Published in final edited form as:

Pediatr Diabetes. 2018 November ; 19(7): 1322–1330. doi:10.1111/pedi.12713.

Diabetes management mediating effects between diabetes symptoms and health-related quality of life in adolescents and young adults with type 1 diabetes

James W Varni¹, Alan M Delamater², Korey K Hood³, Kimberly A Driscoll⁴, Jenise C Wong⁵, Saleh Adi⁵, Joyce P Yi-Frazier⁶, Ellen K Grishman⁷, Melissa A Faith⁷, Sarah D Corathers⁸, Jessica C Kichler⁹, Jennifer L Miller¹⁰, Jennifer K Raymond¹¹, Elena M Doskey¹², Vincent Aguirre¹³, Robert W Heffer¹³, and Don P Wilson¹⁴ Pediatric Quality of Life Inventory 3.2 Diabetes Module Testing Study Consortium

¹Department of Pediatrics, College of Medicine, Department of Landscape Architecture and Urban Planning, College of Architecture, Texas A&M University, College Station, Texas

²Department of Pediatrics, Mailman Center for Child Development, University of Miami Miller School of Medicine, Miami, Florida

³Division of Pediatric Endocrinology and Diabetes, Stanford University School of Medicine, Stanford, California

⁴Department of Pediatrics, Barbara Davis Center for Diabetes, University of Colorado Denver, Denver, Colorado

⁵The Madison Clinic for Pediatric Diabetes and Department of Pediatrics, Division of Endocrinology, University of California San Francisco, San Francisco, California

⁶Seattle Children's Research Institute, Seattle, Washington

⁷Department of Pediatrics, Division of Pediatric Endocrinology, University of Texas Southwestern Medical Center, Dallas, Texas

⁸Department of Pediatrics, Division of Endocrinology, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio

⁹Department of Pediatrics, Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio

¹⁰Division of Pediatric Endocrinology, Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, Illinois

Correspondence: James W Varni, PhD, Professor Emeritus, Colleges of Architecture and Medicine, Texas A&M University, 3137 TAMU, College Station, TX 77843-3137. jvarni@tamu.edu.
Melissa A. Faith, Institute for Brain Protection, Sciences, Johns Hopkins All Children's, Hospital, Saint Petersburg, FL.
Elena M. Doskey, University of Oklahoma Health Sciences Center, Oklahoma City, OK.

Conflict of interest

New item development and item modification of the existing PedsQL 3.0 Diabetes Module for the published item generation qualitative methods study for the PedsQL 3.2 Diabetes Module was previously funded by Eli Lilly and Company, Indianapolis. Dr. Varni holds the copyright and the trademark for the PedsQL and receives financial compensation from the Mapi Research Trust, which is a non-profit research institute that charges distribution fees to for-profit companies that use the Pediatric Quality of Life Inventory. Dr. Varni did not receive funding from Eli Lilly and Company for the current quantitative methods field test study. The other authors report no competing interests related to this study.

¹¹Center for Endocrinology, Diabetes, & Metabolism, Children's Hospital Los Angeles, Los Angeles, California

¹²Department of Educational Psychology, Texas A&M University, College Station, Texas

¹³Department of Psychological and Brain Sciences, Texas A&M University, College Station, Texas

¹⁴Cook Children's Medical Center, Fort Worth, Texas

Abstract

Objectives: The primary objective was to investigate the mediating effects of diabetes management in the relationship between diabetes symptoms and generic health-related quality of life (HRQOL) in adolescents and young adults (AYAs) with type 1 diabetes. The secondary objective explored patient health communication and perceived treatment adherence barriers as mediators in a serial multiple mediator model.

Methods: The PedsQL 3.2 Diabetes Module 15-item diabetes symptoms summary score, 18-item diabetes management summary score, and PedsQL 4.0 generic core scales were completed in a 10-site national field test study by 418 AYA aged 13 to 25 years with type 1 diabetes. Diabetes symptoms and diabetes management were tested for bivariate and multivariate linear associations with overall generic HRQOL. Mediation analyses were conducted to test the hypothesized mediating effects of diabetes management as an intervening variable between diabetes symptoms and generic HRQOL.

Results: The predictive effects of diabetes symptoms on HRQOL were mediated in part by diabetes management. In predictive analytics models utilizing multiple regression analyses, demographic and clinical covariates, diabetes symptoms, and diabetes management significantly accounted for 53% of the variance in generic HRQOL ($P < 0.001$), demonstrating a large effect size. Patient health communication and perceived treatment adherence barriers were significant mediators in an exploratory serial multiple mediator model.

Conclusions: Diabetes management explains in part the effects of diabetes symptoms on HRQOL in AYA with type 1 diabetes. Patient health communication to healthcare providers and perceived treatment adherence barriers further explain the mechanism in the relationship between diabetes symptoms and overall HRQOL.

Keywords

health-related quality of life; patient-reported outcomes; pediatrics; PedsQL; self-management; symptoms; type 1 diabetes

1 | INTRODUCTION

The worldwide prevalence of type 1 diabetes is increasing in children, adolescents, and young adults.^{1,2} Diabetes self-management is a crucial component of overall diabetes care, and represents a particular challenge during the adolescent and young adult (AYA) developmental period when competing demands may undermine successful disease control.³ As AYA with type 1 diabetes assume greater responsibility for their health and well-being between childhood and emerging adulthood, they must also navigate the transition from

pediatric to adult healthcare providers and settings.⁴ These factors in combination may undermine the achievement of adequate diabetes management, and may be associated with less than optimal glycemic control and impaired overall health-related quality of life (HRQOL).

Patient-reported outcomes (PROs), including HRQOL and symptom-specific measurement instruments,⁵ have assumed a greater role in determining the impact of pediatric diseases and treatments from the perspective of pediatric patients.⁶ Particularly with the advent of the Food and Drug Administration (FDA) guidelines regarding PROs,⁷ there has been a significantly increased emphasis on the integration of PROs with clinical and biological data in the evaluation of treatment efficacy for chronic health conditions.

Generic (general or non-disease-specific) HRQOL measures provide a common metric on which to compare interventions both within and across patient groups.⁸ Generic HRQOL is a multidimensional construct, consisting at the minimum of the physical, psychological (including emotional and cognitive), and social health dimensions delineated by the World Health Organization.^{7,9} While generic HRQOL measurement instruments enable comparisons across patient populations and facilitate benchmarking with healthy population norms, diabetes-specific measurement instruments are essential to understanding symptoms and problems most relevant for patients with diabetes.¹⁰ Further, based on the conceptualization of disease-specific symptoms and problems as causal indicators of generic HRQOL,¹¹ it would be expected that diabetes-specific symptoms and problems would be significant predictors of impaired generic HRQOL.

Recently, we described the item development and 10-site national field test study for the PedsQL 3.2 Diabetes Module.^{12–14} The PedsQL 3.2 Diabetes Module is a revised and updated version of the PedsQL 3.0 Diabetes Module, the most widely used internationally validated PRO instrument to measure the diabetes-specific HRQOL of children, adolescents, and young adults with type 1 or type 2 diabetes.^{10,15–17} From the factor analysis of the 33 items contained in the PedsQL 3.2 Diabetes Module, two summary scores were empirically derived as most parsimonious in explaining the factor structure.^{13,14} Specifically, the diabetes symptoms summary score and the diabetes management summary score demonstrated internal consistency reliability and construct validity in type 1 and type 2 diabetes.^{13,14} Previously, in a predictive analytics model utilizing hierarchical multiple regression analysis controlling for relevant demographic and clinical covariates, we demonstrated that the PedsQL diabetes symptoms summary score explained 38% of the variance in patient-reported generic HRQOL for type 1 diabetes, representing a large effect size.¹⁸ However, to our knowledge, and unique to the present study, no prior research has investigated patient-reported diabetes management as a mediator in the relationship between diabetes symptoms and overall generic (non-disease-specific) HRQOL in AYA with type 1 diabetes. The delineation of patient-reported diabetes management mediators derived from a standardized measurement instrument may facilitate interventions designed to improve diabetes self-management behaviors and enhance overall generic HRQOL.

To address this significant gap in the empirical literature, the primary objective of the present study was to investigate the hypothesized mediating effects of diabetes management

as a mechanism or intervening variable in the relationship between diabetes symptoms and overall generic HRQOL in AYA with type 1 diabetes. The secondary objective explored patient health communication and patient perceived treatment adherence barriers as mediators in a serial multiple mediator model based on a conceptual model previously tested in pediatric inflammatory bowel disease.^{19,20}

2 | METHODS

2.1 | Participants and settings

AYA with type 1 diabetes were recruited from 10 clinical sites in the United States for the PedsQL 3.2 Diabetes Module field test (see Appendix A). Data collection for the field test took place between July 2015 and June 2017. For the field test study, the inclusion criteria included physician-diagnosed type 1 or type 2 diabetes, English or Spanish language speaking and reading ability, and ages 2 to 25 years.^{13,14} The exclusion criteria included type 1 or type 2 diabetes was not the primary diagnosis, and youth and/or caregivers whose dominant language was a language other than English or Spanish. All participants for the present sample completed the English language versions of the PedsQL. Parental informed consent and patient assent/consent were obtained. The research protocol was approved by the Institutional Review Board at each site.

2.2 | Measures

2.2.1 | PedsQL diabetes symptoms and diabetes management summary

scores—The 15-item PedsQL diabetes symptoms summary score (eg, “I get shaky”) and the 18-item PedsQL diabetes management summary score (eg, “It is hard for me to do everything I need to do to care for my diabetes”) are derived from the PedsQL 3.2 Diabetes Module, a diabetes-specific HRQOL instrument developed through qualitative and quantitative methods.^{12,13} The instructions ask how much of a problem each item has been during the past 7 days utilizing the PedsQL 5-point Likert-type response scale (0 = never a problem; 1 = almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). Items are reverse-scored and linearly transformed to a 0 to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), so that lower scores demonstrate more diabetes symptoms and diabetes management problems and hence lower diabetes-specific HRQOL. Summary scores are computed as the sum of the items divided by the number of items answered (this accounts for missing data). If more than 50% of the items in the scale are missing, the summary score is not computed.²¹ Although there are other strategies for imputing missing values, this computation is consistent with previous PedsQL peer-reviewed publications as well as other well-established HRQOL measures.⁶ For the current study, the percentage of missing item responses was 0.005% and 0.002% for the diabetes symptoms summary score and diabetes management summary score, respectively.

2.2.2 | PedsQL 4.0 generic core scales—The 23-item PedsQL 4.0 generic core scales encompass: physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (five items).^{22–24} To create the total scale score, the mean is computed as the sum of the items divided by the number of items

answered in the physical, emotional, social, and school functioning scales. The total scale score measures overall generic HRQOL.²² Higher scores indicate better HRQOL.

2.2.3 | PedsQL family information form—Participants completed the PedsQL Family Information Form which contains demographic information including age, gender, and race/ethnicity.²²

2.2.4 | Hemoglobin A1c—Hemoglobin A1c (HbA1c) values were measured at each data collection site utilizing standard point-of-care methods (eg, DCA Vantage Analyzer, Siemens Medical Solutions Diagnostics, Tarrytown, NY, USA). The most recent HbA1c value from the patient's medical record was utilized.

2.2.5 | Body mass index—Body mass index (BMI) values were calculated from height and weight measures at each data collection site following the Centers for Disease Control and Prevention guidelines.²⁵

2.3 | Statistical analysis

Pearson product-moment correlation analyses were conducted to test the bivariate associations between the diabetes symptoms summary score, diabetes management summary score, and the generic core scales total scale score. Bivariate correlation effect sizes are designated as small (0.10), medium (0.30), and large (0.50) in magnitude.²⁶ Predictive analytics models utilizing hierarchical multiple regression analyses were conducted to statistically predict the generic core scales total scale score by the diabetes symptoms summary score and diabetes management summary score after controlling for relevant demographic and clinical variables.²⁷ Hierarchical multiple regression analyses tested the change in the variance accounted for by the diabetes symptoms summary score (R^2 change). In each hierarchical multiple regression analysis predicting the generic core scales total scale score, gender (coded male = 1, female = 2) was entered in Step 1 as a demographic covariate and HbA1c and BMI were entered in Step 2 as clinical covariates. These covariates were included in the multivariate analyses since they were significantly correlated with the generic core scales total scale score in bivariate analyses. Only covariates significantly associated with the dependent variable at the bivariate level of analysis were included in the multivariate analyses. Hierarchical multiple regression analysis is a statistical approach that isolates the effects of a predictor variable on a criterion variable by controlling for the influence of covariates.²⁷

Mediator variables are hypothesized to account in part or fully for the relationship between a predictor variable and an outcome variable.^{28,29} The predictor variable is hypothesized to have a direct effect on the outcome variable, as well as a potentially indirect effect through a mediator variable. Testing for direct and indirect effects may elucidate the mechanisms linking predictors to outcomes. We tested the following single mediator conceptual model: diabetes symptoms → diabetes management → generic HRQOL.

A series of multiple regression analyses were conducted to test the mediation model in which diabetes management mediated the relationship between diabetes symptoms and overall generic HRQOL based on the Baron and Kenny conceptual framework.²⁸ To test for

mediating effects, Baron and Kenny delineated a four-step analytic method. To support mediation, (1) diabetes symptoms must significantly predict HRQOL (direct effect), (2) diabetes symptoms must significantly predict diabetes management, (3) diabetes management must significantly predict HRQOL controlling for diabetes symptoms, and (4) prediction of HRQOL by diabetes symptoms must be significantly attenuated when the predictor and proposed mediator are entered simultaneously in the multiple regression analysis. We report standardized regression coefficients (β) and significance levels for Steps 1 to 3, and R^2 change for Step 4. We utilized the Sobel test to determine whether the indirect effect through the proposed mediator is significantly different from zero.³⁰ Partial mediation would be demonstrated when diabetes management explains only some of the prediction of diabetes symptoms on HRQOL. Full mediation would be demonstrated if diabetes management explained all of the predictive effect of diabetes symptoms on HRQOL.

We report R^2 values for each of the full models. R^2 is the percentage of variability in the outcome variable (HRQOL) explained by the full model (demographic and clinical control variables, predictor, mediator). R^2 effect sizes are designated as small (0.02), medium (0.13), and large (0.26) in magnitude.²⁶ Statistical analyses were conducted using IBM/SPSS (Armonk, New York, New York).

Additionally, an exploratory factor analysis of the diabetes management summary score was conducted in order to determine whether the 18 items might be further grouped into item clusters or “facets”.³¹ A principal component factor analysis with promax rotation of the 18 items was conducted. Based on recommendations from the measurement literature, we included items with a factor loading of 0.40 or greater.³² Cronbach’s coefficient alpha was utilized to determine internal consistency reliability.³³ Internal consistency reliabilities of 0.70 or greater are recommended for comparing patient groups, while an internal consistency reliability criterion of 0.90 is recommended for analyzing individual patient scores.³⁴

Based on a conceptual model previously tested in pediatric inflammatory bowel disease,^{19,20} we also tested a more complex serial multiple mediator model³⁵ with patient health communication and patient perceived treatment adherence barriers as mediators. Specifically, we tested the following serial multiple mediator model: diabetes symptoms → patient health communication → perceived treatment adherence barriers → generic HRQOL.

Finally, we explored a novel conceptual model in which social embarrassment and patient perceived treatment adherence barriers were tested as mediators in a serial multiple mediator model. Specifically, we tested the following serial multiple mediator model: diabetes symptoms → social embarrassment → perceived treatment adherence barriers → generic HRQOL. Indirect effects were tested utilizing 10 000 bias-corrected bootstrapped resamples with replacement yielding 95% confidence intervals (CIs). Significant indirect effects are demonstrated when the 95% CIs do not include zero. These analyses were conducted using the PROCESS macro for SPSS (processmacro.org) as described in Hayes.³⁶

3 | RESULTS

3.1 | Demographic and clinical characteristics

Table 1 contains the demographic and clinical characteristics of the participants. A total of 418 AYA with type 1 diabetes aged 13 to 25 years participated and completed the PedsQL instruments in the current study.

3.2 | Exploratory factor analysis

As shown in Table A1, the 18 diabetes management items may be further delineated into the latent constructs labeled “perceived treatment adherence barriers,” “procedural pain,” “social embarrassment,” “diabetes worry,” and “health communication.” Since the two health communication items loaded on Factor 3 with three items from the original a priori “Treatment Adherence Scale,” an additional principal components factor analysis with promax rotation of the seven items comprising the “perceived treatment adherence barriers” latent variable was conducted. A single unidimensional factor emerged for these seven items (column 6 in Table A1).

3.3 | Bivariate correlations between diabetes symptoms and diabetes management with generic core scales total scale score

Table 2 contains the means, SDs, and bivariate correlations of the diabetes symptoms summary score, diabetes management summary score, perceived treatment adherence barriers, procedural pain, social embarrassment, diabetes worry, and health communication facet/sub-scale scores with the generic core total scale score. All diabetes summary and facet/subscale scores were significantly correlated with the generic core scales total scale score (all P s < 0.001), demonstrating medium to large effect sizes.

3.4 | Mediation analysis predicting generic core scales total scale score

Prior to conducting the hierarchical multiple regression analyses, univariate analyses were conducted with age, gender, race/ethnicity, HbA1c, BMI, and time since diagnosis with the generic core total scale score in order to determine which demographic and clinical covariates to include in the multivariate analyses. HbA1c ($r = -0.17$, $P < 0.001$) and BMI ($r = -0.12$, $P < 0.01$) were significantly correlated with the generic core total scale score. Females demonstrated a lower generic core total scale score than males (80.03 vs 84.62, respectively, $t [416] = 3.51$, $P < 0.001$). Age ($r = -0.01$, $P > 0.05$), race/ethnicity ($F [4, 411] = 0.26$, $P > 0.05$), and time since diagnosis ($r = -0.03$, $P > 0.05$) were not associated with the generic core total scale score, and consequently were not included as covariates in the multivariate analyses.

Controlling for the significant univariate covariates (HbA1c, BMI, and gender), diabetes symptoms significantly predicted HRQOL ($\beta = .65$, $P < 0.001$) and diabetes management ($\beta = .54$, $P < 0.001$), achieving the first two criteria for mediation. Diabetes management predicted HRQOL ($\beta = .38$, $P < 0.001$) controlling for diabetes symptoms and the covariates, supporting the third criterion for mediation. When diabetes symptoms and diabetes management were simultaneously entered into the multiple regression analysis predicting HRQOL, the percentage of variance accounted for by diabetes symptoms was attenuated in

predicting HRQOL ($R^2 = .38$, $P < 0.001$ vs $R^2 = .13$, $P < 0.001$), meeting the criteria for partial mediation. The Sobel test indicated that the indirect effect of diabetes symptoms on HRQOL was significantly different from zero (Sobel test statistic = 7.04, $P < 0.001$). Indirect effects were additionally tested utilizing 10 000 bias-corrected bootstrapped resamples with replacement yielding 95% CIs that did not include zero (.1248, .2205). Thus, diabetes symptoms had both direct and indirect effects on overall generic HRQOL, with the indirect effect partially mediated by diabetes management. The full model accounted for 53% of the variance in overall generic HRQOL, demonstrating a large effect size.

3.5 | Serial multiple mediator models predicting HRQOL

Controlling for the significant univariate covariates (HbA1c, BMI, and gender), the serial multiple mediator model for the diabetes symptoms predictor variable demonstrated that the total indirect effect on HRQOL as estimated by the sum of the indirect effects for patient health communication and perceived treatment adherence barriers was .1466, and different from zero as determined by the bias-corrected bootstrap 95% CIs that were above zero (.1007, .1989). Within the serial multiple mediator model, patient health communication and perceived treatment adherence barriers CIs did not contain zero (.0544, .1592; .1493, .3165, respectively), and together demonstrated serial indirect effects (.0289, 95% CI: .0156, .0486) for the mediator model: diabetes symptoms → patient health communication → perceived treatment adherence barriers → HRQOL. The full serial multiple mediator model for diabetes symptoms accounted for 53% of the variance in HRQOL ($P < 0.001$), demonstrating a large effect size.

Controlling for the significant univariate covariates (HbA1c, BMI, and gender), the serial multiple mediator model for the diabetes symptoms predictor variable demonstrated that the total indirect effect on HRQOL as estimated by the sum of the indirect effects for social embarrassment and perceived treatment adherence barriers was .1218, and different from zero as determined by the bias-corrected bootstrap 95% CIs that were above zero (.0834, .1664). Within the serial multiple mediator model, social embarrassment and perceived treatment adherence barriers CIs did not contain zero (.0227, .1365; .1738, .3403, respectively), and together demonstrated serial indirect effects (.0168, 95% CI: .0084, .0304) for the mediator model: diabetes symptoms → social embarrassment → perceived treatment adherence barriers → HRQOL. The full serial multiple mediator model for diabetes symptoms accounted for 52% of the variance in HRQOL ($P < 0.001$), demonstrating a large effect size.

4 | DISCUSSION

The findings demonstrate that diabetes management partially mediates the relationship between diabetes symptoms and overall generic HRQOL. The mediation model accounted for 53% of the variance in HRQOL, reflecting a large effect size. When patient health communication and perceived treatment adherence barriers were tested within the serial multiple mediator model, the percentage of the variance accounted for in HRQOL was also 53%. Lastly, we explored a serial multiple mediator model in which social embarrassment and perceived treatment adherence barriers were tested as mediators, again demonstrating a

large effect size with 52% of the variance in overall generic HRQOL accounted for in the model.

These findings highlight the relevance of measuring diabetes symptom burden in AYA with type 1 diabetes in addition to measuring HbA1c as the primary outcome variable in diabetes clinical trials. After controlling for HbA1c, BMI, and gender, diabetes symptoms significantly predicted 38% of the variance in overall generic HRQOL. Testing for direct and indirect effects further elucidated the mechanism linking diabetes symptoms to overall generic HRQOL. By conducting the exploratory factor analysis of the diabetes management summary score in AYA with type 1 diabetes, facets, or subscales were additionally identified that potentially further clarify the intervening mechanism.

Identifying health communication, social embarrassment, and perceived treatment adherence barriers in the serial multiple mediator models provides more specific targets for interventions designed to ameliorate impaired HRQOL in AYA with type 1 diabetes. The present study findings indicate that patient health communication and social embarrassment may influence both perceived treatment adherence barriers and overall generic HRQOL serially. That is, patient health communication and social embarrassment in separate serial multiple mediator models had direct effects on patient perceived treatment adherence barriers, and sequentially overall HRQOL. The direct effects of patient health communication on perceived treatment adherence barriers suggests that health communication with health-care providers may be helpful in discussing strategies for overcoming perceived barriers to treatment adherence. Across multiple chronic health conditions, doctor-patient communication has been found to improve patient satisfaction, treatment adherence, and health outcomes.³⁷ For instance, healthcare providers and patients can mutually identify a set of priorities to discuss at a visit, and in a non-judgmental manner, healthcare providers can suggest strategies for addressing these priorities in a collaborative way.³⁸ The finding from the serial multiple mediator model that social embarrassment predicted perceived treatment adherence barriers is consistent with the literature in which individuals with diabetes report social stigma associated with their diabetes and diabetes treatment, which may undermine their attempts to treat their diabetes in social, school, or work environments.³⁹ Interventions to encourage AYA with type 1 diabetes to share their health experiences with their healthy peers may be a useful focus for future research.⁴⁰ This may include an openness about their diabetes diagnosis, symptoms and management with their classmates in the school setting.⁴¹ Finally, perceived treatment adherence barriers may be targeted directly for self-management strategies designed to improve overall HRQOL in AYA with type 1 diabetes who are experiencing diabetes symptoms.⁴²

The present study has several strengths, including the relatively large overall sample size, and the nationwide representation of the participants. Limitations include the lack of information on families who chose not to participate. An additional limitation was the lack of a central laboratory for HbA1c measurement across the sites, although the majority of the sites utilized the same measurement approach. Lastly, the cross-sectional design limits directionality assumptions in statistical prediction. Longitudinal research will be necessary to determine the directionality of the variables tested in the conceptual models.

In conclusion, patient health communication, social embarrassment, and perceived treatment adherence barriers represent mediators in the link between diabetes symptoms and overall generic HRQOL in AYA with type 1 diabetes. These predictive analytics models testing both the direct and indirect effects of diabetes symptoms on overall generic HRQOL may serve a hypothesis generating function for future intervention research for AYA with type 1 diabetes. Interventions directed toward several of the mediators in the serial multiple mediator models may enhance the overall treatment effect of a multicomponent intervention designed to improve HRQOL in AYA with type 1 diabetes.

ACKNOWLEDGEMENTS

The investigators thank the following individuals for their involvement in participant recruitment, data collection, and/or data verification: Marta Pardo, Morgan Drake, Luke Hamilton, Natalie Beauregard, Cisco Pascual, Nora Chokr, Marie Nader, Jacqueline Shea, Kylie Benson, Lisa Keys, Vanessa Guzman, Jeanette Velez, Bianca Agustin, Esti Iturralde and Elizabeth Dabrowski. No funding was specifically designated for the PedsQL 3.2 Diabetes Module field test study data collection effort or manuscript preparation.

APPENDIX A

PEDIATRIC QUALITY OF LIFE INVENTORY (PEDSQL) 3.2 DIABETES MODULE TESTING STUDY CONSORTIUM

The PedsQL 3.2 Diabetes Module Testing Study Consortium sites include a Network and Statistical Center at the Center for Health Systems & Design, Colleges of Architecture and Medicine, Texas A&M University, College Station, TX (PI: James W. Varni, PhD), and 10 primary research data collection sites: Department of Pediatrics, Mailman Center for Child Development, University of Miami Miller School of Medicine, Miami, FL; (PI: Alan M. Delamater, PhD); Division of Pediatric Endocrinology and Diabetes, Stanford University School of Medicine, Stanford, CA (PI: Korey K. Hood, PhD); Department of Pediatrics, Division of Endocrinology, University of Texas Southwestern Medical Center, Dallas, TX (PIs: Ellen K. Grishman, MD, Melissa A. Faith, PhD, ABPP); Center for Endocrinology, Diabetes, & Metabolism, Children's Hospital Los Angeles, Los Angeles, CA (PIs: Jennifer K. Raymond, MD, MCR, Nancy T. Chang, PhD, MSN, FNP); Department of Pediatrics, Barbara Davis Center for Diabetes, University of Colorado Denver, Denver, CO (PI: Kimberly A. Driscoll, PhD); The Madison Clinic for Pediatric Diabetes and Department of Pediatrics, Division of Endocrinology, University of California San Francisco, San Francisco, CA (PI: Jenise C. Wong, MD, PhD); Seattle Children's Research Institute, Seattle, WA (PI: Joyce P. Yi-Frazier, PhD); Department of Pediatrics, Division of Endocrinology and Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH (PIs: Sarah D. Corathers, MD, Jessica C. Kichler, PhD, CDE); Department of Pediatrics, Division of Pediatric Endocrinology, Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL (PI: Jennifer L. Miller, MD); Cook Children's Medical Center, Fort Worth, TX (PI: Don P. Wilson, MD)

APPENDIX B

Table A1

Factor loadings of the 18 items of the PedsQL diabetes management summary score for adolescents and young adults with type 1 diabetes

A priori scales	Items	Factor structure					Perceived treatment adherence barriers
		1	2	3	4	5	
Treatment barriers	It hurts to get my finger pricked					0.89	
	It hurts to get insulin shots					0.80	
	I am embarrassed by my diabetes treatment	0.91					
	My parents and I argue about my diabetes care	—					
Treatment adherence	It is hard for me to do everything I need to do to care for my diabetes		0.54				0.79
	It is hard for me to take blood glucose tests		0.89				0.77
	It is hard for me to take insulin shots		0.78				0.78
	It is hard for me to exercise or do sports			0.56			0.57
	It is hard for me to keep track of carbohydrates		0.48				0.69
	It is hard for me to carry a fast-acting carbohydrate			0.62			0.62
	It is hard for me to snack when I go “low”			0.54			0.49
Worry	I worry about going “low”				0.77		
	I worry about going “high”				0.86		
	I worry about long-term complications from diabetes				0.70		
Communication	It is hard for me to tell the doctors and nurses how I feel			0.73			
	It is hard for me to ask the doctors and nurses questions			0.88			
	It is hard for me to explain my illness to other people	0.75					
	I am embarrassed about having diabetes	0.90					

Factor loadings less than 0.40 are not included. — indicates item did not load on a factor. Factor loadings in bold represent perceived treatment adherence barriers items. See text for details.

Hypothesized latent variables: Factor 1 = social embarrassment; Factors 2 and 3 = perceived treatment adherence barriers, except two items measuring health communication for Factor 3; Factor 4 = diabetes worry; Factor 5 = procedural pain.

Abbreviations:

AYA	adolescent and young adult
FDA	Food and Drug Administration
HbA1c	hemoglobin A1c (glycated hemoglobin)

HRQOL	health-related quality of life
PedsQL	pediatric quality of life inventory
PRO	patient-reported outcome

REFERENCES

1. Dabelea D, Mayer-Davis EJ, Saydah S, et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. *JAMA*. 2014;311:1778–1786. [PubMed: 24794371]
2. You WP, Henneberg M. Type 1 diabetes prevalence increasing globally and regionally: the role of natural selection and life expectancy at birth. *BMJ Open Diabetes Res Care*. 2016;4:e000161.
3. Dabelea D, Stafford JM, Mayer-Davis EJ, et al. Association of type 1 diabetes vs type 2 diabetes diagnosed during childhood and adolescence with complications during teenage years and young adulthood. *JAMA*. 2017;317:825–835. [PubMed: 28245334]
4. Lotstein DS, Seid M, Klingensmith G, et al. Transition from pediatric to adult care for youth diagnosed with type 1 diabetes in adolescence. *Pediatrics*. 2013;131:e1062–e1070. [PubMed: 23530167]
5. Eiser C, Varni JW. Health related quality of life and symptom reporting: similarities and differences between children and their parents. *Eur J Pediatr*. 2013;172:1299–1304. [PubMed: 23715654]
6. Varni JW, Limbers CA. The pediatric quality of life inventory: measuring pediatric health-related quality of life from the perspective of children and their parents. *Pediatr Clin N Am*. 2009;56:843–863.
7. FDA. Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Rockville, MD: Food and Drug Administration, U.S. Department of Health and Human Services; 2009.
8. Varni JW, Seid M, Rode CA. The PedsQL™: measurement model for the pediatric quality of life inventory. *Med Care*. 1999;37:126–139. [PubMed: 10024117]
9. World Health Organization. Constitution of the World Health Organization: Basic Document. Geneva, Switzerland: World Health Organization; 1948.
10. Varni JW, Burwinkle TM, Jacobs JR, Gottschalk M, Kaufman F, Jones KL. The PedsQL™ in type 1 and type 2 diabetes: reliability and validity of the pediatric quality of life inventory™ generic core scales and type 1 diabetes module. *Diabetes Care*. 2003;26:631–637. [PubMed: 12610013]
11. Fayers PM, Hand DJ. Factor analysis, causal indicators and quality of life. *Qual Life Res*. 1997;6:139–150. [PubMed: 9161114]
12. Varni JW, Curtis BH, Abetz LN, Lasch KE, Piau EC, Zeytoonjian AA. Content validity of the PedsQL™ 3.2 diabetes module in newly diagnosed patients with type 1 diabetes mellitus ages 8–45. *Qual Life Res*. 2013;22:2169–2181. [PubMed: 23269541]
13. Varni JW, Delamater AM, Hood KK, Raymond JK, Chang NT, Driscoll KA, et al. PedsQL 3.2 Diabetes Module for Children, Adolescents, and Young Adults: Reliability and Validity in Type 1 Diabetes. Submitted for publication; 2018.
14. Varni JW, Delamater AM, Hood KK, Raymond JK, Chang NT, Driscoll KA, et al. PedsQL 3.2 Diabetes Module for Children, Adolescents, and Young Adults: Reliability and Validity in Type 2 Diabetes. Submitted for publication; 2018.
15. Anderson BJ, Laffel LM, Domenger C, et al. Factors associated with diabetes-specific health-related quality of life in youth with type 1 diabetes: the global TEENs study. *Diabetes Care*. 2017;40:1002–1009. [PubMed: 28546221]
16. Lawrence JM, Yi-Frazier JP, Black MH, et al. Demographic and clinical correlates of diabetes-related quality of life among youth with type 1 diabetes. *J Pediatr*. 2012;161:201–207. [PubMed: 22361221]
17. Hilliard ME, Lawrence JM, Modi AC, et al. Identification of minimal clinically important difference scores of the PedsQL in children, adolescents, and young adults with type 1 and type 2 diabetes. *Diabetes Care*. 2013;36:1891–1897. [PubMed: 23340884]

18. Varni JW, Delamater AM, Hood KK, et al. Diabetes symptoms predictors of health-related quality of life in adolescents and young adults with type 1 or type 2 diabetes. *Qual Life Res.* 2018;10.1007/s11136-018-1884-6.
19. Varni JW, Shulman RJ, Self MM, et al. Patient health communication mediating effects between gastrointestinal symptoms and gastrointestinal worry in pediatric inflammatory bowel disease. *Inflamm Bowel Dis.* 2017;23:704–711. [PubMed: 28394807]
20. Varni JW, Shulman RJ, Self MM, et al. Perceived medication adherence barriers mediating effects between gastrointestinal symptoms and health-related quality of life in pediatric inflammatory bowel disease. *Qual Life Res.* 2018;27:195–204. [PubMed: 28887749]
21. Fairclough DL. *Design and Analysis of Quality of Life Studies in Clinical Trials: Interdisciplinary Statistics.* New York, NY: Chapman & Hall/CRC; 2002.
22. Varni JW, Seid M, Kurtin PS. PedsQL™ 4.0: reliability and validity of the pediatric quality of life inventory™ version 4.0 generic core scales in healthy and patient populations. *Med Care.* 2001;39:800–812. [PubMed: 11468499]
23. Varni JW, Limbers CA. The PedsQL™ 4.0 generic core scales young adult version: feasibility, reliability and validity in a university student population. *J Health Psychol.* 2009;14:611–622. [PubMed: 19383661]
24. Varni JW, Limbers CA, Burwinkle TM, Bryant WP, Wilson DP. The ePedsQL™ in type 1 and type 2 diabetes: feasibility, reliability and validity of the pediatric quality of life inventory™ internet administration. *Diabetes Care.* 2008;31:672–677. [PubMed: 18184893]
25. Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC growth charts for the United States: methods and development. *Vital Health Stat.* 2002; 11:1–190.
26. Cohen J *Statistical Power Analysis for the Behavioral Sciences.* 2nd ed. Hillsdale, NJ: Erlbaum; 1988.
27. Cohen J, Cohen P, West SG, Aiken LS. *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences.* 3rd ed. Mahwah, NJ: Erlbaum; 2003.
28. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol.* 1986;51:1173–1182. [PubMed: 3806354]
29. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods.* 2008;40:879–891. [PubMed: 18697684]
30. Sobel ME. Asymptotic confidence intervals for indirect effects in structural equation models. *Sociol Methodol.* 1982;13:290–312.
31. Costa PT, McCrae RR. Domains and facets: hierarchical personality assessment using the revised NEO personality inventory. *J Pers Assess.* 1995;64:21–50. [PubMed: 16367732]
32. Floyd FJ, Widaman KF. Factor analysis in the development and refinement of clinical assessment instruments. *Psychol Assess.* 1995;7: 286–299.
33. Cronbach LJ. Coefficient alpha and the internal structure of tests. *Psychometrika.* 1951;16:297–334.
34. Nunnally JC, Bernstein IR. *Psychometric Theory.* 3rd ed. New York, NY: McGraw-Hill; 1994.
35. Hayes AF, Rockwood NJ. Regression-based statistical mediation and moderation analysis in clinical research: observations, recommendations, and implementation. *Behav Res Ther.* 2017;98:39–57. [PubMed: 27865431]
36. Hayes AF. *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach.* New York, NY: Guilford; 2013.
37. Street RL. How clinician-patient communication contributes to health improvement: modeling pathways from talk to outcome. *Patient Educ Couns.* 2013;92:286–291. [PubMed: 23746769]
38. Grant RW, Altschuler A, Uratsu CS, et al. Primary care visit preparation and communication for patients with poorly controlled diabetes: a qualitative study of patients and physicians. *Prim Care Diabetes.* 2017; 11:148–153. [PubMed: 27916628]
39. Schabert J, Browne JL, Mosely K, Speight J. Social stigma in diabetes: a framework to understand a growing problem for an increasing epidemic. *Patient.* 2013;6:1–10. [PubMed: 23322536]

40. Vaala SE, Lee JM, Hood KK, Mulvaney SA. Sharing and helping: predictors of adolescents' willingness to share diabetes personal health information with peers. *J Am Med Inform Assoc.* 2018;25:135–141. [PubMed: 28575462]
41. Holmström MR, Häggström M, Audulv A, Juneag L, Coyne I, Söderberg S. To integrate and manage diabetes in school: youth's experiences of living with Type 1 diabetes in relation to school – a qualitative study. *Int Diabetes Nurs.* 2017;14:46–51.
42. Floyd BD, Block JM, Buckingham BB, et al. Stabilization of glycemic control and improved quality of life using a shared medical appointment model in adolescents with type 1 diabetes in suboptimal control. *Pediatr Diabetes.* 2017;18:204–212. [PubMed: 26919322]

TABLE 1

Demographic and clinical characteristics of participants

Characteristics	<i>n</i> (%) or mean (SD)
Total number	418
Age	16.3 (2.2)
Gender	
Male	210 (50.2%)
Female	208 (49.8%)
Race/ethnicity	
White non-Hispanic	265 (63.7%)
Hispanic	52 (12.5%)
Black non-Hispanic	61 (14.7%)
Asian/Pacific islander	5 (1.2%)
Other	33 (7.9%)
Diabetes duration (y)	6.3 (4.1)
HbA1c (%)	8.9 (2.1)
BMI (kg/m ²)	24.1 (6.6)

Abbreviation: BMI, body mass index. Subgroup sample sizes may differ given missing data.

TABLE 2

PedsQL diabetes symptoms summary score, diabetes management summary score and facets bivariate intercorrelations with the generic core scales total scale score in adolescents and young adults with type 1 diabetes

Diabetes symptoms and management summary scores and facets	Items	α	Mean	SD	r^{*a}	r^{*b}	r^{*c}
Diabetes symptoms summary score	15	0.89	64.90	15.95	–	–	0.67
Diabetes management summary score	18	0.89	78.89	15.07	0.62	–	0.63
Perceived treatment adherence barriers	7	0.80	85.21	13.89	0.51	0.82	0.56
Procedural pain	2	0.78	84.06	19.19	0.30	0.46	0.34
Social embarrassment	3	0.83	84.77	18.51	0.33	0.64	0.39
Diabetes worry	3	0.69	67.91	19.96	0.34	0.46	0.28
Health communication	2	0.87	84.86	20.54	0.45	0.63	0.49
Generic core total scale score	23	0.92	82.33	13.53	–	–	–

α , Cronbach's alpha internal consistency reliability; r , Pearson product-moment correlation coefficient; dash line, not applicable. Effect sizes for Pearson r designated as small (0.10), medium (0.30), and large (0.50) in magnitude. Lower scores demonstrate worse symptoms and more problems.

* All P s < 0.001.

^a Bivariate correlations with the diabetes symptoms summary score.

^b Bivariate correlations with the diabetes management summary score.

^c Bivariate correlations with the generic core scales total scale score.