Efficacy of an innovative Herbst appliance with TADs for patients with hyperdivergent class II malocclusion: study protocol for a randomised controlled trial

Yuhui Wang 1,2, Yichen Xu 1,2, Zhicheng Gong 2,3, Jie Pan 1,2, Yuehua Liu 1,2

ABSTRACT

Introduction Class II treatment with mandibular retrusion often involves the Herbst appliance due to its efficiency and low requirement of cooperation. Despite its advantages, it causes side effects concerning the occlusal plane and pogonion in terms of clockwise rotation that hinder the desired mandibular advancement for hyperdivergent patients. In this study, we will use a newly designed Herbst appliance, and a protocol that is accompanied by TADs for vertical control to avoid maxillary clockwise rotation. We hypothesise that the effect of the Herbst appliance with the vertical control approach will be beneficial for maintaining or even decreasing the skeletal divergence in hyperdivergent class II patients compared with conventional Herbst treatment.

Methods and analysis This study is a randomised, parallel, prospective controlled trial that will study the efficacy of Herbst with or without vertical control in children with hyperdivergent skeletal class II malocclusion. A total of 44 patients will be enrolled and randomised in a ratio of 1:1 to either Herbst treatment or Herbst treatment with vertical control. Participants will be recruited at the Shanghai Stomatological Hospital, Shanghai, China. The primary endpoint is the change in the angle indicating the occusal plane and Sella-Nasion plane from baseline (T0) to the primary endpoint (T2) on cephalometric measurements by lateral X-ray examination. Important secondary outcomes include the root length of the anterior teeth, and the assessment score of the Visual Analogue Scale Questionnaire, etc. Safety endpoints will also be evaluated.

Ethics and dissemination This study has been approved by the ethics committee of the Shanghai Stomatological Hospital (Approval No. (2021) 012). Before enrolment, a qualified clinical research assistant will obtain written informed consent from both the participants and their guardians after full explanation of this study. The results will be presented at national or international conferences and published in peer-reviewed journals.

Trial registration number ChiCTR2100049860, Chinese Clinical Trial Registry

INTRODUCTION

Malocclusion is one of the most common oral abnormalities in adolescents, which results in abnormal dental relationships and facial aesthetic disorders. Class II malocclusion is one of the most prevalent malocclusions in Chinese children, with a prevalence of 50.9%.1,2 Typical features of class II malocclusion include deep overjet, deep overbite and mandibular retrusion, leading to a reduced chin projection and a convex facial profile, which impair oral function and facial attractiveness.3 The skeletal characteristics of class II malocclusion include mandibular retrognathism, maxillary prognathism or a combination of both, along with discrepancies in the horizontal and vertical directions.3 To improve patients’ facial aesthetics, promoting mandibular growth or advancement is applied in orthodontic treatment for growing patients.

A wide range of functional appliances have been introduced to stimulate mandibular growth and correct the bite by forward positioning of the mandible in children who are in the growth and development stage.4-6 One of the representative appliances, the
Herbst appliance, a fixed occlusal device that keeps the mandible in the forward extension position and stimulates the growth of the condyle and mandible. Studies have proven that the Herbst appliance can induce improvements in mandibular position and increases in mandibular length. During the treatment, the Herbst device generates both skeletal and dental effects, which mainly yield proclination of the mandibular incisors, distalisation and intrusion of the maxillary molars. The intrusion of upper molars contributes to a clockwise rotation of the occlusal plane. This undesired effect can minimise the skeletal effects and impede the desired forward displacement of the mandible, thereby preventing the establishment of a solid class I final dental relationship and facial profile, especially for patients with hyperdivergent pattern. Studies have shown that with conventional Herbst treatment, patients with hyperdivergent pattern experienced a deleterious backward true mandibular rotation and an increment in facial height. Adequate control of tooth eruption and extrusion would result in a steeper occlusal plane, an increase in lower face height and a tendency for posterior mandibular rotation, which is not conducive to the chin advancement and straight facial profile aesthetics for the patients with hyperdivergent pattern.

For angle class II division 1 patients with high angle, the key for orthodontic treatment is to maintain or even decrease the skeletal divergence (mandibular plane (MP) angle), achieving counterclockwise rotation of the mandible and a promising profile. One of the studies showed that the Herbst appliance attached to acrylic splints in conjunction with a high-pull headgear can enhance skeletal anchorage and have a better control of the vertical dimension for hyperdivergent patients. The use of extraoral devices to enhance anchorage can prevent the proclination of the lower incisors, effectively maintain the vertical height, and prevent the mandible from rotating clockwise, but the effect is still controversial. There is still great concern with the treatment of hyperdivergent class II malocclusion in the clinic due to the lack of randomised controlled studies comparing the vertical pattern change after different treatment approaches.

With the intention of solving these problems, we developed a version of the Herbst appliance that covers the occlusal surface of lower molars, and a protocol that is accompanied by miniscrew implants to intrude upper anterior teeth for occlusal plane levelling. Mini-implants were used to improve vertical control and thus to allow full expression of the sagittal correction by preventing the chin from swinging backward and downward. We hypothesise that using Herbst treatment with the vertical control approaches will maintain or even decrease the skeletal divergence in hyperdivergent class II patients compared with conventional Herbst treatment. The purpose of this study is to recruit children who are diagnosed with hyperdivergent skeletal class II malocclusion and compare the clinical effects of Herbst treatment with or without vertical control in terms of dental and maxillofacial development, mandible position and profile attractiveness. Here, we present the rationale and methodology for a parallel randomised controlled trial to compare the efficacy of such treatment methods in Chinese children with hyperdivergent skeletal class II malocclusion.

**Objectives**

This study is designed to evaluate the clinical effect of Herbst treatment with or without vertical control in children diagnosed with class II malocclusion with a hyperdivergent facial pattern.

**METHODS AND ANALYSIS**

The study protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) reporting guidelines.

**Study design**

This study is a parallel randomised controlled trial. It will involve children with class II malocclusion. The study was designed following the SPIRIT guidelines and will be reported in accordance with the Consolidated Standards of Reporting Trials (http://www.consort-statement.org/). The recruitment announcements were published at the hospital and on the official website of Shanghai Stomatological Hospital. We will enrol 44 children aged 10–13 years who are diagnosed with hyperdivergent angle class II malocclusion. The participants will undergo a series of medical tests, including physical examinations and maxillofacial radiography, to verify the diagnosis. Once enrolled in the study, subjects will be randomly divided into one of two treatment groups—the Herbst group, or the Herbst with vertical control group—in a ratio of 1:1. All participants will be treated with a Herbst appliance with or without miniscrew implants and followed until the end of the Herbst treatment. Regardless of the group assignment, assessments will be conducted at the end of the Herbst treatment (T2). The flow chart of this trial can be seen in figure 1. The SPIRIT checklist with the recommended items to address in a clinical trial protocol is available in online supplemental file 1.

**Patient and public involvement**

There will be no patient or public involvement in the design and conduct of this study.

**Study patients**

A total of 44 eligible patients will be recruited after screening at the study site.

The inclusion criteria are as follows:

1. Patients aged 10–13 years old who are at or right before the peak of the pubertal spurt assessed using vertebral analysis.
2. Class II, division 1 malocclusion characterised by mandibular retrognathism and normal or mild maxillary protrusion (A point, Nasion, B point (ANB) ≥ 4).
3. Minimum overjet of 4 mm in permanent dentition.
4. Hyperdivergent growth pattern (FMA > 33).
5. Good oral health condition (healthy periodontal tissue, no periapical disease and no unfilled caries).
6. Patients whose guardians agree to their participation in this trial and sign the informed consent forms.

The exclusion criteria are as follows:
1. Previous orthodontic or orthopaedic treatment.
2. History of temporomandibular joint dysfunction.
3. Existence of bone islands, osteomas, periapical cysts, root resorption in the tooth movement area.
4. Concurrent systemic diseases, metabolic syndromes or other special needs.
5. Poor oral health (presence of periodontitis, gingival recession or active white spots).
6. Abnormal bone metabolism (history of medication with antibone resorption drugs, hormone drugs or immunosuppressants).
7. Mental or motor disorder.

**Recruitment and randomisation process**
Before enrolment, there will be one pretreatment screening visit at the study site office, during which a qualified clinical research assistant will obtain written informed consent from both the participants and their guardians after full explanation of this study (online Figure 1).
supplemental file 2). Participants will be recruited at Shanghai Stomatological Hospital, Shanghai, China, from August 2021 to December 2023. The hospital comprises relevant diagnostic and treatment departments. Notification of subject recruitment will be published in the hospital and on official websites.

After the baseline assessment, eligible participants will be randomly assigned to one of two groups. The random number table method will be used in this trial. An electronic table of random numbers will be used to allocate the participants into either the Herbst group or the Herbst with vertical control group in a 1:1 ratio using the simple randomisation method. An independent researcher will use SPSS V.24.0 to generate a random number sequence. Sequentially numbered, sealed, opaque envelopes will be used for concealment of this trial. After randomisation, an email will be submitted to the clinical research coordinator (CRC) with the random number and the allocation group information of the participants. The CRC will contact participants to start the treatment. To minimise bias, the analyst will be blinded to the patients’ information during the measurements.

The randomisation sequence is concealed by opaque envelopes from both researchers and subjects until final assignment.

Description of the interventions
The enrolled subjects will undergo Herbst treatment or Herbst treatment with vertical control within 4 weeks after randomisation. Both treatment methods will be implemented by experienced doctors.

Subjects receiving Herbst treatment will be fitted with a standard Herbst appliance for 10 months. Routine follow-up will be conducted every 4 weeks until the end of the treatment.

Subjects receiving Herbst with vertical control treatment will be fitted with a Herbst appliance accompanied by miniscrew implants for occlusal plane levelling. Miniscrew implants will be inserted 1 week after the Herbst appliance is settled. After rinsing with chlorhexidine gluconate 0.12% for 1 min, patients will be given local infiltration anaesthesia (articaine 4% with 100 000 epinephrine). Once anaesthesia has set, miniscrew implants will be placed bilaterally between the root of the lateral incisor and canine in the attached gingiva depending on the subject’s anatomy. After the surgery, the miniscrews will be ligated with elastic chains to the power hooks bilaterally with a the force of 30 g to intrude the upper anterior teeth. Patients will be given appointments at 4-week intervals. The group receiving Herbst treatment with vertical control is depicted in figure 2.

Study visits
Three study visits per subject will be scheduled in the study as follows: baseline assessment visit (T0), initiation of Herbst therapy visit (T1) and end of Herbst therapy visit (T2) (table 1). These visits will occur at the study site office. Additional services will be provided for participants through WeChat or phone for the guardians to have direct access to their doctors. After the placement of the Herbst appliance or the miniscrew implants, excessive care and follow-ups will be provided 1 week after the operation to improve their adherence. At scheduled visits, data relating to lateral cephalometric radiographs, CBCT scanning, subjective assessment of VAS, adverse events, etc, will be recorded and collected.

Participants may quit the study at their guardians’ discretion or defer to the supervisory team. Circumstances that will suspend participants from the study include adverse events and detection of evidence that may influence the outcomes of the research. Patients with adverse events will be treated promptly and followed up until they are stable.

Outcome measures
Primary outcome
Endpoint measurements will be performed at the baseline assessment visit (T0) and after the removal of the Herbst device (T2). The primary endpoint of the trial is the angle between the occlusal plane and the Sella-Nasion plane (OPSN). Participants will take lateral radiographs at T0 and T2 for cephalometric measurements to obtain OPSN. The OPSN angle is usually considered as the key index to evaluate the occlusal plane inclination of the patient.

Secondary outcomes
The secondary endpoints include the change in cephalometric analysis, root length of anterior teeth measured by CBCT and subjective assessment of VAS.

All subjects will take lateral cephalometric radiographs at the intercuspal occlusion using the same X-ray machine, and the same operator. Radiographs will be traced and digitised using the Dolphin imaging software (Dolphin Imaging & Management Solutions

Figure 2 The innovative Herbst appliance combined with TADs for occlusal plane levelling in the Herbst with vertical control group.
Corporation, Chatsworth, California, USA). The cephalometric measurements are presented in figure 3. An expert investigator blinded to the allocation of participants will be responsible for the measurements. The measurement items are as follows: SNA, angular indicator for maxillary protrusion; SNB, angular indicator for mandibular protrusion; ANB, angular indicator for the sagittal relationship between the jaws; MP-SN, angle between the MP and Sella-Nasion plane; OP-SN, angle between OP-SN; U1-SN, angular indicator for upper anterior teeth protrusion; L1-MP, angular indicator for lower anterior teeth protrusion; U1-PP, distance for upper incisor to PP; L1-MP, distance for lower incisor to MP.

Table 1  Schedule of enrolment, interventions and assessments (recommended by SPIRIT)

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<thead>
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<td>VAS*</td>
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<td>Adverse event monitoring (side effects and complications)</td>
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</tbody>
</table>

*VAS will be filled out daily for 7 days postoperatively.

OP-SN, occlusal plane and Sella-Nasion plane; SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials.

Figure 3  The cephalometric landmarks and indicators. A, subspinale; ANS, anterior nasal spine; B, supramental, Go, gonion; Li, lower incisor; Lir, lower incisor root; Me, menton; MP, mandibular plane; N, Nasion; OP, occlusal plane; PNS, posterior nasal spine; PP, palatal plane; S, Sella; SN, frontal cranial base plane; Ui, upper incisor; Uir, upper incisor root.
between the upper incisor and the palatal plane; U6-PP, distance between the upper first molar and the PP; L1-MP, distance between the lower incisor and the MP; L6-MP, distance between the lower first molar and the MP; anterior nasal spin-menton (Me)/N-Me×100%, percentage of the lower anterior face height relative to the total anterior face height.

The root length of each examined tooth will be measured by CBCT and recorded as the perpendicular distance from the root apex to the cementoenamel junction (CEJ), which will be constructed as the line connecting the CEJ on both the labial and lingual sides as shown in figure 4.

The VAS Questionnaire will be performed to analyse the pain scale 1 week after mini-implants insertion. Briefly, pain will be graded on a scale from 0 to 10, where a 0 denotes no pain and 10 represents maximum intensity of pain. Guardian(s) and each subject will complete the study questionnaire without help to ensure reliability and validity.

**Sample size calculation**

The sample size was calculated using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA) in this study. Our expectation hypothesis is that the angle between the OP-SN may decrease after application of the Herbst device accompanied by vertical control. According to our previous pilot study, the mean OP-SN angle decreased by 2.5±2.8° in adolescents who were treated with the innovative Herbst appliance with vertical control, while the average change of the OP-SN angle in the standard Herbst group was 0±2.8°. Eighteen participants in each group can provide 95% power to detect a minimum clinically significant difference in OP-SN of 0.7° (using $\alpha=0.05$). The sample size calculation was based on a two-sided hypothesis. Considering an anticipated 20% dropout rate, the final sample size is a total of 44, with 22 participants in each group.

**Data collection and statistical analysis**

The data surveyor will be blinded to the subjects’ groups during the measurements. The full analysis set, based on the intent-to-treat principle, will be established as the primary efficacy analysis population. A two-sided value of $p<0.05$ will be considered to indicate significance for any statistical tests. Demographics, baseline characteristics and safety data will be summarised based on treatment groups.
The primary endpoint of this study is the change in OP-SN from T0 to T2. Intergroup comparisons will be performed using an analysis of covariance to adjust for baseline OP-SN. Paired and unpaired t tests will further be used to test OP-SN reduction within each group and between groups, respectively. The 95% CIs for the least square mean difference between the two groups will also be calculated.

The analysis of the root length of the anterior teeth, and the lateral cephalometric measurements in the secondary endpoints will use similar statistical methods as those used for the OP-SN. Descriptive statistical analysis will be used for the measurements of lateral cephalometric radiographs and CBCT.

Statistical analysis will be conducted using IBM SPSS Statistics V.24.0. Continuous data will be presented as mean±SD and categorical data as frequency. The 95% CIs will be calculated using the exact method. Descriptive analysis will be performed on all variables (frequency and percentage of categorical variables, mean and SD of continuous variables). The log-rank test will be used to assess the correlation between OP-SN (primary endpoint) and the vertical control therapy. The T test or Mann-Whitney test will be used for comparison between groups of continuous variables, and χ² test or Fisher’s exact test will be used for categorical variables. The statistical tests used in the study will be two-sided. When p<0.05, it will be considered statistically significant. Categorical data will be tested using Pearson’s χ² test or Fisher’s exact test, as appropriate. Continuous secondary endpoints will be analysed similarly to the primary endpoint. Missing data will be disposed with the last-observation-carried-forward method.

**ETHICS AND DISSEMINATION**

**Ethical considerations**

The independent ethics committees of Shanghai Stomatological Hospital have approved the study protocol (protocol V.3.0, issue date: 12 May 2021) for the respective participating sites (Approval No. (2021)012). Written informed consent will be obtained from both the participants and their guardians after full explanation of this study. They will be informed that they can also withdraw from the study as they wished at any time. The ethics committee has agreed that this study will not raise patients’ risk or cause extra harm to study subjects.

The ethics committee has further agreed that the study is in accordance with the Declaration of Helsinki and that the study will be conducted without ethical problems.

**Dissemination**

The final clinical report will be published in a medical journal and presented at national or international conferences. A formal report or publication of the data from the study will be jointly published by a person appointed by the principal investigators. A report of the results of this study will be sent to the guardians of the participants by mail.

**DISCUSSION**

A wide range of functional appliances have been introduced to stimulate mandibular growth and correct the bite by forward positioning of the mandible for children in the growth and development stage. Of these, the Herbst appliance is a fixed forward occlusal device widely used across the world. However, there are concerns that this appliance can result in intrusion of the upper molars, which contributes to a clockwise rotation of the occlusal plane. If this is not controlled vertically, it may result in an increase in skeletal divergence, which is not conducive to the treatment of patients with high-angle class II malocclusion. In this trial, our hypothesis is that the key for mandibular counterclockwise rotation is the levelling of the occlusal plane, which is determined by the vertical height of both the molars and the incisors. Therefore, we have developed a version of the Herbst appliance that covers the occlusal surface of the lower molars and a protocol that is accompanied by miniscrew implants to intrude upper anterior teeth for occlusal plane levelling. With vertical control of the upper anterior teeth, we aim to achieve a better outcome for patients with a class II hyperdivergent pattern.

Although new treatment patterns with skeletal anchorage have recently been proposed to avoid protrusion of the lower anterior teeth and promote distalisation of the upper molars, treatment methods for children with vertical growth patterns are still challenging. Studies have shown that patients with hyperdivergent pattern experience a deleterious backward true mandibular rotation and increase in facial height with conventional Herbst treatment. The inclination of the occlusal plane is crucial to the direction of mandibular advancement with the Herbst appliance. Patients with a flatter occlusal plane will experience less backward rotation of the mandible than those with a steeper occlusal plane after mandible advancement. Studies have proven that the hypodivergent patients undergo more significant anterior displacement of the pogonion with Herbst treatment than hyperdivergent patients, which is beneficial to facial aesthetics. Since patients with hyperdivergent pattern often have steeper occlusal planes than patients with hypodivergent pattern, it is important to level the occlusal plane during the treatment for patients with vertical growth tendency to achieve a forward rotation of the mandible. The Herbst appliance, in combination with the mini-implants to intrude upper incisors, has not yet been standardised into a treatment protocol or reported in clinical trials. We inserted the miniscrews in the anterior part of the maxilla to intrude the incisors and level the occlusal plane. Along with the intrusive effect of the Herbst appliance on upper molars, we expect to achieve counterclockwise rotation of the mandible. There is still great controversy concerning the treatment of class II malocclusion with hyperdivergent...
facial pattern in the clinic due to the lack of randomised controlled studies comparing the vertical pattern change after different treatment approaches.

This preliminary study describes how a combination of miniscrews and Herbst appliance can control the inclination of the occlusal plane during treatment. A standard Herbst appliance may cause side effects with retroclination of the maxillary incisors and proclination of the mandibular incisors, which could reduce the mandibular growth response because of the reduction of the space for mandibular advancement. To have better control of unfavourable tooth movements to lead to greater skeletal effects, we used TADs to intrude the upper incisors and maintain the inclination of the upper incisors. Our newly designed Herbst appliance is attached to both molars and the palatal surfaces of the upper incisors. After inserting the miniscrews in the anterior part of the maxilla, with the power chain applied on the hooks welded to the Herbst appliance, they will apply the intruding and backward force to the upper arch. The lower arch will be guided by the inclination of occlusal plane and the telescope rod, which will experience counterclockwise rotation.

In this study, a randomised controlled trial was designed to investigate the efficacy of the Herbst appliance with/without vertical control treatment for children with hyperdivergent pattern with mandibular retrognathia. Elimination of anterior inferences by orthodontic repositioning of the front teeth, preventing extrusion of the posterior teeth at the same time, will allow an anterior rotation of the mandible, with further improvement of the sagittal correction and a beneficial reduction in lower face height. In this study protocol, lateral cephalometric measurements of the subjects will be conducted for skeletal and dental analysis of treatment efficacy. The anterior tooth root length will also be evaluated in this study to evaluate the effect of intrusion of the teeth. VAS will also be included to assess the subjective feelings of mini-implant anchorage insertion.

The results of this study will provide valuable evidence for the merits and long-term efficacy of different therapeutic approaches and contribute to facilitating the treatment of mandibular retrognathia for patients with hyperdivergent patterns.

**Trial status**

The study is ongoing. The recruitment is expected to be completed by the end of December 2023. Thirty patients have been enrolled in this trial. The data for 16 patients, including 10 for standard Herbst appliance and 6 for Herbst treatment with vertical control, have been collected.

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**Contributors**

YW participated in the design of the clinical trial and drafted the first version of the manuscript. YL and JP designed the research protocol and revised the final manuscript. YX assisted in the preliminary research design and implementation of the trial. ZG designed of this study. All authors participated in the proposal discussion and approved the submission. YW and YX contributed equally to this manuscript.

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**Competing interests**

None declared.

**Patient and public involvement**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication**

Consent obtained from parent(s)/guardian(s).

**Provenance and peer review**

Not commissioned; externally peer reviewed.

**Supplemental material**

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**REFERENCES**


### SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

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<td>Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities</td>
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<td>Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)</td>
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## Introduction

### Background and rationale
6a Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention______________________________
6b Explanation for choice of comparators______________________________

### Objectives
7 Specific objectives or hypotheses______________________________

### Trial design
8 Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)______________________________

## Methods: Participants, interventions, and outcomes

### Study setting
9 Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained______________________________

### Eligibility criteria
10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)______________________________

### Interventions
11a Interventions for each group with sufficient detail to allow replication, including how and when they will be administered______________________________
11b Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)______________________________
11c Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)______________________________
11d Relevant concomitant care and interventions that are permitted or prohibited during the trial______________________________

### Outcomes
12 Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended______________________________

### Participant timeline
13 Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)______________________________
<table>
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</tbody>
</table>

**Methods: Assignment of interventions (for controlled trials)**

**Allocation:**

<table>
<thead>
<tr>
<th>Sequence generation</th>
<th>16a</th>
<th>Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment mechanism</td>
<td>16b</td>
<td>Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned</td>
</tr>
<tr>
<td>Implementation</td>
<td>16c</td>
<td>Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions</td>
</tr>
</tbody>
</table>

**Blinding (masking):**

<table>
<thead>
<tr>
<th>Blinding (masking)</th>
<th>17a</th>
<th>Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>17b</td>
<td>If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial</td>
</tr>
</tbody>
</table>

**Methods: Data collection, management, and analysis**

<table>
<thead>
<tr>
<th>Data collection methods</th>
<th>18a</th>
<th>Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18b</td>
<td>Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Section</th>
<th>Text</th>
<th>Page References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data management</td>
<td>Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol</td>
<td>12, 13</td>
</tr>
<tr>
<td>Statistical methods</td>
<td>Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Methods for any additional analyses (eg, subgroup and adjusted analyses)</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)</td>
<td>13</td>
</tr>
<tr>
<td>Methods: Monitoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data monitoring</td>
<td>Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed</td>
<td>12, 13</td>
</tr>
<tr>
<td></td>
<td>Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>No analysis is planned in the study</td>
<td></td>
</tr>
<tr>
<td>Harms</td>
<td>Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct</td>
<td>9</td>
</tr>
<tr>
<td>Auditing</td>
<td>Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor</td>
<td>n/a, supervised by Shanghai Hospital Development Center quarterly</td>
</tr>
<tr>
<td>Research ethics approval</td>
<td>24</td>
<td>Plans for seeking research ethics committee/institutional review board (REC/IRB) approval</td>
</tr>
<tr>
<td>--------------------------</td>
<td>----</td>
<td>-----------------------------------------------------------------</td>
</tr>
<tr>
<td>Protocol amendments</td>
<td>25</td>
<td>Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)</td>
</tr>
<tr>
<td>Consent or assent</td>
<td>26a</td>
<td>Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)</td>
</tr>
<tr>
<td></td>
<td>26b</td>
<td>Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable</td>
</tr>
<tr>
<td>Confidentiality</td>
<td>27</td>
<td>How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial</td>
</tr>
<tr>
<td>Declaration of interests</td>
<td>28</td>
<td>Financial and other competing interests for principal investigators for the overall trial and each study site</td>
</tr>
<tr>
<td>Access to data</td>
<td>29</td>
<td>Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators</td>
</tr>
<tr>
<td>Ancillary and post-trial care</td>
<td>30</td>
<td>Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation</td>
</tr>
<tr>
<td>Dissemination policy</td>
<td>31a</td>
<td>Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions</td>
</tr>
<tr>
<td></td>
<td>31b</td>
<td>Authorship eligibility guidelines and any intended use of professional writers</td>
</tr>
<tr>
<td></td>
<td>31c</td>
<td>Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code</td>
</tr>
<tr>
<td>Appendices</td>
<td></td>
<td>Model consent form and other related documentation given to participants and authorised surrogates</td>
</tr>
<tr>
<td>Biological specimens</td>
<td>33</td>
<td>Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable</td>
</tr>
</tbody>
</table>

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported license.*
Informed consent form · Informed notification page

Dear patient:

You are diagnosed as malocclusion by your doctor. You are invited to participate in a clinical study “The efficacy of TADs assisted Herbst appliance for Angle Class II division I hyperdivergent patients with early permanent dentition”. The project is funded by Shanghai Commission of Science and Technology (20Y11904100, 20YF1442400), Shanghai Municipal Health commission (20224Y0391) and the Clinical Innovation Team of Shanghai Stomatological Hospital (SSDC-2020-CXTD-A04). This study protocol has been reviewed by the Medical Ethics Committee of Shanghai Stomatological Hospital.

Before you decide whether to participate in this study, please read the following carefully. It can help you understand the aim, procedure and duration of the study, and the benefit, risk and discomfort you may have. If you wish, you can also discuss with your relatives and friends, or ask a doctor to explain it to help you make a decision.

1. Why we conduct this study?

1.1 Disease burden and the current status of the treatment

Class II malocclusion is a common maxillofacial deformity, characterized with mandibular retrognathism as the main feature in the Chinese population. Functional appliances have been introduced to children who are in the growth and development stage. Among them, the representative Herbst appliance was first proposed by German scholar Herbst at the International Dental Conference in Berlin in 1909. Herbst appliance is a fixed occlusal forward device. The Herbst appliance, is a fixed forward occlusal device that keeps the mandible in the forward extension position and stimulates the growth of the condyle and mandible.

Compared to other functional appliances, Herbst appliance can result in intrusion of
upper molars, which contributes to a clockwise rotation of the occlusal plane. If this is not controlled vertically, it may result in an increase in skeletal divergence, which is not conducive to the treatment of angle II high angle patients. Since the close relationship between occlusal plane and the mandible position, the key for orthodontic treatment is to maintain or even decrease the inclination of occlusal plane, achieving the counterclockwise rotation of the mandible and a promising profile.

1.2 The purpose of this study
The purpose of this study is to compare the clinical effects of Herbst treatment with or without vertical control in terms of dental and maxillofacial development, mandible position and profile attractiveness in children who were diagnosed with hyperdivergent skeletal Class II malocclusion.

1.3 Study participants and the number of expected participants
The study will be conducted in Shanghai Stomatological Hospital. According to our previous pilot study, the mean OP-SN angle decreased by 2.5±2.8 in adolescents who were treated with innovative Herbst appliance with vertical control, while the average change of OP-SN angle in the standard Herbst group was 0±2.8 degrees. 18 participants in each group can provide 95% power to detect a minimum clinically significant difference in the OP-SN of 0.7 degrees (using α=0.05). The sample size calculation was based on a two-sided hypothesis. Considering an anticipated 20% dropout rate, the final sample size is a total of 44, and 22 participants in each group.

2. Who were invited to join the study?
1) Patients aged from 10 to 13 years old who are at or right before the peak of the pubertal spurt assessed using vertebral analysis
2) Class II, division 1 malocclusion characterized by mandibular retrognathism and normal or mild maxillary protrusion (A point, Nasion, B point [ANB] ≥ 4)
3) Minimum overjet of 4 mm in permanent dentition
4) Hyperdivergent growth pattern (FMA>33)
5) Good oral health condition (healthy periodontal tissue, no periapical disease and no unfilled caries)
3. How was the study conducted?

We will enroll 44 children aged from 10 to 13 years who are diagnosed with angle Class II malocclusion. The participants will undergo a series of medical tests, including physical examinations and maxillofacial radiography, to verify the diagnosis. Once enrolled in the study, subjects will be randomly divided into one of two treatment groups - the Herbst group, or the Herbst with vertical control group - at a ratio of 1:1. The enrolled subjects will undergo Herbst treatment or Herbst treatment with vertical control within 4 weeks after randomization. Both treatment methods will be implemented by experienced doctors.

Subjects receiving Herbst treatment will be fitted with a standard Herbst appliance for 10 months. Routine follow-up will be conducted every 4 weeks until the end of the treatment. Subjects receiving Herbst with vertical control treatment will be fitted with a Herbst appliance accompanied by miniscrew implants for occlusal plane leveling. Miniscrew implants will be inserted 1 week after the Herbst appliance is settled. Patients will be given appointments at 4-week intervals. The patients and their guardians will be well informed by the doctor for the study content, and sign the informed consent after full consideration. Three study visits per subject will be scheduled in the study as follows: baseline assessment visit (T0), initiation of Herbst therapy visit (T1), and end of Herbst therapy visit (T2). At scheduled visits, data relating to lateral cephalometric radiographs, CBCT scanning, subjective assessment of VAS, adverse events will be recorded and collected.

4. The possible impact of participating in the study on the subjects’ daily life

When you decide whether to participate in this study, please carefully consider the possible impact of the examination and follow-ups as listed above on your daily life, etc. Consider the time schedule for each visit and the traffic. If you have any questions about the examinations and steps involved in the test, you can consult with us. Considering your safety and to ensure the validity of the study results, you cannot participate in any other clinical studies on drugs and medical devices during the study.
5. Possible adverse effects, risks and discomfort, and inconvenience of participating in the study

The discomfort you may undergo after the placement of the Herbst appliance, including the discomfort in tongue, mucosa and temporomandibular joint area. Mini-implants insertion may cause the risk of implant breaking, loosening, and soft tissue local inflammation. The oral appliance may affect the appearance, causing inconvenience during speech and eating.

6. Potential benefits of participating in the study

Although Studies have proven the satisfactory outcome of Herbst appliance in skeletal Class II treatment, this does not guarantee the treatment outcome for you. The protocol used in this study is not the only way to treat mandibular retrognathism. If the Herbst appliance is not beneficial to your condition, you can ask for alternative treatment methods. The examination fee will be covered in this study. All the patients will get the free orthodontic planning for second stage treatment.

7. Confidentiality of personal information

Your medical records (study records / CRFs, laboratory sheets, etc.) will be kept in the hospital where you visit. Your doctor will record the results of the laboratory tests and other tests on your medical record. The investigator and the ethics committee will be allowed to access to your medical records. No public report on the results of this study will disclose your personal identity. We will make every effort to protect the privacy of your personal medical information as permitted by law.

According to medical research ethics, in addition to personal privacy information, trial data will be available for public inquiry and sharing, and it will be limited to electronic databases, ensuring that no personal privacy information will be leaked.

8. Related expenses

The examination fee is RMB 400 yuan, and the subsequent phase II treatment plan is free. You need to pay for the Herbst appliance, mini-implants and orthodontic treatment.

When your health condition is compromised by participating in this study, please inform the investigator, and we will immediately take the necessary medical methods
to protect your health. According to the relevant laws and regulations of China, the sponsor of this study will cover the corresponding medical expenses and the corresponding economic compensation in the event of any injury related to the study.

9. Do you have to attend and complete this study?
You may choose not to participate in this study, which will not have any adverse effect on your standard medical care. You will not suffer any discrimination accordingly. Even if you consent to participate, you may withdraw from the study at any time without any reason, and this will not affect your access to standard medical services. When you decide not to participate in this study, you need to inform your study doctor that the study doctor can provide advice and guidance on your health status.

We will inform you of any information that may affect your decision to continue your participation in this study.

In case of gingival recession, dental disease or systemic disease during the treatment, the treatment should be stopped in time and transferred to relevant departments for treatment to ensure the safety and rights and interests of patients.

In the event of an early termination of this study, or for your best interest, your doctor may suspend you during the course of the study. Your doctor will advise you on your next treatment plan based on your health status.

Other information required to inform the subject:
For dropout subjects, we have a final follow-up plan and you have the right to refuse. If any unused study drug or device should be returned to your doctor. If you withdraw and find new information about your health and rights, we may contact you again.
After the withdrawal, it should be clear that no new data will be collected. Participants will also be given detailed instructions on how to handle previously collected study data and withdrawal data due to adverse events.
If you withdraw from the study for any reason, you may also be required to have a laboratory examination and a physical examination if your doctor thinks it is necessary.

10. What should I do now?
Whether or not to participate in this study is up to you (and your family members).
Ask your doctor for questions before making your decision to participate in the study.
Please call (office number with area code during working hours), after work hours,
weekends and holidays (24 hours landline or mobile phone with area code). the
supervision number for hospital ethical committee is 021-54668034.
Thank you for reading. If you decide to participate in this study, please tell your
doctor that he/she will arrange for you about the study. Please keep this information.
The researcher's statement

I have informed the subject and the subject's guardian about the background, purpose, steps, risks and benefits regarding to the study “The efficacy of TADs assisted Herbst appliance for Angle Class II division 1 hyperdivergent patient with early permanent dentition”.

The subject and his/her guardians had enough time to read the informed consent form and discuss it with others. I have answered all the questions about the research. I have informed the subject that he/she can access to Dr. Jie Pan with any related questions about the study. He/she can reach the hospital medical Ethics Committee when encountering problems related to your own rights/interests. I have provided the accurate contact information. I have informed the subject that he/she may withdraw from the study without any reason. I have informed the subject that he/she will have a copy of this informed consent form. It contains me and his/her signatures. I confirm that the patient has been explained all the details of this trial, including his/her authority and possible benefits and risks, and given a copy of the signed informed consent form.

Doctor's signature: ____________________  Date: ______________

The Doctor's work phone number: ____________________
Subject statement

My child and I have been fully informed of the background, purpose, steps, risks and benefits regarding to the study “The efficacy of TADs assisted Herbst appliance for Angle Class II division 1 hyperdivergent patient with early permanent dentition”.

I had plenty of time and opportunities to ask questions. I was pleased with the answers. I was also told who I should contact when I had problems, difficulties, concerns. I have read this informed consent form, and I have agreed to participate in this study. I know that at any time during the study I can have my child withdraw from the study without any reason. Furthermore, I have discussed this research project with my child, and my child agreed to participate in this study, knowing that without any reason at any time during the study I could request him/her to withdraw from the study. I was informed that I would have a copy of this informed consent form containing the signatures of me and the investigator.

Subject guardian signature: _______________ Date: _______________
Contact number: _______________