

# INPLASY PROTOCOL

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**Review Stage at time of this submission:** The review has not yet started.

**Conflicts of interest:**  
The authors declare no conflicts of interest.

## The Efficacy of Bloodletting Therapy in Patients with Postherpetic Neuralgia: A Protocol for Systematic Review and Meta-analysis

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**Review question / Objective:** To summarize and evaluate the effects of Bloodletting therapy for postherpetic neuralgia. **Condition being studied:** Postherpetic neuralgia (PHN) is the most common chronic complication of herpes zoster. It is characterized by paroxysmal or persistent burning pain, anxiety, depression or even insomnia. The management of PHN is an effective long-term therapy. The first-line drugs for PHN are nonsteroidal anti-inflammatory drugs (NSAIDs), Mecobalamin and Vitamin. However, above western medicine have high risk for acquiring low compliance and severe side effects in cardiovascular and gastrointestinal systems. Therefore, taking a view on alternative medicine has become another popular way. Amounts of clinical randomized controlled trials have showed that Bloodletting therapy is effective in treating PHN with less adverse events.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 September 2020 and was last updated on 21 September 2020 (registration number INPLASY202090077).

### INTRODUCTION

**Review question / Objective:** To summarize and evaluate the effects of Bloodletting therapy for postherpetic neuralgia.

**Condition being studied:** Postherpetic neuralgia (PHN) is the most common chronic complication of herpes zoster. It is characterized by paroxysmal or persistent burning pain, anxiety, depression or even insomnia. The management of PHN is an

effective long-term therapy. The first-line drugs for PHN are nonsteroidal anti-inflammatory drugs (NSAIDs), Mecobalamin and Vitamin. However, above western medicine have high risk for acquiring low compliance and severe side effects in cardiovascular and gastrointestinal systems. Therefore, taking a view on alternative medicine has become another popular way. Amounts of clinical randomized controlled trials have showed that Bloodletting therapy is effective in treating PHN with less adverse events.

## METHODS

**Search strategy:** Database: Chinese Database: China Biology Medicine (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Data, Chinese Scientific Journal Database (VIP); English Database: PubMed, Cochrane Library, EMbase. Search Strategy and Search Terms: Chinese: Postherpetic neuralgia, Bloodletting therapy, randomized controlled trials; English: A. Search strategy to locate 'Neuralgia, Postherpetic' #1 "Neuralgia, Postherpetic"[MeSH] #2 "Postherpetic Neuralgia" #3 #1 OR #2 B. Search strategy to locate 'Bloodletting' #4 "Bloodletting"[MeSH] C. Search strategy to locate RCTs #5 "Randomized Controlled Trial as Topic"[MeSH] #6 "Clinical Trials, Randomized" #7 "Trials, Randomized Clinical" #8 "Controlled Clinical Trials, Randomized" #9 #5 OR #6 OR #7 OR #8 D. Search strategy to locate studies for this review #3 AND #4 AND #9.

**Participant or population:** Patients with a diagnosis of Postherpetic Neuralgia (PHN). There are no restrictions of age, sex, course of disease, race, etc.

**Intervention:** Bloodletting Therapy.

**Comparator:** Western medicine or other terms of external treatments of Traditional Chinese Medicine (TCM).

**Study designs to be included:** Randomized controlled trials.

**Eligibility criteria:** Randomized controlled trials that compared bloodletting therapy and western medicine or another external treatment of TCM for patients with Postherpetic Neuralgia (PHN).

**Information sources:** Chinese Database: China Biology Medicine (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Data, Chinese Scientific Journal Database (VIP); English Database: PubMed, Cochrane Library, EMbase.

**Main outcome(s):** Effective rate; pain intensity (VAS, NRS, MPQ, etc.).

**Quality assessment / Risk of bias analysis:** Two authors assessed the risk of bias of the included studies using the methods recommended by the Cochrane Collaboration for the following terms. Six domains should be scored: sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting and other sources of bias. The risk of bias was graded as low, high and unclear.

**Strategy of data synthesis:** RevMan 5.3 software (Cochrane Collaboration) was used for the meta-analysis. Dichotomous data were reported as risk ratio (RR) with 95% confidence intervals (CI), while continuous data were reported as standardized mean difference (SMD) with 95% CIs. The Higgins  $I^2$  test was used to test heterogeneity with a significance level set at 50%. If heterogeneity was not significant ( $I^2 \leq 50\%$ ), the fixed effects model was used for meta-analysis. Otherwise, the random effects model was used ( $I^2 \geq 50\%$ ). If possible, we investigated the potential explanations for heterogeneity and conducted subgroup analysis.

**Subgroup analysis:** Subgroup analysis will be conducted for heterogeneity arising from control type (acupuncture, drug, other external treatment of Traditional Chinese Medicine), treatment frequency duration, course of disease, the amounts of blood letting out, and acupoints, etc.

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**Sensibility analysis:** Sensibility analysis will be conducted to assess the influence of each individual study, leave-one-out sensitivity analysis was performed iteratively by removing one study at a time to confirm that the findings were not influenced by any single study.

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

**Keywords:** Postherpetic neuralgia; Bloodletting Therapy; Randomized Controlled Trials; Systematic Review.

**Contributions of each author:**

**Author 1 - Sihui Li -** Author 1 drafted the manuscript.

**Author 2 - Weishang Hu -** Author 2 contributed to the development of the selection criteria, and the risk of bias assessment strategy.

**Author 3 - Qiaofeng Wu -** Author 3 checked the manuscript.