

Good Metabolic Control Is Associated With Better Quality of Life in 2,101 Adolescents With Type 1 Diabetes

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Patients from ethnic minorities had poorer scores for impact ($P < 0.0001$), worries ($P < 0.05$), and health perception ($P < 0.01$). There was no correlation between adolescent and parent or between adolescent and professional scores.

CONCLUSIONS— In a multiple regression model, lower HbA_{1c} was significantly associated with better adolescent-rated QOL on all four subscales and with lower perceived family burden as assessed by parents and health professionals.

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OBJECTIVE— It is unclear whether the demands of good metabolic control or the consequences of poor control have a greater influence on quality of life (QOL) for adolescents with diabetes. This study aimed to assess these relations in a large international cohort of adolescents with diabetes and their families.

RESEARCH DESIGN AND METHODS— The study involved 2,101 adolescents, aged 10–18 years, from 21 centers in 17 countries in Europe, Japan, and North America. Clinical and demographic data were collected from March through August 1998. HbA_{1c} was analyzed centrally (normal range 4.4–6.3%; mean 5.4%). Adolescent QOL was assessed by a previously developed Diabetes Quality of Life (DQOL) questionnaire for adolescents, measuring the impact of diabetes, worries about diabetes, satisfaction with life, and health perception. Parents and health professionals assessed family burden using newly constructed questionnaires.

RESULTS— Mean HbA_{1c} was 8.7% (range 4.8–17.4). Lower HbA_{1c} was associated with lower impact ($P < 0.0001$), fewer worries ($P < 0.05$), greater satisfaction ($P < 0.0001$), and better health perception ($P < 0.0001$) for adolescents. Girls showed increased worries ($P < 0.01$), less satisfaction, and poorer health perception ($P < 0.01$) earlier than boys. Parent and health professional perceptions of burden decreased with age of adolescent ($P < 0.0001$).

The main aims of diabetes care in children and adolescents are to achieve optimal glycemic control (1–6), normal psychosocial development, and support for the young person and family in developing strategies to cope with a lifetime of diabetes. A major challenge is to maximize quality of life (QOL) for the adolescent in the context of effective therapeutic intervention (7,8).

The relation, however, between QOL and psychosocial issues, diabetes treatment regimens, and metabolic control in adolescence is controversial (9–14). Some studies suggest a link between QOL and metabolic control (11,12), whereas others find no association (9,13,14). Furthermore, both parents and health professionals make assumptions about adolescent QOL in the context of diabetes. These assumptions may play a major role in diabetes management (12). For other medical conditions, there is evidence that the views of adults and children with illness are discordant (15,16). It is important, therefore, to understand whether such discrepancies exist in diabetes. Sex differences have been noted in the clinical context of diabetes. Girls enter puberty at an earlier age than boys and have more unsatisfactory blood glucose control for a number of reasons (3). These may involve decreasing adherence to different aspects of the treatment regimen

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The parent and health professional questionnaires used in this study are available from H.H.

Abbreviations: DQOL, Diabetes Quality of Life; QOL, quality of life.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—Adolescent demographic characteristics, clinical profile, and treatment regimen

| | Boys | Girls | P |
|---|-------------|-------------|----------|
| n | 1,085 | 1,016 | |
| Age (years) | 13.8 ± 2.1 | 13.8 ± 2.1 | 0.86* |
| Diabetes duration (years) | 5.1 ± 3.8 | 5.4 ± 3.8 | 0.06† |
| BMI (kg/m ²) | 20.8 ± 3.2 | 21.8 ± 3.6 | <0.0001‡ |
| HbA _{1c} (%) | 8.6 ± 1.6 | 9.0 ± 1.7 | <0.01‡ |
| Daily insulin injections | | | |
| 1 | 8 (1) | 10 (1) | |
| 2 | 472 (44) | 380 (37) | <0.05 |
| 3 | 295 (27) | 287 (28) | |
| ≥4 | 307 (28) | 339 (33) | |
| Premixed insulin | 445 (41) | 407 (40) | 0.66 |
| Insulin dose (units · kg ⁻¹ · day ⁻¹) | 0.94 ± 0.32 | 1.01 ± 0.32 | <0.0001‡ |
| Severe hypoglycemic events (incidence per 100 patient years) | 15.5 | 15.7 | 0.90‡ |

Data are means ± SD or n (%), unless otherwise indicated. *Adjusted for center; †adjusted for center and age; ‡adjusted for center, age, and duration of diabetes.

(11,13) and decreasing insulin sensitivity of peripheral tissues (17). These changes in metabolic control may affect QOL differently in male and female patients.

This study addressed the relations between QOL and HbA_{1c}, age, sex, duration of diabetes, BMI, insulin regimen, severe hypoglycemia, and family structure in a large international population of adolescents with diabetes. Furthermore, the study aimed to compare adolescent QOL with parent and health professional perceptions of family burden related to diabetes.

RESEARCH DESIGN AND METHODS

The study involved 21 centers in 17 countries in Europe, Japan, and North America. Between March and August 1998, adolescent patients with type 1 diabetes who were born between 1980 and 1987 (i.e., aged 10–18 years) at each study center were invited to participate; 2,101 patients consented, and 2,077 had HbA_{1c} measurements taken. Samples and information from 79% of the patients registered at the centers were obtained (Table 1). Written informed consent was obtained in advance from patients and parents according to national ethical regulations.

Differences in emphasis on particular aspects of QOL across countries have been reported (18). Therefore, center was included as a factor in the statistical model, implying that the effects found for the variables of sex, age, and metabolic control are evaluated within centers, but

combining the information from all centers. The center effect will be analyzed separately in future papers.

QOL questionnaire for adolescents with diabetes

QOL in adolescents was assessed using the adolescent version of the Diabetes Quality of Life (DQOL) questionnaire developed by Ingersoll and Marrero (9), which ensured that a theoretical rationale was provided for how the items were selected. The questionnaire contains 52 items in four sections: impact of diabetes, worries about diabetes, satisfaction with life, and health perception.

Questions were scored from 1 to 5, except health perception, which was scored from 1 to 4; a lower score indicates better QOL. In the original Ingersoll and Marrero instrument (9), lower scores on satisfaction subscale indicated poorer QOL. For ease of comparison across subscales, we have scored all scales in the same direction.

Parent and health professional questionnaires

To evaluate perceptions of the family burden related to diabetes among parents and health professionals, two short questionnaires were constructed for this study. We assessed family burden as one aspect of QOL in the family setting, which is of particular concern to health professionals. For each adolescent, one parent and one health professional completed a five-item questionnaire about their per-

ceptions of the family burden related to the adolescent's diabetes. Questions were scored from 1 to 5; a lower score indicates less burden.

Forward and backward translation of questionnaires

Translation and cross-cultural adaptation of the questionnaires to each of the 14 languages in the study was performed by a forward translation from English followed by an independent backward translation into English. Subsequently, the translation was tested by a lay panel before final endorsement by the originators.

Completion of the questionnaires

Patients and parents completed questionnaires confidentially and returned them in sealed envelopes during a routine clinic visit. Staff members completed questionnaires independently. All forms were forwarded to the coordinating center and were received within 2–3 weeks of blood collection for HbA_{1c}.

Study procedure

Questionnaires. Questionnaire completion rates were very high for adolescents, parents, and health professionals (93, 89, and 94%, respectively), as were item completion rates for all three groups (98.6–99.8%). Cronbach's α coefficient values for the questionnaires were: adolescent DQOL impact 0.79, worries 0.84, and satisfaction 0.92; parents 0.80; and health professionals 0.86, indicating good internal validity and consistency of the multiple-item instruments. Values of 0.8–0.9 are preferable (19).

Clinical data. Age, sex, height, weight, age at diagnosis, number of insulin injections, use of premixed insulin, total daily insulin dose, number of serious hypoglycemic incidents (i.e., convulsions or unconsciousness) in the last 3 months, family structure, and ethnic status were recorded. Ethnic minority was defined as a minority group differentiated from the main population of the community by racial or cultural background. Using this classification, ethnic minority groups in Europe and Japan comprised ~10% of the population. Ethnic status was not obtained in Canada ($n = 224$) because of the multicultural nature of the population. Family structure was classified by whether one or two parents lived at home.

Blood samples. A blood sample was taken from each patient and sent to the

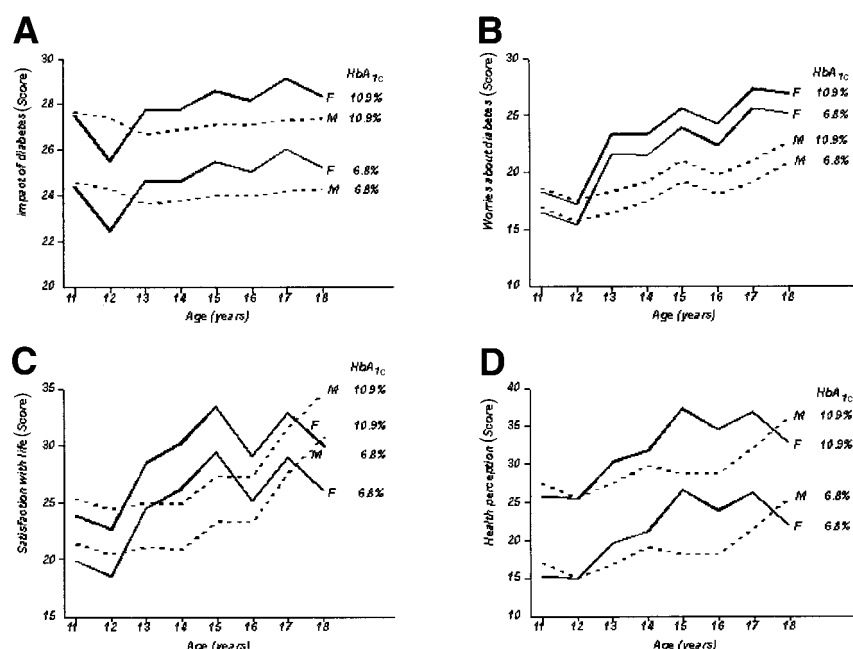


Figure 1—The association of HbA_{1c} (6.8 or 10.9%) and sex on (A) the impact of diabetes with the age of patient (lower score = less impact), (B) worries score by age, (C) satisfaction score by age, and (D) health perception score by age.

Steno Diabetes Center (Gentofte, Denmark) for determination of HbA_{1c}. Normal mean HbA_{1c} is 5.4% (range 4.4–6.3). The intra- and interassay variability (SD) for HbA_{1c} was 0.06 and 0.15, respectively. Details of this assay and transport of specimens have been published previously (3). Patients, parents, and health professionals were blinded to the HbA_{1c} result.

Statistical analysis

Summary statistics were expressed as the means \pm SD or the means \pm SE. Comparisons were based on normal distribution methods. Multiple regression analysis was performed to explore the relation between QOL scores and HbA_{1c}, sex, age, and duration of diabetes. In addition, the relation between parent- and health professional-rated family burden and HbA_{1c}, sex, and age was analyzed.

The three main hypotheses that were evaluated were: 1) lower HbA_{1c} is associated with better QOL in adolescents and less perceived burden as assessed by parents and health professionals; 2) there are significant sex differences in adolescent QOL (specifically, girls have poorer self-rated QOL than boys); and 3) parent and health professional perceptions of burden offer unique complementary information to that derived from adolescent self-rated

QOL, as reflected by nonsignificant correlation of scores.

Primary QOL end points were summary scores for the four subscales of impact, worries, satisfaction, and health perception as identified by Ingersoll and Marrero (9). Primary parent and health professional end points were summary scores for family burden. All QOL scores were linearly transformed so that the best and worst possible scores were 0 and 100, respectively. To illustrate the spread of the scores, the mean and SD were calculated.

The clinical parameters and HbA_{1c} were tested for having a potential effect on responses in a multiple regression model. Center, sex, age, and duration of diabetes were included in analyses to control for confounding effects; age was treated as a class variable, allowed to have a different effect for each sex, and duration of diabetes was treated as a regression variable. The total effect of the explanatory variables is described by the proportion of variance they explain (R^2). To illustrate the effect of sex, age, and HbA_{1c} in the model, the predicted course for combinations of sex and HbA_{1c} (6.8 and 10.9%, respectively, in the population) are shown as a function of age. To fix the level of other factors, age at diagnosis is chosen as 5 years, and the center average is used.

Other choices would change only the level of the curve. Age 10 years is not shown because of low patient numbers.

Pearson's χ^2 test was applied to test for sex differences in both the number of daily injections and the use of premixed insulin. All statistical analyses were performed using SAS version 6.12 with a UNIX platform on a DEC axp 2100 5/250 computer.

RESULTS—The HbA_{1c} (mean \pm SD) was $8.7 \pm 1.7\%$ (range 4.8–17.4) and was 0.22% (95% CI 0.08–0.35) higher in girls ($P < 0.01$). HbA_{1c} increased with age ($P < 0.05$) and by 0.07% (CI 0.05–0.09) per year of diabetes ($P < 0.0001$) (Table 1). The overall incidence of severe hypoglycemic episodes was 15.6 per 100 patient years. The insulin dose (in units per kilogram body weight) was 0.07 (CI 0.04–0.09) higher in girls ($P < 0.0001$), and it increased with age ($P < 0.0001$) and by 0.02 (0.02–0.03) per year of diabetes ($P < 0.0001$). BMI was 1.02 kg/m² (CI 0.76–1.27) greater in girls than in boys ($P < 0.0001$); it increased with age ($P < 0.0001$) and by 0.04 kg/m² (0.002–0.074) per year of duration ($P < 0.05$).

Figure 1A, B, C, and D show the QOL scores as function of age and sex and high or low HbA_{1c}, as perceived by adolescents. Impact of diabetes (Fig. 1A) was similar for boys and girls, with no effect of age or duration of diabetes on the scoring. Impact was significantly ($P < 0.001$) associated with HbA_{1c}, with the lowest scores (least impact) occurring with the lowest HbA_{1c} value. There was a statistically significant increase in worries ($P < 0.01$) by age for girls compared with boys (Fig. 1B). Before 12 years there was no sex difference, whereas after 12 years girls were significantly more worried. The mean score was 19 (Table 2), indicating that adolescents perceive themselves to be only slightly worried, despite having a chronic disease. Lower HbA_{1c} was associated with fewer worries ($P < 0.05$). Likewise, age had a marked effect on satisfaction (Fig. 1C). It deteriorated earlier in girls (at ~ 12 years) than boys (16 years). Variation in satisfaction scores across centers was extremely large, and this was the reason for the R^2 value being 0.31 (Table 2). Higher HbA_{1c} was associated with significantly ($P < 0.001$) less satisfaction. Girls' health perceptions were significantly ($P < 0.01$) poorer than that of boys (Fig. 1D), with increased

Table 2—Population range of adolescent QOL scores, parent and health professional ratings of family burden, and the impact of the variables, age, sex, diabetes duration, center, and HbA_{1c} on the variation in score (R²)

| QOL category and respondent | Items | Respondents | Score | Effect of HbA _{1c} (regression coefficients) | Variance* |
|-----------------------------|-------|-------------|---------|--|-----------|
| Adolescent | | | | | |
| Impact | 23 | 1,945 | 25 ± 11 | 0.76 (0.16) | 0.06 |
| Worries | 11 | 1,935 | 19 ± 16 | 0.43 (0.22) | 0.16 |
| Satisfaction | 17 | 1,919 | 25 ± 18 | 0.97 (0.23) | 0.31 |
| Health perception | 1 | 1,895 | 33 ± 25 | 3.47 (0.34) | 0.18 |
| Parent | | | | | |
| Family burden | 5 | 1,864 | 38 ± 21 | 1.20 (0.29) | 0.17 |
| Health professional | | | | | |
| Family burden | 5 | 1,983 | 38 ± 21 | 1.86 (0.25) | 0.33 |

All scores coded so that the range is 0–100, with low values meaning good QOL. The regression coefficients express the change in score for a 1% change in HbA_{1c}. *Proportion of variance (R²) due to the explanatory factors, which was calculated as $1 - \text{SD}^2(\text{residual})/\text{SD}^2(\text{total})$. Data are *n* and means ± SD.

scores at ~12 years old. The effect of HbA_{1c} was highly significant for both sexes ($P < 0.001$), indicating that poor control was associated with significantly ($P < 0.001$) poorer health perception.

Table 2 shows the population range of QOL scores for adolescents and family burden as assessed by parents and health professionals. Adolescent answers tended toward the more positive part of the scoring system for impact, worries, and satisfaction, whereas parent and health professional answers tended to span the whole scale. There was little or no correlation between adolescent self-reported QOL scores and either parent or health professional perceptions of family burden (correlations ranged from 0.1 to 0.32 and from –0.001 to 0.17 for parents and health professionals, respectively). Equally, parent and professional ratings were only modestly correlated (correlation coefficient 0.36).

The joint effect of variables (age, sex, diabetes duration, center, and HbA_{1c}) influencing the QOL scores (R²) was evaluated by multiple regression analysis. Up to 33% of the variation in QOL scores could be explained in this way (Table 2). Parent assessment of family burden was adjusted for patient sex, duration of diabetes, and center and showed that burden decreased with adolescent age. Change in burden with age was similar across the sexes, but parents of boys reported higher burden over the whole age range. The effect of HbA_{1c} was highly significant ($P < 0.0001$). Thus, families of children with good metabolic control (i.e., low HbA_{1c} values) reported lower burden than those

with poor control. As with parents, the health care providers perceived family burden to decrease with adolescent age. Contrasting with parents, health professionals considered family burden to be the same for girls and boys, but the effect of HbA_{1c} remained very significant, higher HbA_{1c} associated with greater burden. The center variation was extremely significant ($P < 0.001$); hence R² was 0.33 (Table 2).

Hypoglycemia and QOL

Adolescents having at least one severe hypoglycemic episode in the previous 3 months were more worried than those without, with an increase in the score for worries (4.2 [CI 0.3–8.2]; $P < 0.05$). Hypoglycemia was also related to greater family burden as perceived by health professionals, with an increase in family burden score (6.7 [2.1–11.2]; $P < 0.01$). Parents' assessments did not show such an increase.

Insulin regimen and QOL

There was no significant relation between the number of insulin injections per day (or use of premixed insulin) and adolescent QOL or with family burden as assessed by parents and health professionals, even after adjustment for the effects of center, sex, age, and duration of diabetes. Higher daily insulin doses were associated with poorer health perception (score change 0.6 per 0.1 unit/kg [CI 0.2–1.0]; $P < 0.001$), greater health professional-rated family burden (score change 3.7 per 0.1 unit/kg [2.0–5.5]; $P < 0.0001$), and, to a lesser extent, impact of diabetes (score

change 0.16 per 0.1 unit/kg [0.001–0.32]; $P < 0.05$).

BMI and QOL

Greater BMI was associated with poorer adolescent-rated QOL, including lower satisfaction (score change 0.24 per kg/m² [CI 0.00–0.48]; $P < 0.05$), and worse health perception (score change 0.80 per kg/m² [0.45–1.16]; $P < 0.0001$). It was not associated with impact of diabetes, worries, or family burden as described by parent or health professional.

Family structure, ethnicity, and QOL

Adolescents having two parents at home ($n = 1,530$) had significantly lower HbA_{1c} values ($8.6 \pm 1.6\%$) compared with single-parent families ($9.0 \pm 1.8\%$; $n = 298$; $P < 0.001$). Health professional-rated family burden was significantly lower in two-parent than single-parent families (mean score 38 ± 21 vs. 41 ± 22 ; $P < 0.01$). Family structure had no significant effect on either parent scores for burden or adolescent scores for impact of diabetes, worries, satisfaction, or health perception.

In the ethnic minority group ($n = 161$), HbA_{1c} levels were significantly higher than in the nonethnic group (9.2 vs. 8.7% ; mean difference in HbA_{1c} 0.49 [CI 0.21–0.78]; $P < 0.001$). Adolescent QOL scores were markedly poorer for impact of diabetes (mean increase in score 4.2 [2.2–6.2]; $P < 0.0001$), worries (increase in score 3.3 [0.4–6.2]; $P < 0.05$), and health perception (increase in score 6.0 [2–11]; $P < 0.01$), but not satisfaction, nor were they poorer for family burden as perceived by parents or health professionals.

CONCLUSIONS— This is the first large international multilanguage study evaluating the relation between metabolic control and QOL in adolescents with diabetes. Although the importance of QOL assessment in adolescents with type 1 diabetes has been highlighted (10), studies on the relation between metabolic control and QOL have been small and inconclusive. This study suggests that better metabolic control is associated with a better QOL for adolescents and with a lesser perceived burden by parents and health professionals.

Few adolescents rated the disease impact as major. Moreover, a lower impact score was significantly associated with

better HbA_{1c}. More worries were evident with increasing age, and more so in girls. This may reflect the higher incidence of psychological disturbance widely reported in population studies of adolescent girls (20,21). There may be cultural differences to explain these findings (18), and further studies are recommended to evaluate the significance of these differences. The relation between HbA_{1c} and worry was just significant. As metabolic control deteriorated during adolescence (3), so did worry, particularly in girls. It was not possible from the information here to ascertain whether lower levels of worry in boys reflect more or less appropriate worrying. As yet, there is insufficient published information about the DQOL to anchor particular score levels on the worry subscale to concepts such as excessive worry about diabetes or insufficient worry/attention to the necessary aspects of good clinical management of diabetes treatment. The relation of disease-related worry to more general psychological well-being (e.g., anxiety) should be evaluated directly in a separate study.

The scores for satisfaction followed the same pattern as worries, showing less satisfaction with increasing age, with the trend again more pronounced in girls. The highly significant center variation for satisfaction may reflect cultural, socioeconomic, or treatment differences across centers (18,22). This will be further analyzed in a separate report.

Teenage girls had poorer health perception and more difficulties with diabetes control than boys. Girls had higher BMI and significantly poorer overall QOL at an earlier age than boys. These findings may be associated with earlier hormonal and pubertal changes in teenage girls (17,23–25), and with their relative lack of physical activity and abnormal eating behaviors (26,27).

The lack of correlation between adolescent QOL and burden perceived by parents and health professionals may reflect significant differences in perceptions of diabetes impact between adolescents and adults. Adolescents expressed less difficulty with diabetes than both adult groups. Also, patient and health professional ratings were only modestly correlated. These findings suggest the importance of assessing the perceptions of all three groups in the adolescent diabetes management triad. In contrast to the

increasing worry and poorer satisfaction described by adolescents, parental assessment of family burden decreased with adolescent age, with parents of girls reporting the lowest burden. Because girls enter puberty earlier than boys, with an earlier transfer of responsibility for self-care management from parent to child, the parent's burden is perhaps correspondingly decreased. By contrast, health professional scores for family burden showed no sex difference. For both parent and health professional ratings, higher HbA_{1c} levels were associated with greater family burden. It may be that knowledge of the consequences of poor control results in increased parental and health professional concern.

It is surprising that severe hypoglycemic episodes were not related to family burden. However, because the number of episodes reported was low (2), it may be that for most parents, the absence of episodes reduces worry.

There was no significant relation between insulin regimen and adolescent QOL or family burden. Thus, whereas 59% of the adolescents received three or more injections daily, this regimen was not related adversely to QOL. Some professionals may perceive multiple injection treatment as being more intrusive and distressing than a twice-daily regimen (28). This study provided no evidence for a difference across regimens. Also surprising was the lack of association between the use of premixed insulin and better QOL.

Despite a statistically significant association between higher BMI and poorer QOL, large changes in BMI resulted in only small changes in adolescent QOL. Furthermore, neither parent nor health professional ratings of family burden were associated with BMI scores.

Adolescents from single-parent families and ethnic minority groups both showed higher HbA_{1c}, as reported elsewhere (11,13). Moreover, adolescents from ethnic minority groups had markedly poorer QOL across several dimensions. These findings highlight the importance of meeting the needs of these particularly vulnerable adolescents. Communication problems, poor understanding of the social regulations, and differences in culture and diet result in increased time expenditure and specific requirements, including meetings with municipalities/social security offices regarding support arrangements.

In conclusion, we have found that HbA_{1c} is significantly associated with QOL in adolescent diabetes; that sex differences exist, with girls reporting greater difficulties; and that perceptions of family burden by parents and health professionals are not correlated with patient-rated QOL but rather provide complementary and relevant information.

The most important finding is that lower HbA_{1c} is associated with better QOL. Although this study cannot determine a cause-and-effect relation, efforts to achieve optimal metabolic control now appear justified on QOL as well as clinical grounds (1). The size and international nature of the study adds credence to this assertion. Because individuals with a higher QOL may be better equipped physically and psychologically to deal with the burdens of diabetes management, better QOL may facilitate better metabolic control through improved self-care as part of a positive circle. Therefore, we propose that QOL assessment be an integral part of clinical management in adolescents with diabetes, and we suggest yearly examination on a routine basis.

We suggest that specific attention should be given to the management of girls, single-parent families, and ethnic minorities, because QOL evaluations indicate particular problems in these groups. Assessments by parents and health professionals are recommended for use in diabetes care, because these appear to be unique end points that may influence treatment outcome independent of patient QOL.

Future studies are warranted to evaluate cross-cultural differences in diabetes-related QOL and longitudinal relations between QOL and clinical outcomes. This study provides a useful basis for such investigations.

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