0.036	0.044	0.751**	—

*$p < 0.05$; **$p < 0.01$.

the extent to which treatment recommendations are followed did not mediate the association between parental emotional distress and HbA_{1c}. Even though parental emotional distress and HbA_{1c} after 1 year were not significantly related, we did proceed to test and report on the hypotheses concerning mediation to avoid overlooking possible suppression effects.[34]

These findings are contrary to our a priori expectations. This may suggest that adolescents are more resilient in the face of parental emotional distress than previously expected, possibly due to positive adolescent characteristics (such as self-efficacy).[35] However, there are several alternative explanations. First, whether or not there is a relationship between parental and adolescent, emotional health may be dependent on the method of assessment. Similar to our study, Wiebe et al.[17] reported maternal depressive symptoms not to be directly related to distress in adolescents with type 1 diabetes, seemingly contradicting other studies in the general population[14,15] that did suggest parental psychiatric disorders as a risk factor for psychopathology in their children. One other study, in the context of type 1 diabetes mellitus, did report maternal distress to be a risk factor for child psychopathology.[16] Self-reported symptoms of distress do not equal a diagnosis of a psychiatric disorder and this may explain the inconsistencies in the (nonsignificant) results of our study and the significant results of studies focusing on psychiatric disorders determined with diagnostic interviews.[14–16] The impact of the problems is higher in the latter group of studies. Psychiatric disorders by definition indicate a certain level of severity or impairment in areas of daily life, while symptom severity based on questionnaires can range from nonexistent to severe. In our sample, only 4% of parents reported to have a current diagnosed mood disorder, while 7% reported an anxiety disorder. When looking at symptom severity, the majority or parents reported no or mild depressive and anxiety symptoms, and few parents had high scores. This restriction of range could have attenuated the associations and lowered power to detect the hypothesized associations.[36] A second explanation for our unexpected findings concerns selection of the participating parent in the present study; the parent who was most involved in the diabetes care of the adolescent was invited. This is not necessarily the parent to whom the adolescent feels the most (emotional) attachment or by whom the adolescent is most emotionally affected. Also, the presence of emotional support by other important people in the social network of the adolescent could have buffered the negative effects of emotional distress in the participating parent,[37] but this fell beyond the scope of the present study. Third, other unmeasured factors outside the adolescent–parent relationship could be important contributors to adolescent emotional distress, such as emotional distress of the other parent, adolescent distress regarding life with diabetes,[38] or problems with peers.[39]

With regard to the expected association between parental depressive and anxiety symptoms, and HbA_{1c}, previous research has suggested both direct[18] and indirect associations for maternal depressive symptoms.[19,20] However, these studies had a cross-sectional design. Less is known about parental anxiety. Parental fear of hypoglycemia, specifically, has been cross-sectionally related to higher HbA_{1c}. However, anxious parents could also engage in (over)controlling parenting behaviors (in this case, more involvement in diabetes care) in attempts to avoid adverse outcomes in their children (thus achieving lower HbA_{1c} values).[40] These reverse effects could have played a part in the found results. While we examined whether parental distress was associated with HbA_{1c} at follow-up, it is also imaginable that suboptimal HbA_{1c} precedes parental distress.

Alternatively, parental diabetes-specific distress may be of more importance than general parental well-being, as suggested in a longitudinal study by Eilander et al.[41]. While general emotional distress can arise as the result of a myriad of reasons,

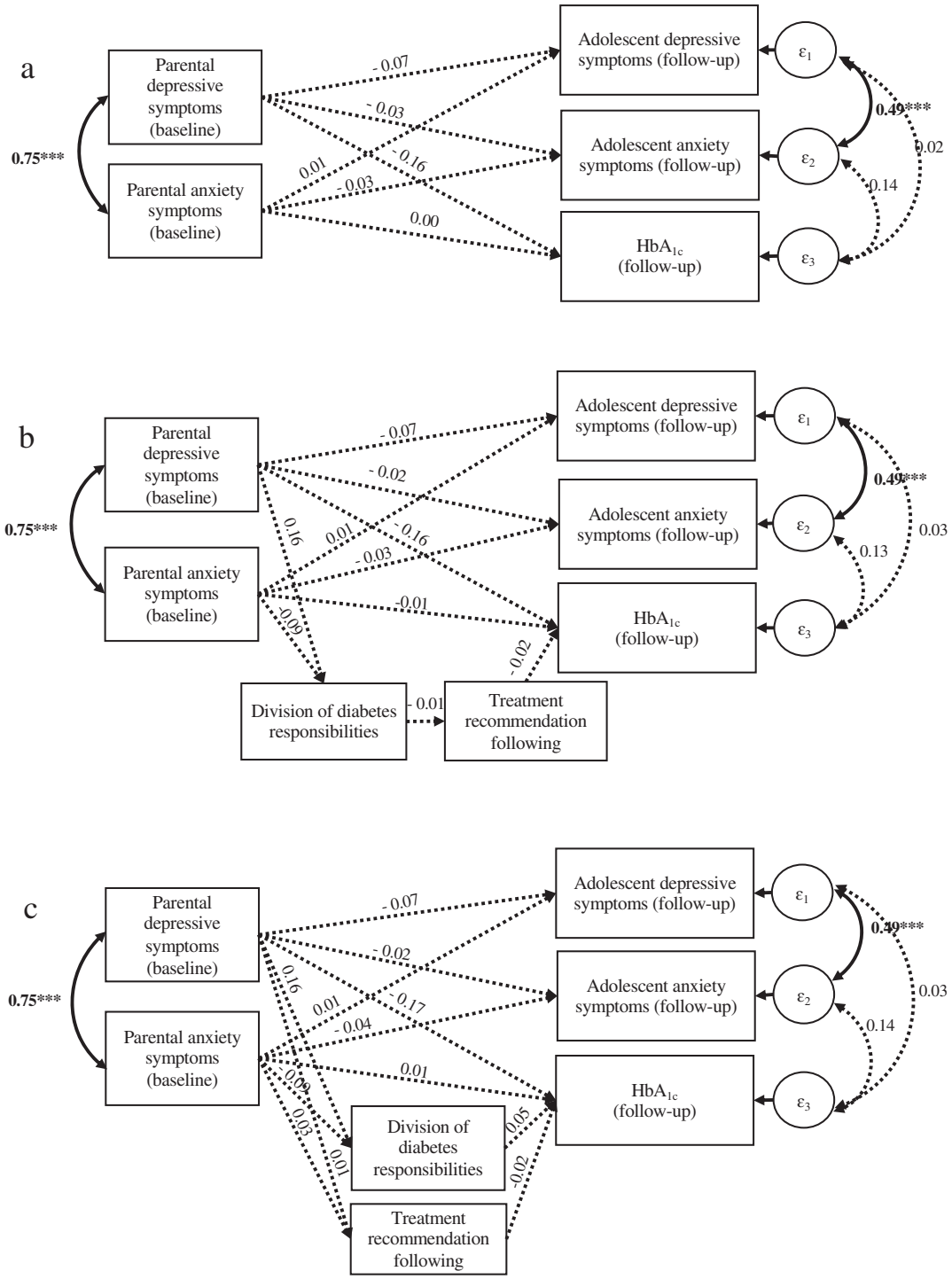

Fig. 2 Structural models of the 1-year associations between parental distress and adolescent health outcomes. a Direct effects model. **b** Sequential mediation model. **c** Simultaneous mediation model. Note: For readability, covariates (parental sex, adolescent sex, parental anxiety and depressive symptoms at follow-up, baseline adolescent anxiety and depressive symptoms, and baseline HbA_{1c}), correlations of exogenous variables, and correlations of error terms are not depicted in the structural models. Double-headed curved arrows reflect Pearson's product–moment correlations and single-headed straight arrows reflect standardized regression coefficients. Solid arrows concern statistically significant effects and dotted arrows nonsignificant effects. In the direct effects model, we also adjusted for the division of diabetes responsibilities and treatment recommendation following.

diabetes-specific distress clearly relates to life with diabetes and might be more directly related to HbA_{1c}.

Parental involvement has been suggested as a mediator in the association of parental distress and adolescent HbA_{1c}, but this hypothesis was rejected in the present study. However, previous studies have defined this involvement as parental monitoring,[19,20] or conflict, and warmth of involvement,[20] while we focused on the quantity of involvement in diabetes-related responsibilities, possibly explaining the differences in results. Both aspects may be of importance for the diabetes management of youth with type

1 diabetes mellitus.[42] Also, the DFRQ total score may have been less suitable to assess the level of involvement of the parent of interest. For example, the DFRQ assesses the involvement of both parents as one entity, meaning over or under involvement of the parent of interest may have been masked by the activities of the other parent. Furthermore, similar sum scores can be assigned to families where adolescent and parents are equally sharing all diabetes responsibilities versus families where the tasks are distinctly divided. It could also be the case that the division of diabetes responsibility per se is less important than the match of this division to the adolescent's readiness and ability to (adequately) perform these tasks. The Adherence in Diabetes Questionnaire measures how often a diabetes-related task is performed, yet it does not assess whether the tasks are optimally timed and/or appropriately executed (leading to the desired outcomes).

The prospective design, the focus on adolescent mental health and diabetes outcomes, as well as the use of validated questionnaires are strengths of our study. However, several limitations should be recognized as well. First, as we did not collect (mental health) data in adolescents and parents who opted out of participation, we cannot rule out selection bias during recruitment. This could threaten the generalizability of the results. Second, despite the large sample size, we must also note that the rates of self-reported physician/specialist diagnosed parental mood and anxiety disorders were low, thus analyses restricted to the group with psychopathology could not be executed. Third, it should be noted that the percentage of parents with elevated depressive/anxiety symptoms was also low and might not be representative of the population. Fourth, we focused on the parent who had indicated to be most involved in the diabetes care, thereby possibly overlooking (the role of) significant others in the social network of the adolescent. Fifth, not all adolescents and parents who participated in the baseline wave were retained in the follow-up wave, which could have induced attrition bias. However, by using an inclusive method (Full Information Maximum Likelihood) to handle missing data and assuming the data were missing at random, we aimed to maximally use the available data in order to estimate the parameters as accurately as possible.[31] We note that it is not clear whether the dropout at follow-up was caused by high depressive or anxiety symptoms. Nevertheless, we found no significant differences between completers and dropouts on any of the baseline variables included in our model. Sixth, different associations may exist for early adolescents versus late adolescents as this developmental stage is characterized by fast-paced changes, and should be addressed in future studies. Moreover, more frequent and intensive follow-ups could uncover prospective associations between parental depressive and anxiety symptoms and adolescent health outcomes and vice versa.

To our best knowledge, this is the first prospective study in which parental depressive and anxiety symptoms are examined in relation to both emotional and diabetes health outcomes in adolescents with type 1 diabetes mellitus. We did not find significant longitudinal associations between parental emotional distress and adolescent health outcomes after 1 year. However, it might be premature to discard the notion of parental emotional distress affecting adolescent outcomes, given the limitations of the present study. Previous studies focusing on diagnoses did suggest transgenerational links of emotional distress, thus future research should focus specifically on the group with psychopathology. Moreover, future studies are advised to examine which aspects of parental involvement may be of importance in these associations, in order to inform avenues for targeted supportive intervention for families at risk for adverse outcomes.

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AUTHOR CONTRIBUTIONS

L.A.N., F.P., H.-J.A., and G.N. substantially contributed to the conception and design of the study, the acquisition of data, the analysis and interpretation of data, the drafting of the article, and critically revised the article for important intellectual content. E.H. and P.W. substantially contributed to acquisition of data, the interpretation of data, and critically revised the article for important intellectual content. P.L. substantially contributed to the analysis and interpretation of data, the drafting of the article, and critically revised the article for important intellectual content. All authors gave approval of the version to be published.

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

Patient consent: Informed consent from adolescents and their parents was obtained.

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