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# Early-stage pain trajectory and analgesic use in fixed versus clear aligner treatment across different malocclusion classes: a prospective cohort study

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## Abstract

# Background

Pain and discomfort during orthodontic treatment are important clinical factors that can influence patient compliance. Although previous studies have reported differences between fixed appliances (FA) and clear aligners (CA), the effect of malocclusion type on this experience is still not well understood. This study aimed to compare early-stage pain and analgesic use between clear aligners and fixed appliances.

# Methods

This prospective cohort study included 150 patients (FA: n = 75; CA: n = 75), with equal distributions of Angle Class I, II, and III malocclusions in both groups (n = 25 each). The FA group was treated with 0.014-inch NiTi archwires, whereas the CA group was subjected to a 7–10-day aligner change protocol. Pain intensity was assessed using a 0–100 mm visual analogue scale (VAS) on days 1, 2, 7, 14, and 21. Patient-reported subscales were scored on a 0–4 scale. Repeated measurements were analysed using linear mixed-effects models. Analgesic use (yes/no) and tablet counts were analysed using logistic and negative binomial GEE models, respectively. All analyses were adjusted for age and sex.

# Results

VAS scores decreased over time and differed between treatment groups. Pain scores were lower in the CA group during the first 14 days, with no difference at day 21. Analgesic use and tablet counts were lower in the CA group. Pain and mechanical irritation scores were also lower in the CA group. Differences decreased over time.

# Conclusions

Clear aligner treatment was associated with lower pain levels and reduced analgesic use during the early phase of orthodontic treatment. However, these differences decreased over time and were no longer evident by the third week.

## INTRODUCTION

Orthodontic treatment is widely used to correct malocclusions and improve both function and aesthetics. However, pain and discomfort during treatment remain important clinical factors that can influence patient compliance and overall treatment experience.

Pain, particularly in the early stages of treatment, can reduce patient motivation and, in rare cases, lead to premature termination of treatment [1]. Orthodontic pain is associated with an inflammatory response in the periodontal ligament, vascular changes, and the release of mediators resulting from mechanical forces applied to the teeth.

Following the application of force, vascular changes occur in areas of compression and tension; an increase in inflammatory mediators such as prostaglandins and cytokines enhances nociceptor sensitivity, thereby lowering the pain threshold [2-4]. Clinically, pain typically begins within the first few hours, peaks at approximately 24 hours, and then gradually decreases over the following days [5,6].

Fixed orthodontic appliances and clear aligner systems represent the two main treatment approaches in contemporary orthodontic practice. It has been suggested that clear aligners may provide greater patient comfort due to their removable nature and differences in force delivery mechanisms. Randomized clinical trials and systematic reviews have shown that patients treated with clear aligners report lower pain levels, particularly during the early stages of treatment [6]. However, pain perception is not solely dependent on the type of appliance; it is influenced by multiple factors, including the individual pain threshold, applied force characteristics, and type of malocclusion [7].

Although the current literature compares early-stage pain levels between clear aligners and fixed appliances, longitudinal cohort studies that incorporate balanced malocclusion classes, multidimensional patient-reported outcomes, and analgesic consumption as a behavioral measure are limited. This gap creates uncertainty regarding the generalizability of observed comfort differences between treatment modalities. In this context, understanding early orthodontic discomfort as a dynamic and multidimensional adaptive process, rather than merely a comparison between appliance types, may provide additional clinical insight.

The primary aim of this study was to compare early-stage pain intensity among patients with different types of Angle malocclusion treated with fixed orthodontic appliances and clear aligners. The secondary aim was to evaluate analgesic use and patient-reported outcomes, including functional, mechanical, and psychosocial dimensions, according to treatment modality. The temporal course of treatment-related pain was assessed longitudinally at predefined time points.

**Specific objectives or hypotheses**

(1) The orthodontic treatment modality (clear aligner vs. fixed appliance) is associated with early-stage pain perception;

(2) The orthodontic treatment modality is associated with analgesic use during early treatment;

(3) Malocclusion class is associated with differences in at least some dimensions of patient-reported outcomes, particularly functional impact.

# METHODS

**Study design**

This prospective comparative cohort study was conducted to evaluate early-stage pain perception and temporal changes in patient-reported outcomes in patients treated with fixed orthodontic appliance (FA) and clear aligner system (CA). Participants were recruited consecutively during routine clinical visits. Treatment allocation was based on clinical indications and patient preference; therefore, the study was not randomized.

To enhance comparability between groups, the malocclusion classes were equally distributed, and the baseline demographic characteristics were similar. In addition, standardized initial biomechanical protocols were applied in both groups to reduce potential confounding.

The study was conducted in a university-based orthodontic clinic and reported in accordance with the STROBE guidelines for observational studies. Ethical approval was obtained from the Institutional Clinical Research Ethics Committee (Approval No: 25.20.70), and the study was carried out in accordance with the principles of the Declaration of Helsinki. The study was designed to reflect real-world clinical conditions.

**Participants, eligibility criteria, and setting**

Participants were recruited consecutively from patients attending the university-based orthodontic clinic between February 2025 and January 2026. Before the main study, a pilot phase was carried out with 15 patients to develop the questionnaire.

The inclusion criteria were permanent dentition, absence of systemic disease or chronic pain conditions, and no previous orthodontic treatment. Patients who regularly used analgesic or anti-inflammatory medication, had active periodontal disease, or did not comply with the study protocol were excluded.

All participants completed the scheduled follow-up assessments, and outcome data were collected at each time point. There was no loss to follow-up, and complete outcome data were available for all participants.

**Exposures, predictors, potential confounders, and effect modifiers**

The primary exposure variable was orthodontic treatment modality (fixed appliance vs clear aligner). Time (measurement points) and malocclusion class were included as predictors.

Age and sex were considered potential confounders and were included as covariates in all the models. Effect modification was assessed using treatment-by-time interaction terms.

**Outcomes (primary and secondary)**

The primary outcome was overall pain intensity, which was assessed using a 0–100 mm visual analogue scale (VAS), with endpoints defined as “no pain” and “unbearable pain” [8].

The secondary outcomes included functional pain, mechanical irritation, psychosocial impact, and analgesic use.

Functional pain was evaluated using a five-item subscale, including pain during chewing, pain at rest, pain during biting with the anterior and posterior teeth, and pain during tooth clenching. This structure was based on previously published studies assessing orthodontic pain experience [9–11]. Each item was scored on a scale from 0 (none) to 4 (very severe), and mean scores were calculated.

Mechanical irritation was assessed using a subscale evaluating soft tissue sensitivity and discomfort related to orthodontic appliances. This construct was also based on previously reported discomfort patterns during orthodontic treatment [9,11]. The items were scored on a 0–4 scale.

Psychosocial impact was assessed using a brief two-item subscale evaluating effects on school/work performance and social communication. This measure was developed on the basis of studies examining the social and adaptive aspects of orthodontic treatment and was used for exploratory purposes [10,12]. This measure was included to provide an exploratory perspective on patient experience and should be interpreted accordingly.

Analgesic use was recorded at each time point both as a binary variable (use vs no use) and as the total number of tablets consumed. Analgesic consumption has been reported as a behavioral indicator of the experience of orthodontic pain [5,13].

The internal consistency of the subscales was assessed using Cronbach's alpha coefficient.

**Sample size calculation**

The sample size was determined on the basis of an a priori power analysis assuming a clinically meaningful difference of at least 15 mm in VAS score ($\alpha=0.05$, power=0.80). The minimum required sample size was calculated as 29 patients per group. The final sample size of 75 patients per group provided sufficient statistical power for the planned analyses.

**Sources of Bias and comparability between exposure groups**

Owing to the nonrandomized design, selection bias cannot be completely excluded, as treatment allocation was based on clinical indications and patient preference. However, to improve comparability between groups, the malocclusion classes were equally distributed, and the baseline demographic characteristics were similar.

In addition, standardized initial biomechanical protocols were applied in both groups to reduce potential performance bias. Adjustment for age and sex was also performed in the statistical models to control for potential confounding factors. Potential sources of bias were considered during the study design and analysis, and efforts were made to minimize their impact through balanced group allocation and

statistical adjustment. Patients choosing clear aligner treatment may also have had different expectations regarding comfort, which could have influenced their pain reporting.

### Statistical analysis

All the statistical analyses were performed using Python software (version 3.10). Descriptive statistics are presented as mean(SD) for continuous variables and as counts and percentages for categorical variables.

VAS scores and subscale measures were analysed using linear mixed-effects models to account for repeated measurements within individuals and to capture subject-specific variability. Fixed effects included treatment group, time, malocclusion class, and their interactions, while age and sex were included as covariates. A random intercept was included to account for within-subject correlation.

Analgesic use (yes/no) was analysed using logistic generalized estimating equations (GEEs), and the total number of tablets was analysed using a negative binomial GEE model to account for overdispersion in the count data. An exchangeable working correlation structure was used for the GEE models.

The selection of statistical models was based on the structure of the data and the interpretation of interest. Continuous outcomes were analysed using linear mixed-effects models to obtain subject-specific estimates by accounting for within-subject variability, whereas generalized estimating equations (GEE) were employed to obtain population-averaged estimates for binary, count, and continuous outcomes. The assumptions of the mixed-effects models pertain to the distribution of residuals rather than the outcome variables themselves. Thus, model selection was guided by the research question and the desired interpretation of effects rather than solely by outcome distribution.

Interaction terms between treatment and time were tested in all models. For outcomes where the interaction was not statistically significant, overall treatment effects were reported.

Model assumptions were evaluated using residual diagnostics. Statistical significance was set at $p < 0.05$. This approach allowed appropriate modelling of different outcome structures while accounting for within-subject correlation. Mixed-effects models provide subject-specific estimates, whereas GEE models provide population-averaged estimates. Given the different nature of the outcomes (continuous vs binary/count), this combined approach was considered the most appropriate to obtain clinically interpretable results. No missing data were observed; therefore, no imputation methods were applied.

## RESULTS

### Participant flow

Overall, 162 patients were assessed for eligibility. Twelve patients were excluded because they did not meet the inclusion criteria or declined to participate. The remaining 150 patients were included in the

study (FA: n = 75; CA: n = 75). All participants completed the scheduled follow-up assessments at the predefined time points, and no loss to follow-up or missing data was observed (Figure 1).

**Baseline data**

Baseline demographic characteristics of the participants are presented in Table 1. The mean age was similar between the FA and CA groups (17.16 (5.98) vs 17.74 (6.05) years). The distribution of sex was also comparable between groups, indicating comparable baseline characteristics. Pain scores at the first measurement (Day 1), obtained after appliance placement, were lower in the clear aligner group compared with the fixed appliance group (Table 1).

Table 1. Baseline characteristics of the study population

| Variable | Fixed Appliance (n=75) | Clear Aligner (n=75) | p value |
|---|---|---|---|
| **Age (years), mean (SD)** | 17.16 (5.98) | 17.74 (6.05) | 0.62 |
| **Sex, n (%)** | | | 0.58 |
| Female | 40 (53.3%) | 37 (49.3%) | |
| Male | 35 (46.7%) | 38 (50.7%) | |
| **Malocclusion class, n (%)** | | | Not applicable |
| Class I | 25 (33.3%) | 25 (33.3%) | |
| Class II | 25 (33.3%) | 25 (33.3%) | |
| Class III | 25 (33.3%) | 25 (33.3%) | |
| **VAS score at Day 1, mean (SD)** | 62.6 (18.4) | 49.6 (17.2) | <0.001 |

Values are presented as mean (SD) or number (percentage).

**Numbers analysed for each outcome, estimation and precision**

All 150 participants (FA: n=75; CA: n=75) were included in the analyses for all outcomes. All participants were included in all analyses, and estimates are presented with corresponding measures of precision (95% confidence intervals).

**Primary outcome (VAS pain score)**

In the linear mixed-effects model, a significant effect of time was observed ($p<0.001$). The treatment × time interaction was also significant ($p<0.001$), indicating that changes in pain over time differed between the treatment groups.

VAS scores were lower in the CA group during the first 14 days (Table 2, Figure 2), with no difference between groups at day 21.

Table 2. Differences in VAS pain scores between clear aligners and fixed appliances over time (linear mixed-effects model)

| Variable | β | 95% CI | p |
|---|---|---|---|
| Time (overall effect) | — | — | <0.001 |
| Treatment × Time | — | — | <0.001 |
| CA vs FA (Day 1) | −18.5 | −25.0 to −12.0 | <0.001 |
| CA vs FA (Day 2) | −18.1 | −24.6 to −11.6 | <0.001 |
| CA vs FA (Day 7) | −20.7 | −27.3 to −14.1 | <0.001 |
| CA vs FA (Day 14) | −11.3 | −17.8 to −4.8 | <0.001 |
| CA vs FA (Day 21) | −5.8 | −12.3 to 0.7 | 0.079 |

**Abbreviations:** VAS, visual analogue scale; CA, clear aligner; FA, fixed appliance; CI, confidence interval. Negative β values indicate lower VAS scores in the CA group.

**Analgesic use and tablet counts**

Analgesic use and tablet counts were lower in the CA group (Table 3, Figure 3).

Table 3. Analgesic use and tablet counts (GEE models)

A) Logistic GEE (Analgesic use: Yes/No)

| Variable | OR | 95% CI | p |
|---|---|---|---|
| CA vs FA (overall) | 0.35 | 0.21–0.58 | <0.001 |

The results are presented as odds ratios (ORs) for the logistic model and incidence rate ratios (IRRs) for the negative binomial model.

B) Negative binomial GEE (Tablet count)

| Variable | IRR | 95% CI | p |
|---|---|---|---|
| CA vs FA (overall) | 0.41 | 0.27–0.63 | <0.001 |

The interaction terms were not statistically significant; therefore, overall estimates are presented.
**Abbreviations:** OR, odds ratio; IRR, incidence rate ratio; CI, confidence interval. An OR or IRR < 1 indicates lower analgesic use in the CA group.

Estimates were obtained from generalized estimating equations (GEE) models with an exchangeable correlation structure, adjusted for age and sex. The reference category for treatment was fixed appliance (FA).

**Other analyses (patient-reported subscales)**

Pain and mechanical irritation scores were lower in the CA group (Table 4). Psychosocial scores differed according to treatment and time (Table 5). Although malocclusion class was not significantly associated with pain, irritation, or psychosocial subscales (Table 4), a significant association was observed for functional impact (p=0.009; Table 5), with Class II malocclusion showing lower scores than Class I in post-hoc comparisons.

Table 4. Mixed-effects model results for patient-reported outcomes (adjusted for age and sex)

| Variable | β (Clear aligner vs Fixed appliance) | 95% CI | p |
|---|---|---|---|
| **A. Pain subscale** | | | |
| Treatment (CA vs FA) | -0.80 | -1.10 to -0.50 | <0.001 |
| Time (overall effect) | - | - | <0.001 |
| Malocclusion (overall) | - | - | 0.38 |
| Treatment × Time | - | - | 0.11 |
| **B. Irritation subscale** | | | |
| Treatment (CA vs FA) | -0.55 | -0.82 to -0.28 | <0.001 |
| Time (overall effect) | - | - | <0.001 |
| Malocclusion (overall) | - | - | 0.44 |
| Treatment × Time | - | - | 0.08 |
| **C. Psychosocial subscale** | | | |
| Treatment (CA vs FA) | -0.36 | -0.63 to -0.09 | 0.009 |
| Time (overall effect) | - | - | <0.001 |
| Malocclusion (overall) | - | - | 0.43 |
| Treatment × Time | - | - | 0.003 |

Estimates are presented as β coefficients with 95% confidence intervals. Models were adjusted for age (continuous) and sex ( female vs male). The reference category for treatment was fixed appliance (FA). *For malocclusion, p-values are from omnibus Wald tests (not pairwise comparisons).*

Table 5. Functional impact and post hoc comparisons

A) Mixed-effects model (Wald tests)

| Term | $\chi^2$ (df) | p |
|---|---|---|
| Treatment | 19.90 (1) | <0.001 |
| Time | 499.11 (4) | <0.001 |
| Malocclusion | 9.44 (2) | 0.009 |
| Treatment × Time | 27.92 (4) | <0.001 |

B) Post hoc comparisons (Bonferroni-adjusted)

| Comparison | β | 95% CI | Adjusted p |
|---|---|---|---|
| Class 2 vs Class 1 | −0.359 | −0.595 to −0.123 | 0.009 |
| Class 3 vs Class 1 | −0.249 | −0.480 to −0.018 | 0.103 |
| Class 3 vs Class 2 | 0.110 | −0.126 to 0.346 | 1.000 |

Estimates were obtained from a linear mixed-effects model adjusted for age and sex. The reference category for treatment was fixed appliance (FA).

# DISCUSSION

**Main findings in the context of the existing evidence, interpretation**

In this prospective comparative cohort study, early-stage pain experience and patient-reported outcomes were evaluated in patients treated with fixed orthodontic appliances and clear aligners across different malocclusion classes. These findings indicate that pain scores and analgesic use were lower in the clear aligner group during the early phase of treatment; however, this difference disappeared by the third week. These findings support the concept that orthodontic pain is a transient biological response that decreases over time.

The temporal pattern observed in both groups, with pain peaking within the first 24–48 hours and gradually declining thereafter, is consistent with the inflammatory response following orthodontic force application [2-4]. An increase in inflammatory mediators such as prostaglandins and cytokines is known to increase nociceptor sensitivity and contribute to early pain perception [5].

The observed difference in VAS scores in the early period exceeds the minimal clinically important difference reported in the literature [14], suggesting that the early comfort advantage associated with clear aligners may be clinically relevant. However, given the observational design of the study, these findings should be interpreted as associations rather than causal effects. This also reflects the time-

dependent nature of the observed treatment differences, as supported by the significant treatment-by-time interaction.

The temporal pattern of analgesic use paralleled the pain scores, with greater consumption in the fixed appliance group during the early phase and a marked decline over time in both groups. These findings support previous evidence indicating that orthodontic pain is related primarily to the acute inflammatory phase [15,16]. Including analgesic use as an additional outcome helped support the findings of pain in addition to self-reported scores.

Previous studies have reported lower pain levels with clear aligner treatment, particularly during the initial stages [6, 17, 18]. However, some studies have not reported consistent differences at later time points, suggesting that pain may also be influenced by force dynamics and treatment protocols rather than appliance type alone [18, 19]. These findings are consistent with the present results and highlight the multifactorial nature of orthodontic pain.

The lower mechanical irritation scores observed in the clear aligner group may be explained by the absence of brackets and archwires, which are known sources of mucosal irritation and soft tissue discomfort [20,21]. In contrast, fixed appliances may contribute to localized irritation, particularly during the initial adaptation period.

Similarly, the lack of a significant effect of age and sex suggests that demographic factors alone may not sufficiently explain the variability in early orthodontic pain experience, which is consistent with previous studies [22, 23]. The observed difference in pain scores at the first measurement (Day 1) suggests that early pain perception may have been influenced by factors other than treatment modality. Therefore, subsequent comparisons should be interpreted with caution, and the treatment-by-time interaction becomes particularly important in understanding the temporal evolution of pain. The baseline difference in the Day 1 VAS score may indicate pretreatment differences between the groups. However, the inclusion of treatment-by-time interactions and repeated measures modelling partially accounts for these differences. As baseline pain before appliance placement was not assessed, residual baseline differences between groups cannot be excluded.

**Strengths and limitations**

The strengths of this study include the balanced distribution of malocclusion types, the standardization of initial biomechanical protocols, and the use of statistical models appropriate for repeated measurements. The combined use of linear mixed-effects and GEE models allowed for appropriate handling of within-subject dependence and provided robust estimates for different outcome types. Furthermore, the multidimensional assessment of patient experience—including visual analogue scale (VAS) scores, functional impairment, mechanical irritation, psychosocial impact, and analgesic consumption—offers a more comprehensive evaluation of orthodontic discomfort.

However, several limitations should be considered. Although the study was prospective, it was not randomized, and treatment allocation was based on clinical indications and patient preference, which may have introduced selection bias and residual confounding. It is also possible that unmeasured factors related to patient preference or expectations may have influenced the observed differences between groups. While baseline comparability and covariate adjustment reduce this risk, they cannot be completely excluded. Therefore, causal inferences should be made with caution. Potential confounding was further addressed through statistical adjustment for age and sex; however, residual confounding cannot be completely excluded.

In addition, compliance with clear aligner use was assessed on the basis of patient reports and clinical observations rather than objective digital tracking systems, which may have limited the accuracy of adherence assessment. The use of digital wear-time monitoring systems may improve compliance evaluation in future studies.

Furthermore, the study focused only on the first three weeks of treatment, and inflammatory biomarkers were not assessed. Therefore, the underlying biological mechanisms could not be directly evaluated.

**Clinical implications**

The early reduction in pain associated with clear aligners may be clinically relevant when counselling patients and planning initial treatment strategies.

**Generalizability**

The findings of this study are generalizable to adolescent and young adult patients undergoing initial orthodontic treatment with either fixed appliances or clear aligners in a university clinic setting. The balanced distribution of malocclusion classes supports applicability across different angle classifications. However, the results may not be directly generalizable to younger children, adults with complex medical histories, or treatment protocols involving different biomechanical force levels or aligner change intervals. Additionally, as the study was conducted in a single center, multicenter studies are needed to confirm the external validity of these findings.

**Future directions**

Future studies integrating clinical pain scales with biochemical or physiological parameters may contribute to a better understanding of the biological basis of orthodontic pain. Randomized controlled trials would allow for improved control of confounding factors.

Additionally, studies evaluating masticatory muscle activity using electromyography (EMG) and investigating the biomechanical load distribution in the periodontal ligament across different malocclusion types may help clarify the mechanisms underlying functional differences. Long-term follow-up studies are also needed to assess how comfort perception, treatment compliance, and oral health-related quality of life evolve over time.

# CONCLUSION

The findings of this prospective cohort study indicate that differences in patient-reported pain levels and analgesic use may occur depending on the type of appliance used in the early phase of orthodontic treatment. Clear aligner treatment was associated with lower pain scores and less analgesic consumption, particularly in the initial days. However, this observed difference decreased over time and was no longer significant by the third week. The significant treatment-by-time interaction observed for the VAS score suggested that the difference in pain between the two treatment modalities was not constant over time. While clear aligner therapy was associated with lower pain levels in the early phase, this difference gradually diminished, and by the third week, the groups presented comparable pain levels. The clinically significant difference observed in the early period should be considered, particularly in managing patient expectations and in the appliance selection process at the start of treatment.

# Abbreviations

FA – Fixed appliances

CA – Clear aligners

VAS – visual analogue scale

# Declarations

### OTHER INFORMATION

#### Ethics approval and consent to participate

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Clinical Research Ethics Committee (Approval No: 25.20.70). Written informed consent was obtained from all participants and/or their legal guardians prior to inclusion in the study.

#### Consent for publication

Not applicable.

#### Registration and protocol accessibility

As this was an observational cohort study conducted within routine clinical practice, prospective registration in a clinical trial registry was not needed.

#### Support & Funding

This research received no external funding.

**Competing interests**

The authors declare that they have no competing interests.

**Availability of data, code and other materials**

The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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# Figures

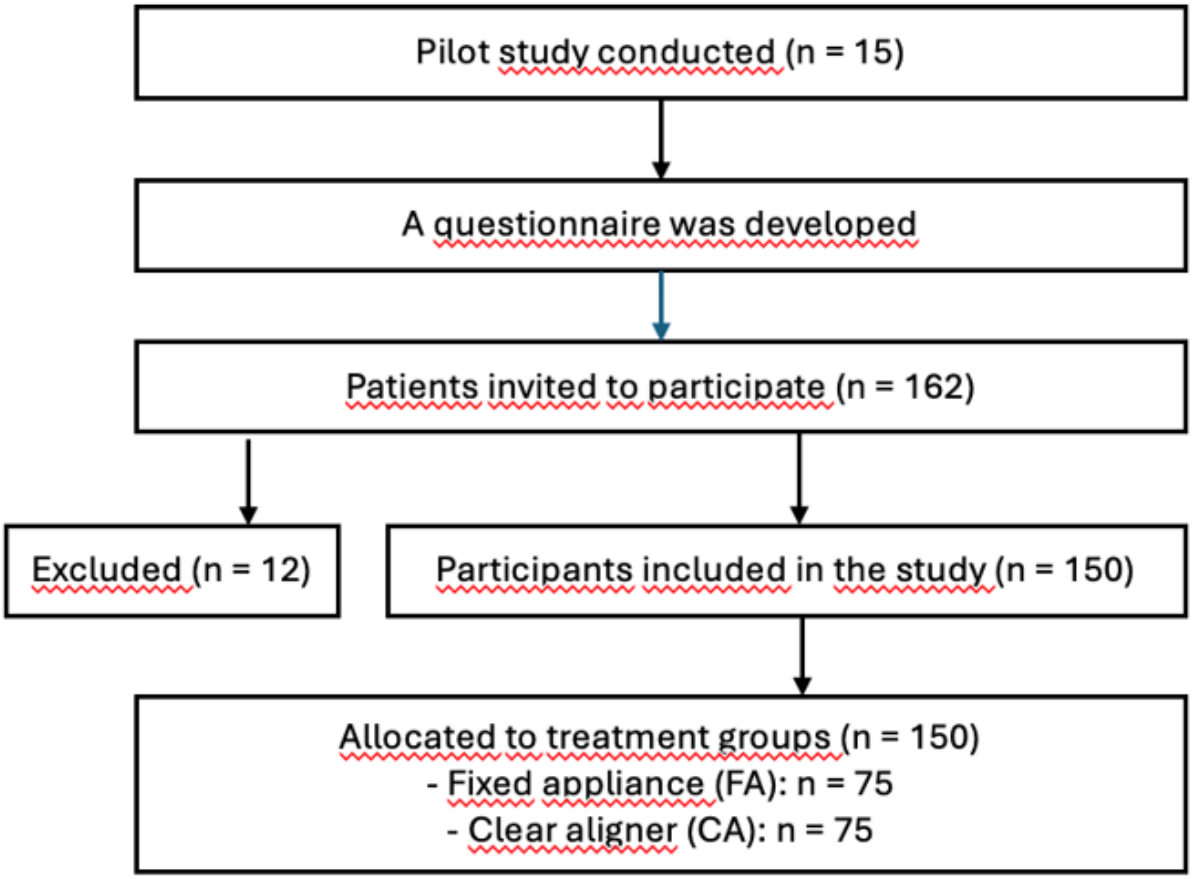



**Figure 1**

Flow diagram of participant enrollment and follow-up

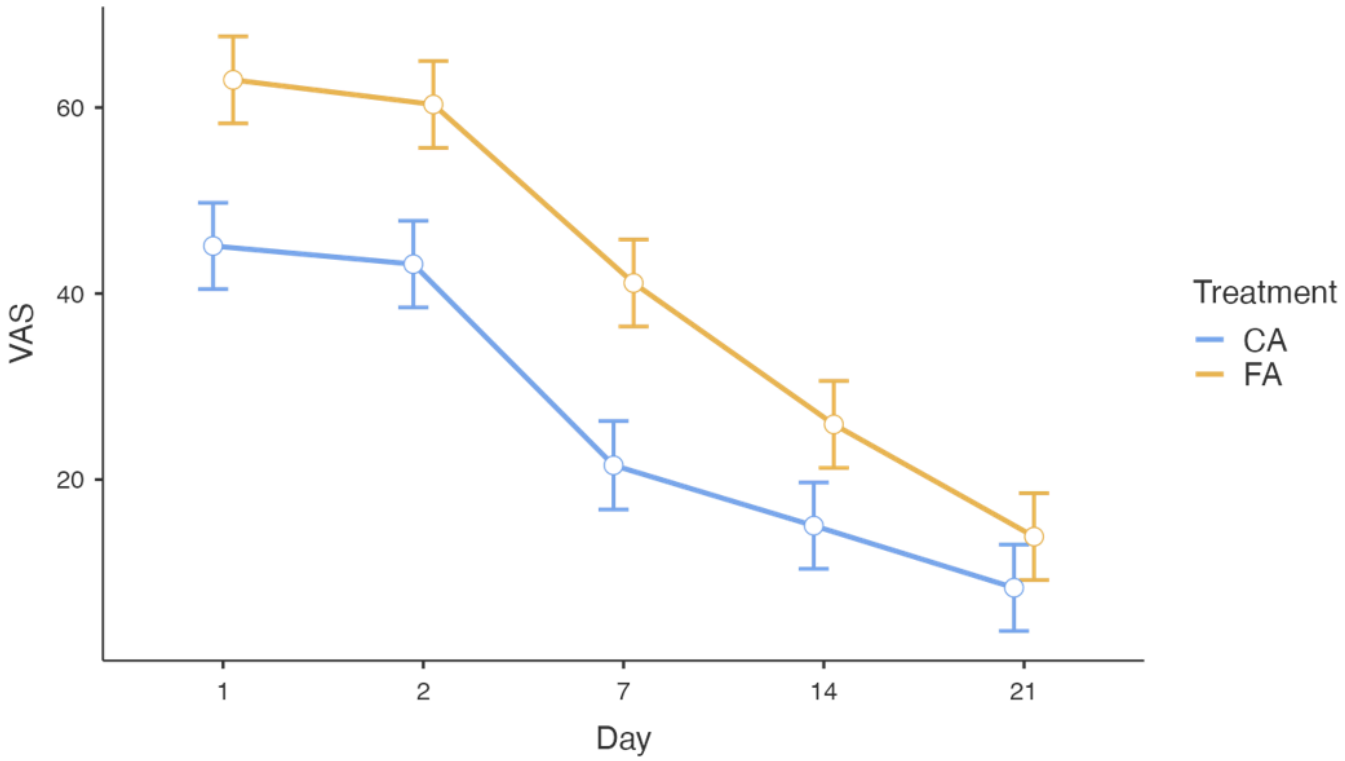



**Figure 2**

Changes in VAS pain scores over time according to treatment group. Estimated marginal means with 95% confidence intervals are shown for the fixed appliance (FA) and clear aligner (CA) groups across follow-up.

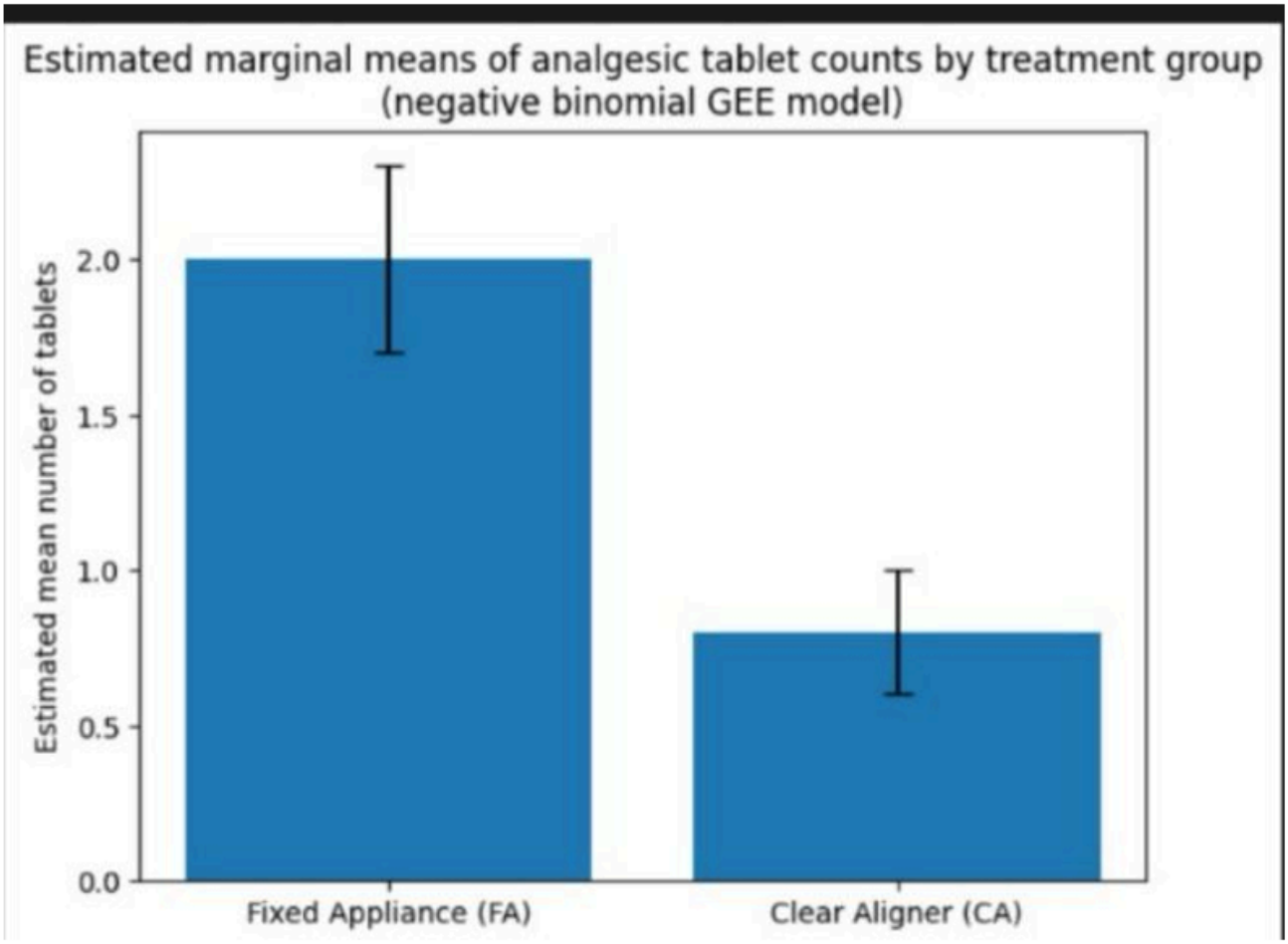



**Figure 3**

Overall estimated marginal means of analgesic tablet counts according to treatment group. Estimates were obtained from a negative binomial GEE model and represent population-averaged effects. The error bars indicate 95% confidence intervals.