

Health Related Quality of Life in Children and Adolescents with Type 1 Diabetes Mellitus in Spain: Results from the CRYSTAL Study

Luis Alberto Vázquez,¹ Juan Pedro López-Siguero,² Renata Villoro,³ Dingfeng Jiang,⁴ Maria Merino,³ Jesus Reviriego,¹ Magaly Perez-Nieves⁴

¹Eli Lilly and Company, Madrid, Spain; ²Hospital Universitario Carlos Haya, Málaga, Spain; ³Instituto Max Weber, Madrid, Spain; ⁴Eli Lilly and Company, Indianapolis, IN USA

ABSTRACT

Background: CRYSTAL (Costs and Health Related quality of Life Study for Type 1 diabetes mellitus paediatric patients in Spain) is an observational study conducted in 2014 on a representative sample of 275 patients aged 0-17 years with Type 1 Diabetes Mellitus (T1DM) in Spain. The study collects diabetes specific health related quality of life (HRQoL) using the Diabetes Module of the Paediatric Quality of Life Inventory™ (PedsQL). This scale has been identified to be one of the best scales to describe HRQoL in paediatric population.

Objective and hypotheses: The objective was to describe the HRQoL for paediatric patients with T1DM in Spain and to compare results by HbA1c level.

Method: PedsQL is modular instrument composed of 28 items comprising 5 dimensions (diabetes, treatment I, treatment II, worry, and communication) graded on a scale from 0 to 100, where higher scores indicate higher HRQoL. The questionnaire was self-administrated on patients 8-17 and proxy completed by the caregiver for children 2-7. The overall and itemized mean scores by age ranges were calculated. Results by HbA1c level (HbA1c <7.5% vs HbA1c ≥ 7.5%) were analyzed by Mann-Whitney U test.

Results: Valid results were obtained for 268 patients. The proxy results indicated an overall HRQoL of 65.5 for patients with HbA1c ≥ 7.5% and 70.6 for those with HbA1c < 7.5% in patients aged 2-7. For patients 8-17, the self-report indicated an overall HRQoL of 72.0 for patients with HbA1c ≥ 7.5% and 73.2 for those with HbA1c < 7.5%. Results by age range were consistently lower among patients with HbA1c ≥ 7.5%, although differences by HbA1c level were not statistically significant. The "Worry" dimension had the highest negative score on QoL across all age ranges.

Conclusion: CRYSTAL is the first study to evaluate HRQoL in a representative sample of children and adolescents with T1DM in Spain. Interventions are needed to include HRQoL measures as part of the regular practice while managing diabetes for better assessment of diabetes care.

INTRODUCTION

- Recent incidence rates for type 1 diabetes in the Spanish paediatric population are considered high or very high depending on the regions and they are even increasing in some areas.¹
- Assessing quality of life in clinical practice in chronic illnesses, including diabetes, has been recognized as an important way to improve diabetes care in paediatric population.
- Previous research has demonstrated that better glycaemic control (lower HbA1c) is associated with higher quality of life.²
- Routine HRQoL assessment is likely to facilitate detection and discussion of psychological issues related to diabetes.
- Sharing the information regarding HRQoL as part of ongoing clinical care is crucial and may help to tailor care to the needs of the children and adolescents with diabetes.
- Structured and current information about quality of life in paediatric population with type 1 diabetes in Spain is very limited.³

Costs and Health Related quality of Life Study for Type 1 Diabetes Mellitus in Paediatric Patients in Spain (CRYSTAL)

- This is a non-interventional, cross sectional observational study conducted in 2014 on a representative sample of 275 paediatric patients aged 0-17 years with Type 1 Diabetes Mellitus (T1DM) in Spain.
- The study was designed to estimate total annual costs (direct and indirect) and describe health related quality of life and adherence behaviors in paediatric patients with T1DM in Spain.

Objective

- The objective of this investigation was to describe the HRQoL for paediatric patients with T1DM in Spain and to compare results by HbA1c level.

Exclusion Criteria:

- Patients diagnosed with any other type of diabetes (i.e. latent autoimmune diabetes in adults "LADA", monogenic forms of DM, gestational diabetes, Type 2 diabetes, etc.).
- Are considered to be "inpatient."
- Patient or caregiver has a limitation (i.e. not able to understand local language or any cognitive impairment) that in opinion of the investigator, could affect the reliability of the responses or will not be able to complete the questionnaires.
- Patient is participating in any clinical trial.

METHODOLOGY

Patient Population

- Inclusion Criteria:
 - Include patients with T1DM (World Health Organization [WHO] classification).
 - Include patients less than 18 years of age.
 - Have been diagnosed with T1DM for at least 12 months.
 - Have given informed consent to release information from caregivers and assent from patients to participate in the study in accordance with local regulations.

Figure 1. Sites Distribution



- H. U. 12 de Octubre, Madrid.
- H. U. Fundación Alcorcón, Madrid.
- H. U. Vall d'Hebron, Barcelona.
- H. U. Sant Joan, Reus.
- H. U. de Cruces, Barakaldo.
- H. U. i Politécnica la Fe, Valencia.
- H. General Nuestra Señora del Prado, Talavera de la Reina.
- H. U. Virgen del Rocío, Sevilla.
- H. Comarcal de la Axarquía, Vélez-Málaga.
- H. Clínico U. San Cecilio, Granada.
- C. H. U. Insular Materno Infantil, Las Palmas de Gran Canaria.
- H. U. A Coruña, A Coruña.

The Autonomous Communities of Spain were then grouped into 8 regions based on population size, history and culture. The regions are the following:

- Madrid
- Cataluña
- Northwest (Galicia, Asturias, Cantabria, Castilla y León)
- North (Aragón, Navarra, La Rioja, País Vasco)
- East (Valencia, Baleares)
- Center (Castilla la Mancha, Extremadura)
- South (Andalucía, Murcia, Ceuta, Melilla)
- Canary Islands

The 12 centers were distributed across the 8 regions following the size of centers by region. Patients were distributed across all sites keeping the age distribution. Patients were included as they came in and meet inclusion/exclusion criteria. In this way T1DM paediatric population was sampled representatively as it is being treated in the country.

Table 1. PedsQL – Diabetes Module

Variable	Description ^{4,5,6,7}																		
Purpose	The PedsQL 3.0 Type 1 Diabetes Module was developed to measure disease specific health related quality of life for patients with type 1 diabetes.																		
No. of Items	Composed of 28 items comprising 5 dimensions																		
Dimensions	Diabetes (DM) symptoms (11 items), treatment 1 or Tx barriers (4 items), treatment 2 or Tx adherence (7 items), worry (3 items), and communication (3 items)																		
Recall Period	7 days																		
Rating and Interpretation	5-point liker scale from 0 (Never) to 4 (Almost always). Scores are converted from 0 to 100, where higher scores indicate lower problems and better HRQoL.																		
Administration	The study used proxy by caregivers for ages 2 to 7 and direct patient self-report on patients ages 8 to 18. No instrument is available for ages less than 2.																		
Validation	Only empirically validated paediatric instrument with item and scale construct consistency and both child and parent proxy reports across a broad age range. Linguistically validated translations for Spanish speaking population in Spain. Instrument has been identified as one of the best instruments to measure HRQoL in paediatric population with Type 1 Diabetes. ⁸																		
Example	<p><i>In the past 7 days, how much of a problem has this been for you ...</i></p> <p>TREATMENT - I (problems with...)</p> <table border="1"> <thead> <tr> <th></th> <th>Never</th> <th>Almost Never</th> <th>Sometimes</th> <th>Often</th> <th>Almost Always</th> </tr> </thead> <tbody> <tr> <td>1. It hurts to get my finger pricked</td> <td>0</td> <td>1</td> <td>2</td> <td>3</td> <td>4</td> </tr> <tr> <td>2. It hurts to get insulin shots</td> <td>0</td> <td>1</td> <td>2</td> <td>3</td> <td>4</td> </tr> </tbody> </table> <p>Example</p>		Never	Almost Never	Sometimes	Often	Almost Always	1. It hurts to get my finger pricked	0	1	2	3	4	2. It hurts to get insulin shots	0	1	2	3	4
	Never	Almost Never	Sometimes	Often	Almost Always														
1. It hurts to get my finger pricked	0	1	2	3	4														
2. It hurts to get insulin shots	0	1	2	3	4														

- HRQoL scores (mean and standard deviation) were calculated for each dimension as well as the overall score.
- Differences in scores by HbA1c level were statistically analyzed, comparing patients with adequate glycaemic control (HbA1c <7.5%) vs those with inadequate control (HbA1c ≥ 7.5%), using the Mann-Whitney U test.

Acknowledgements:

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RESULTS

Table 2. Patient Characteristics

Variable*	N**	% or Mean (95% CI)
Age (years)	268	11.02 (10.57 - 11.48)
Gender		
Female	127	47.4%
Male	141	52.6%
Time from Diagnosis (Years)	268	4.98 (4.59 - 5.36)
Puberty status *		
No (Pre-pubertal)	113	42.3%
Yes (Post-pubertal)	154	57.7%
Pump Usage (%)*	28 (out of 267)	10.5%
CGMS Usage (%)*	27 (out of 262)	10.3%
HbA1c level		
<7.5%	156	58.2%
≥7.5 - <9%	93	34.7%
≥9%	19	7.1%
HbA1c (%)	268	7.43 (7.31 - 7.54)
Center size *		
Small size	36	13.4%
Medium size	71	26.5%
Large size	161	60.1%

Abbreviations: Bca = bias-corrected and accelerated bootstrap; CI = confidence interval; Max = maximum; Min = minimum; N = number of patients; SD = standard deviation; T1DM = Type 1 Diabetes Mellitus.
* Total sample for this variable is affected by missing values. ** Total sample analyzed for PedsQL was 268 (out of 275 total participants); missing cases include 5 patients with more than 50% of the items in the scale missing and 2 children that were less than 2 years old (no scale was available for this age group). * Size categories were: <50 patients per year, small; 50-149, medium; ≥150, large.

Health Related Quality of Life

Figure 2. PEDsQL (All Ages) – Per Dimension and Overall

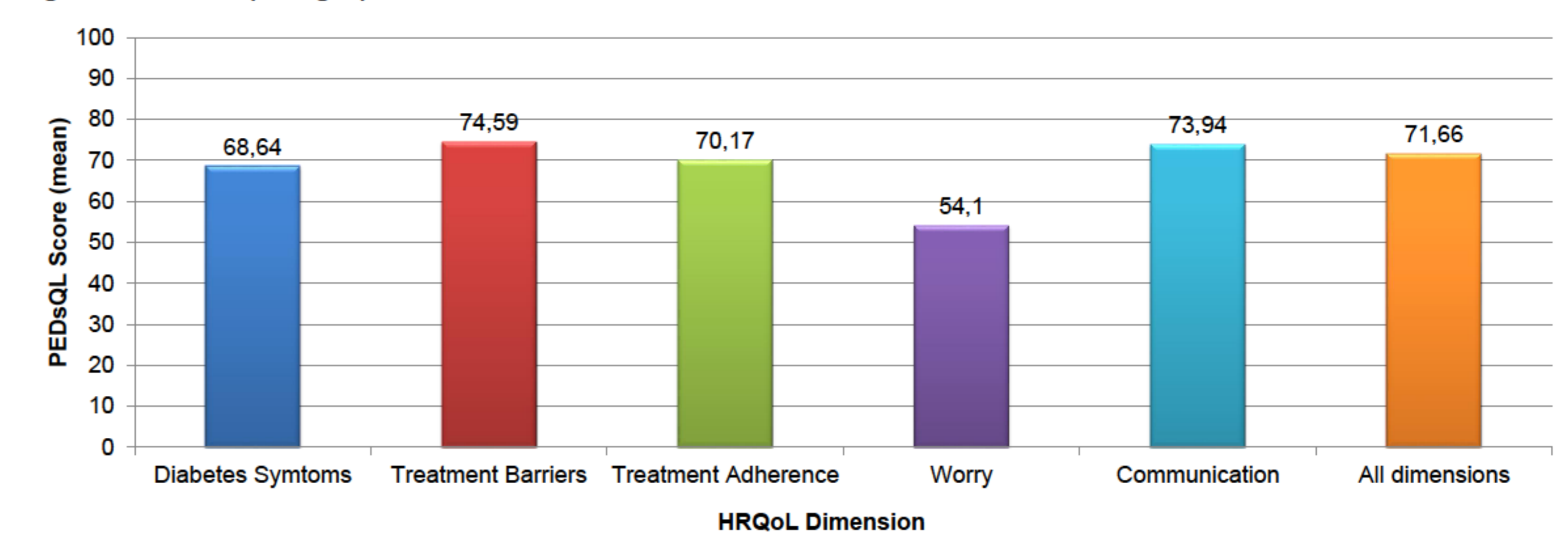


Figure 3. PEDsQL per HbA1c by Age Groups – Per Dimension and Overall (Proxy by Caregivers)

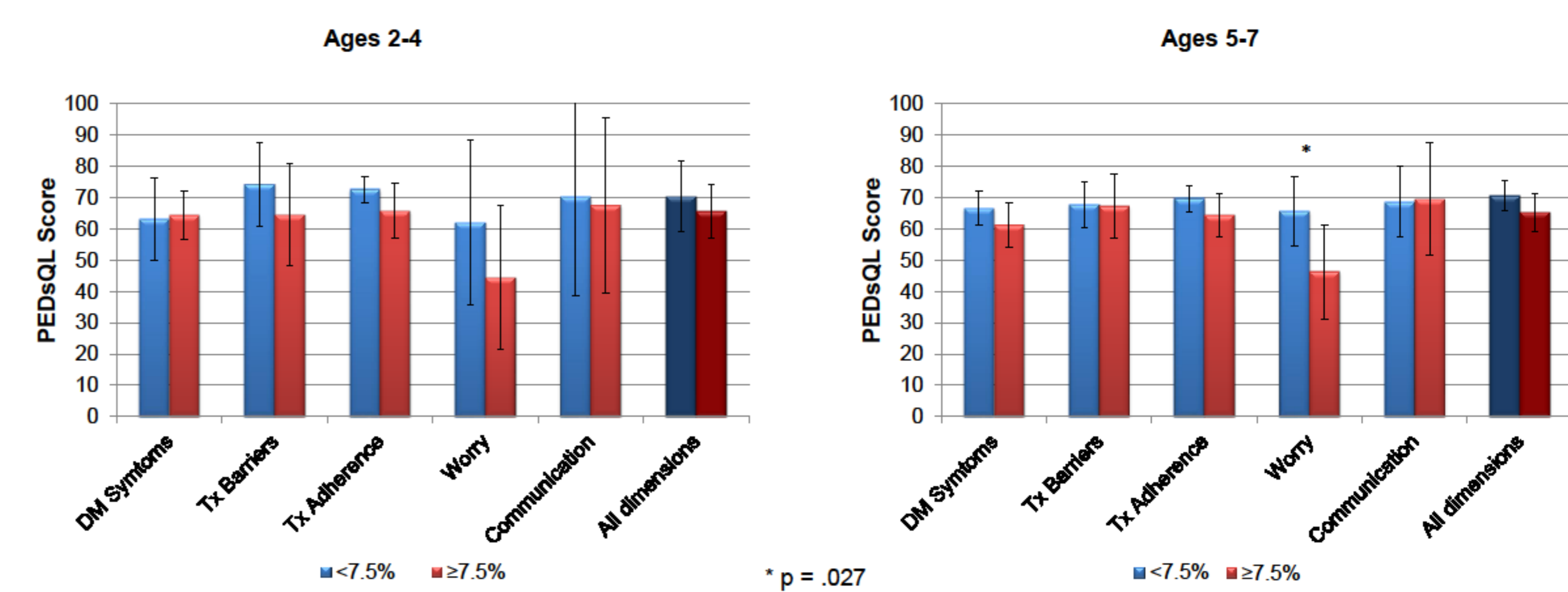
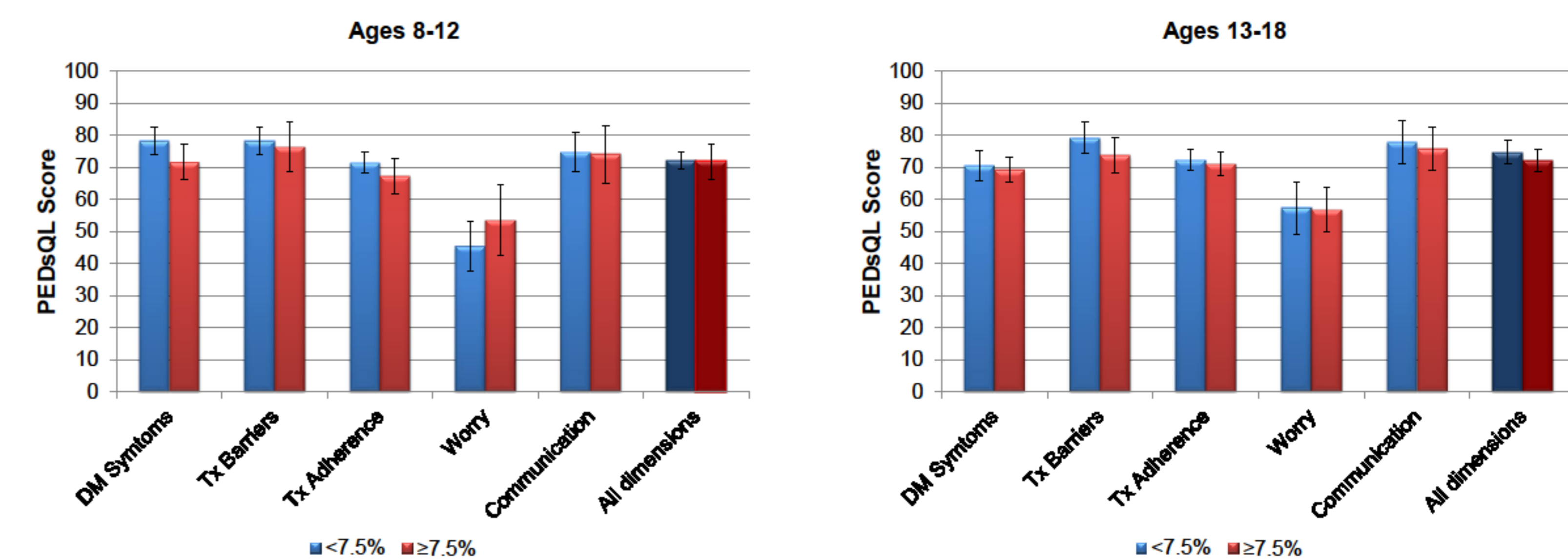


Figure 4. PEDsQL per HbA1c by Age Groups – Per Dimension and Overall (Self-Reported)



STRENGTHS AND LIMITATIONS

Strengths

- This study captured the first structured information in HRQoL comprising representative sample from Spain
 - Data collected directly from patients, caregivers and health care providers
 - Representative sample per age from different regions and from different types of paediatric endocrinology units
- Use of a well recognized tool for evaluating HRQoL specifically in paediatric population with diabetes.

Limitations

- Participants aged less than 2 years old were not evaluated due to lack of instrument for this age range.
- As all studies based on self report, results lack a "golden standard" comparison and can only be interpreted in a subjective manner.
- Quality of life evaluated as proxy by the caregivers for children aged 2-7 may be underestimated since parents may not be aware of their child's "quest for normality" when asked to rate the child's perceived health and may be correlated to their own HRQoL.

CONCLUSIONS

- CRYSTAL is the first study to evaluate HRQoL in a representative sample of children and adolescents with T1DM in Spain.
- Overall HRQoL is consistently lower among patients with HbA1c ≥ 7.5%, although differences by HbA1c level are not statistically significant. The "Worry" dimension has the highest negative impact on HRQoL across all age ranges, with significant differences by HbA1c only in children 5-7 years old.
- The results of this study bring good representation of the current quality of life for paediatric population with T1DM in Spain that has probably changed substantially from previous decades due to the introduction of new drugs and techniques for better glucose control and more convenient therapies.
- Interventions are needed to include HRQoL measures as part of the regular practice while managing diabetes for better assessment of diabetes care.

