



## Evaluation of the Relationship between Orthodontic Treatment Need and Oral Health-Related Quality of Life of 11-15 Year Old Children With Different Malocclusions: A Cross-Sectional Study

11-15 Yaş Arası Farklı Malokluzyonlara Sahip Çocuklarda Ortodontik Tedavi İhtiyacı ve Ağız Sağlığına İlişkin Yaşam Kalitesi Arasındaki İlişkinin Değerlendirilmesi: Kesitsel Bir Çalışma

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### ABSTRACT

**Objective:** The aim of this cross-sectional study is to determine the orthodontic treatment need and oral health-related quality of life (OHRQoL) in children aged 11-15 and to evaluate the effect of orthodontic treatment need on OHRQoL in different malocclusion groups.

**Material and Method:** 261 children (158 girls, 103 boys) aged 11-15 years (mean 13.03±1.93 years in girls, 12.66±1.75 years in boys) who deserved orthodontic treatment constituted the material of this study. Individuals were divided into 3 groups according to their dental malocclusions as Angle Class I, Class II and Class III. Data collection tools; Index of Orthodontic Treatment Need (IOTN) Dental Health Component (IOTN-DHC), IOTN Aesthetic Component (IOTN-AC), Oral Health Impact Profile-14 (OHIP-14) and Clinical Examination Data Form. OHIP-14 was used to measure OHRQoL. IOTN-DHC and IOTN-AC (orthodontist & self-perception) were used to determine the need for orthodontic treatment. Data were collected through questionnaires, personal interviews, and intraoral examinations. Mann Whitney U test, Kruskal-Wallis test and Kendall tau-b correlation test were used to evaluate the data and the significance level was determined as P<0.05.

**Results:** It was determined that there was no difference between the genders in terms of OHIP-14, IOTN-DHC and IOTN-AC variables (P>0.05). While there was no significant difference between malocclusion groups in terms of OHIP-14 scores, IOTN-DHC scores indicating the orthodontic treatment need were found to be significantly higher in the Class III malocclusion group (P<0.001). The IOTN-AC (self-perception) scores, in which children with Class II malocclusion evaluated their dental status according to their own aesthetic perceptions, were found to be significantly higher. While IOTN-DHC and IOTN-AC scores were highly correlated in all malocclusion groups, the correlation between IOTN scores and OHIP-14 scores was not statistically significant.

**Conclusion:** The orthodontic treatment need determined in different malocclusion groups may not affect the OHRQoL of the patients. In children aged 11-15 years, OHRQoL indices may be helpful in determining treatment priority as an adjunct to traditional diagnostic methods.

**Keywords:** Malocclusion, oral health-related quality of life, index of orthodontic treatment need, OHIP-14, child

### ÖZ

**Amaç:** Bu kesitsel çalışmanın amacı 11-15 yaş arası çocuklarda ortodontik tedavi ihtiyacının ve ağız sağlığı ile ilgili yaşam kalitesinin (OHRQoL) belirlenmesi ve farklı malokluzyon gruplarında ortodontik tedavi ihtiyacının, OHRQoL üzerindeki etkisinin değerlendirilmesidir.

**Gereç ve Yöntem:** Ortodontik tedavi görme isteği bulunan 11-15 yaş arası (kızlarda ort. 13,03±1,93 yıl, erkeklerde ort. 12,66 ±1,75 yıl) 261 çocuk (158 kız, 103 erkek) çalışmanın gerecini oluşturdu. Bireyler dental malokluzyonlarına göre Angle Sınıf I, Sınıf II ve Sınıf III olarak 3 gruba ayrıldı. Veri toplama araçları; Ortodontik Tedavi İhtiyacı Diş Sağlığı Bileşeni indeksi (IOTN-DHC), IOTN Estetik Bileşeni indeksi (IOTN-AC), Ağız sağlığı etki profili (Oral Health Impact Profile-14 (OHIP-14)) ve klinik muayene veri formuydu. OHRQoL'yi ölçmek için OHIP-14 ölçeği kullanıldı. IOTN-DHC ve IOTN-AC (ortodontist & kendi algısı) ise ortodontik tedavi gereksinimini belirlemek amacıyla kullanıldı. Veriler; anketler, kişisel görüşmeler ve intraoral muayeneler yoluyla toplandı. Verilerin değerlendirilmesinde Mann Whitney U testi, Kruskal-Wallis testi ve Kendall tau-b korelasyon testi kullanıldı ve anlamlılık düzeyi P<0,05 olarak belirlendi.

**Bulgular:** Cinsiyetler arasında OHIP-14, IOTN-DHC ve IOTN-AC değişkenleri açısından farklılık bulunmadığı belirlendi (P>0,05). Malokluzyon grupları arasında OHRQoL ölçme verisi olan OHIP-14 skorları açısından anlamlı farklılık bulunmazken ortodontik tedavi gereksinimini belirten IOTN-DHC skorları Sınıf III malokluzyon grubunda anlamlı derecede yüksek olduğu bulundu (P<0,001). Sınıf II malokluzyona sahip çocukların dental durumlarını kendi estetik algılarına göre değerlendirdikleri IOTN-AC (kendi algısı) skorları ise anlamlı derecede yüksek bulundu. Tüm malokluzyon gruplarında IOTN-DHC ve IOTN-AC skorları yüksek korelasyon gösterirken, IOTN skorları ve OHIP-14 skorları arasındaki korelasyon istatistiksel olarak anlamlı değildi.

**Sonuç:** Farklı malokluzyon gruplarında belirlenen ortodontik tedavi ihtiyacı, hastaların OHRQoL'sini etkilemeyebilir. 11-15 yaş arası çocuklarda OHRQoL indeksleri geleneksel teşhis metotlarına yardımcı olarak tedavi önceliğinin belirlenmesinde faydalıdır.

**Anahtar Kelimeler:** Malokluzyon, ağız sağlığı ile ilişkili yaşam kalitesi, ortodontik tedavi gereksinim indeksi, OHIP-14, çocuk

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## INTRODUCTION

According to the World Health Organization (WHO) being healthy is not just the absence of disease or infirmity, holistic health is a state of complete mental, physical and social well-being of individuals (1). While evaluating the quality of life (QoL) of individuals, their perceptions, expectations and anxiety attitudes about their health status are evaluated (2). It is known that QoL is related to oral health, and poor oral health can affect individuals' QoL (3). Oral health-related quality of life (OHRQoL) subjectively examines the impact of oral health on the functional, psychosocial and physical states of individuals (4). Oral health is an important part of the general health of individuals and is considered to be an effective factor in their perception of their own health (5, 6). By determining the effect of applications in different fields of dentistry on the quality of life, the positive and negative effects of oral health on general health can be determined, it can be used in oral health research, clinical research and examining the results of clinical procedures (7, 8). In recent years, the interest in the effects of OHRQoL has increased considerably, and for this purpose, many different scales have been developed that question the various symptoms, problems and mental states of the patients (7). The Oral Health Impact Profile (OHIP) scale is commonly used for this purpose. OHIP, which was first developed in Australia and accepted and used internationally by WHO, is the most comprehensive and subjective tool in the measurement of oral health (7, 9,10). Since the first developed OHIP was long with 49 items, it was seen that it caused a waste of time and created difficulties for the respondents. For this purpose, abbreviated 14-item OHIP scales (OHIP-14), which are easier to administer and answer, have been developed as an alternative to the original 49-item version of the OHIP (10). The OHIP-14 scale was found to be a valid and highly reliable scale in longitudinal and clinical research studies (7, 10).

Dentofacial aesthetics has a very important role in the social communication of individuals and children such as people's ability to make friends, personal development, participating in school activities, communicating with people, and making themselves accepted by the society (11). Malocclusions can negatively affect facial aesthetics, functions such as chewing, speaking, smiling, and self-esteem and reduce the QoL of children (12). Evaluating the perception of orthodontic malocclusions on the patient is important in terms of determining the need for treatment. Studies have shown that the use of subjective scales together with the need for orthodontic treatment determined by objective scales is beneficial in orthodontic treatment planning (13, 14). Various quantitative malocclusion indices such as Index of Orthodontic Treatment Need (IOTN), Index of Complexity, Outcome and Need (ICON) and Dental

Aesthetic Index (DAI) are frequently used to classify malocclusions in epidemiological studies, to classify patients according to treatment needs, and to evaluate treatment success (15,16). IOTN assesses the need for orthodontic treatment in terms of two components (17). These are the Dental Health Component (DHC), which examines the teeth for dental components such as Missing teeth, Overjet/Reverse Overjet, Crossbite, Displacement of Contact Point, Overbite/Openbite, and the Aesthetic Component (AC) which examines the teeth aesthetically. While the IOTN AC subjectively evaluates the psychosocial treatment needs of the patients, the IOTN DHC objectively evaluates the treatment need by the dental professional based on dental malocclusion (18).

There are conflicting results in the literature regarding the relationship between orthodontic malocclusion and OHRQoL of children. In some studies, it is stated that there is no relationship between malocclusions and OHRQoL (19, 20), while in some studies it is stated that these two phenomena are related to each other (21, 22). Therefore, this study aims to determine the relationship between 3 different types of dental malocclusion (Class I, Class II, and Class III) (**Figure 1**) and OHRQoL of 11-15-year-old children. The null hypothesis is (H<sub>0</sub>); there is no difference between OHRQoL levels in different malocclusion groups and H<sub>1</sub> hypothesis is; there is difference between OHRQoL levels in different malocclusion groups.



**Figure 1.** Different types of orthodontic malocclusion groups. **A:** Angle Class I Malocclusion, **B:** Angle Class II Malocclusion, **C:** Angle Class III Malocclusion

## MATERIAL AND METHOD

This cross-sectional study was approved by the Non-Invasive Clinical Trials Publication Ethics Committee at Nevşehir Hacı Bektaş Veli University (Reference No: 2022.02.10.). Informed consent forms that described the study method and requested consent were obtained separately from the children and their families who contributed to the study.

### Study Design and Study Subjects

In the power analysis, the minimum sample size calculated for this study was 252 children, with 5% significance level, 90% test power, and the minimum detectable probability ratio of 1:5. The effect size was calculated based on the mean quality of life scores in a similar article (23). This cross-sectional study was carried out on 261 randomly selected patients aged between 11 and 15 who applied to Ordu University Faculty of Dentistry Department of Orthodontics for orthodontic treatment. Inclusion criteria for the participants were age (11-15

years), patients who voluntarily applied to the clinic for orthodontic examination, and no previous orthodontic treatment history. The exclusion criteria were; patients with a diagnosed psychiatric problem, who already had a fixed or removable prosthetic restoration, and any cranio-facial syndrome. Data collected from 261 children (158 girls, 103 boys) between the ages of 11-15 who accepted to participate in the study and met the criteria formed the material of the study. No incentives or rewards were made for participation. Data were obtained through self-administered questionnaires, personal interviews, and intraoral and extraoral examinations.

### Evaluation of OHRQoL Measurements and Orthodontic Treatment Need (IOTN/DHC & IOTN/AC)

Assessment of orthodontic treatment need, OHRQoL measurements, and sociodemographic information were collected using a structured questionnaire from individuals and their parents who agreed to participate in this study. The children self-completed the OHIP-14 questionnaire in the dental clinic waiting room just prior to the dental examination. The way to improve OHRQoL requires oral function, chewing, preventing oral disease, repairing oral tissue, and addressing patient complaints. Slade and Spencer developed a scale in 1994 to measure the functional, social, and psychological consequences of oral conditions based on 49 questions known as OHIP-49 (10). The OHRQoL measurement is a subjective indicator that provides information about the effects of oral conditions on an individual's life and the perceived need for dental treatment. The Oral Health Impact Profile (OHIP) is a survey that measures people's perception of the social impact of oral disorders on their health. In 1997, Slade developed a short form of this questionnaire called OHIP-14, consisting of 14 questions, which showed good reliability, validity, and precision (24). In terms of the subjects that OHIP-14 will measure, it is divided into seven main dimensions as functional limitations, physical pain, mental distress, physical disability, social disability, mental disability and handicap. OHIP-14 is widely used around the world for a variety of research purposes (7). Turkish version of the OHIP-14 scale that the reliability, validity, intelligibility and reproducibility have been proven Başol et al. (7) was used in our study. Lower scores from the scale represent better QoL, while higher scores indicate worse OHRQoL.

IOTN index which was developed in 1989 by Brook and Shaw (17), evaluates malocclusion in order to identify the need for orthodontic treatment. This index consists of two components, the DHC and the AC. DHC is an objective component developed to reduce subjectivity in measurements. The need for treatment was divided into five different groups: 5 (very great), 4 (great), 3 (moderate), 2 (little), 1 (no need for treatment) (17). Specific conditions such as contact point disorders, overjet, overbite, missing or erupted teeth are evaluated,

and the score of the occlusal feature with the highest score is the DHC score. IOTN-AC evaluation is carried out with the ten-point scale of the Standardized Continuum of Aesthetic Need index (SCAN) (17, 25). These ten photographs taken from the frontal side are selected from intraoral photographs taken from one thousand 12-year-old children, and the number one photograph is the most attractive and the tenth is the least attractive photograph. The IOTN-AC component was evaluated both by the orthodontist (IOTN-AC; orthodontist) and by the children's self-perception (IOTN-AC; self-perceived) in our study. The person's need for orthodontic treatment is scored in terms of orthodontics according to IOTN-DHC scale and ten photographs of the AC component are scored in terms of aesthetics and processed into the questionnaire form. As a result of the questionnaire made according to the IOTN index, if the individual is IOTN-DH  $\geq 4$  and/or IOTN-AC (orthodontist)  $\geq 8$ , it is evaluated that needs for orthodontic treatment.

### Statistical Analysis

All measurements were analyzed with a statistical analysis program (SPSS for Windows version 20.0; SPSS Inc, Chicago, IL, USA). After applying the normal distribution test to the data, while applying the parametric tests to the data showing normal distribution; non-parametric tests were applied to the data that did not show normal distribution.

Mann-Whitney U test was used to compare data between genders. The Kruskal-Wallis test was used to compare data in subjects with different malocclusions. Kendall tau-b correlation was used to evaluate the relationship between OHIP-14 scores and IOTN parameters in different malocclusions.  $P < 0.05$  was considered statistically significant in all tests.

## RESULTS

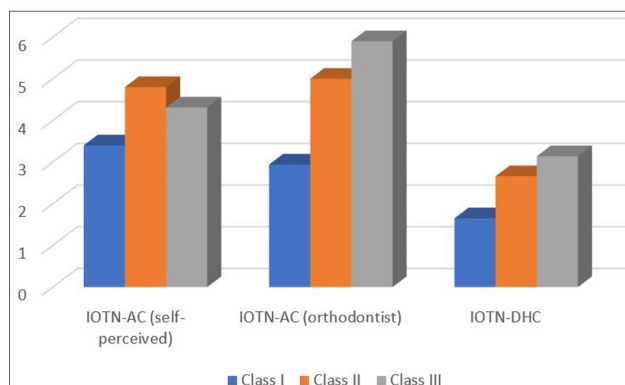
A total of 261 child-parent dyads participated in this cross-sectional study. The distribution of clinical and socio-demographic variables by gender is shown in Table 1. The distribution of clinical and demographic characteristics by dental malocclusions is shown in Table 2 and the distribution of aesthetic and dental components of IOTN according to dental malocclusion groups is shown in Figure 2. 158 of the children participating in the study were girls (mean age:  $13.03 \pm 1.93$ ) and 103 were boys (mean age:  $12.66 \pm 1.75$ ). While 58.62% of the participants were born by vaginal birth, 41.48% of them were born by cesarean section and it was determined that only 44 of the participants (16.86%) had nasal breathing. While the mean OHIP-14 score was  $8.80 \pm 6.70$  in girls, it was  $7.77 \pm 6.67$  in boys, and this difference between genders was not statistically significant ( $P = 0.162$ ). IOTN-AC (self-perceived) values, were  $3.82 \pm 2.65$  on average for girls and  $3.99 \pm 2.56$  for boys. There was no significant



difference between the genders in terms of mean IOTN-DHC and IOTN-AC scores ( $P>0.05$ ). While there was no significant difference between the dental malocclusion groups in terms of age and distribution of OHIP-14 scores, there was a statistically significant difference in terms of IOTN-DHC and IOTN-AC scores. In patients with dental Class III malocclusion, IOTN-DHC scores were found to be significantly higher than other malocclusion groups ( $P<0.001$ ). Dental Class II malocclusion group's IOTN-AC (self-perceived) scores, in which individuals scored their own dental aesthetic appearance, were significantly higher than Class I malocclusion group ( $P<0.001$ ).

Demographic Variables	Male (n=103)	Female (n=158)	P-value
	Mean (SD)	Mean (SD)	
Age (years)	12.66 (1.75)	13.03 (1.93)	0.174#
Type of Birth			0.830*
Normal Birth	66	87	
Cesarian Section	37	71	
Breathing Pattern			0.148*
Mouth Breathing	18	26	
Nose Breathing	85	132	
Clinical Variables			
OHIP-14	7.77 (6.67)	8.80 (6.70)	0.162#
IOTN-AC (self-perceived)	3.99 (2.56)	3.82 (2.65)	0.370#
IOTN-AC (orthodontist)	4.03 (2.87)	3.70 (2.61)	0.484#
IOTN-DHC	2.25 (1.21)	1.99 (1.02)	0.116#

# Results of Mann-Whitney U test. \* Results of Pearson Chi-Square test.



**Figure 2.** The distribution of aesthetic and dental components of IOTN according to dental malocclusion groups.

The evaluation of the correlation between OHIP-14 data and IOTN scores by dental malocclusion groups is shown in Table 3. Accordingly, IOTN-AC (self-perceived), IOTN-AC (orthodontist) and IOTN-DHC scores showed a positive correlation with each other in all malocclusion groups. There was no statistically significant difference in the correlation between OHIP-14 scores and IOTN scores in any malocclusion group, so the null hypothesis was accepted and H1 hypothesis was rejected.

**Table 3. Kendal tau-b correlations between OHIP-14 scores and IOTN parameters in Class I malocclusion subjects.**

	OHIP-14	IOTN-AC (self-perceived)	IOTN-AC (orthodontist)	IOTN-DHC
<b>Dental Class I Malocclusion</b>				
OHIP-14	-	0.082	0.050	0.062
IOTN-AC (self-perceived)	0.082	-	0.588**	0.525**
IOTN-AC (orthodontist)	0.050	0.588**	-	0.746**
IOTN-DHC	0.062	0.525**	0.745**	-
<b>Dental Class II Malocclusion</b>				
OHIP-14	-	0.054	-0.029	0.040
IOTN-AC (self-perceived)	0.054	-	0.288*	0.267*
IOTN-AC (orthodontist)	-0.029	0.228*	-	0.679**
IOTN-DHC	0.040	0.267*	0.676**	-
<b>Dental Class III Malocclusion</b>				
OHIP-14	-	0.041	-0.079	0.067
IOTN-AC (self-perceived)	0.041	-	0.347*	0.332*
IOTN-AC (orthodontist)	-0.079	0.347*	-	0.539**
IOTN-DHC	0.067	0.332*	0.539**	-

Significance levels, \* $P < 0.05$  \*\* $P < 0.01$ .

## DISCUSSION

Evaluation of OHRQoL in addition to traditional diagnostic tools and normative measures can be applied to interpret treatment need and priority in orthodontic malocclusions that affect psychosocial status in children (26). In this study, the possible effects of orthodontic treatment need defined in different malocclusion groups and aesthetic perception determined by both the physician and patient on OHRQoL were evaluated. 261 children participated in our study and 60.5% of the

**Table 2. Clinical and demographic characteristic of participants by dental malocclusion.**

	Class I (n=161)	Class II (n=71)	Class III (n=29)	P-value#	Post Hoc Test*		
	Mean (SD)	Mean (SD)	Mean (SD)		I-II	I-III	II-III
Age (years)	12.82 (1.72)	13.06 (2.18)	12.86 (1.92)	0.611	0.318	0.757	0.776
OHIP-14	8.48 (6.77)	8.42 (6.94)	7.83 (5.77)	0.973	0.922	0.815	0.900
IOTN-AC (self-perceived)	3.40 (2.53)	4.80 (2.65)	4.31 (2.32)	<0.001	<0.001	0.019	0.504
IOTN-AC (orthodontist)	2.94 (2.47)	5.00 (2.22)	5.90 (2.96)	<0.001	<0.001	<0.001	0.152
IOTN-DHC	1.65 (0.91)	2.66 (0.98)	3.14 (1.03)	<0.001	<0.001	<0.001	0.034

# Results of Kruskal Wallis H test. \*Results of Mann Whitney U test.



participants were girls. In similar studies, it was stated that female participants who applied with the desire to receive orthodontic treatment were more than males (26-28). This may be related to the increased desire for orthodontic treatment because parents pay more attention to the physical appearance of their daughters. Likewise, it is known that girls have higher anxiety about their own physical appearance than boys (26). In our study, it was found that OHIP-14 scores, which measure OHRQoL, were higher in girls than boys, but this difference was not statistically significant.

While determining the need for orthodontic treatment in routine clinical examinations, factors such as patient demand, dental malocclusion, skeletal malocclusion, loss of function and aesthetic requirements are evaluated. Although the popularity of OHRQoL indices is increasing day by day, its use as an indicator of routine treatment needs is controversial. Psychosocial development of children is affected by aesthetic concerns, self-confidence, and free expression. It is thought to be a part of this chain due to dental malocclusions associated with oral health. While planning the treatment, it is important to evaluate both aesthetic and dental factors and patient expectations comprehensively. In this study, aesthetic perception was evaluated by both the physician and the patient using the IOTN-AC index. There was no significant difference between the genders in terms of mean IOTN-AC scores. Similar to this finding in some studies, it was found that the OHRQoL scores of female and male patients were not significantly different (29, 30). However, Buyukbayraktar and Doruk found that female patients had higher OHRQoL scores than males because of that female patients give more attention to their physical appearance than male patients (31).

Orthodontic malocclusions influence physical appearance dissatisfaction in the child-adolescent population (29, 32). It was determined that there was no difference between the Class I, Class II and Class III malocclusion groups in terms of OHIP-14 scores. It is noteworthy that the OHIP-14 scores of patients with increased overjet seen with dental Class II malocclusion or negative overjet with Class III malocclusion were not affected by this dental condition. Although Soh et al. (33) reported that increased overjet seen in Class II division 1 malocclusions, in the Asia population was perceived by lay people as the main occlusal feature affecting dental aesthetics. However, Tessarollo et al. (30) reported that increased overjet and anterior diastema did not affect OHRQoL in their study evaluating the effects of malocclusions on dental appearance satisfaction and oral functions of adolescents. It is worth noting that molar relationship, a condition that represents an important aspect of normative orthodontic diagnosis, was not associated with OHRQoL scores of the children

in this study. The effect of OHRQoL scores according to malocclusion types is various according to the studies because of it is related to the sociocultural level of the population in which the study was conducted. However, the effect of children's dental conditions on the OHRQoL is more related to the child's self-perception rather than the type of malocclusion. Physical self-concept development of the children is based on their own physical qualities, their reactions perceived by the people around them, the comparisons they make among themselves, and cultural differences between the populations (30). While children were determining their OHRQoL, malocclusion types did not affect the results, but they scored according to their own individual perceptions.

IOTN-AC (self-perceived), IOTN-AC (orthodontist) and IOTN-DHC scores showed a positive correlation with each other in all malocclusion groups. In terms of aesthetic scoring, the children's self-perception scores and the orthodontist evaluation were found to be compatible with each other. It can be concluded that the aesthetic perceptions of the children in the study group are realistic. In addition, it was found that patients with high aesthetic IOTN scores also had high IOTN dental scores. This shows that the IOTN index is a reliable measurement tool in determining the need for orthodontic treatment.

Although studies on OHRQoL in children have increased in the literature, studies on this subject in Turkey are limited. OHRQoL affected by many factors such as gender, age, sociocultural and socioeconomic level, so OHRQoL cannot be determined using only a verified measurement (26). This study has some limitations. Even though we planned our study between the ages of 11-15, some children in the mixed dentition period are also included in the study because dental age and chronological age do not always match. Since it is known that different results can be obtained in IOTN-AC scores in mixed and permanent dentition, children with permanent dentition may be included in the sample in future studies. Another limitation of the study is that the sociocultural and geographical background is limited to a limited population and only the individuals in the relevant location are evaluated. Therefore, the study sample may not be representative of all Turkish children at this age, and future studies using larger sample sizes from different geographical regions may be planned. Socioeconomic levels, one of the factors affecting OHRQoL scores, were not evaluated in this study. Since the main goal of the study was to determine OHRQoL values among malocclusion types, other variables were ignored. However, the findings of this cross-sectional study evaluating the relationship between malocclusions and OHRQoL may offer recommendations for future longitudinal studies with large samples.



## CONCLUSIONS

According to results of this study it was concluded that;

- OHRQoL is not adversely affected in children with a defined need for orthodontic treatment,
- There was no difference between the malocclusion groups in terms of OHRQoL levels,
- The IOTN is an effective method used to determine the orthodontic treatment need in children aged 11-15,
- Considering the limitations of the study, it would be beneficial to conduct further longitudinal studies involving larger sample size and different geographical areas.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** This cross-sectional study was approved by the Non-Invasive Clinical Trials Publication Ethics Committee at Nevşehir Hacı Bektaş Veli University (Reference No: 2022.02.10.).

**Informed Consent:** Informed consent forms that described the study method and requested consent were obtained separately from the children and their families who contributed to the study.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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