INTRODUCTION

Review question / Objective: Does CO2 laser therapy (COLT) effectively treat acne depressed scar (ADS)?

Condition being studied: CO2 laser therapy; acne depressed scar.

METHODS

Participant or population: We will only include subjects who had a confirmed clinical diagnosis of ADS. No limitations upon the race, gender, age, economic status and educational background will be placed.
**Intervention:** In the experimental group, we will include all involved studies that focus on COLT management.

**Comparator:** In the control group, control interventions could be any treatments, except any forms of COLT.

**Study designs to be included:** All randomized controlled trials (RCTs) on use of COLT for patients with ADS will be included with no limitation of language and publication time.

**Eligibility criteria:** All RCTs on use of COLT for patients with ADS will be included with no limitation of language and publication time.

**Information sources:** Electronic databases sources - We will search all following electronic databases from the beginning of each one to the March 31, 2020: Cochrane Library, PUBMED, EMBASE, Web of Science, Allied and Complementary Medicine Database, VIP Database, CBM database, and China National Knowledge Infrastructure. All electronic databases will be searched without restrictions of language and publication time by two independent authors. If any different views occur, a third author will help to solve them through discussion. The detailed strategy for searching the Cochrane Library will be built. We will also adapt similar detailed search strategies for any other electronic databases. Other literature sources - We will also search conference papers, clinical trial registries, and reference lists of relevant reviews.

**Main outcome(s):** The primary outcome is severity of acne scars, as measured by Echelle D’Evaluation Clinique des Cicatrices D’Acne grading scale or other associated scales. The secondary outcomes are scar improvement (as assessed by Vancouver Scar Scale or other scales), crust time, time to complete molting, edema time, erythema duration, depression (as checked by Self-rating Depression Scale or other scores), anxiety (as evaluated by Self-rating Anxiety Scale or other tools), quality of life (as identified by Global Quality of Life Scale or other scales), and adverse events.

**Data management:** Two authors will extract data from all selected studies independently. Any discrepancies between two authors will be solved through discussion by a third author. This data collect form will consist of reference identification, first author, year of publication, basic characteristics of patient, diagnostic criteria, inclusion and exclusion criteria, randomization, blinding, intervention and control indicators, outcome measurements, research results, follow-up information, adverse events, and other detailed information. If necessary, we will contact primary trial author for further information when we find insufficient or missing data from the included studies.

**Quality assessment / Risk of bias analysis:** Two independent authors will identify the risk of bias for each eligible trial using Cochrane risk of bias tool. It covers 7 aspects and each one will be classified as low risk of bias, unclear risk of bias, or high risk of bias. Any disagreements between two authors will be resolved by a third author through arbitration.

**Strategy of data synthesis:** RevMan 5.3 software will be used for statistical analysis. We will express enumeration data with risk ratio and 95% confidence intervals (CIs), and measurement data with mean difference or standardized mean difference and 95% CIs. We will use I² statistic test to determine the heterogeneity of the research results. If I² ≤50%, the heterogeneity among the studies will be considered as acceptable; and a fixed-effect model will be used. Otherwise, if I² >50%, it will be considered evidence of substantial heterogeneity among the trials, and a random-effect model will be utilized. We will undertake meta-analysis if there is not significant statistical heterogeneity in the outcome results. If we identify substantial heterogeneity, we will further explore the sources of such obvious heterogeneity using subgroup analysis. In addition, we will present outcome results as descriptive summary.
**Subgroup analysis:** If there is obvious heterogeneity among included trials, we will undertake a subgroup analysis in accordance with the basic information of study and patient, different managements, comparators, and outcomes.

**Sensibility analysis:** If possible, we will also perform sensitivity analysis to verify the robustness of conclusions by removing low quality studies.

**Country(ies) involved:** China.

**Keywords:** CO2 laser therapy; acne depressed scar; randomized controlled trial; effectiveness; safety.