THE EFFECTIVENESS OF MANDIBULAR ADVANCEMENT ALIGNERS, WITH AND WITHOUT VERTICAL BITE OPENING, IN GROWTH MODIFICATION OF CLASS II DIVISION 1 MALOCCLUSION: A RANDOMISED CONTROLLED TRIAL

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METHODOLOGY

1.1 Study design

The study was designed based on the guidelines from the Consolidated Standards of Reporting Trials (CONSORT) statement updated in 2025 (Hopewell et al., 2025), and registered in Clinicaltrials.gov for a prospective randomised clinical trial. All methods were performed in accordance with the relevant guidelines and regulations. The study was conducted in accordance with the Declaration of Helsinki as revised in 2013 (World Medical Association, 2013).

This study is a three-arm parallel, prospective, single-center randomised controlled trial. Participants were recruited voluntarily through non-probability convenience sampling at the Orthodontic Postgraduate Clinic, Universiti Malaya. Participants were screened according to the inclusion and exclusion study criteria. Informed and written consent were taken from the parent or legal guardian of the participants after details of the research and the accompanying risks were explained thoroughly. This research was conducted in three phases: the pre-treatment phase, treatment phase, and post-advancement phase. Figure 3.1 illustrates the flow chart of the whole study.

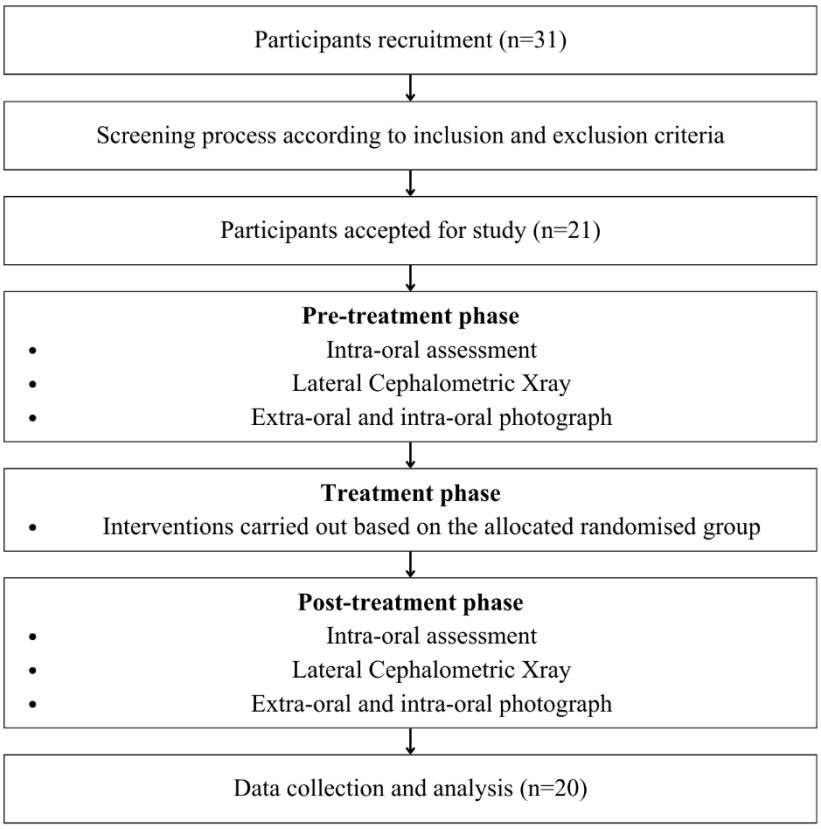

Figure 3.1 Flow chart of the study

1.2 Ethics clearance and approval

Ethical approval for the study was obtained from the Research and Ethics Committee of the Faculty of Dentistry, Universiti Malaya (Ethics Approval No. DF CD 2421/0057 (P), approved on 4th July 2024) (Appendix A).

All data and information collected were handled with strict confidentiality and were accessible only to members of the research team. Only participants who had provided written informed consent were recruited into the study. Furthermore, all participants retained the right

to withdraw from the study at any stage without prejudice and were assured of rights to continued treatment.

1.2 Participants

1.2.1 Recruitment of participants

Volunteer sampling (self-selection sampling), a form of non-probability sampling, was selected in this study. This method involved two steps: publicising the need for participants and subsequently screening their suitability, followed by either inviting or excluding them.

Participants were sourced from patients who sought orthodontic treatment from the Orthodontic Postgraduate Clinic, Universiti Malaya. The name list was compiled by the principal investigator (AKD), who then contacted the potential participants for the screening process. Both participants and their parents were provided with patient information sheets to ensure a clear understanding of the clinical trial prior to enrolment.

Although this sampling method is susceptible to selection bias, it was deemed essential and appropriate for the current study. It offered a more pragmatic and convenient approach for recruitment in a real-world clinical setting. While probability sampling is generally preferred for its robustness in generating representative numerical data, properly executed volunteer sampling can produce results of comparable quality. Furthermore, non-probability sampling was advantageous in this context as it allowed for quicker recruitment and reduced costs, given that the sample was already known to the researcher.

1.2.2 Sample size calculations

The sample size was calculated based on the standard deviation of the Wit's analysis value from a previous study by Hassan Al Subaie et al. 2023. The value was chosen for sample size calculation because it is one of the parameters that was included in this study and is significant in assessing the skeletal pattern of the participant. The sample size is calculated using G*Power software 3.1.9.7, with the consideration of α equals to 0.05, with the power set to 80%, and an effect size of 1.83mm is used. Thus, the sample size per group is 5, and the total sample size needed is 15 participants (2 intervention groups and 1 control group). This number is increased by 30% to account for the attrition range to produce the final sample size of 21 (7 samples in each group).

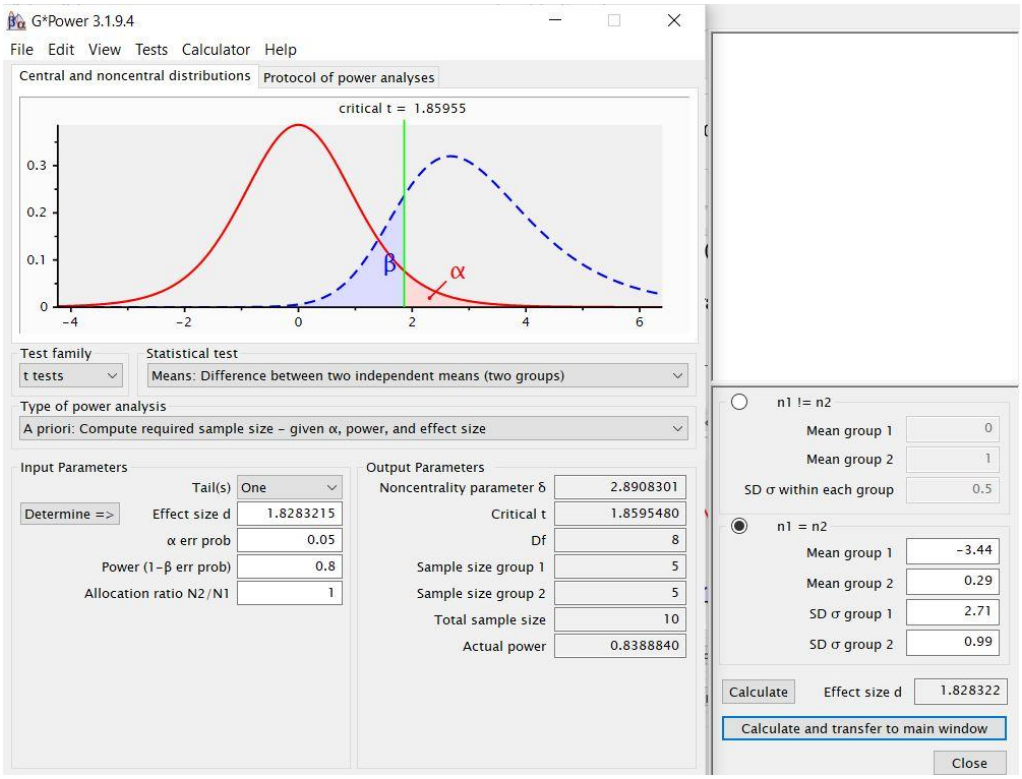

Figure 3.2 Sample size calculation

1.3 Inclusion and exclusion criteria

Participants were selected from May 2024 to May 2025 at the Orthodontic Postgraduate Clinic, Universiti Malaya, and screened according to the inclusion and exclusion criteria outlined in Table 3.1 and Table 3.2:

Table 3.1 Inclusion criteria of the participants

	Inclusion Criteria
1	Cervical Vertebrae Maturity: CS3-CS4 (Growing participants)
2	Chronological age: 10-14 years old (Female), 12-16 years old (Male)
3	Average or reduced lower anterior facial height (LAFH<57%)
4	Mild to moderate skeletal Class II (4°<ANB<9°)
5	Retrognathic mandible (SNB<78°)
6	Increased overjet (7mm≤OJ≤11mm)
7	Increased overbite by more than 30%
8	Molar relationship by more than ½ unit Class II bilaterally
9	Mild to moderate crowding

Table 3.2 Exclusion criteria of the participants

	Exclusion criteria
1	Participant with an anterior open bite
2	Participant with syndromic dentofacial anomalies
3	Participant with a previous history of orthodontic intervention
4	Participant with signs and symptoms of temporomandibular disorder

5	Participant with severe facial asymmetry (Deviation ≥4mm)
6	Not being consented to by both parents and participants
7	Poor quality of pre-treatment Lateral Cephalometric records
8	Participant with mental or physical disabilities affecting the ability to wear an appliance

1.4 Method of randomisation and blinding

In this study, blinding was only implemented during data analysis. This is due to the nature of the clinical trial, which makes it impossible for the principal investigator (AKD) and the outcome assessor to be blinded during the study. Selected participants were informed beforehand regarding the chance of getting the control or experimental interventions in their treatment.

In this study, a block sampling method was employed to ensure a balanced representation across treatment groups. The randomisation process utilised a pseudo-randomly generated code through randomisation software, employing random permuted blocks of the same size. Gender-based randomisation was also being incorporated to maintain gender equality within each group. To ensure equal representation of all treatments, seven blocks of three participants each were created: one for MAA with VBO, one for MAA without VBO, and the other for Twin Block. These represent the smallest blocks where each treatment is proportionally represented.

The sequence of intervention allocation within each block (MAA with VBO, MAA without VBO, and TB) was randomly determined. Participants were then randomly assigned to these blocks. The assignment of participants within the blocks and the order of treatments are both conducted randomly, ensuring a fair distribution of biases introduced by sequential processing across the treatment groups. The randomisation process for this study was carried out using MinimPy, a commonly used randomisation software in clinical trials (Saghaei, 2011).

An independent assistant (AQ) was appointed in this study to help in the randomisation and blinding process, as the principal investigator (AKD) was blinded during the process to prevent potential bias. The independent assistant (AQ) held the protected file with the password master list of the participants throughout the randomisation process without revealing it to the principal investigator (AKD). The independent assistant (AQ) was responsible for the randomisation process by using the MinimPy and allocated a special code to the participant without the knowledge of the principal investigator (AKD).

Figure 3.3 shows the flow chart of the method used in blinding and randomisation that has been applied in this study.

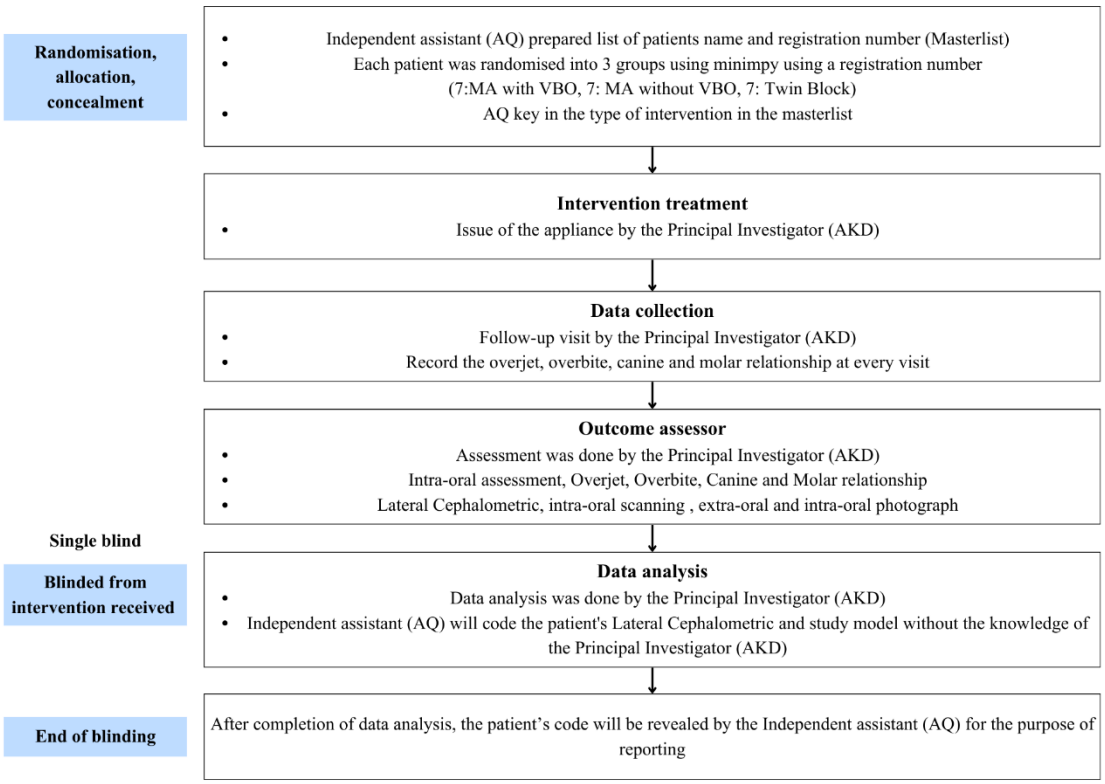

Figure 3.3 Flow chart of randomisation and blinding

1.5 Pre-treatment phase (T0)

The pre-treatment phase involved obtaining the participant's consent from the parent or legal guardian, collection of the participant's demographic data, examination and diagnosis, extra-oral and intra-oral assessment, extra-oral and intra-oral photographs of the participant, intra-oral scanning, and a pre-treatment lateral cephalometric radiograph.

1.5.1 Participant's consent

The process of obtaining informed consent from the participant's parents or legal guardians was carried out before the commencement of the study. Patient information sheets

and consent forms were issued to all participants who met the inclusion and exclusion criteria (Appendix B and Appendix C). The consent form outlined the purpose of the study, the procedures involved, potential risks and benefits, measures to ensure confidentiality, costs of the treatment, and the voluntary nature of participation.

Participants and their guardians were given sufficient time to review the consent form and raise any questions before providing written consent. It was also emphasised that participants had the right to withdraw from the study at any time without facing any consequences. The informed consent process adhered to ethical guidelines and regulations to safeguard the rights and well-being of the participants.

1.5.2 Participant's demographic information

Basic demographic information of the participants, including age, gender, and home address, was collected to establish the baseline characteristics of the study sample. Age and gender were relevant for identifying potential confounding factors that could influence treatment outcomes, particularly differences in growth stage and sex-related growth patterns. The collection of home address was undertaken solely for administrative and follow-up purposes, serving as an additional means of contacting participants to issue appointment reminders and study-related correspondence, thereby reducing the risk of loss to follow-up. Table 3.3 summarises the demographic information collected in this study.

Table 3.3 Participant's demographic information

Participant's Demographic Information
Name
Registration Number
Date of birth
Address
Contact Number
Gender

The confidentiality of participants' information was meticulously managed to ensure privacy and adherence to ethical standards. All participant data, including personal and medical information, was securely stored in password-protected electronic databases accessible only to authorised research personnel. Each participant was assigned a unique identifier code to anonymise their data, and any identifying information was kept separate from the research dataset to maintain confidentiality.

Access to participant information was restricted to research team members directly involved in data collection, analysis, and management. Furthermore, any published or disseminated findings were presented in aggregate form to prevent the identification of individual participants. Before the data collection, participants were informed about the confidentiality measures in place and were required to provide informed consent for their participation, including the use and storage of their data. Compliance with data protection

regulations and ethical guidelines was ensured throughout the study to safeguard the confidentiality and privacy of the participants.

1.5.3 Intra-oral assessment

The intra-oral assessments that are very important in assessing the progress of the treatment are incisor relationship, canine relationship, and molar relationship. These assessments are explained and defined in Tables 3.4 to 3.6 and Figure 3.4.

Table 3.4 Definition of incisor relationship (British Standards Institute, 1936)

Classification	Description
Class I	The lower incisor tips occlude or lie below the cingulum plateau of the upper incisors
Class II	The lower incisor tips occlude or lie posterior to the cingulum plateau of the upper incisors. The classification is further subdivided into 2 divisions
Class II Div 1	The overjet is increased with upright or proclined upper incisors
Class II Div 2	The upper incisors are retroclined, with a normal or occasionally increased overjet
Class III	The lower incisor tips occlude or lie anterior to the cingulum plateau of the upper incisors.

Table 3.5 Definition of canine relationship

Classification	Description

Class I	The maxillary permanent canine should occlude directly in the embrasure between mandibular canine and first premolar
Class II	The maxillary permanent canine occludes in front of the embrasure between mandibular canine and first premolar
Class III	The maxillary permanent canine occludes behind the embrasure between mandibular canine and first premolar

Table 3.6 Definition of molar relationship

Classification	Description
Class I	The mesiobuccal cusp of the maxillary first molar occludes on the anterior buccal groove of the mandibular first molar
Class II	The mesiobuccal cusp of the maxillary first molar occludes anteriorly to the anterior buccal groove of the mandibular first molar
Class III	The mesiobuccal cusp of the maxillary first molar occludes posteriorly to the anterior buccal groove of the mandibular first molar

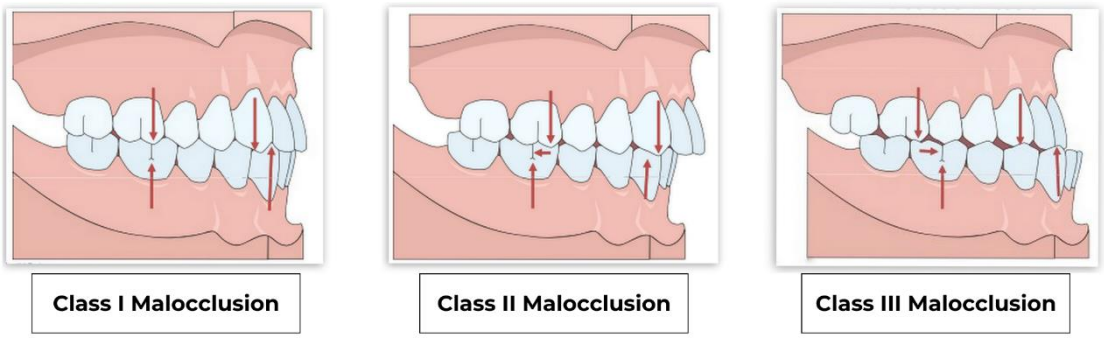

Figure 3.4 The Angle's classification of canine and molar relationship

1.5.4 Extra-oral and Intra-oral Photographs

Figures 3.5 and 3.6 illustrate the extra-oral and intra-oral photographs of the participant that will be taken at the pre-treatment phase (T0). Extra-oral photographs are essential for documenting the participant's facial proportions, symmetry, profile, and soft-tissue relationships at baseline, which are particularly important in participants with Class II malocclusion, where sagittal discrepancies and facial convexity are key diagnostic features. These images serve as a reference for evaluating treatment-induced alterations in facial aesthetics following mandibular advancement therapy.

Intra-oral photographs provide a detailed record of the dental arches, occlusal relationships, overjet, overbite, and transverse discrepancies prior to treatment. They are crucial for diagnosing the severity of malocclusion, identifying dentoalveolar compensations, and

planning appliance design and activation protocols. Furthermore, standardised intra-oral photographs enable longitudinal comparison of occlusal changes before and after treatment, facilitating assessment of treatment effectiveness and stability.

Figure 3.5 Extra-oral photographs of the participant

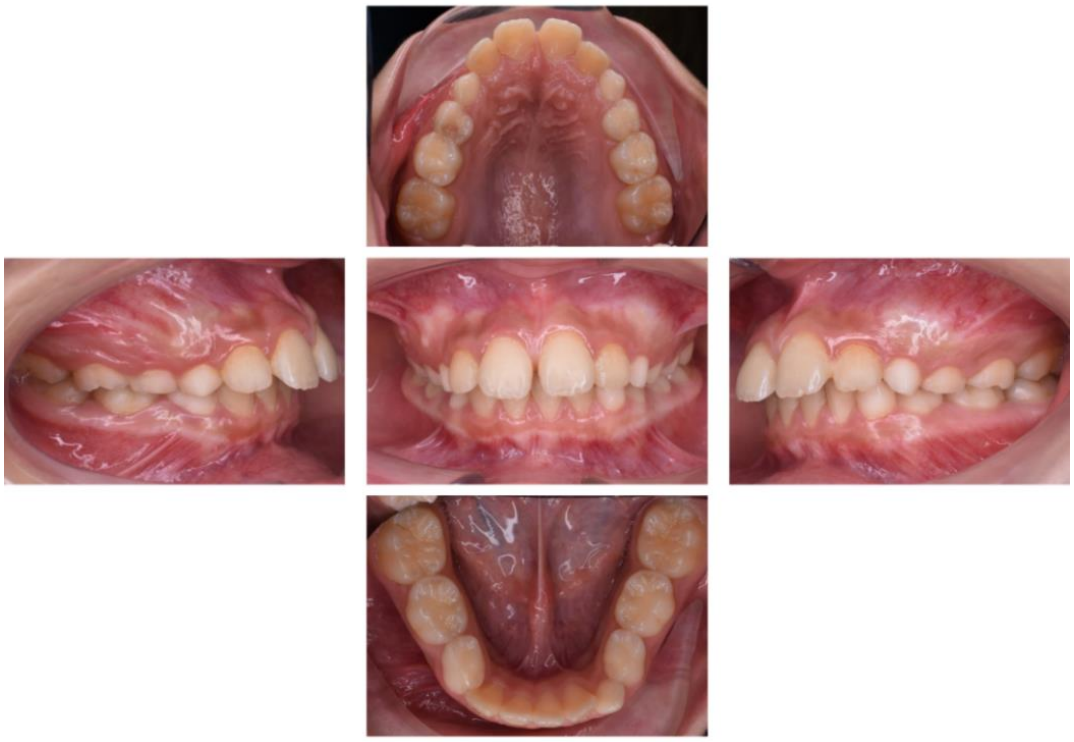

Figure 3.6 Intra-oral photographs of the participant

1.5.5 Intra-oral scanning

Intra-oral scanning of all participants was performed using the iTero Element 2 digital scanner by the principal investigator (AKD). The scans were converted to .stl files and submitted to the software of the developers for the construction of the Mandibular Advancement Aligner (MAA). For participants in the control group, alginate impressions were taken for fabrication of the Twin Block appliance. Figure 3.7 illustrates the iTero Element 2 scanner used in this study.

Figure 3.7 iTero Element 2 scanner

1.5.6 Radiograph

All participants were then referred to the Radiographic Unit, Faculty of Dentistry, Universiti Malaya, for lateral cephalometric radiographs. The x-ray machine used for each radiograph was recorded to ensure the same machine was utilised during the post-advancement phase. The magnification scale was standardised at 1:1. The flowchart outlining the pre-treatment phase, from participant recruitment to intervention selection and preparation, is illustrated in the figure below.

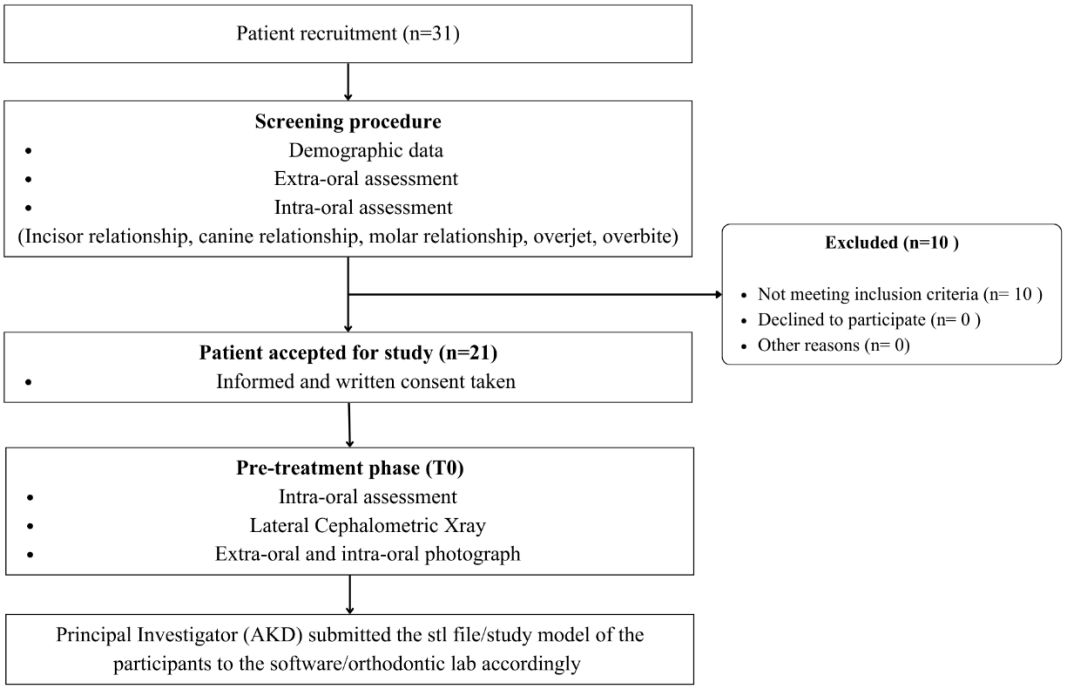

Figure 3.8 Flow chart during pre-treatment phase

1.6 Treatment phase

1.6.1 Questionnaire

A questionnaire was given to the participant to be answered prior to the issuance of the appliance. The CPQ questionnaire was selected as it is one of the most widely used instruments globally, with age being a critical factor in assessing patient-reported outcomes in children (Wallander & Koot, 2016). This period, when malocclusion becomes evident following incisor eruption, provided meaningful insights into children requiring interceptive treatment.

The short-form version of CPQ 11-14 consisted of 16 items for patients aged 11–14 years, using closed-ended questions across four domains: oral symptoms, functional limitations, emotional well-being, and social well-being. The instrument captured children's

perceptions and emotional responses regarding their oral health over the preceding four weeks. The CPQ 11–14 had been validated and translated into Bahasa Melayu, and it can be employed in cross-national comparisons because of its similarity to the English-language form. (Amirul et al., 2011)

The CPQ was administered at two time points: prior to appliance issuance (T0) and after the post-advancement phase (T1). Participants completed the questionnaire independently, choosing either the English or Malay version. The principal investigator (AKD) was available if any help was needed by the participants. The CPQ questionnaires are presented in Appendix D.

1.6.2 Treatment protocol

All treatments were carried out by the principal investigator (AKD). Approximately three weeks were allocated from the pre-treatment phase to appliance delivery. Once the appliance was fabricated, the independent assistant (AQ) scheduled the participant's appointment. Appliance issuance was performed by the principal investigator under the supervision of an orthodontist. Participants were instructed to wear the appliance for a minimum of 22 hours per day, removing it only for eating, contact sports, and toothbrushing.

Standard oral and appliance hygiene instructions were provided to participants and their parents, supplemented with written information. All treatments were conducted at the Postgraduate Orthodontic Clinic, Faculty of Dentistry, Universiti Malaya.

Advancement was considered complete when an anterior edge-to-edge incisal relationship and/or a Class I molar relationship were achieved without the appliance in situ and without the ability of participant to retrude the mandible.

1.6.2.1 Control group (Twin Block) protocol

The Twin Block appliance (Figure 3.9) used in this study was constructed with standard inclined planes angulated at 70° to the occlusal plane, providing 4 mm inter-premolar clearance, with specific design modifications incorporated to optimise function and participant comfort. The mandibular component included Adams clasps on the first molars and premolars, supported by ball-ended clasps between the anterior teeth, while the maxillary component followed a similar retentive design. Particular attention was given to the posterior bite block thickness, which was adjusted according to the participant's vertical dimension needs.

Participants were instructed to wear the appliance for at least 22 hours per day, although it was acknowledged that participants with pronounced deep bites may experience greater functional interference, such as difficulty in speech, mastication, and aesthetics, which could negatively affect their oral-health-related quality of life and subsequently influence compliance.

The midline expansion screw was activated by the participant with a quarter turn per week until the maxillary palatal cusps aligned over the mandibular buccal cusps, after which expansion ceased while appliance wear continued.

The advancement protocol consisted of a single advancement to achieve an edge-to-edge incisal relationship, except in cases with an overjet >10 mm, where advancement was staged in two steps. Upon completion of the advancement phase, participants in the twin-block group entered a transition phase designed to stabilise the achieved correction.

During this period, the appliance was worn part-time, primarily at night, to facilitate occlusal settling while allowing continued condylar growth and eruption of posterior teeth. The thickness of the upper bite blocks was progressively reduced during this stage to encourage intercuspation. The transition phase lasted for a minimum of two months, although the exact duration varied depending on individual growth and occlusal development.

Following the transition period, participants were reassessed clinically to determine the need for further intervention. If dental development and skeletal relationships were favourable, participants proceeded to Phase 2 treatment with comprehensive fixed appliances. Figure 3.9 illustrates participant with the Twin Block appliance in mouth.

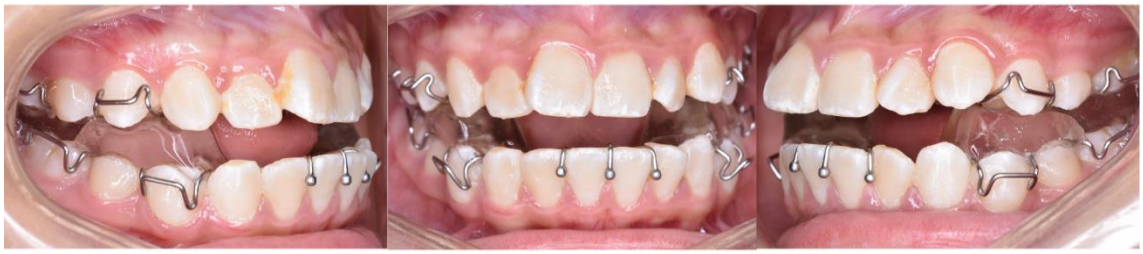

Figure 3.9 Participant with the Twin Block appliance

1.6.2.2 Mandibular Advancement Aligner with Vertical Bite Opening Protocol

Mandibular advancement aligners with vertical bite opening (MAA with VBO) were delivered using the Angelalign system and planned with iOrtho software version 11.3.11 (Angelalign Technology) as illustrated in Figure 3.10. Prior to study commencement, the principal investigator (AKD) completed certified training with the system developer to ensure standardised appliance planning and delivery.

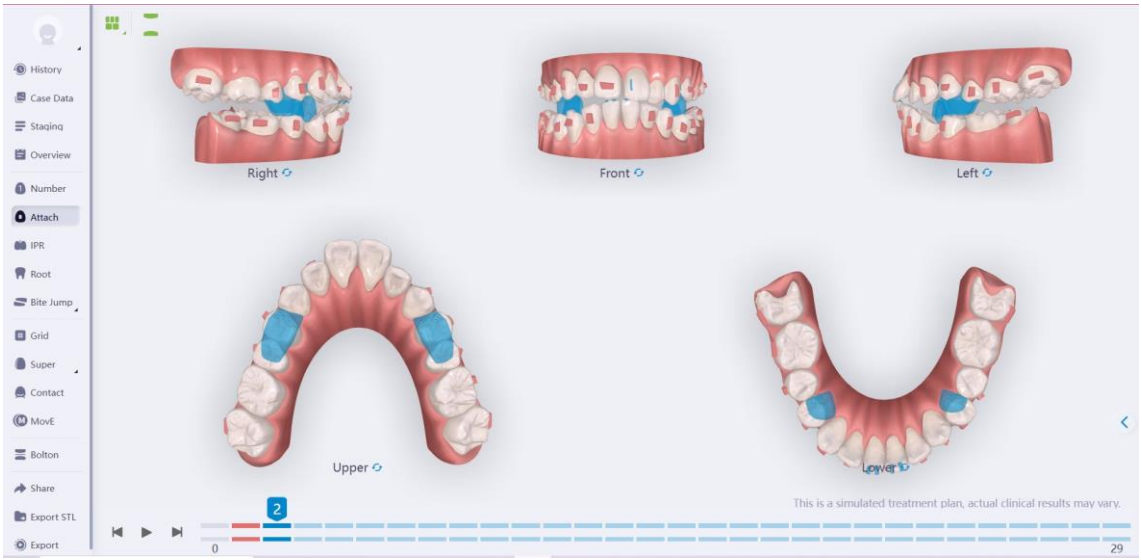

Figure 3.10 iOrtho software version 11.3.11

All treatment setups were generated using the software's default planning protocols, with no manual modification or optimisation of force systems by the principal investigator. The investigator's input was limited solely to predefined treatment constraints, whereby levelling and alignment were permitted during the mandibular advancement phase, while interproximal reduction, dental extractions, and molar distalisation were not permitted to maintain comparability with the Twin Block control group.

The occlusal blocks were designed to increase the vertical dimension, prevent premature posterior occlusal contacts, and facilitate controlled forward positioning of the mandible during

functional advancement. Maxillary arch expansion was programmed digitally to achieve an ideal buccal occlusion during the advancement phase.

Attachments were placed on premolars and molars, including vertical rectangular and mandibular anchorage attachments, to enhance aligner retention, improve surface engagement, and ensure controlled force transmission during mandibular repositioning. These attachments also served to counteract aligner dislodgement during forward mandibular posturing and to stabilise the mandible throughout functional advancement.

Mandibular advancement was planned as a single-step advancement to achieve an edge-to-edge incisal relationship. However, in participants presenting with an initial overjet exceeding 8–10 mm, a two-stage advancement protocol was employed. This staged approach was adopted to minimise excessive strain on the temporomandibular joints, reduce participant discomfort, and maintain compliance while ensuring biologically safe sagittal correction.

For the MAA with VBO group, each aligner set was worn according to the manufacturer's protocol, consisting of 7 days for stage A followed by 3 days for stage B. Upon completion of the initial mandibular advancement phase, participants were reassessed clinically. If off-tracking or insufficient advancement was detected, rescanning and refinement were performed, and new aligners were fabricated to ensure accurate continuation of treatment.

For both MAA groups, a minimum daily wear time of 22 hours was prescribed. Aligners were removed only during meals, toothbrushing, and participation in contact sports. This wear protocol was standardised across groups to minimise compliance-related variability and allow meaningful comparison with the Twin Block control group. Figure 3.11 illustrates the participant wearing the MAA with VBO at the time of delivery.

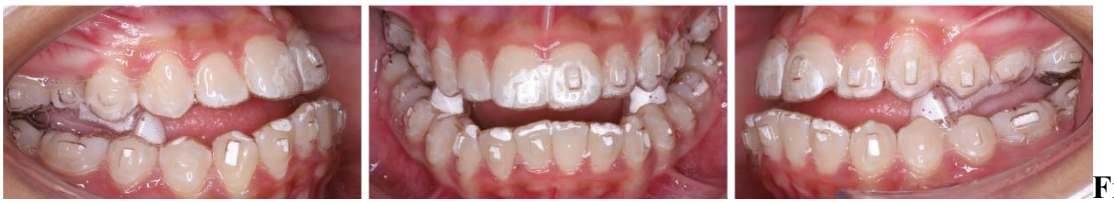

Figure 3.11 MAA with vertical bite opening.

1.6.2.3 Mandibular Advancement Aligner without Vertical Bite Opening Protocol

Mandibular advancement aligners without vertical bite opening (MAA without VBO) were delivered using the Invisalign system and planned with ClinCheck Pro software version 6.0 (Align Technology) as illustrated in Figure 3.12. Prior to study commencement, the principal investigator (AKD) completed certified training with the system developer to ensure standardised appliance planning and delivery.

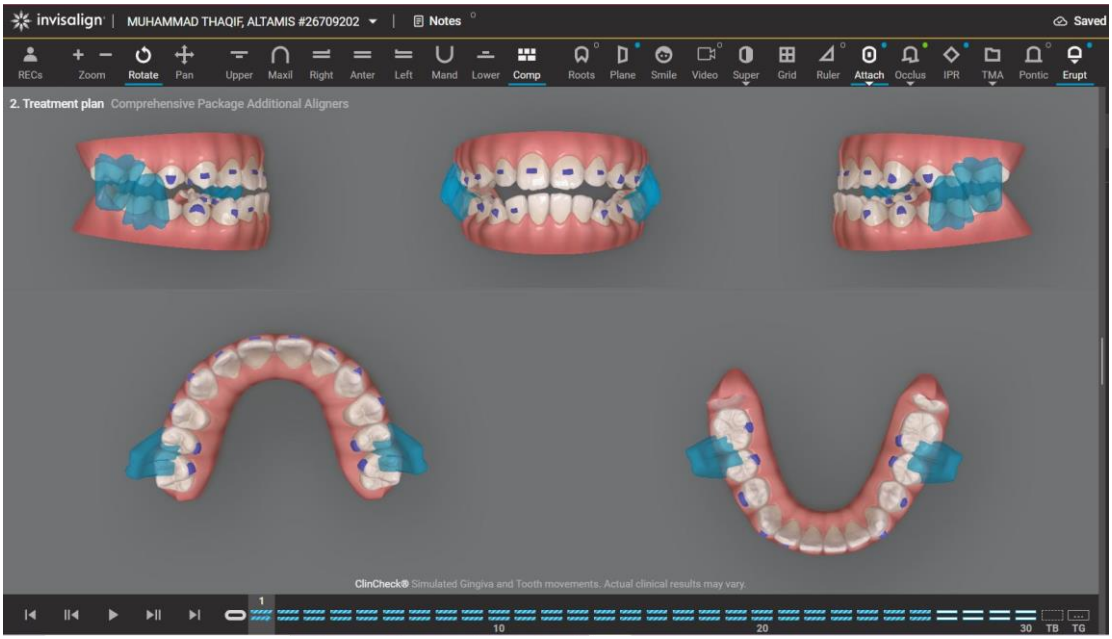

Figure 3.12 ClinCheck Pro software version 6.0

All treatment setups were generated using the software's default planning protocols, with no manual modification or optimisation of force systems by the principal investigator. The investigator's involvement was restricted to predefined treatment constraints, whereby levelling and alignment were permitted during the mandibular advancement phase, while interproximal reduction, dental extractions, and molar distalisation were deliberately excluded to ensure comparability with both the MAA with VBO group and the Twin Block control group.

Attachments were placed on premolars and molars, including vertical rectangular and mandibular anchorage attachments, to improve aligner retention, enhance surface contact, and stabilise force delivery during mandibular advancement. These attachments were particularly important for maintaining aligner engagement and mandibular positioning during functional advancement, especially in participants with deep curves of Spee.

Mandibular advancement was planned as a single-step advancement to an edge-to-edge incisal relationship. For participants with an initial overjet greater than 8–10 mm, a two-stage advancement protocol was implemented to reduce participant discomfort, minimise functional loading of the temporomandibular joints, and support compliance.

Participants in the MAA without VBO group changed aligners every 7 days, in accordance with manufacturer recommendations. Following completion of the initial advancement phase, clinical reassessment was performed, and rescanning and refinement were initiated if off-tracking or inadequate advancement was observed. New aligners were subsequently issued to ensure accurate continuation of treatment.

For both MAA groups, a minimum daily wear time of 22 hours was prescribed. Aligners were removed only during meals, toothbrushing, and participation in contact sports. This wear protocol was standardised across groups to minimise compliance-related variability and allow meaningful comparison with the Twin Block control group. Figure 3.13 illustrates the participant wearing the MAA without VBO at the time of delivery.

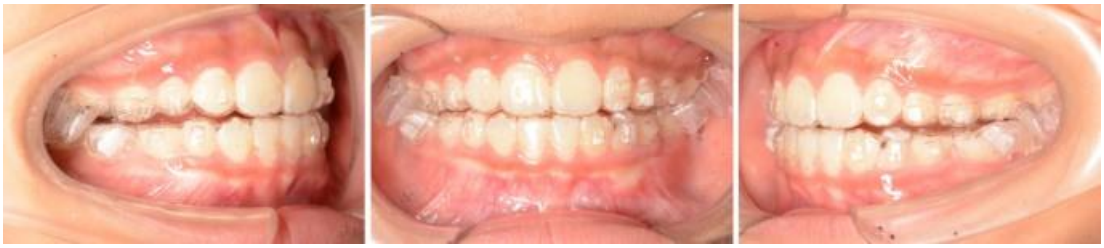

Figure 3.13 MAA without vertical bite opening.

Figure 3.14 illustrates the differences between the MAA with VBO and MAA without VBO in the participant's mouth. The notable differences are the occlusal bite block and the precision wing used to protrude the mandible forward, and the amount of occlusal clearance between the maxillary and mandibular teeth.

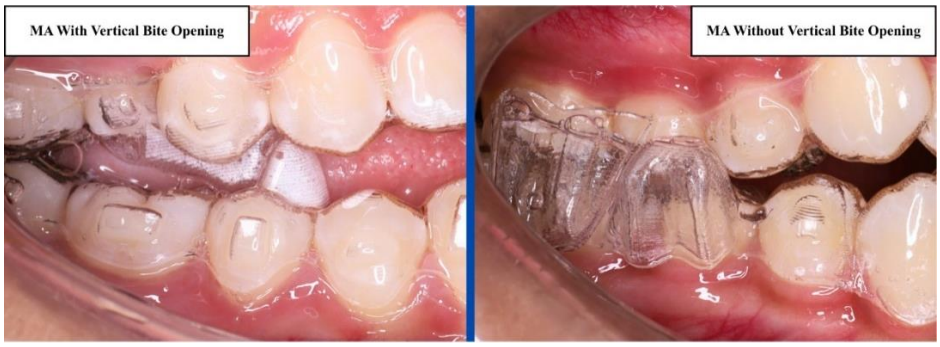

Figure 3.14 Differences between MAA with VBO and MAA without VBO

1.6.3 Follow-up visits

Participants were scheduled for monthly follow-up appointments. At each visit, assessments were conducted by the principal investigator (AKD) under orthodontic supervision. Clinical records included overjet, overbite, incisor, canine, and molar relationships. Appliance condition was also evaluated for objective signs of wear, such as surface dullness or loss of shine, to assess compliance.

Follow-up intervals were adjusted as needed until at least to a Class I molar relationship and/or edge-to-edge incisal contact were achieved. Participants who failed to meet these criteria despite continued mandibular advancement therapy were classified as non-compliant, and records were taken for final data analysis.

To enhance compliance, participants were provided with a diary to record their daily appliance wear and experiences. These entries were reviewed and discussed with the investigator at follow-up visits, focusing on duration and consistency of wear.

1.6.3.1 Participants' compliance

Participants were classified as non-compliant if they: (i) failed to wear the appliance for at least 22 hours daily, (ii) experienced appliance breakage more than three times (as reported during follow-up visit), or (iii) demonstrated insufficient clinical progress, defined as <10% reduction in overjet after six months of appliance wear.

Non-compliant participants were managed according to the intention-to-treat protocol and continued treatment as appropriate, either with a fixed functional appliance or by monitoring until growth cessation for subsequent fixed appliance therapy. Participants who demonstrated non-compliance during the study period were identified and classified accordingly; however, in accordance with the intention-to-treat principle, their data were retained in the final analysis. All available outcome data up to the point at which non-compliance was identified were included to preserve the original group allocation and minimise attrition bias. This approach ensures that the analysis more accurately reflects real-world clinical conditions and maintains the validity of the treatment effect estimates.

In cases of appliance loss, a replacement appliance was fabricated at the participant's expense. This policy was explained to participants and parents during the consent process. All appliance losses and breakages were documented. In this study, all participants were compliant with the treatment, and only one participant in the Twin Block was recorded as a dropout due to missing as participant cannot be contacted even though multiple attempts were made.

1.7 Post-advancement phase (T1)

General inclusion criteria required that cases treated with MAA to continue their treatment according to the prescribed aligner treatment plan. In contrast, cases treated with Twin Block appliances subsequently progressed to Phase 2, which involved comprehensive fixed appliance therapy.

Immediately after participants met the completion criteria, intra-oral scans and extra-oral/intra-oral photographs were obtained. Participants were then referred to the Radiographic Unit, Faculty of Dentistry, Universiti Malaya, for lateral cephalometric radiographs, taken with the same machine as the pre-treatment records at a 1:1 magnification scale. Participants subsequently completed the questionnaire (Appendix D and Appendix E).

1.8 Intention to treat

The study adopted an Intention-to-Treat (ITT) approach to preserve the validity of its findings. In accordance with ITT principles, all enrolled participants were included in the final

analysis regardless of treatment completion. This maintained the randomised nature of the trial, minimised selection bias, and reflected real-world clinical conditions.

The ITT analysis accounted for non-compliance, dropouts, and protocol deviations, thereby providing a comprehensive evaluation of the effectiveness of mandibular advancement aligners with and without vertical bite opening, and the Twin Block appliance in Class II malocclusion growth modification.

1.9 Lateral Cephalometric Analysis

To carry out blinding and to prevent the principal investigator from identifying radiographic images, randomised numbering was generated by the independent assistant (AQ) and assigned to each radiograph. The radiographic images were then copied into another folder to protect the originals during renaming. The copied radiographic images were then renamed according to the randomisation sequence, with the randomisation key stored under password protection accessible only to the independent assistant (AQ).

1.9.1 Tracing method

Lateral cephalometric analysis was performed using a semi-manual tracing method with AI-powered WebCeph software (AssembleCircle Corp, Korea). All radiographs were first uploaded as randomised and anonymised files via Google Drive. They were then calibrated for magnification within the WebCeph software to ensure a 1:1 scale prior to landmark identification and analysis. Tracing was carried out on the same computer system under standardised conditions.

Each cephalogram was labelled with 13 hard tissue landmarks (S, N, ANS, PNS, Point A, Ui, Li, upper incisor root apex, lower incisor root apex, Point B, Menton, Gonion, Condylion) and 4 soft tissue landmarks (Pogonion, Pronasale, Labrale Superius, Labrale Inferius) as illustrated in Figure 3.15. Landmarks were initially identified using the software's AI digitisation function, with manual corrections applied when necessary. Lines, planes, and angular measurements were generated using a modified cephalometric analysis protocol incorporating parameters from Steiner, Downs, McNamara, Tweed, and Jacobson (Wit's) analysis. Data were tabulated for subsequent statistical analysis.

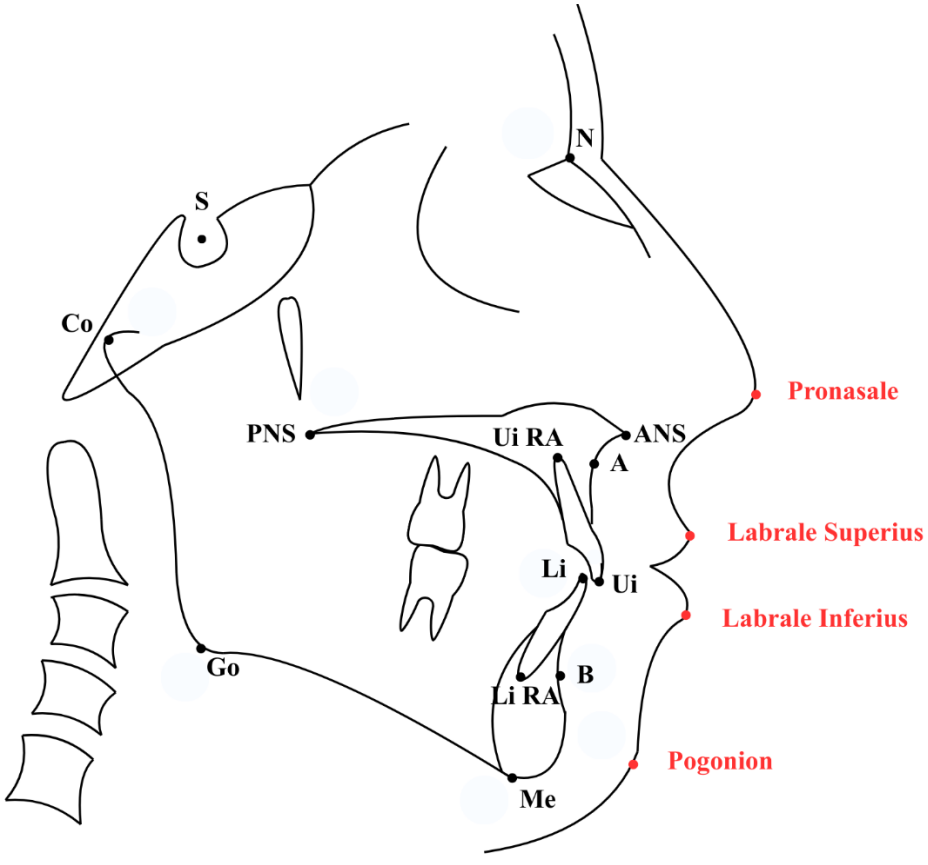

Figure 3.15 Landmarks of lateral cephalometric analysis

1.9.2 Lateral cephalometric parameters

The lateral cephalometric parameters selected for analysis were determined in accordance with the anticipated biological and clinical effects of the respective interventions. For clarity and systematic evaluation, these parameters were categorised into three effects: skeletal effects, dentoalveolar effects, and soft tissue effects. This classification facilitated targeted assessment of treatment outcomes corresponding to each anatomical component influenced by mandibular advancement treatment. The full list of parameters and their operational definitions is presented in Table 3.7. To enhance conceptual understanding, the parameters are also visually illustrated according to their respective categories in Figure 3.16 (Skeletal Effects), Figure 3.17 (Dentoalveolar Effects), and Figure 3.18 (Soft Tissue Effects).

Table 3.7 Definitions of lateral cephalometric parameters

Parameters	Definitions
	SNA (°): *The SNA angle is formed by connecting the sella, nasion, and A-point.*
	SNB (°): *The SNB angle is formed between sella, nasion and point B*
	ANB (°): *The ANB angle evaluates the anteroposterior relationship between the maxilla and mandible. The angle formed between point A, nasion and point B*

Skeletal Effects Parameters	**Wit's Analysis (mm):** *Drawn perpendiculars from points A and B onto the occlusal plane and measured the distance between these two points*
	Co-Gn (mm): *The distance between condylion and gonion*
	SN-Maxillary Plane Angle (°): *The angle formed between the sella-nasion plane and maxillary plane.*
	SN-Mandibular Plane Angle (°): *The angle formed between the sella-nasion plane and mandibular plane.*
	Maxillary-Mandibular Plane Angle (°): *The angle formed between the maxillary plane and mandibular plane.*
	Lower Anterior Facial Height (%): *The ratio of lower anterior facial height to the total face height.*

	Overjet (mm): *The distance between the incisal ridges of the upper incisor teeth labially and the incisal ridges of the lower incisor teeth.*
	Overbite (%): *Vertical (superior-inferior) overlap of the maxillary central incisors over the mandibular central incisors.*
Dentoalveolar Effects Parameters	**Upper incisal angle (°):** *The angle between the long axis of the maxillary central incisor and the palatal plane.*
	Lower incisal angle (°): *The angle between the long axis of the mandibular central incisor and the mandibular plane.*
	Inter incisal angle (°): *The angle formed by the intersection of lines drawn through the long axis of the maxillary and mandibular incisors.*

Upper lip- E-line (mm): *The distance from the upper lip to Rickett's E-line.*

Lower lip- E-line (mm): *The distance from the lower lip to Rickett's E-line.*

Soft tissue Effects

Parameters

Nasolabial angle (°): *The angle formed by drawing a line tangent to the base of the nose and a line tangent to the upper lip.*

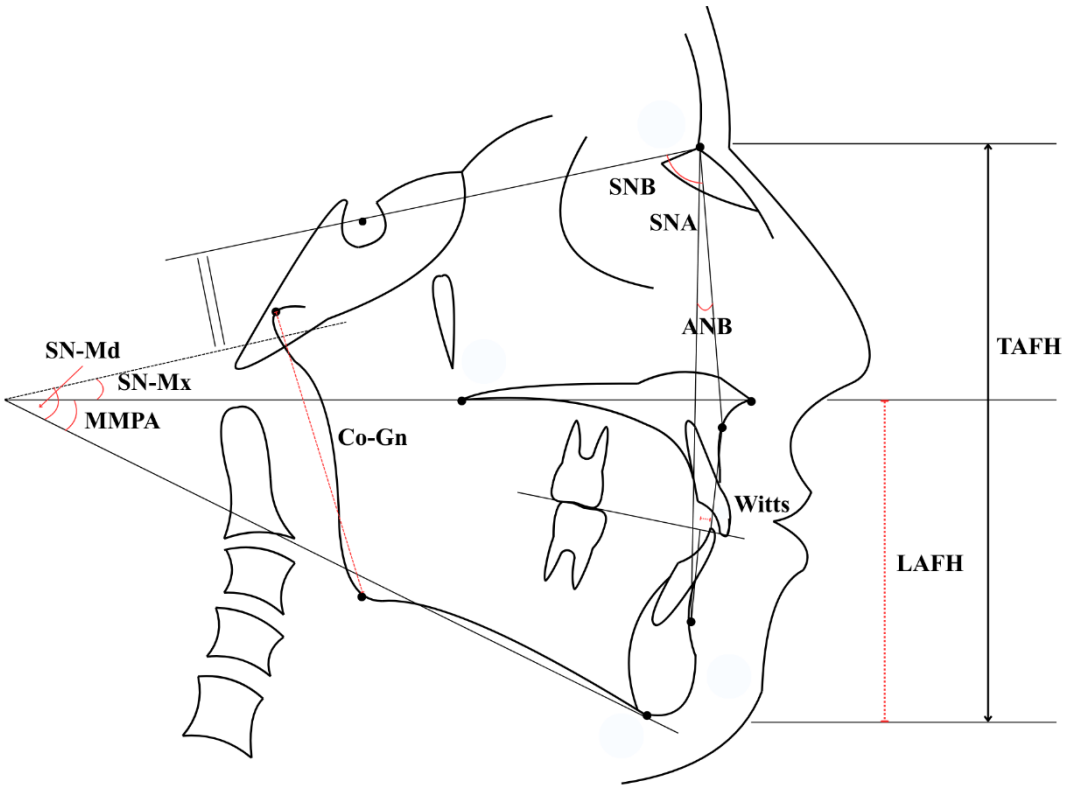

Figure 3.16 Skeletal Effects Parameters

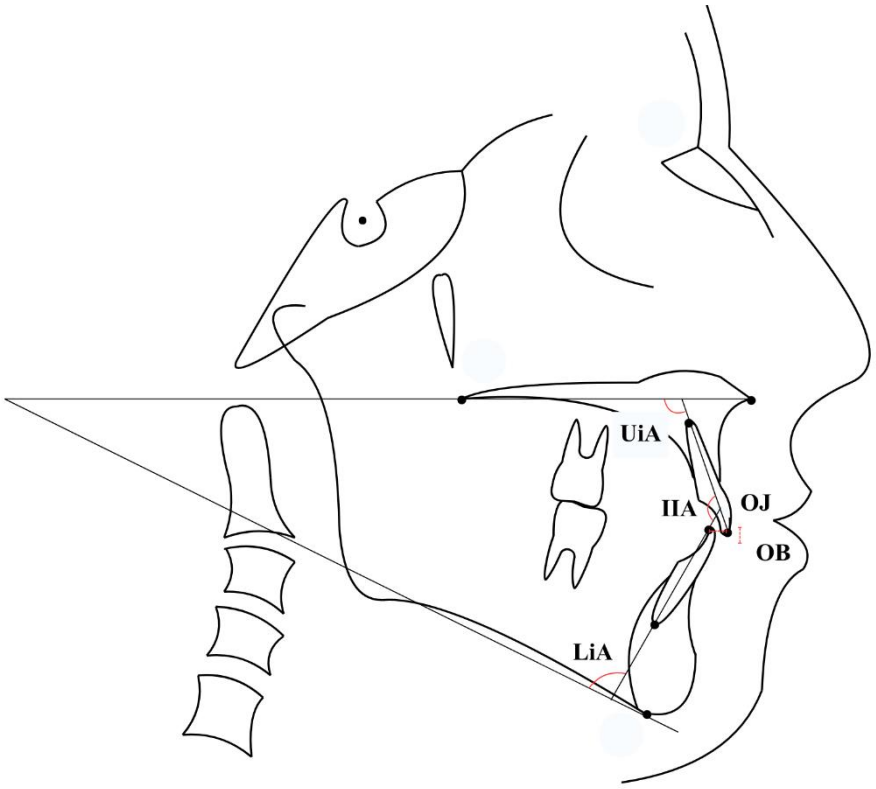

Figure 3.17 Dentoalveolar Effects Parameters

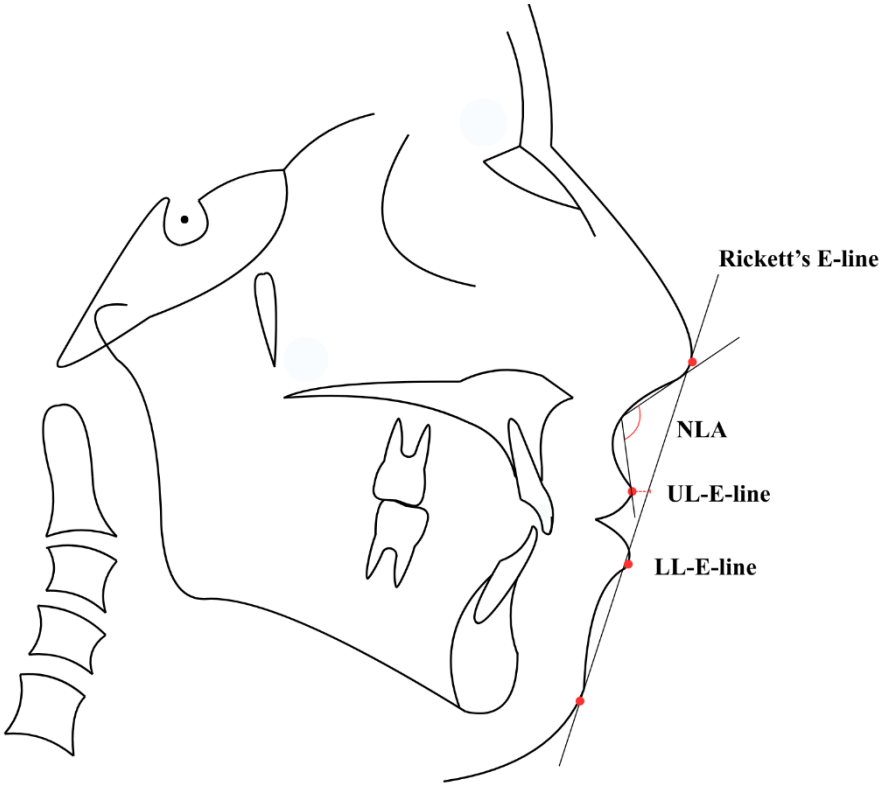

Figure 3.18 Soft Tissue Effects Parameters

1.9.3 Examiner calibration

For inter-examiner validity, 20 randomised lateral cephalometric images were traced by the principal investigator (AKD) and compared with tracings by an experienced orthodontist, serving as the reference standard. For intra-examiner reliability, the principal investigator repeated tracings of the same 20 images two weeks after the initial session. Linear and angular measurement differences were recorded and tabulated. Intra-class correlation coefficients (ICC) were interpreted according to Koo & Li (2016) as shown in Table 3.8.

Table 3.8 Interpretation of intra-class correlation coefficient (ICC)

ICC Score	Interpretation
<0.5	Poor agreement
0.5 to < 0.75	Moderate agreement

0.75 to <0.9	Good agreement
0.9 to 1.0	Excellent agreement

1.10 Data analysis

All data were recorded using a standardised data collection form. The information was subsequently entered into Microsoft Excel to generate a master dataset, which was then coded and exported into SPSS software version 26.0 (IBM Corp., Armonk, NY, USA) for statistical analysis. Descriptive statistics were computed to summarise study variables such as age and gender.

1.10.1 Statistical Tests

For all statistical tests, the level of significance was set at *p-value* < 0.05 with a 95% confidence interval. In addition, results with *p-value*< 0.001 were considered highly significant to further emphasise the strength of these findings.

For within-group comparisons of skeletal, dentoalveolar, and soft tissue changes between the pre-treatment phase (T0) and immediately after the advancement phase (T1), paired t-tests were performed for all the normally distributed data, and for between-group comparisons of skeletal, dentoalveolar, and soft tissue changes, one-way ANOVA was employed.

For assessment of participants' perceptions, responses to the questionnaire were recorded as follows: "never" = 1, "hardly ever" = 2, "sometimes" = 3, "fairly often" = 4, and "very often" = 5. Total scores were computed and compared between pre- and post-intervention using paired t-tests. One-way ANOVA was employed for comparisons between intervention and control groups.

For intra-rater and inter-rater reliability, the Intra-class Correlation Coefficients (ICC) score was employed to assess the reliability and accuracy of the measurement. The ICC score was interpreted according to Koo & Li (2016).

Table 3.11 Statistical analysis of this study

Objectives	Variables	Statistics
Objective 1	Changes in the skeletal effects at pre- and post-intervention: *SNA (°), SNB (°), ANB (°), Wit's analysis (mm), Co-Gn (mm), SN-Maxillary Plane (°), SN-Mandibular Plane (°), Maxillary-Mandibular Plane (°)*	Paired t-test
Objective 1	Changes in the skeletal effects of the three groups: *SNA (°), SNB (°), ANB (°), Wit's analysis (mm), Co-Gn (mm), SN-*	ANOVA test

	Maxillary Plane (°), SN-Mandibular Plane (°), Maxillary-Mandibular Plane (°)	
Objective 2	Changes in the dentoalveolar effects at pre- and post-intervention: *Overjet (mm), Overbite (%), Upper incisor angle (°), Lower incisor angle (°), Inter-incisor angle (°)*	Paired t-test
Objective 2	Changes in the dentoalveolar effects of the three groups: *Overjet (mm), Overbite (%), Upper incisor angle (°), Lower incisor angle (°), Inter-incisor angle (°)*	ANOVA test
Objective 3	Changes in the soft tissue effects at pre- and post-intervention: *Upper lip-E-line (mm), Lower lip-E-line (mm), Nasolabial angle (°).*	Paired t-test
Objective 3	Changes in the soft tissue effects of the three groups: *Upper lip-E-line (mm), Lower lip-E-line (mm), Nasolabial angle (°).*	ANOVA test
Objective 4	Participant's perception (pre- and post-intervention)	Paired t-test
Objective 4	Participant's perception (intervention groups vs control group)	ANOVA test

	Intra-rater reliability	Intra-class-correlation (ICC)
	Inter-rater reliability	Intra-class-correlation (ICC)

1.11 Funding

This study was supported by the Universiti Malaya Research Grant under the Dental Postgraduate Research Grant (DPRG), Universiti Malaya, with Grant Number UMG051E-2024, approved on 1st July 2024.

Appendix A Ethical Approval

UNIVERSITY OF MALAYA

MEDICAL ETHICS COMMITTEE
FACULTY OF DENTISTRY
ADDRESS: 50603, KUALA LUMPUR, MALAYSIA
TELEPHONE: 03-79676460 FAXIMILE: 03-79676456

NAME OF ETHICS COMMITTEE/IRB: Medical Ethics Committee, Faculty of Dentistry **ADDRESS:** Faculty of Dentistry, University of Malaya, 50603, Kuala Lumpur	**ETHICS COMMITTEE/IRB REFERENCE NUMBER:**
TITLE: Effects of Mandibular Advancement Aligners in Growth Modification of Class II Division 1 Malocclusion: A Randomised Controlled Trial	**DF CD 2421/0057 (P)**
PRINCIPAL INVESTIGATOR: Assoc Prof. Dr. Wey Mang Chek / Akmal Khalis bin Doreyat **TELEPHONE:** 03-79674562	

The following item [√] have been received and reviewed in connection with the above study to be conducted by the above investigator.

[√] Application Form	Ver date: 13 February 2024
[√] Brief CV of Main Investigator	Ver date: 4 July 2024
Patient Information Sheet (PIS):	Ver date:
[ ] BM version	
[ ] English version	
[ ] Others: _____	
Consent Form:	
[ ] BM version	
[ ] English version	
[ ] Others: _____	
[ ] Questionnaire	

and have been

[√] Approved
[ ] Conditionally approved (identify item and specify modification below or in accompanying letter)
[ ] Rejected (identify item and specify reasons below or in accompanying letter)

Appendix B Participant Information Sheet and Consent form (English)

UNIVERSITI MALAYA
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PARTICIPANT INFORMATION SHEET

Pleasereadthefollowinginformation carefully. Do not hesitate to discuss any questions you may have with your doctor.

Study Title

EffectsOfMandibularAdvancement Aligners in Growth Modification of Class II Division 1 Malocclusion:ARandomised Controlled Trial

Introduction

Malocclusion is a common dental problem that affects a significant proportion of the population. Class II Division 1 malocclusion can be characterised by a forward upper jaw and a backward lower jaw, resulting in an imbalance in the bite and facial appearance. In approximately 80% of cases, skeletal Class II malocclusions resulted from the backward of the lower jaw. The treatment approach in this case always involves modifying the lower jaw growth using functional appliances, and one of the most common functional appliances employed is the twin-block appliance that being developed since 1950's. However, in recent years, the use of mandibular advancement (MA) aligners for growth modification in this type of malocclusion has gained increasing attention. There are a few designs of the mandibular advancement (MA) aligners available in the market, the one with bite plane and the one with side wing but the mechanism remains the same. Up to date, there is still lack of study done in comparing the effects of these different designs in mandibular advancement (MA) aligners.

What isthepurpose ofthisstudy?

This research aims to fill the existing gap in knowledge by providing evidence-based insights into the optimal treatment approach for achieving favourable outcomes in patients with Class II division 1 malocclusion during the growth phase.

What are the procedures to be followed?

Participants will be selected based on inclusion and exclusion criteria. Participants will be randomly assigned to three groups: mandibular advancement (MA) aligners with vertical bite opening, mandibular advancement (MA) aligners without vertical bite opening, and twin-block appliances. The intervention groups will receive specific instructions on how to wear the appliance accordingly. The trial will span an estimated 6-9 months for each sample, during which monthly follow-up visits will be carried out to monitor the changes and compliance of the appliance. The primary outcome measures include the measurements in the x-ray, changes in the intraoral assessment, measurements of the intraoral scans, and questionnaires.

Who should not enter the study?

1. More than 17 years old
2. Moderate to severe teeth crowding
3. Patients with gum disease
4. Patients with systemic disease
5. Syndromic patients
6. Unable to read and understand in English or Bahasa Melayu

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7. Patients with a previous history of orthodontic intervention

What will be the benefits of the study?

(a)To participant?

Participants will be treated accordingly as the study will adopt the Intention-To-Treat protocol. The participants will also receive an oral hygiene kit, including a toothbrush, toothpaste, and mouthwash.

(b) To the investigator?

To see the effects of different designs of mandibular advancement (MA) aligners in growth modification of participants with Class II Division 1 malocclusion

To see the participant's perception of the treatment outcome with the type of intervention.

Do I receive any compensation/honorarium/reimbursement?

Yes,participantswillreceiveanhonorariumofRM50uponagreeing to participate in the study.

Whatarethepossiblerisks / complications / adverseeffectsthatmayhappen?

Participants might feel mild discomfort, pain, and sensitivity during the interventions. In the early period of the intervention, participants will have interference with their speech due to the presence of the retainer against the lips and tongue. Some participants may accidentally bite their cheeks or cut their tongue on the appliances as they adjust to their presence in their mouths. Some adverse clinical events reported that polyurethane and isocyanate materials that make up the mandibular advancement (MA) aligners may cause allergic reactions. For some participants, the reaction may be minor gum and mouth irritation, while others may experience more severe effects such as difficulty breathing, swelling of the throat or lips, blisters, or anaphylactic reactions. It is essential to discuss any discomfort and irritation associated with an allergic reaction immediately when symptoms occur. Besides that, participants might also experience dry mouth, especially in the initial period of the wearer because the appliances will fully cover the teeth and obstruct the natural flow of saliva, and it is essential to drink sufficient amounts of water and brush teeth often to keep the mouth hydrated and clean.

Can I refusetotakepartinthestudy?

Your participation is totally voluntary. You need not have to explain why you prefer not to take part in the study and it will not affect your dental treatment. Your data obtained from this study will be anonymized and kept confidential.

Who will have access to my research data?

The research data will only be accessible to the team members of the research including the Principal Investigator, Co-investigators, Research Assistant, and Clinical Assistant.

How did my records/data being kept confidential?
The confidentiality and security of participant recordsanddataareofutmost importance. Several measures are implemented to ensure the participants'informationiskeptconfidential:

- Participants' data will be collected and reportedinawaythatdoesnot reveal the identity of individual participants. Personal identifiersarereplacedwithcodesand kept confidential from the research data.
- All data, whether in electronic or paperformat,willbestoredsecurely. Electronic data is stored on a password-protected hard disk,andphysicalrecordsarekept in labeled folders in a locked cabinet. All data will be storedintheDepartmentofPaediatric Dentistry and Orthodontics, Faculty of Dentistry, UniversitiMalaya.
- All participants' data will be disposed permanentlyafter7yearsfrom the end of the study. This includes permanently deleting electronicrecordsand,ifapplicable, shredding physical documents.

• The Personal Data Protection Act 2010(PDPA)inMalaysiaregulates the processing of personal data. This study will comply withthePDPA,whichincludes obtaining consent, ensuring data accuracy, and implementingsecuritymeasurestoprevent unauthorized access.

Who shall I contact if I have additional questions/complications during the course of the study?

(1) Investigator's Name: Dr Akmal Khalis Bin Doreyat
Mobile No.: 017-7585262
Address: Faculty of Dentistry, Universiti Malaya, Kuala Lumpur, Malaysia
Official email address: s2149633@siswa.um.edu.my

(2) Investigator's Name: Associate Professor Dr Wey Mang Chek
Mobile No.: 017-6355746
Address: Faculty of Dentistry, Universiti Malaya, Kuala Lumpur, Malaysia
Official email address: weymc@um.edu.my

(3) Investigator's Name: Dr Aufa Dahlia Bahar
Mobile No.: 010-2588588
Address: Faculty of Dentistry, Universiti Malaya, Kuala Lumpur, Malaysia
Official email address: aufa.dahlia@um.edu.my

(4) Investigator's Name: Dr Nurul Aliaa Ahmad Fauzi
Mobile No.: 011-13070708
Address: Faculty of Dentistry, Universiti Malaya, Kuala Lumpur, Malaysia
Official email address: aliaafauzi@um.edu.my

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CONSENT BY PARTICIPANT FOR RESEARCH
FACULTY OF DENTISTRY, UM, K.L.

I,…… Identity Card No ……
(Name of participant)

of ……
(Address)
hereby agree to take part in the research specified below:

Title of Study:

EffectsOfMandibularAdvancementAlignersinGrowthModificationofClassIIDivision 1 Malocclusion: A Randomised Controlled Trial

Thenatureandpurposeoftheresearchhasbeenexplainedtomeby……
(*Name&designation of doctor*)
andinterpreted(whennecessary)by…….....tothebest of his/her ability in
(*Name & designation*)
……(*specify language*).Afterknowingandunderstandingallthepossible advantages anddisadvantagesofthisresearch,Ivoluntarilyconsentofmyownfreewilltoparticipate.

IunderstandthatIcanwithdrawfromthisresearchatanytimewithoutassigningmy reason whatsoever.

Signature …… Date……
(*Participant*)

IN THE PRESENCE OF

Name ……,

I/C No. ……., Position ……...

Signature …… Date .....
(Witness for signature of participant)

Iconfirm that I have explained to the participant the nature and purpose of the above-mentioned research.

Signature …….. Date ……....
(Attending doctor)

Complaints on unethical conduct can be forwarded to Faculty of Dentistry Medical Ethics Committee (FDMEC), UM at 03-79676460 or via email to ethics_dental@um.edu.my.

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CONSENT BY PARTICIPANT'S PARENT/GUARDIAN FOR RESEARCH
FACULTY OF DENTISTRY, UM, K.L.

I,…….. Identity Card No. …… of
**(Name of participant's parent/guardian)*

…… hereby agree
(*Address)*
to allow my daughter/son named …….. to take part in the
(Name of participant)
research specified below:

Titleof Study:EffectsOf Mandibular Advancement Aligners in Growth Modification of Class II Division 1 Malocclusion: A Randomised Controlled Trial

Afterknowingandunderstandingallthepossibleadvantagesand disadvantages of this research, I voluntarily consent of my own child to participate.

Iunderstandthatmychildcanwithdrawfromthisresearchatany time.

Signature…… Date ……
**(Participant's parent/ guardian)*

INTHEPRESENCEOF

Name ……,

I/C No. ……., Position ……..

Signature …… Date .....

**(Witness for signature of participant's parent/ guardian)*

Iconfirm that I have explained to the *participant's parent/guardian the nature and purpose of the above mentioned research.

Signature …….. Date ……....
(Attending doctor)

* **Delete where not applicable**

Complaints on unethical conduct can be forwarded to Faculty of Dentistry Medical Ethics Committee (FDMEC), UM at 03-79676460 or via email to ethics_dental@um.edu.my.

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Appendix D Child Perceptions Questionnaire (English Version)

Child Perceptions Questionnaire 11-14 (CPQ11-14)

Subject Number:
Age:
Gender:
Date today:

Hello,
Thank you for helping us with our study!
We are doing this study to understand what may happen to children because of their teeth and mouth.

Please Remember:

- Don't write your name on the questionnaire
- This is not a test, and there are no right or wrong answers
- Answer as honestly as you can
- No one you know will see your answers
- Read each question carefully and think about what has happened to you in the last 4 weeks.
- Before you answer,ask yourself:"Hasthishappenedtomebecauseofmyteethormouth?"
  Circle the best answer.

A. QUESTIONS ABOUT YOUR TEETH & MOUTH

No	Questions	Never 0	Once/ twice 1	Sometimes 2	Often 3	Ev ery day / Almost every day 4
In the past 4 weeks, have you ever had						
1	Pain in your teeth, lips, jaws, and mouth?	0	1	2	3	4
2	Bad breath / smelly mouth?	0	1	2	3	4
3	Sore spots (ulcers) in your mouth?	0	1	2	3	4
4	Food stuck in between your teeth?	0	1	2	3	4
In the past 4 weeks, have you ever had						
5	Difficult to drink or eat hot or cold foods?	0	1	2	3	4
6	Difficulty biting or chewing food like apples, corn on the cob or steak?	0	1	2	3	4
7	Difficulty saying any words?	0	1	2	3	4
8	Taken longer than others to eat a meal?	0	1	2	3	4
B. QUESTIONS ABOUT YOUR FEELING.						
In the past 4 weeks, have you ever felt						
9	Been upset because of your teeth or mouth?	0	1	2	3	4
10	Irritable or frustrated because of your teeth or mouth?	0	1	2	3	4
11	Shy or embarrassed because of your teeth or mouth?	0	1	2	3	4
12	Been concerned what other people think about your teeth, lips, mouth or jaws?	0	1	2	3	4
C. QUESTIONS ABOUT YOU BEING WITH OTHER PEOPLE						
In the past 4 weeks, have you ever						
13	Had other children ask you questions about your teeth, lips, jaws or mouth?	0	1	2	3	4
14	Other children teased you or called you names?	0	1	2	3	4
15	Avoided smiling or laughing when around other children?	0	1	2	3	4
16	Argued with other children or your family because of your teeth or mouth?	0	1	2	3	4