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Article type : Original

Medical clown support is associated with better quality of life of children with food allergy starting oral immunotherapy

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Running Title: The effect of medical clowning on quality of life

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There are no conflicts of interest for any of the authors.

Dr. Goldberg is funded by a Kamea grant from the Ministry of Health, Israel.

This study was supported by a grant from Dream Doctors Project.

Word count: 2878

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/PAI.13445](#)

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CONFLICTS OF INTEREST

Naama Epstein Rigbi does not have any conflicts of interest to disclose.

Michael R Goldberg does not have any conflicts of interest to disclose.

Michael B Levy does not have any conflicts of interest to disclose.

Liat Nachshon does not have any conflicts of interest to disclose.

Arnon Elizur does not have any conflicts of interest to disclose

ABSTRACT

Background: The start of oral immunotherapy (OIT) for food allergy is a critical period in the treatment process, with a potential to influence patient quality of life (QOL) and subsequently treatment outcome. The association of medical clowning with QOL at OIT initiation was examined.

Methods: Children aged 4-12 years supported by a medical clown (MC) during the induction week of OIT for food allergy were studied. Children in the same age range starting OIT without the support of a MC served as controls. Parents of all children completed the Food Allergy Quality of Life Questionnaire - Parent Form (FAQLQ-PF) and children aged 8-12 years completed the Food Allergy Quality of Life Questionnaire - Child Form (FAQLQ-CF). QOL scores of parents and children with and without a MC support were compared.

Results: Children with (n=88) and without (n=212) the support of a MC were comparable in demographics and clinical characteristics. The study group had a significantly lower single highest tolerated dose compared to controls (57 ± 83 vs 162 ± 274 mg protein. respectively, $p < 0.001$). Parental perception of the QOL of children was not associated with a MC support ($p = 0.81$) but rather with previous reaction severity ($p < 0.01$). In contrast, the QOL of children aged 8-12 years (n=119) was positively associated primarily with a MC support, Total Score 3.7 ± 1.1 vs. 4.6 ± 1.3 ($p < 0.001$).

Conclusions: While the perception of QOL of parents of children with food allergy at OIT initiation, is mainly associated with previous reaction severity, the QOL of the children themselves is primarily positively associated with MC support .

KEY WORDS

Quality of Life, Oral Immunotherapy, Medical Clown, Anxiety

BACKGROUND

Oral Immunotherapy (OIT) is effective in desensitizing patients with food allergy (1–4) but the process itself is challenging for both patients and their caregivers (5–7). Patients might experience anxiety regarding the consumption of the allergenic food, due to fear of potential anaphylactic reactions, and aversion towards the food they need to consume (5).

We previously demonstrated a significant improvement in the QOL of children with food allergy during OIT with further improvement on follow-up (6,8–10). We also observed in children aged 4–12 years that an initial deleterious effect on QOL can be seen during the first dose-escalation week of OIT (17). Interestingly, we noted that parents of children aged 8–12 years undergoing OIT, consistently perceived the QOL of their children to be better than the QOL reported by the children themselves (10,11). These differences in perspective between parents and children can be attributed to the various difficulties they each face during OIT. While parents are mostly concerned with safety aspects, and alleviating uncertainty improves their QOL (7) children are forced to cope with consuming food to which they have an aversion, and may not fully understand the long-term benefits of the process. This stresses the importance of supporting children during OIT, as well as actively engaging them and encouraging them to succeed in the process itself.

Medical Clowns (MC) support was shown to effectively decrease anxiety induced by medical procedures in children, as well as in relieving pain during medical interventions (12–18). Most studies, however, focused on relatively short-term procedures, such as drawing blood, perioperative processes, or performing allergy skin prick tests (16). We aimed to examine whether the support of a MC affects the QOL of children during the initiation of OIT.

METHODS

Patients. Children aged 4–12 years who began OIT for IgE-mediated food allergy to milk, peanut, egg, sesame or tree nuts at Shamir Medical Center (formerly Assaf Harofeh) between May 2018 and January 2019, were prospectively recruited for the MC arm of the study. A control group comprised of children aged 4–12 years (2.5 to 1 ratio) who previously underwent a similar OIT protocol without the support of a MC. Exclusion criteria were uncontrolled asthma, eosinophilic gastro-intestinal disease, or chronic inflammatory disease other than asthma. Epidemiological data, past medical

history, and the nature and severity of previous food-related reactions were obtained from the parents of each participant. The diagnosis of food allergy was based on a positive skin prick test (SPT) and/or specific serum IgE, together with a positive oral food challenge (OFC), or a clinical history of an allergic reaction following accidental ingestion in the past year. SPTs to the treated food and histamine control (ALK-Abello, Port Washington, NY) were performed in all patients on the volar surface of the forearm and read after 15 minutes. The study was approved by the institutional ethics committee and Informed oral consent was obtained from parents of all study participants.

Oral immunotherapy. The initial dose-escalation of OIT phase consisted of 4 consecutive day visits in an ambulatory clinic at Shamir Medical Center. On day 1, an oral food challenge-desensitization protocol was performed. Doses were administered at 10-30 minute intervals until a clinical reaction occurred. If no reaction occurred on day one, the protocol continued to increase on day two until the eliciting dose was established. On subsequent days 2 and 3, the single highest tolerated dose (SHTD) approximating 25% less than the eliciting dose was established. On day four this dose was administered under supervision again to ensure its safety. The individual SHTD served as the starting dose for OIT. Children in the study group were accompanied by a MC designated for this study throughout their initial dose-escalation week.

Food Allergy Quality of Life Questionnaire- Child Form (FAQLQ-CF) and Parent Form (FAQLQ-PF).

The FAQLQ-CF was developed to evaluate the QOL of school-aged food allergic children aged 8-12 years (19). The FAQLQ-PF was developed to examine quality of life in children aged 0-12 years, as perceived by their parents (20). Both questionnaires are comprised of several domains examining different aspects of QOL (Emotional Impact, Food Anxiety and Social and Dietary limitations in the FAQLQ-PF and Emotional Impact, Allergen Avoidance, Risk of Allergen Exposure and Dietary limitations in the FAQLQ-CF). Items are scored on a 1-7 scale, ranging from not troubled (1) to extremely troubled (7). A higher score represents a higher impact or burden and hence, worse health related quality of life. The total FAQLQ-CF/PF score is the sum of all items divided by the number of the items and ranges from 1 (minimally impaired QOL) to 7 (extremely impaired QOL). Both questionnaires were previously translated to Hebrew and validated (10). Children and their

parents were given the FAQLQ-CF and FAQLQ-PF, respectively, during the third day of the initial induction, at a point when the SHTD had been determined. Only patients who answered $\geq 80\%$ of the questions in the FAQLQ-CF/FAQLQ-PF were included.

Medical clowning. In this study we used a MC who graduated his studies in the Dream Doctors organization. A specific MC was designated for this study and participated throughout the whole process. The MC first met the patients at their arrival to the allergy clinic on the first day of OIT and supported them throughout the first up dosing days (up to 6 hours/day). This support entailed presence during the different intake procedures at the clinic, including skin prick testing, spirometry, and most importantly the presence and support while consuming increasing doses of the allergenic foods. The MC involvement included techniques for distraction, anxiety reduction and the creation of a positive experience for the patients and their caregivers.

Statistics. Statistical analyses were performed using SAS 9.4 software. Continuous variables were normally distributed based on Q-Q plots, and were expressed as means and standard deviations (SDs) unless otherwise indicated, and categorical variables as numbers and percentages.

Comparisons of categorical and continuous variables between children with and without a MC support were assessed by Chi-square or Fisher's Exact test and t-tests, respectively. The association between categorical variables and the QOL scores was assessed by t-tests. The association between continuous variables and the QOL scores were explored using Spearman Correlation Coefficient. QOL scores of children and their parents were compared using Wilcoxon signed rank test. Multivariable analysis were performed using analysis of co-variates (ANCOVA) modeling. A difference of >0.5 was considered the minimal clinical important difference (MCID) on HRQL questionnaires with a 7 point scale(21). All analyses were 2-tailed and a p-value of less than 0.05 was considered significant.

RESULTS

Demographic and clinical characteristics

A total of 300 children aged 4-12 years (88 with MC support and 212 without) were studied. Mean age $\pm$ SD was 7 ± 2.5 years and 178 (59.3%) were males. Asthma was diagnosed in 130 (43.3%) children. Most children (34.7%) began milk OIT, followed by peanut (32.3%), tree nuts (19.3%), sesame (7.7%) and egg (6.0%). Multiple food allergies were diagnosed in 119 (39.7%) children. Previous anaphylactic reactions to the treated foods were experienced by 137 (45.7%) children, and 122 (40.7%) children required emergency room visits, 85 (28.3%) required intra-muscular adrenaline and 25 (8.3%) were hospitalized for such reactions. During the initial 4-day dose-escalation week, 39 (13%) children required intra-muscular adrenaline for treatment of reactions.

Children with and those without the support of a MC were comparable in gender ($p=0.51$) and age ($p=0.36$) (**Table 1**). The two groups were also comparable in their clinical characteristics, having similar rates of asthma ($p=0.61$) and of multiple food allergies ($p=0.12$), in the severity of their prior reactions to the treated food, and in reactions requiring adrenalin during the first week of OIT ($p=0.35$) (**Table 1**). A lower mean SHTD (indicating more severe allergy) was found in the study population (57 ± 83 mg protein) compared to controls (162 ± 274 mg protein), $p<0.001$ (**Table 1**). There was also a significant difference in the foods treated between the two groups with more children treated for tree nuts and sesame in the study group and more milk, egg and peanut treated children in controls (**Table 1**). However, the two groups were comparable for foods which are frequently present in Israeli households and are more difficult to avoid (milk, egg and sesame) vs. those who are less available and easier to avoid (peanut and tree nuts), ($p=0.17$).

The association of different parameters with parent perception of quality of life of children aged 4-12 years (n=300)

Several parameters were associated with worse QOL of children aged 4-12 years, as perceived by their parents, including a female gender, age ≥ 8 years, and having asthma or multiple food allergies (**Table 2**). The severity of previous reactions to the treated food had the most significant and consistent association with worse QOL in children, as perceived by their parents. The FAQLQ-PF

Total score and sub-scales of children with a history of anaphylaxis, adrenalin injection, emergency room visit and hospital admission were significantly higher (worse) ($p<0.01$). In addition, children treated for milk, egg or sesame had significantly higher EI ($p=0.027$), SDL ($p<0.001$) and Total scores ($p=0.004$), on the FAQLQ-PF, compared to those treated for peanut or tree nuts. In contrast, the SHTD at the beginning of OIT and a reaction requiring adrenalin during the first week of treatment did not impact children's QOL, as perceived by their parents. Also, the support of a MC did not significantly impact children's QOL, as perceived by their parents, mean total score 3.65 ± 1.26 versus 3.69 ± 1.29 in children with and without the support of a MC, respectively ($p=0.81$) (**Table 2**). The parameters that remained significantly associated with children's QOL as perceived by their parents on multivariate analysis were mainly age (independent factor for EI, FA and total score), multiple food allergies (independent factor for EI, FA and total score), previous admission (independent factor for FA, SDL and total score) and previous anaphylaxis (independent factor for FA, SDL and total score), $p\leq0.01$ for all.

The association of different parameters with children (aged 8-12 years) perception of quality of life (n=119).

A total of 119 children (36 with the support of a MC and 83 without) were studied. These groups were comparable in their demographics and clinical characteristics, including the allergenic foods treated. Similar to the entire cohort of children aged 4-12 years, the mean SHTD of children aged 8-12 years was lower in the study group compared to controls (58.1 ± 87.8 versus 121.6 ± 225.4 mg protein) but statistical significance was not met, ($p=0.11$) (**Table1s**). Similar to the finding in all 4-12 year-old children, parental perception of QOL scores of the sub-group of children aged 8-12 years with and without a MC support was comparable. In contrast, the support of a MC was associated with better children's QOL, as they perceived it, with significantly lower mean QOL scores in the Allergen Avoidance (AA) domain (3.35 vs 4.64, $p<0.01$), Dietary Restrictions (DR) domain (2.46 vs 4.18, $p<0.01$), and the Total score (3.74 vs 4.64, $p<0.01$) (**Table 3, Figure 1**). The differences in these domains between children with and without a MC were also clinically significant (exceeding 0.5). An additional factor associated with worse QOL as perceived by the children, was the need for

adrenalin injection during the first up-dosing week (a parameter for reaction severity), $p=0.01$ (**Table 3**). Given the differences in SHTD between the groups, we re-analyzed the data after excluding 10 patients with the highest SHTD in the control group. The remaining 73 patients without MC and the 36 patients with MC support had comparable SHTD (59.8 vs. 58.1 mg protein, respectively, $p=0.9$). In this analysis as well, QOL scores were significantly better in patients with MC support ($p<0.001$ for the AA and DR domains as well as for the total score). Multivariate analysis demonstrated that the support of a MC was most significantly associated with better QOL scores of children in AA ($p<0.001$), and DR ($p<0.001$) domains and the Total score ($p<0.001$) (**Table 4**). While children, in the absence of MC support, perceived their QOL as worse compared to their parents ($p<0.001$), the reverse was observed when a MC was present, as children perceive their QOL to be better compared to their parents ($p=0.002$) (**Figure 1s**).

DISCUSSION

In this study, we evaluated the impact of MC support on the QOL of children, as perceived by them and by their caregivers, during the initiation of OIT for food allergy. Our main findings were that parents' and children's perception of QOL during OIT were influenced by different factors. Parent perception was primarily affected by factors unrelated to OIT, factors which increase the child's risk for severe reactions, i.e. older age, asthma, multiple food allergies, allergy to common Israeli foods (milk, egg, sesame), and the severity of previous reactions. In contrast, the QOL of children aged 8-12 years was primarily affected by events occurring during the first week of treatment, and was significantly improved by the presence of a MC.

Food allergy is associated with reduced QOL mainly due to anxiety, caused by fear of unexpected allergic reactions, and as a result of the social limitations inflicted on patients (22–25). We have previously shown that OIT significantly improves QOL in desensitized patients, with further improvement as time on treatment continues (11,12). However, patients are required to face significant challenges during the treatment process, such as daily consumption of foods they find aversive, limitations surrounding the administration of the daily dose, and fear of an allergic reaction to the dose taken. These challenges might have deleterious effects on patients QOL which could be apparent as early as the first week of treatment (10). Moreover, increased anxiety could in turn lead to treatment failure (26). Our finding, that the deleterious effects at the beginning of OIT could be overcome by the presence of a MC, support the importance of implementing child-oriented procedures directed at relieving anxiety during the course of OIT.

The effect of MCs on reducing anxiety in patients has been extensively studied. Much of the research focused on relatively short, painful or stressful procedures (12,13,18) using pain-, stress- and anxiety-specific scales. Our study examined the impact of MC support in a more complicated setting, involving a several day-process during which patients must cope not only with anxiety but also with food aversion and with potential disappointment. The positive effect found in the study group, especially given their lower SHTD, demonstrates the utility of MCs even in more extended procedures.

Children were primarily affected by events that occurred during the first week of OIT, i.e. the support of a MC and the occurrence of reactions requiring adrenaline. In contrast, parents' perception of the QOL of their children was primarily affected by characteristics determined before OIT. It was previously shown that parents of children with food allergy (27), including those undergoing OIT (10,28), tend to estimate the QOL of their children to be better than the children's own estimation. It was also demonstrated that the epidemiologic and demographic backgrounds affects the child's QOL, primarily as perceived by the parents (29). Parents and children face different difficulties throughout OIT. While parents have a broader perspective and may carry the burden of the child's past medical history, children, on the other hand, are influenced by the evolving present. Therefore, while parental anxiety may be alleviated by the active initiative taken by starting OIT, and by the extensive information and the availability of expert support during treatment (7,29,30), children need a child-oriented approach.

This study has several limitations. First, we did not examine QOL of patients before starting OIT and therefore we do not know their baseline. We therefore cannot report an actual effect on QOL but rather an association. Second, the two groups differed in their SHTD. It is, however, important to stress the point that the baseline SHTD of the study group was lower. As a lower SHTD was previously shown to have a negative effect on QOL during the first up-dosing of OIT (10), this point serves to empower our findings that the QOL of children in the study group, despite having a lower SHTD, was actually reported to be better. Additionally, unlike other studies examining the impact of MCs by using specific anxiety scales, we chose to use the FAQLQ questionnaires, which may not accurately reflect the encounter with a MC, even if relatively prolonged. Our decision was based on several reasons. The FAQLQ forms were developed and validated as disease specific questionnaires, taking into consideration social and developmental characteristics, and distinguishing parents from children (19). Moreover, these questionnaires were used in numerous studies related to food allergy, were previously shown to identify changes in QOL already within the first week of OIT and enable comparisons to other studies and populations. Finally, this study focused only on the initial dose-escalation period to assess the effect of MCs. The impact MC support throughout the entire treatment deserves further research.

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In summary, in this study we show that children undergoing OIT with the support of a MC report a better QOL at the initiation of the process. These findings likely reflect the alleviation of anxiety in allergic children and the distraction from the need to consume a food they find aversive. Future studies should examine whether the positive influence of MC support throughout OIT has an impact on the treatment and its outcome. Child-oriented procedures should be considered by OIT treatment program to better engage children in the process.

ACKNOWLEDGEMENTS

We would like to thank the large staff of the Shamir Medical Center Allergy Clinic in their daily work and efforts: nurses, dieticians, respiratory technicians, laboratory workers and secretaries. We would especially like to thank Alex Vinegart, our medical clown, who brought much laughter and joy to our patients, parents and staff. Finally, we would also like to thank our patients and their parents for participating in this study.

KEY MESSAGE

This study highlights the differences in the perception of quality of life between food allergic children and their caregivers at the start of oral immunotherapy. A medical clown support was associated with better quality of life as perceived by children but not by their caregivers. These differences emphasize the importance of actively engaging children in oral immunotherapy, using child-oriented procedures.

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Accepted Article

AUTHOR CONTRIBUTIONS

Naama Epstein Rigbi contributed in conception and design of the study, acquisition of data and in analysis and interpretation of data and in drafting the article.

Naama Schwartz contributed to the statistical analysis

Michael R Goldberg contributed in interpretation of data and in drafting the article

Michael B Levy contributed in interpretation of data and in drafting the article

Liat Nachshon contributed in interpretation of data and in drafting the article

Arnon Elizur contributed in conception and design of the study, acquisition of data and in analysis and interpretation of data and in drafting the article.

Table 1: Comparison of patients with and without a clown

Parameter		EI	FA	SDL	Total Score
Male gender	No (n=122)	3.8±1.3	4.3±1.5**	3.5±1.5	3.8±1.3
Parameter		No clown (n=212)	Clown (n=88)	P value	
Male gender		123 (58%)	55 (62.5%)	0.51	
Age (years)		7.2±2.2	7±2.6	0.36	
Multi food allergies		78 (36.8%)	41 (46.6%)	0.12	
Asthma		94 (44.3%)	36 (40.9%)	0.61	
Anaphylaxis		103 (48.6%)	34 (38.6%)	0.13	
Adrenaline		54 (25.5%)	31 (35.2%)	0.09	
Emergency room		81 (38.2%)	41 (46.6%)	0.2	
Admission		17 (8.0%)	8 (9.1%)	0.82	
Adrenaline on OFC		25 (11.8%)	14 (15.9%)	0.35	
SHTD (mg)		56.6±83	162.4±274.2	<0.001	
Food	Egg	13 (6.1%)	5 (5.7%)	0.026	
	Milk	81 (38.2%)	23 (26.1%)		
	Peanut	72 (34%)	25 (28.4%)		
	Sesame	14 (6.6%)	9 (10.2%)		
	Tree nuts	32 (15.1%)	26 (29.5%)		

OFC= oral food challenge; SHTD= single highest tolerated dose

Table 2: The association of different parameters with parent perception of children's QOL (n=300)

	Yes (n=178)	3.6±1.3	3.7±1.5	3.3±1.5	3.6±1.3
	Mean difference (95% CI)	NS	0.54 (0.2, 0.88)	NS	NS
Age ≥8 years	No (n=178)	3.6±1.3*	3.7±1.5**	3.3±1.4	3.5±1.2*
	Yes (n=122)	3.9±1.3	4.3±1.4	3.5±1.5	3.9±1.3
	Mean difference (95% CI)	-0.31 (-0.6, -0.01)	-0.58 (-0.92, -0.24)	NS	-0.39 (-0.68, -0.09)
Medical clown	No (n=212)	3.6±1.3	3.9±1.5	3.4±1.5	3.7±1.3
	Yes (n=88)	3.8±1.3	3.9±1.6	3.3±1.4	3.6±1.3
	Mean difference (95% CI)	NS	NS	NS	NS
Multi food allergies	No (n=181)	3.6±1.2*	3.8±1.5*	3.3±1.5	3.5±1.3*
	Yes (n=119)	3.9±1.3	4.2±1.5	3.6±1.5	3.9±1.3
	Mean difference (95% CI)	-0.34 (-0.64, -0.05)	-0.38 (-0.73, -0.03)	NS	-0.33 (-0.63, -0.04)
Asthma	No (n=170)	3.6±1.3	3.8±1.5	3.2±1.5*	3.5±1.3*
	Yes (n=130)	3.9±1.3	4.1±1.5	3.6±1.4	3.8±1.3
	Mean difference (95% CI)	NS	NS	-0.41 (-0.74, -0.07)	-0.3 (-0.59, -0.01)
Previous anaphylaxis	No (n=163)	3.4±1.3**	3.7±1.5**	3.0±1.5**	3.4±1.3**
	Yes (n=137)	4.0±1.3	4.2±1.5	3.8±1.4	4.0±1.2

	Mean difference (95% CI)	-0.57 (-0.85, -0.28)	-0.58 (-0.92, -0.24)	-0.78 (-1.11, -0.45)	-0.63 (-0.92, -0.35)
Previous adrenaline	No (n=215)	3.5±1.2**	3.7±1.5**	3.2±1.4**	3.5±1.3**
	Yes (n=85)	4.3±1.2	4.4±1.4	4.0±1.4	4.2±1.2
	Mean difference (95% CI)	-0.77 (-1.1, -0.46)	-0.65 (-1.0, 0.28)	-0.85 (-1.21, -0.48)	-0.75 (-1.1, -0.44)
Previous ER visit	No (n=178)	3.4±1.2**	3.7±1.5**	3.1±1.4**	3.4±1.2**
	Yes (n=122)	4.1±1.3	4.3±1.4	3.8±1.5	4.0±1.3
	Mean difference (95% CI)	-0.66 (-0.95, -0.37)	-0.57 (-0.91, 0.23)	-0.72 (-1.1, -0.38)	-0.62 (-0.91, -0.33)
Previous admission	No (n=275)	3.6±1.3**	3.8±1.5**	3.3±1.5**	3.6±1.3**
	Yes (n=25)	4.4±1.4	5.0±1.1	4.5±1.2	4.6±1.2
	Mean difference (95% CI)	-0.78 (-1.3, 0.26)	-1.15 (-1.75, -0.54)	-1.21 (-1.8, -0.61)	-1.0 (-1.53, -0.5)
Adrenaline on OFC	No (n=261)	3.7±1.3	3.9±1.5*	3.3±1.5	3.6±1.3*
	Yes (n=39)	4.0±1.4	4.4±1.6	3.8±1.6	4.1±1.4
	Mean difference (95% CI)	NS	-0.56 (-1.1, -0.06)	NS	-0.46 (-0.89, -0.03)
Food treated	Milk/egg/Sesame (n=145)	3.9±1.3*	4.1±1.5	3.8±1.4**	3.9±1.2**
	Peanut / Tree nuts (n=155)	3.5±1.3	3.8±1.5	3.1±1.5	3.5±
	Mean difference (95% CI)	0.33 (0.04, 0.62)	NS	0.71 (0.38, 1.0)	0.42 (0.13, 0.71)

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*For comparisons with significance of $p<0.05$; **For comparisons with significance of $p<0.01$

Differenced in QOL exceeding the 0.5 clinically important difference are bolded

Table 3: The association of different parameters with children's perception of their QOL (n=119)

Parameter		AA	RAE	EI	DR	Total Score
Male gender	NO (n=52)	4.5±1.6	4.7±1.4	5.3±1.3*	3.9±1.6	4.6±1.3
	Yes (n=67)	4.1±1.5	4.4±1.6	4.7±1.5	3.5±1.6	4.2±1.2
	Mean difference (95% CI)	NS	NS	0.56 (0.03, 1.1)	NS	NS
Medical clown	No (n=83)	4.6±1.6**	4.4±1.5	5.1±1.4	4.2±1.4**	4.6±1.3**
	Yes (n=36)	3.3±1.1	4.9±1.5	4.6±1.4	2.5±1.3	3.7±1.1
	Mean difference (95% CI)	1.3 (0.8, 1.8)	-0.47 (-1.1, 0.13)	NS	1.72 (1.18, 2.26)	0.9 (0.42, 1.4)
Multi food allergies	No (n=78)	4.3±1.6	4.5±1.6	5.0±1.5	3.6±1.5	4.4±1.3
	Yes (n=41)	4.2±1.4	4.6±1.4	4.9±1.3	3.8±1.7	4.3±1.3
	Mean difference (95% CI)	NS	NS	NS	NS	NS
Asthma	No (n=62)	4.3±1.5	4.7±1.5	5.1±1.4	3.6±1.6	4.4±1.2
	Yes (n=57)	4.2±1.6	4.4±1.6	4.9±1.5	3.7±1.5	4.3±1.4
	Mean difference (95% CI)	NS	NS	NS	NS	NS
Previous anaphylaxis	No (n=60)	4.1±1.6	4.3±1.5	5.0±1.5	3.6±1.7	4.3±1.3
	Yes (n=59)	4.4±1.6	4.8±1.5	4.9±1.4	3.7±1.5	4.5±1.3
	Mean difference (95% CI)	NS	NS	NS	NS	NS

Previous adrenaline	No (n=80)	4.2±1.6	4.3±1.5*	4.9±1.5	3.7±1.7	4.3±1.3
	Yes (n=39)	4.4±1.5	5.0±1.5	5.2±1.4	3.6±1.4	4.6±1.2
	Mean difference (95% CI)	NS	-0.64 (-1.2, -0.05)	NS	NS	NS
Previous ER visit	No (n=65)	4.2±1.6	4.4±1.5	4.9±1.5	3.7±1.6	4.3±1.3
	Yes (n=54)	4.3±1.5	4.8±1.6	5.0±1.4	3.6±1.5	4.4±1.3
	Mean difference (95% CI)	NS	NS	NS	NS	NS
Previous admission	No (n=110)	4.2±1.6	4.5±1.5*	4.9±1.5	3.7±1.6	4.3±1.3
	Yes (n=9)	5.2±1.1	5.6±1.8	5.5±1.4	3.7±1.6	5.1±1.2
	Mean difference (95% CI)	NS	-1.16 (-2.2, -0.13)	NS	NS	NS
Adrenaline on OFC	No (n=91)	4.1±1.5	4.3±1.5**	4.9±1.5	3.5±1.6	4.2±1.3*
	Yes (n=28)	4.7±1.6	5.2±1.5	5.2±1.3	4.1±1.4	4.9±1.2
	Mean difference (95% CI)	NS	-0.89 (-1.5, 0.25)	NS	NS	-0.71 (-1.25, -0.17)
Food treated	Milk/egg/Sesame (n=60)	4.5±1.5	4.7±1.6	4.9±1.4	3.9±1.4	4.5±1.2
	Peanut / Tree nuts (n=59)	4.0±1.7	4.4±1.5	5.1±1.5	3.4±1.7	4.2±1.4
	Mean difference (95% CI)	NS	NS	NS	NS	NS

All numbers are provided as mean ± SD

AA= allergen avoidance, RAE= risk of allergen exposure, EI= emotional impact, DR= dietary restrictions, ER= emergency room, OFC= oral food challenge.

*For comparisons with significance of $p < 0.05$; **For comparisons with significance of $p < 0.01$

Differenced in QOL exceeding the 0.5 clinically important difference are bolded

Table 4: Multivariable analyses for the effect of medical clowning on children's perception of their quality of life.

QOL sub-core	Parameter	Mean	Mean difference	P value
AA	No clown	4.76	1.33	<0.001
	Clown	3.43	(0.73 - 1.92)	
RAE	No clown	4.49	-0.39	0.12
	Clown	4.88	(-1 - 0.22)	
EI	No clown	5.21	0.55	0.07
	Clown	4.66	(-0.04 - 1.14)	
DR	No clown	4.27	1.69	<0.001
	Clown	2.58	(1.12 - 2.26)	
Total Score	No clown	4.73	0.94	<0.001
	Clown	3.79	(0.44 - 1.44)	

QOL= quality of life

AA= allergen avoidance, RAE= risk of allergen exposure, EI= emotional impact, DR= dietary restrictions

Variables are adjusted for: age, gender, adrenalin, starting dose, type of food allergy

Analysis was performed with ANCOVA models

FIGURE LEGENDS

Figure 1. Comparison between the FAQLQ-CF scores of children (8-12 years) with (n=36) and without (n=83) medical clown support during the initiation of OIT treatment. The scores are shown as mean $\pm$ SD for each domain (Emotional Impact, Allergen Avoidance, Dietary Restrictions, Risk of Allergen Exposure) and for the total score. There were significantly lower QOL scores (better QOL) for children supported by a MC in the AA (allergen avoidance), DR (dietary restriction) and Total score, $p < 0.01$.

Figure 1s. Comparison of QOL total scores between children (8-12 years) and their parents, with (n=36) and without (n=83) medical clown support during the initiation of OIT treatment. The scores are shown as mean $\pm$ SD for the total score of children and their parents, with and without the support of a MC. The QOL was statistically better for children with a MC support ($p < 0.01$), but there was no difference between the parents.

Figure 1. Comparison between the FAQLQ-CF scores of children (8-12 years) with (n=36) and without (n=83) medical clown during the initiation of OIT treatment.

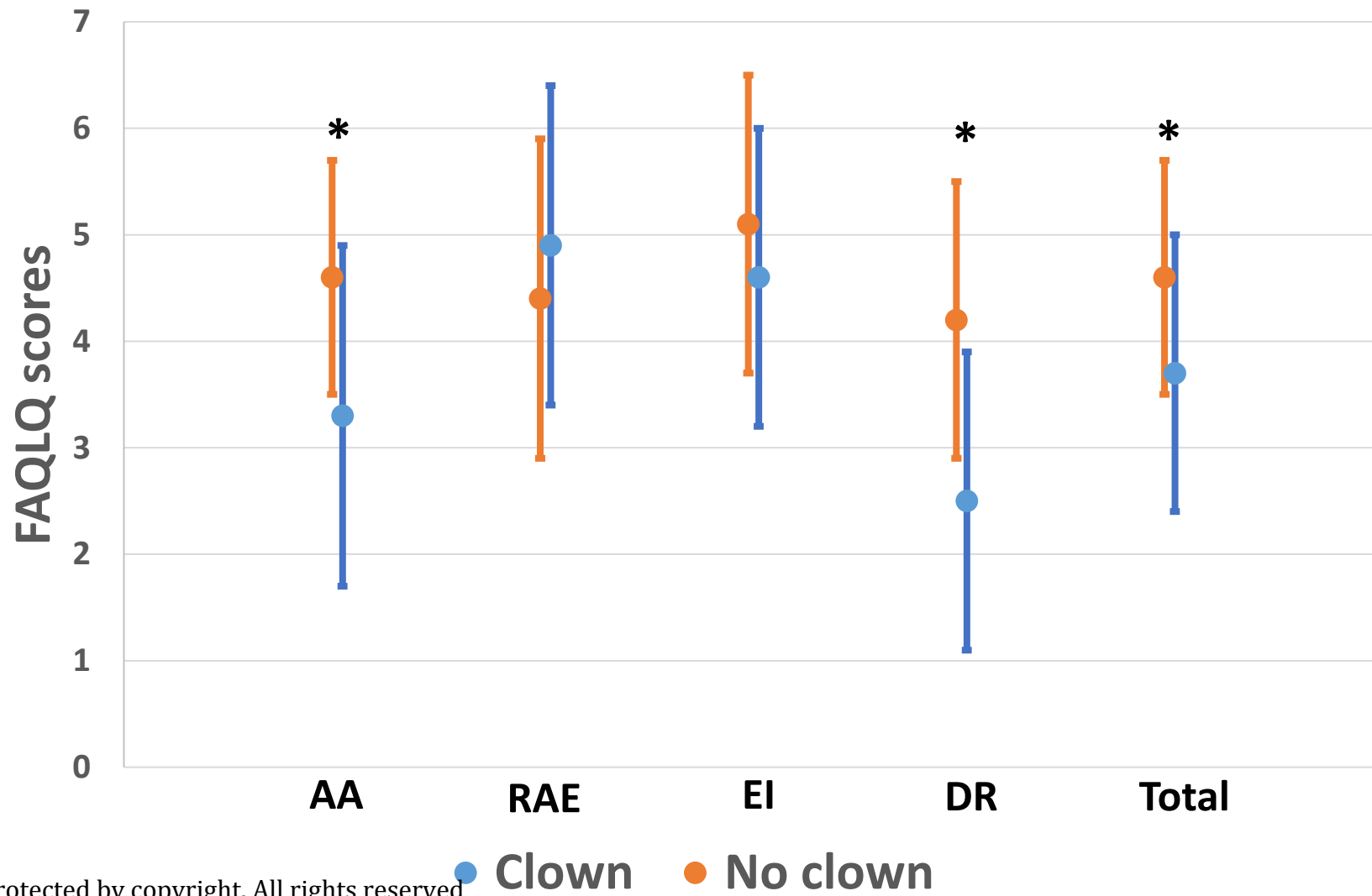


Figure 1s. Comparison of QOL total scores between children (8-12 years)and their parents, with (n=36) and without (n=83) a clown during the initiation of OIT treatment.

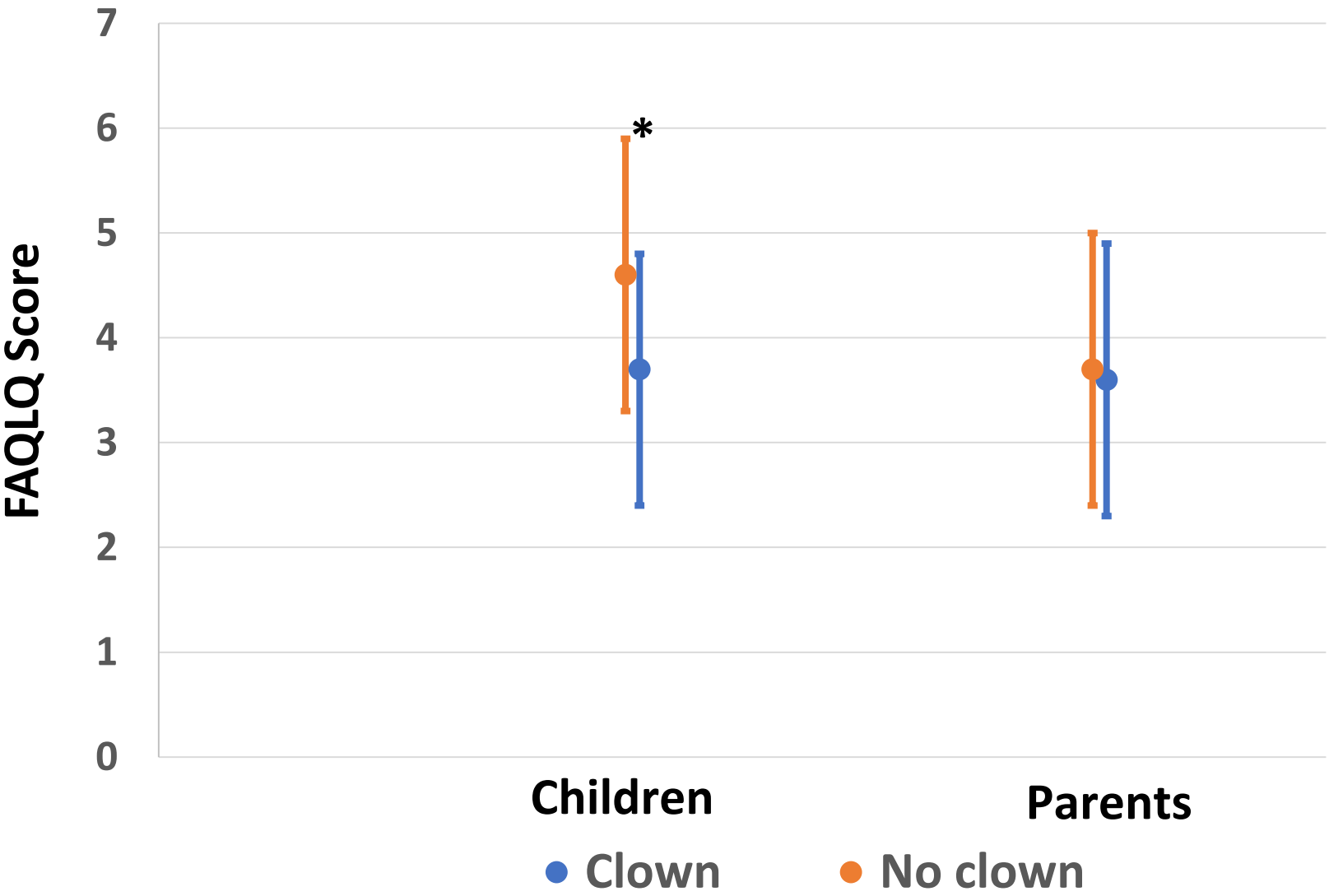


Table 1s: Comparison of children with and without a clown

Parameter		No clown (n=83)	Clown (n=36)	P value
Male gender		44 (53%)	23 (63.9%)	0.32
Age (years)		9.8±1.4	9.5±1.5	0.29
Multi food allergies		25 (30.1%)	16 (44.4%)	0.15
Asthma		42 (50.6%)	36 (40.9%)	0.43
Anaphylaxis		43 (51.8%)	15 (41.7%)	0.55
Adrenaline		25 (30.1%)	14 (38.9%)	0.4
Emergency room		34 (41%)	20 (55.6%)	0.16
Admission		5 (6.0%)	4 (11.1%)	0.45
Adrenaline on OFC		19 (22.9%)	9 (25%)	0.82
SHTD (mg)		121.6±225.4	58.1±87.8	0.11
Food	Egg	8 (9.6%)	3 (8.3%)	0.91
	Milk	28 (33.7%)	11 (30.6%)	
	Peanut	19 (22.9%)	10 (27.8%)	
	Sesame	8 (9.6%)	2 (5.6%)	
	Tree nuts	20 (24.1%)	10 (27.8%)	

OFC= oral food challenge; SHTD= single highest tolerated dose