

# INPLASY PROTOCOL

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The authors declare that they  
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## Comparison of the antihypertensive efficacy of morning and bedtime dosing on reducing morning blood pressure surge

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**Review question / Objective:** Comparison of the  
antihypertensive efficacy of morning and bedtime dosing on  
reducing morning blood pressure surge.

**Condition being studied:** It is well-known that morning blood  
pressure surge increases the risk of myocardial events in the  
first several hours, post-awakening. This meta-analysis was  
performed to compare the antihypertensive efficacy of  
morning and bedtime dosing on decreasing morning blood  
pressure surge.

**Information sources:** The Literature search was performed in  
Pubmed, Embase, Cochrane and ISI Web of Science.

**INPLASY registration number:** This protocol was registered with  
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### INTRODUCTION

**Review question / Objective:** Comparison  
of the antihypertensive efficacy of morning  
and bedtime dosing on reducing morning  
blood pressure surge

**Condition being studied:** It is well-known  
that morning blood pressure surge  
increases the risk of myocardial events in  
the first several hours, post-awakening.  
This meta-analysis was performed to  
compare the antihypertensive efficacy of

morning and bedtime dosing on decreasing morning blood pressure surge.

## METHODS

**Participant or population:** Adult patients who satisfied diagnosis of hypertension using office measurements of blood pressure (SBP  $\geq$  140 mmHg or DBP  $\geq$  90 mmHg), including essential hypertension and secondary hypertension.

**Intervention:** Intervention was defined as one or more anti-hypertensive drugs administered at bedtime (from 5:00 p.m. to 12:00 midnight).

**Comparator:** The control group was matched to the experimental group by drug and dose but with a morning regimen or in awaking time (from 6:00 a.m. to 12:00 noon).

**Study designs to be included:** Experimental trials with at least 6 weeks' treatment duration of antihypertensive drugs (angiotensin-converting enzyme inhibitors, calcium channel blockers, beta-blockers, diuretics, angiotensin receptor blockers, and alpha-blockers).

**Eligibility criteria:** 1) Adult patients who satisfied diagnosis of hypertension using office measurements of blood pressure (SBP  $\geq$  140 mmHg or DBP  $\geq$  90 mmHg), including essential hypertension and secondary hypertension; 2) Experimental trials with at least 6 weeks' treatment duration of antihypertensive drugs (angiotensin-converting enzyme inhibitors, calcium channel blockers, beta-blockers, diuretics, angiotensin receptor blockers, and alpha-blockers); 3) Intervention was defined as one or more anti-hypertensive drugs administered at bedtime (from 5:00 p.m. to 12:00 midnight), the control group was matched to the experimental group by drug and dose but with a morning regimen or in awaking time (from 6:00 a.m. to 12:00 noon); 4) The pre- and post-treatment SBP and DBP of each patient were measured by ABPM, which is now the gold standard measurement and the most cost-effective

strategy for diagnosing hypertension, evaluating true BP level.

**Information sources:** The Literature search was performed in Pubmed, Embase, Cochrane and ISI Web of Science.

**Main outcome(s):** The morning blood pressure surge: SBP and DBP.

**Quality assessment / Risk of bias analysis:** Six criteria were applied as follows: 1) selection bias (random-sequence generation and allocation concealment); 2) performance bias (blinding of participants and personnel); 3) detection bias (blinding of outcome assessment); 4) attrition bias (incomplete outcome data); 5) reporting bias (selective reporting); 6) other bias. There were three potential bias judgments: 1) low risk; 2) high risk; 3) unclear risk. A study was rated as having an unclear risk when insufficient details were reported regarding the methods and outcome, the risk of bias was unknown, a metric was not relevant to the study, particularly for assessing blinding and incomplete outcome data, or when the outcome assessed by the metric had not been measured in the study.

**Strategy of data synthesis:** The following search terms: Antihypertensive-drugs, Antihypertensive, Antihypertensive effect, Antihypertensive treatment, morning, awakening, blood pressure, Blood Pressure Monitoring, Ambulatory, bedtime, without imposed language restrictions.

**Subgroup analysis:** When there is heterogeneity between research results, we will conduct a comprehensive and systematic analysis of the reasons for heterogeneity and carry out hierarchical treatment according to different sources of heterogeneity. If it is due to the variation between studies, the intervention measures are consistent, and the research objects come from different populations. The following aspects will be used: age, course of the disease, gender.

**Sensibility analysis:** Statistical heterogeneity among studies was

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assessed using I<sup>2</sup> and Q test statistic. Mild, moderate, and severe heterogeneity were defined by I<sup>2</sup> values of 25%, 50%, and 75%, respectively. Sensitivity analysis was used to determine whether the included literature had a significant impact on the stability of the study.

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

**Keywords:** Hypertension; Antihypertensive drugs; Bedtime; Morning blood pressure surge; Meta-analysis.

**Contributions of each author:**

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