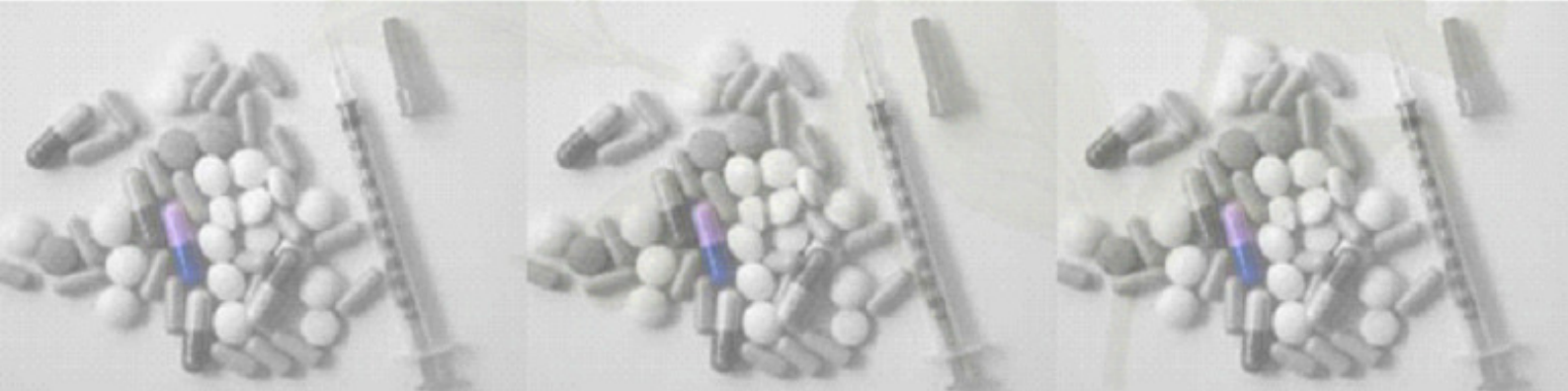
# Short - term and Long - term Effects of Chinese Herbal Medicine in Drug Abuses: A Series of Meta-analysis

# 中藥近期和遠期脫毒療效的薈萃分析



# RESEARCH PROJECT REPORT

# (BDF 070002)


## Principal Investigators:

**XU Min, XU Dong Ying, TIAN Xiao Ying,**
**DENG Ping Xiang, QI Chen, DENG Bin**

(Hong Kong Baptist University)

## Advisors:

**NG Roger, ZIEA Tat Chi**

(Hospital Authority, Hong Kong)

## Participants:

**GU Tie Guang, ZHANG Xiao Ming, CHOI Ching Mei,**
**KONG Hiu Lai, HUANG Ping, CHONG Ling Ling,**
**CHAN Weng Leong**

(Hong Kong Baptist University)


**March 2009**

# ACKNOWLEDGEMENTS

**We would sincerely give our thanks to the sponsorship from the Beat Drugs Fund of Hong Kong Government**

# ABSTRACT

**Background and objectives:** Psychotropic-drug abuse is a study priority of health and social science. A number of randomized controlled clinical trials (RCTs) to treat heroin dependence and psychotropic-drug adverse effects with Chinese herbs (CH) have been conducted. This study aims to (1) assess the quality and data of these trials, and (2) compare the efficacy and safety of CH with WM (Western medications) in short-term and long-term heroin detoxification, and in the treatment of adverse symptoms caused by psychotropic drugs clinically.

**Methods:** (1) Search strategy: electronic databases and hand-search materials were widely searched for screening eligible trials. (2) Inclusive and exclusive criteria: RCTs to compare the efficacy and safety of CH with WM were valid. (3) Data analysis: the quality of eligible trials was assessed by Jadad's scale; and data were estimated by standard mean difference (SMD) and odd ratio (OR) with 95% confidence interval (95% CI) in meta-analyses.

**Results:** (1) 107 RCTs (6,032 treated with CH in total 11,490 patients) that met the inclusion criteria were included from 193 trials and 34 RCTs (32%) were assessed as high-quality trials (scoring 3-5 marks; 13 RCTs for short-term heroin detoxification, 3 RCTs for long-term heroin detoxification, and 18 RCTs for adverse effects of pscychtropic drugs); the rest were low-quality trials (scoring 1-2 marks) owning to poor description of randomization, double-blind methods and dropout reporting.

(2) In short-term heroin detoxification ($\leqq$10 days): 1) Compared with clonidine, CH was more effective to diminish acute abstinent symptoms from the Day 1 to 10 (16RCTs, P=0.01 to P<0.0001) and anxiety on the Day 5 or 10 (9RCTs, P<0.0001 or P=0.0002). 2) Compared with methadone, CH showed a similar effect to diminish acute abstinent symptoms from the Day 1 to 10 (5RCTs, P$\geqq$0.05) and anxiety on the Day 5 or 10 (4RCTs, P>0.05). 3) Compared with nofexidine, CH was more effective to diminish acute abstinent symptoms from the Day 1 to 6 (8RCTs,

P=0.03 to P=0.007) and anxiety on the Day 10 (7RCTs, P=0.04). 4) Compared with buprenorphine, CH showed a similar effect to diminish acute abstinent symptoms from the Day 1 to 10 (5RCTs, P>0.05) in most trials. 5) Compared with diazepam, CH was more effective to diminish acute abstinent symptoms from the Day 4 to 7 and 10 (2RCTs, P=0.02 to P=0.0009). 6) Compared with WM in the number of improved patients (NIP) of acute abstinent symptoms, CH showed more effective than clonidine (5RCTs, P=0.007) and buprenorphine (2RCTs, P=0.01) but similar to methadone (4RCTs, P=0.87). 7) Adverse-effect score of CH was lower than that of WM from the Day 1 to 4 (6RCTs, P=0.01 to P=0.0009), and CH was safer than WM in NIP of adverse effects such as blurred vision (2RCTs, P<0.00001) and dizziness (3RCTs, P<0.00001).

(3) In long-term heroin detoxification (>10 days): 1) Compared with WM (diazepam, oryzanol, tramadol, naltrexone, clonidine, etc.), CH was more effective to diminish protracted abstinent symptoms (3RCTs, P=0.006) and anxiety (2 RCTs, P=0.02), but might be less effective to diminish pain (2RCTs, P=0.04); meanwhile, CH was more effective to improve NIP in all symptoms (2RCTs, P=0.0002), insomnia (3RCTs, P<0.00001), anxiety (2RCTs, P<0.00001), pain (2RCTs, P<0.00001), debility (2RCTs, P=0.0001) and relapse rate (3RCTs, P<0.0001). 2) Compared with placebo, CH was more effective to diminish all symptoms (4RCTs, P=0.0005), insomnia (3RCTs, P=0.002), pain (3RCTs, P<0.00001), palpitation (1RCT, P<0.00001), dysphoria (1RCT, P<0.00001), and to improve relapse rate (1 RCT, P=0.03). 3) CH was safer than WM in long-term treatments, although available data could not be integrated in a meta-analysis.

(4) In the treatment of adverse effects caused by psychotropic drugs: 1) Compared with WM, CH was more effective to improve NIP (8RCTs, P<0.00001), constipation (4RCTs, P=0.001), sialorrhea (7RCTs, P<0.00001), dry mouth (3RCTs, P<0.00001), ECG (4RCTs, P=0.001), amenorrhea (4RCTs, P=0.0009), enuresis (3RCTs, P<0.00001), leucopenia (5RCTs, P<0.00001) and coma (3RCTs, P=0.003). 2) CH showed a less adverse-effect score in nausea (2RCTs, P=0.005) and poor appetite (2RCTs, P=0.002) when compared with WM.

**Conclusion:** CH may be effective and safe for the treatment of heroin withdrawal syndrome and adverse effects caused by other psychotropic drugs, albeit more clinical trials with high-quality study design should be conducted to further verify the evidence in this study. In addition, CH is not a “No-Pain” therapy in heroin detoxification and treatment of adverse effects caused by other psychotropic drugs. It should be concerned in future clinical studies that some toxic herbs can cause typical adverse effects, and the relapse rate is still quite high in patients treated with certain herbal preparations.

***Keywords*:** Chinese herb; drug abuse; heroin detoxification; withdrawal syndrome; psychotropic drug; systematic review; meta-analysis.

# 中文摘要

**背景**：濫用海洛英等毒品和精神藥物引起的毒副作用對身心及社會均造成巨大的影響；是一個困擾全球的問題，也是醫療衛生和社會科學優先關注的研究課題。近年不少臨床試驗研究了中藥在海洛英脫毒的短期和長期療效以及在治療精神藥物引起的毒副作用的意義。本課題按循證醫學的原則與方法，首次對有關的臨床試驗進行系統評價分析。

**目的**：(1) 對相關臨床試驗及其資料進行收集整理，質量評估和資料分析；

(2) 比較中藥和西藥在臨床試驗中的療效及安全性。

**方法**：(1) 文獻檢索: 通過電子文獻資料庫、手工檢索等方法收集包括所有語種的相關臨床試驗。(2) 篩選標準: 選擇所有中藥治療海洛因急性期和稽延期戒斷症狀以及精神藥物引起的毒副作用的隨機對照臨床試驗(RCTs)。(3) 資料分析: 符合納入標準的研究採用 Jadad 計分定量評估其質量。計量資料採用標準化均數差值(SMD)，計數資料採用優勢比(OR)以及 95%可信區間進行 meta 分析。

**結果**：(1) 在系統檢索所獲的 193 項臨床試驗(共計 11,490 例患者中 6,032 例用中藥治療)中 107 項(治療急性戒斷症狀 36 項，治療稽延期戒斷症狀 14 項，治療精神類藥物的毒副作用 57 項)符合納入標準；Jadad 計分評估結果顯示 34 項(32%)屬於高質量研究(分值達 3-5 分；治療急性期戒斷症狀 13 項，治療稽延期戒斷症狀 3 項，治療精神藥物的毒副作用 18 項)，其餘研究在描述隨機化、盲法及報告病例退出率等方面不達要求而不屬高質量研究。

(2) 中藥治療海洛因戒斷急性期症狀(≦10 天): 1) 與可樂定相比，中藥治療於 1-10 天緩解急性戒斷症狀較好(16RCTs, P=0.01 to P<0.0001)； 於 5 和 10 天緩解焦慮較好(9RCTs, P<0.0001 or P=0.0002)；2) 與美沙酮相比, 中藥在 1-10 天緩解戒斷症狀 (5RCTs, P≧0.05) 或 5 和 10 天緩解焦慮療效相似(4RCTs, P>0.05)； 3) 與諾啡西定相比, 中藥治療於 1-6 天緩解戒斷症狀(8RCTs, P=0.03 to P=0.007)和於 10 天緩解焦慮(7RCTs, P=0.04)較好；4) 與丁丙諾啡相比, 大多數研究報告中藥治療的療效相似(5RCTs, P>0.05)； 5) 與舒樂安定相比, 中藥治療於 4 至 7 和 10 天緩解

戒斷症狀較好(2RCTs, P=0.02 to P=0.0009)； 6) 與西藥相比，中藥在改善戒斷症狀人數(有效率)方面優於可樂定(5RCTs, P=0.007)和丁丙諾啡(**2RCTs, P=0.01**)，而與美沙酮相似(4RCTs, P=0.87)；7)與西藥比較，中藥治療 1-4 天的不良反應分值較低(6RCTs, P=0.01 to P=0.0009)；在視物模糊(2RCTs, P<0.00001)和頭暈(3RCTs, P<0.00001)發生人數上較西藥少。

(3) 中藥治療海洛因稽延期戒斷症狀(>10 day): 1) 與西藥(安定，穀維素，曲馬朵，納曲酮，可樂定，等)相比，中藥對治療稽延期綜合症狀(3RCTs, P=0.006)和焦慮(**2RCTs, P=0.02**)較優，但西藥緩解疼痛較優(2RCTs, P=0.04)； 而中藥組在獲改善總人數上較優(2RCTs, P=0.0002)，以及在失眠(3RCTs, P<0.00001),焦慮(2RCTs, P<0.00001)，疼痛(2RCTs, P<0.00001)，乏力(2RCTs, P=0.0001)的改善人數上，或複吸率(3RCTs, P<0.0001)上較優； 2) 與安慰劑相比，中藥對治療稽延期綜合症狀(4RCTs, P=0.0005)以及失眠(3RCTs, P=0.002)，疼痛(3RCTs, P<0.00001)，心悸(1RCT, P<0.00001)，煩躁(1RCT, P<0.00001)，複吸率(1RCT, P=0.03)上較優；3) 中藥治療較少發生不良反應。

(4) 中藥治療精神藥物引起的毒副作用: 1)與西藥相比，中藥在獲改善總人數上較優(8RCTs, P<0.00001)，對改善便秘(4RCTs, P=0.001)，流涎(7RCTs, P<0.00001)，口幹(3RCTs, P<0.00001)，心電圖異常(4RCTs, P=0.001)，閉經(4RCTs, P=0.0009)，遺尿(3RCTs, P<0.00001)，白細胞減少(5RCTs, P<0.00001)，急性中毒昏迷(3RCTs, P=0.003)等較優； 2) 中藥組發生噁心(2RCTs, P=0.005)和食欲降低(2RCTs, P=0.02)等不良反應比西藥組少。

**結論**：中藥療法在治療海洛英急性戒斷症狀方面具有一定優勢；在改善戒斷後期稽延症狀和降低複吸率方面也顯示了治療意義；因此中藥應用於海洛英脫毒應該是一種有效的療法。同時，中藥對精神藥物引起的多種臨床不良反應也具有療效，而且中藥療法較爲安全。但是中藥應用於海洛英戒毒和治療精神藥物的不良反應並非是一種輕鬆的脫毒途徑。含有某些毒性中藥的中藥製劑在臨床上也可以引起典型的不良反應。此外，中藥治療者中複吸率仍較高，尚有待改进。由於現有研究方法和資料的局限性，進一步開展高質量的臨床研究以驗證本工作的結果是必要的。

**關鍵字**：中草藥； 藥物濫用；海洛因戒毒；戒斷症狀；精神藥物；系統評價；薈萃分析

# CONTENT

# CHAPTER 1

# General Introduction

## 1.1 Evidence-based medicine

Evidence-based medicine (EBM) is defined as the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. EBM is a process of turning clinical problems into questions and then systematically locating, appraising and using research findings as the basis for clinical decisions. In the last decades, the computerisation of bibliographies and the development of software that can rapidly locate and analyse relevant data have made it easier to find available evidence in the published literatures. Clinicians who devote their scarce reading time to selective, efficient, patient driven search, appraisal and incorporation of the current best evidence can practise EBM.

Traditional Chinese medicine has been serving people over 2000 years and remains an important part of health care provision in Hong Kong and Mainland China. Chinese herbs (CH) are potential resources of new medications, and their efficacy and safety need to be identified by EBM. It is undoubted that systematic review and meta-analysis can also significantly increase the power and precision in estimates of treatment effects and risks of traditional Chinese medicine, and EBM should be an important approach to develop traditional Chinese medicine in modern society. Meanwhile, many researches of CH have been published in Chinese and most of them are not readily accessed by Western experts. It should be valuable to draw together and make more accessible findings from clinical trials largely published in China.

## 1.2 Systematic review and meta-analysis

A systematic review is an evidence-based overview process which uses explicit methods to perform a thorough literature search and critical appraisal to identify the valid and applicable evidence. A meta-analysis is the quantitative use of statistical techniques to integrate the results of included studies. It can be understood as one important part of analyzing and presenting results involved in a systematic review. The usual effect size indicator is the standardized mean difference for measurement data and odd ratios for category data in a 95% confidence interval to yield a quantitative analysis on the size of the treatment effect and a test of homogeneity in the estimate of effect size.

A meta-analysis should be an optional component or step in systematic reviews.

When we conduct a systematic review following a standard procedure that should include finding, selecting, appraising, synthesizing, analyzing and reporting eligible data, meta-analysis as a specific statistical analysis may provide an important way for us to synthesize and analyze the data of individual studies. In practice, systematic reviews may contain meta-analyses of the data but it is not always available. This may happen in a systematic review if the data is insufficient or inappropriate to generate a meta-analysis.

Systematic review and meta-analysis may not be able to prove the authenticities of the sources, neither did other methods. However, the World Health Orgnisation (WHO) regards it as a current best method to provide clinical evidences. It gives the answer for those who criticize systematic review and meta-analysis for not being meaningful if all paper sources are in poor qualities. The logic is that, even if that is the case, we still synthesize all available data and are providing current "best evidence" in this area. In other words, following our results from a meta-analysis should be safer than believing any paper individually.

### 1.3 Study objective

In recent years, more and more RCTs have been conducted in China and claimed that CM therapies have therapeutic effects to manage psychotropic-drug abuse. It is very valuable to identify the quality of these trials and assess the efficacy and safety of CM with principles and measurements of EBM. This study aims to (1) assess the quality and data of these trials, and (2) compare the efficacy and safety of CH with WM in short-term and long-term heroin detoxification, and in the treatment of adverse symptoms caused by psychotropic drugs clinically. The results of this study may provide the current best evidence that should be helpful for clinicians and researchers to design high quality clinical trials; to develop new agents from natural herbs; to establish a new professional database for public health services; and to accumulate unique knowledge and methodology for developing an evidence-based Chinese medicine in future.

### 1.4 Study procedure

Followed the Cochrane Collaboration and other internationally acceptable

strategies and standards, relevant ramdomized controlled trials (RCTs) were retrieved by electronic database searching and hand searching. The quality of eligible trials was evaluated by the Jadad's scale. The measurement and category data on efficacy and safety of CH therapy will be quantitatively assessed and compared with other therapies in meta-analyses by using the Revman 5.0 program (Cochrane software).

### 1.4.1 Data search

In this study, electronic databases including the Cochrane Central Register of Controlled Trials, MEDLINE, CINAHL, AMED, VIP Chinese Science and Technology Periodical Database, Wanfang Chinese Scientific Journal Database, CBMdisc, China National Knowledge Infrastructure, Traditional Chinese Medicine Database, Chinese Medical Current Contents, China Proceedings of Conference Databases, and China Doctorate/Master Dissertations Full Text Databases, etc. were searched. Meanwhile, other databases including WorldCat, MetaPress, SpringerLink, Oxford Journals Online, Blackwell Synergy, ScienceDirect, ProQuest, the National Institute for Drug Addiction Website, the National Clearinghouse for Alcohol and Drug Information, the European Monitoring Center for Drugs and Drug Addiction, the Journal of the American Academy of Child and Adolescent Psychiatry were also searched. The reference lists of retrieved papers were checked for finding any potential clinical trials matching the inclusion criteria. In addition, hand searching was carried out to explore newest papers or other publications in the libraries of Hong Kong Baptist University and Guangzhou University of Chinese Medicine until the latest copy available to November 2008.

### 1.4.2 Data extraction

The key information of each included trial was input into a data extraction form. The titles, methods, interventions, trial periods, outcomes of the trials were summarized and listed in the form (Section 3.2). Key information was extracted by one reviewer and confirmed by the other reviewer. Any disagreement was solved by discussions. Whenever possible we contacted the author of each trial included in the study to verify abstracted data and to obtain further information.

### 1.4.3 Quality assessment

The quality of each included trial was assessed based on the guidelines of Jadad's scale. The randomization, double-blinding and dropout rate of the trials were assessed by ranking them with 1-5 points. The trials scored with 1 or 2 points were considered as low-quality trials, while those scored with 3-5 points were considered as high-quality trials. The process of quality assessment was conducted carefully by two independent reviewers. Any disagreement was solved by discussion.

### 1.4.4 Data analysis

The meta-analysis was carried out by using the Review Manager 5.0 to combine and analyze data from the trials. Weighted mean difference (WMD) or standard mean difference (SMD) and 95% confidence interval (95% CI) were used to pool data for continuous variables. The category data were present as odd ratio (OR) and 95% CI. Overall results of synthetic trials were calculated with a fixed-effect model when heterogeneity was not present. We used the DerSimonian and Laird method to test for heterogeneity among pooled estimates; results were considered significant at the $P<0.05$ level. When heterogeneity was present, a random effect model was used for statistical analysis, and the possible source of heterogeneity was futher analyzed.

# CHAPTER 2

# Review and Analysis

## 2.1 Short-term detoxification of heroin dependence

### 2.1.1 Introduction

Epidemiological survey has shown that the around 16-million people in the world, or 0.4% of the world's population aged 15-64, are opiate abusers. Globally about 71% of the opiate abusers, an estimated 11-million people, are heroin abusers. In China, heroin was the most common drug of abuse. According to the government reports, the registered drug abusers in 2004 were more than 1.14-million (More than 75% were heroin addicts). The problem of heroin dependence is also a priority of health and social care in Hong Kong. In 2004, 14,714 drug-dependent people were reported to the Central Registry of Drug Abuse; amongst them, about 70% were known to be heroin abusers.

The impact of heroin dependence imposes great threat on individual's health, family and society. The central nervous system of heroin addicts is mostly affected; neurobiological alteratations mediate damages in different body organ systems such as digestive system, immunological system, etc. Collapsed veins, bacterial infections, abscesses, infection of heart lining and valves, arthritis and other hematological problems are not uncommon among heroin addicts. These changes impose great harm to the health of heroin addicts. In addiction, risk of overdose happens as heroin tolerance often develops, so larger amount of heroin is often injected or taken by the addicts to result in death. The use of non-sterile needles and syringes promotes the transmission of AIDS and hepatitis among abusers.

Acute heroin abstinence (withdrawal) syndrome includes distinctive symptoms which appear after opioid withdrawal. The acute withdrawal syndrome generally appears 8-12 hours after drug withdrawal, peaks at 36-72 hours, and most of the symptoms disappear after 7 to 12 days. The abstinence symptoms and signs of heroin withdrawal possibly include: (1) cardiovascular system (tachycardia, hypertension), (2) central nervous system (anxiety, papillary dilatation, restlessness, irritability, insomnia, craving), (3) gastrointestinal system (nausea, vomiting, diarrhea), (4) musculoskeletal system (severe muscle and bone pain), (5) skin and mucous membrane (runny nose, lacrimation), etc.

The use of CH therapy to treat opium dependence can be traced back to the 16th

centuries when opium was imported to China. Many clinical experiences on CH for heroin detoxification were accumulated and recorded in ancient medical books, such as *Jie Yian Quan Fa* and *Jie Yian Zhi Nan*. In fact, from 1840 to 1952, case reports of successful treatments with traditional Chinese medicine were preserved. By the end of 1980s, due to the increasing amount of heroin addicts, more and more clinical trials as well as clinical pharmacological researches were conducted. Based on the theories and experiences, CH possessed specific characteristics, and could be effective and safe to treat heroin addicts at any detoxification stages. In the study, we at the first time present the data of meta-analyssi on CH therapy in short-term detoxification of heroin dependence.

### 2.1.2 Method

#### 2.1.2.1 Criteria for considering study

All RCTs that compared the efficacy or safety of CH with WM were included, and all in-patients and outpatients who were heroin addicts were considered. The studies for comparing the effect of CH plus WM versus WM were excluded since they might introduce heterogeneity in the further data synthesis and analysis. In addition, the case reports were excluded. There was no distinction between addicts dependent on heroin alone or on heroin and other drugs. No restriction on age or gender. Interventions included any oral administration of Chinese herbs prepared as capsule, tablet, powder or decoction at any dosage as the principal treatment to manage the signs and symptoms of heroin withdrawal syndrome. The control group was treated with WM. In this study, clonidine, methadone, nofexidine, buprenorphine, diazepam, etc. were the WM of different control groups. The outcome measurement was based on (1) a 10-day withdrawal symptom scores, (2) anxiety scores at day 5 and day 10, (3) adverse effect scores, (4) the number of patients whose heroin withdrawal syndrome was improved (NIP), (5) the incidence of adverse effects occurred during treatments respectively.

#### 2.1.2.2 Search strategy for identification of study

A search strategy was designed to retrieve all the literatures of relevant clinical trials by electronic searching, hand searching and additional searching regardless of

language and publication status (published, unpublished, in press, and in progress). The general structure of the search strategy was “heroin” and “herb”, and their synonyms were applied as keywords. The following keywords as free-text search terms that involved combined terms such as heroin dependence, heroin addiction, heroin abuse, heroin detoxification, withdrawal syndrome, herbal medicine, herbal therapy, Chinese herbs, plant medicine, plant drug, phytomedicine, phytotherapy, etc. were used.

### 2.1.3 Result

#### 2.1.3.1 Included and excluded trial

In literature searching we found 104 trials, and 68 trials were excluded as the following reasons: (1) 11 trials did not treat acute abstinence syndrome; (2) 27 trials did not compare CH with WM (inappropriate comparisons); (3) 21 trials reported insufficient outcomes; and (4) 9 trials were duplicated data. Finally, a total of 36 RCTs involved 5212 participants met the inclusion criteria.

In the 36 included RCTs, the group size in these included RCTs ranged from 20 to 580 participants. 3277 participants were treated with CH, while 1935 participants were treated with WM including clonidine (672 cases), nofexidine (406 cases), methadone (501 cases), buprenorphine (238 cases), diazepam (38 cases) and tramadol (80 cases).

#### 2.1.3.2 Outcome measurement

For outcome assessments of the efficacy, abstinence symptom scores were measured in 34 RCTs [*1-13,*15-35]. Among them, 22 RCTs used CINA score, 12 RCTs used other scores such as OWS, Himmelsbach score, or self-prepared score. Meanwhile, anxiety symptom was assessed by Hama score in 18 RCTs [*1,*2,*4,*6,*7,*9-11,*15,*17-21,*23,*26-28]. In addition, 12 included trials provided the number of improved patients (NIP) whose withdrawal syndrome was reduced after treatments [*4,*6,*7,*9,*14,*23,*25-27,*32,*33,*36].

For outcome assessments of the safety, treatment emergent symptom scale (TESS) was observed for measuring adverse effects in comparisons between CH and clonidine [*2,*3,*10,*13]. In addition, adverse-effect scores were observed by 26 trials, 7 trials

[*2,*3,*10,*13,*22,*23,*30] reported the data of everyday changes of scores, while 5 trials [*4,*5,*6,*9,*21] reported the curve-graphs of everyday changes of scores. 8 trials [*8,*12,*15-17,*19,*26,*36] reported the incidence of adverse effects occurred during treatments. However, other 6 trials [*1,*7,*14,*25,*28,*29] described the adverse effects without exact case number or score value, and 10 trials [*11,*18,*20,*24,*27,*31-35] did not report any adverse effect.

#### 2.1.3.3 Quality assessment

The assessment by Jadad's scale showed that 13 RCTs were classified as high-quality trials (HQT, 3-5 points) [*2,*3,*5-10,*12,*13,*18,*20,*27], and other 23 RCTs were low-quality trials (LQT, 1-2 points), due to poor description of randomization, blindness and withdrawal rate in the trials. In all 36 trials, inclusion criteria were described clearly, and random allocation was performed; but the concrete methods for randomization were only explained in 7 trials [*2,*3,*5-7,*9,*27]; double- or single-blindness was mentioned in 14 trials [*2,*3,*5,*6,*8-10,*12,*13,*18-20,*27,*33]; the concrete methods for blindness were described in 9 trials [*2,*3,*5,*6,*10,*12,*18,*20,*33]; and the withdrawal rate was reported and discussed in 14 trials. In addition, statistical methods used for data analyses were described in 23 trials [*1-3,*5,*8,*12,*13,*15-19,*21-24,*26-33] (Appendix, Chapter 3).

#### 2.1.3.4 Meta-analysis on efficacy

**(1) CH vs. clonidine**

**(A) Abstinence symptom score**

By using the random effect model, Fig.1 (1.1.1 to 1.1.10, Section 3.1.1) showed an analysis on the combined effects of 16 RCTs (9 HQT), involving 1404 cases out of 2056 patients treated with CH. CH was statistical significantly more effective than clonidine to diminish acute abstinence symptoms from the Day 1 to 10 (SMD: D1: -0.23 (-0.41, -0.05), D2: -0.33 (-0.50, -0.15), D3: -0.48 (-0.72, -0.24), D4: -0.61(-0.85, -0.37), D5: -0.69 (-0.93, -0.45), D6: -0.50 (-0.70,-0.29), D7: -0.48 (-0.67, -0.28), D8: -0.50 (-0.72, -0.28), D9: -0.39 (-0.59, -0.20), D10: -0.39 (-0.60, -0.18), P=0.01 to P<0.0001). There was a statistically significant heterogeneity presented in the analyses for the Day 1 to 10 (P<0.0001 to P<0.00001).

**(B) Anxiety score**

By using the random effect model, Fig. 2 (1.2.1 and 1.2.2, Section 3.1.1) showed an analysis on the combined effects of 9 RCTs (4 HQT), involving 913 cases treated with CH out of 1442 patients. CH was more effective to alleviate anxiety both on the Day 5 (SMD: -0.33 (-0.51, -0.16), P=0.0002) and Day 10 (SMD: -0.30 (-0.45, -0.15), P<0.0001). There was a statistically significant heterogeneity presented in the data analysis on the Day 5 (P=0.03).

**(C) NIP of acute abstinent symptoms**

By using the fixed effect model, a meta-analysis was conducted on the combined effects of 5 trials (3 HQT) that 895 patients were involved (Fig.10 (1.10.1), Section 3.1.1). The result indicated that 434 cases out of 556 patients (78.06%) treated with CH had significant improvement in heroin withdrawal syndrome, while 173 cases out of 249 patients (69.48%) treated with clonidine had significant improvement. The efficacy of CH was significantly higher than that of clonidine (5 RCTs; OR, 1.60; 95% CI, 1.13-2.25; P=0.007). There was no statistically significant heterogeneity presented in the data analysis.

**(2) CH vs. methadone**

**(A) Abstinence symptom score**

By using the random effect model, Fig. 3 (1.3.1 to 1.3.10, Section 3.1.1) showed an analysis on the combined effects of 5 RCTs (1 HQT), involving 272 cases treated with CH out of 495 patients, CH showed a similar effect on methadone in diminishing abstinence symptoms from the Day 1 to 10 (SMD: D1: 1.04 (-0.02, 2.11), D2: 1.45 (-0.14, 3.03), D3: 1.57 (-0.17, 3.31), D4: 1.44 (-0.26, 3.15), D5: 0.86 (-0.33, 2.05), D6: 0.51 (-1.08, 2.11), D7: -0.44 (-2.52, 1.64), D8:-0.39 (-1.92, 1.14), D9: -1.07 (-3.21, 1.07), D10, -0.46 (-1.92, 0.99) , P≥0.05). There was a statistically significant heterogeneity presented in the analyses for the Day 1 to 10 (P<0.00001).

**(B) Anxiety score**

By using the random effect model, Fig.4 (Section 3.1.1) showed an analysis on the combined effects of 4 RCTs (1 HQT), involving 424 cases treated with CH out of 825 patients, CH showed a similar effect as methadone in diminishing anxiety symptoms on the Day 5 (SMD: -0.40 (-0.87, 0.07), P=0.09) and Day 10 (SMD: -0.12

(-0.59, 0.36), P=0.63). There was a statistically significant heterogeneity presented in the analyses on the Day 5 and 10 (P=0.0002 to P<0.0001).

**(C) NIP of acute abstinent symptoms**

By using the fixed effect model, a meta-analysis was conducted on the combined effects of 4 trials (1 HQT) that 825 patients were involved. The result indicated that 391 cases out of 424 patients (92.22%) treated with CH were improvement, while 367 cases out of 401 patients (91.52%) were improved when treated with methadone (Fig.10 (1.10.2), Section 3.1.1). There was no statistically significant difference between two groups. There was no statistically significant heterogeneity presented in the analysis.

**(3) CH vs. nofexidine**

**(A) Abstinence symptom score**

By using the random effect model, Fig.5 (1.5.1 to 1.5.10, Section 3.1.1) showed an analysis on the combined effects of 8 RCTs (3 HQT), involving 896 cases out of 1302 patients treated with CH, and CH was significantly more effective than nofexidine to diminish abstinence symptoms from the Day 1 to 6 (SMD: D1: -0.33 (-0.57, -0.09), D2: -0.48 (-0.86, -0.09), D3: -0.68 (-1.18, -0.18), D4: -0.92(-1.66, -0.18), D5: -1.46 (-2.54, -0.38), D6: -1.10 (-2.07, -0.13), P<0.05). CH showed a similar effect to diminish abstinence symptoms from the Day 7 to 10 (D7: -0.63 (-1.29, 0.04), D8: -0.69 (-1.54, 0.15), D9: -0.61 (-1.42, 0.19), D10: -0.54 (-1.16, 0.09), P>0.05). There was a statistically significant heterogeneity presented in the analyses for the Day 1 to 10 (P=0.01 to P<0.00001).

**(B) Anxiety score**

By using the random effect model, Fig.6 (Section 3.1.1) showed an analysis on the combined effects of 7 RCTs (3 HQT), involving 831 cases out of 1197 patients treated with CH, CH was more effective than nofexidine to diminish anxiety symptoms on the Day 10 (SMD: -1.05 (-2.06, -0.03), P=0.04), while CH had a similar effect in diminishing anxiety symptoms on the Day 5 (SMD:-0.63 (-1.36, 0.10), P=0.09). There was a statistically significant heterogeneity presented in the analyses on the Day 5 and 10 (P<0.00001).

**(4) CH vs. buprenorphine**

**(A) Abstinence symptom score**

By using the random effect model, Fig.7 (1.7.1 to 1.7.10, Section 3.1.1) showed an analysis on the combined effects of 5 RCTs (0 HQT), involving 250 cases treated with CH out of 488 patients, CH showed a similar effect as buprenorphine in diminishing abstinence symptoms on the Day 1 to 7 and 9 and 10 (9 days) (SMD: Day 1: 0.42 (-0.18, 1.02), D2: 0.63 (-0.51, 1.77), D3: 0.55 (-0.32, 1.43), D4: 0.34 (-1.13, 1.82), D5: -0.05 (-0.78, 0.68), D6: 0.31 (-2.11, 2.73), D7: 0.31 (-0.52, 1.14), D9: -0.57 (-2.17, 1.04), D10: -0.65 (-2.67,1.37), $P>0.05$). The data on Day 8 was only included from one trial of Yian Decoction [*29]; and this herbal decoction showed a lower efficacy than that of buprenorphine (SMD: 1.33 (0.76, 1.89), $P<0.00001$). There was a statistically significant heterogeneity presented in the analyses for the Day 1 to 10 ($P<0.0001$ to $P<0.00001$).

**(B) Anxiety score**

There was no report on the anxiety score to compare CH with buprenorphine in the included trials.

**(C) NIP of acute abstinent symptoms**

By using the fixed effect model, a meta-analysis was also conducted on the combined effect of 2 trials (0 HQT), in which 322 patients were involved. The result indicated that 158 cases out of 165 patients (95.76%) treated with CH were improved in heroin withdrawal syndrome, while 138 cases out of 157 patients (87.90%) were improved when treated with buprenorphine (Fig.10 (1.10.3), Section 3.1.1). The efficacy of CH was significantly higher than that of buprenorphine (2 RCTs; OR, 3.08; 95% CI, 1.26-7.53; P=0.01). There was no statistically significant heterogeneity presented in the analysis.

**(5) CH vs. diazepam (abstinence symptom score)**

By using the random effect model, Fig.8 (1.8.1 to 1.8.10, Section 3.1.1) showed an analysis on the combined effects of 2 RCTs (0 HQT), involving 33 cases treated with CH out of 71 patients. CH was more effective to diminish abstinence symptoms from the Day 4 to 7 and 10 (SMD: D4: -0.58 (-1.06, -0.10), D5: -0.82 (-1.31, -0.34), D6: -0.81 (-1.30, -0.32), D7: -0.77 (-1.26, -0.28), D10: -1.97 (-3.08, -0.86), $P<0.05$),

while CH showed a similar effect as diazepam in diminishing abstinence symptoms from the Day 1 to 3 and 8 and 9 (D1: 0.04 (-0.71, 0.79), D2: -0.02 (-0.96, 0.92), D3: -0.05 (-0.80, 0.71), D8: -0.84 (-1.98, -0.30), D9: -1.19 (-2.38, -0.00), P>0.05). There was no statistically significant heterogeneity presented in the analyses.

**(6) CH vs. tramadol (abstinence symptom score)**

One trial (0 HQT) [*36] compared the efficacy of CH with tramadol in the treatment of heroin dependence. The result indicated that 58 cases out of 80 patients (72.50%) treated with CH were improved in abstinence symptoms, while 48 cases out of 80 patients (60.00%) were improved when treated with tramadol. The efficacy of CH was similar to tramadol (P=0.095).

### 2.1.3.5 Meta-analysis on safety

The common reported side effects from included trials involved multiple systems, mainly related with gastrointestinal, cardiovascular and neurological systems such as diarrhea, constipation, anorexia, vomiting, tachycardia, orthostatic hypotension, faint, conscious disturbance, blurred vision, lethargy, headache, dry mouth, sweating etc. The most side effects were minor in the patients treated by CH.

**(1) TESS (CH vs. WM)**

By using the random effect model, Fig. 9 (1.9.1 to 1.9.10, Section 3.1.1) showed analyses on the combined effects of 7 RCTs (3 HQT), involving 570 treated with CH out of 885 patients. CH had a lower score of adverse effects than WM including methadone from the Day 1 to 4 (SMD**:** D1: -0.43 (-0.69, -0.18), D2: -0.62 (-1.06, -0.19), D3: -0.64(-1.08, -0.21), D4: -0.52(-0.94, -0.10) , P< 0.05), but had a similar score from the Day 5 to 10 (D5: -0.30 (-0.66, 0.06), D6: -0.23 (-0.56, -0.10), D7: -0.17 (-0.45, 0.11), D8: -0.11 (-0.35, 0.14), D9: -0.12 (-0.27, 0.03), D10: -0.13 (-0.29, 0.04), P >0.05). The TESS mainly based on the assessment of headache, lethargy, nausea, vomiting, dry mouth, cardiac dysfunction, blood-pressure disorder, etc. There was a statistically significant heterogeneity presented in the analyses for the Day 1 to 7 (P=0.04 to P<0.00001); but there was no statistically significant heterogeneity presented in the analyses for the Day 8 to 10.

**(2) NIP of adverse symptoms (CH vs. WM)**

Three trials provided the incidence of blurred vision and dizziness in patients treated by CH or clonidine and methadone [*6,*7,*26], and results of meta-analyses indicated that blurred vision (2 RCTs; OR, 0.18; 95%CI, 0.09-0.36; P<0.00001) and dizziness (3 RCTs; OR, 0.10; 95% CI, 0.05-0.19; P<0.00001) were significantly less in patients treated by CH than those by WM. There was no statistically significant heterogeneity presented in the analyses (Fig. 11, Section 3.1.1).

In addition, 2 included trials [*6,*8] reported that clonidine caused serious hypotension in 5 cases and the patients had to discontinue the clonidine treatment. Serious adverse effects were reported in nofexidine groups of 6 included trials [*15-20]. Sinus bradycardia occurred in 22 cases and syncope occurred in 2 cases that had to discontinue the nofexidine treatment. One trial [*30] reported that CH had less adverse effect from the Day 1 to 3 (P<0.05) than buprenorphine.

### 2.1.3.6 Meta-analysis on high-quality trials

Based on the assessment of Jadad' scale, only high-quality RCTs in above analyses were selected for further sub-group analyses, and the results from these available high-quality RCTs were basically similar to those results from all included RCTs (Fig. 10-12 in the Section 3.1.2).

## 2.1.4 Summary

The results of meta-analyses indicated that CH might be an effective and safe way to treat acute heroin abstinence syndromes. It possessed a higher efficacy than clonidine or nofexidine in alleviating abstinence symptoms over the whole period of detoxification program, whereas it had similar efficacy as methadone or buprenorphine to relieve acute abstinence symptoms at some timepoints and tended to show a higher efficacy during the later stages. Meanwhile, CH was more effective to relieve anxiety than clonidine or methadone but has similar efficacy as nofexidine at certain timepoints. In addition, CH showed a lower adverse effect than WM and might be safer for heroin detoxification. However, CH therapy was not a "no pain" therapy in heroin detoxification. Some herbal preparations like *Fu-Kang* tablet containing

toxic herbs such as *Flos Daturae* or *Radix Aconiti Lateralis Preparata* could cause occurrence of some typical adverse effects in patients who eventually had to cease the treatment. As a significant heterogeneity presented in meta-analyses on continuous data, and a quite high percentage of low-quality trials was included in this review, further trials with high quality of study design should be performed to verify the current evidence in this study.

## 2.2 Long-term detoxification of heroin dependence

### 2.2.1 Introduction

Major heroin withdrawal symptoms peak between 48–72 hours after the last does and subside after about a week. Acute withdrawal syndrome will be followed by a "protracted abstinence syndrome" which can continue for up to 32 weeks afterwards. Protracted abstinence syndrome also is named as protracted withdrawal syndrome, chronic withdrawal syndrome, protracted withdrawal state, extended withdrawal state, etc. The symptoms that continue over this time are restlessness, disturbed sleep patterns, abnormal blood pressure and pulse rate, dilated pupils, cold feeling, irritability, change of personality and feeling, as well as an intense craving for heroin.

Protracted abstinence syndrome is a major cause of drug relapse. Relapse is definite as the return to drug-seeking and drug-taking behavior after a prolonged period of abstinence. People with heroin protracted abstinence syndrome beset by nearly irresistible urges to continue or to resume drug-taking. Even after detoxification and long periods of abstinence, relapse frequently occurs despite sincere efforts to refrain. People or situations previously associated with drug use produce involuntary reactions and may provoke a relapse. High rates of relapse to drug-taking are widely reported following drug detoxification. A survey found that a half-year relapse rate caused by protracted withdrawal syndrome could be 95% in Mainland China.

Some WM such as deanxit, mirtazapine, trazodone, paroxetine, etc. may be helpful to decrease heroin protracted abstinence syndrome clinically. However, current medications only focus on certain symptoms and may not treat all symptoms. Developing more effective medications to treat heroin protracted abstinence syndrome and reduce relapse rate remains one of the most important research targets. In recent

years, some clinical trials were performed to compare the effect of CH with WM or placebo in the treatment of heroin protracted abstinence syndrome. In this study current available CH trials were retrieved, and the quality and data of trials were systematically evaluated.

### 2.2.2 Method

#### 2.2.2.1 Criteria for considering study

All RCTs that compared the effects and/or adverse events of CH with WM or placebo were included. All inpatients and outpatients show protracted abstinence syndromes after heroin detoxification was considered. There was no limit in enrolling patients who abused heroin alone or heroin and other drugs. No restriction on age or gender. Interventions included any oral administration of CH prepared as capsule, tablet, powder or decoction at any dosage as the principal treatment to manage the signs and symptoms of protracted abstinence syndromes. The control group was treated with WM or placebo. The outcome measurement was based on total or single protracted abstinence syndrome score, anxiety score, NIP, relapse rate, adverse effect score, etc.

#### 2.2.2.2 Search strategy for identification of study

A search strategy was designed to retrieve all the literatures of relevant clinical trials by electronic searching, hand searching and additional searching regardless of language and publication status (published, unpublished, in press, and in progress). The general structure of the search strategy was “heroin”, “protracted abstinence syndrome” and “herb”, and their synonyms were applied as keywords. The following keywords as free-text search terms that involved combined terms such as heroin dependence, heroin addiction, heroin abuse, heroin detoxification, protracted withdrawal symptoms, herbal medicine, herbal therapy, Chinese herbs, plant medicine, plant drug, phytomedicine, phytotherapy, etc. were used.

### 2.2.3 Result

#### 2.2.3.1 Included and excluded trial

In literature searching we found 21 trials, and 7 trials were excluded as the

following reasons: (1) 3 trials did not treat protracted withdrawal syndrome; (2) one trial did not compare CH with WM (inappropriate comparisons); (3) 3 trials were duplicated data. Finally, a total of 14 RCTs involved 1894 participants met the inclusion criteria.

In the 14 included trials, the group size in these included RCTs ranged from 14 to 208 participants. 1117 participants were treated with CH preparations; while 342 participants were treated with WM including naltrexone, clonidine, diazepam, oryzanol, ibuprofen, atropine, etc., and 435 participants were treated with placebo or allocated in a blank-control group.

#### 2.2.3.2 Outcome measurement

In trials of CH vs. WM groups, NIP was reported by 3 RCTs (3 RCTs on insomnia, 2 on all abstinent symptom, anxiety, pain and debility), relapse rate was described by 3 RCTs, score of all abstinent symptoms and six single abstinent-symptom scores (insomnia, pain, inappetence, palptation, dysphoria and debility) were reported by 4 RCTs. In trials of CH vs. placebo groups, relapse rate was described in 1 RCT, score of all abstinent symptoms and five single abstinent symptoms (insomnia, pain, inappetence, palptation and debility) were reported by 4 RCTs. The treatment emergent symptom scale (TESS) was observed by 1 RCT, and there were 6 RCTs that reported the incidence of adverse effects occurred during treatments.

#### 2.2.3.3 Quality assessment

The assessment by Jadad scale showed that 3 out of 14 included trials were classified as high-quality trials (3 points) [*38,*41,*46], and the other 11 trials were low-quality trials (1-2 points), due to poor description of randomization, blindness and withdrawal rate. Within the 11 included RCTs, inclusion criteria were described clearly in the papers in 11 RCTs; random allocation was done in 11 RCTs but the concrete methods for randomization were only explained by 6 RCTs; double- or single-blinding was mentioned in 5 RCTs but the concrete methods for blindness were only described in 2 RCTs. In addition, the withdrawal rate was reported and discussed in 5 RCTs (Chapter 3, Appendix).

#### 2.2.3.4 Meta-analysis on efficacy and safety

**(1) CH vs. WM**

By using the fixed effect model, Figure1 showed an analysis on the NIP of 3 included RCTs (0 HQT), in which 98 out of 230 patients treated with CH were involved.

By using the fixed effect model, Figure 1 (2.1.1, Section 3.1.3) showed a meta-analysis on the NIP in the treatment of total abstinent symptom. 130 patients were involved from 2 included RCTs (0 HQT). The result indicated that 84 out of 86 patients (97.67%) were significantly improved after CH treatments, whereas 30 out of 44 patients (68.18%) showed a significant improved after WM treatments, and was lower than CH (OR=19.18; 95% CI: 4.14, 88.90; P=0.0002). No heterogeneity presented in all the data synthesis and analysis (P=0.50).

By using the fixed effect model, Figure 1 (2.1.2, Section 3.1.3) showed a meta-analysis on the NIP of insomnia, 165 patients were involved from 3 included RCTs (0 HQT). The result indicated that 94 out of 98 patients (95.91%) were significantly improved after CH treatments; whereas 35 out of 67 patients (52.24%) showed a significant improved after WM treatments. CH was higher than WM (OR=23.54; 95% CI: 7.67, 72.23; P<0.00001). No heterogeneity presented in all the data synthesis and analysis (P=0.69).

By using the fixed effect model, Figure 1 (2.1.3, Section 3.1.3) showed a meta-analysis on the NIP of anxiety, 106 patients were involved from 2 included RCTs (0 HQT). The result indicated that 62 out of 68 patients (91.18%) were significantly improved after CH treatments; whereas 13 out of 38 patients (34.21%) showed a significant improved after WM treatments. CH was higher than WM (OR=19.85; 95% CI: 6.79, 58.03; P<0.00001). No heterogeneity presented in all the data synthesis and analysis (P=0.83).

By using the fixed effect model, Figure 1 (2.1.4, Section 3.1.3) showed a meta-analysis on the NIP of pain, 84 patients were involved from 2 included RCTs (0 HQT). The result indicated that 53 out of 56 patients (94.64%) were significantly improved after CH treatments; whereas 7 out of 28 patients (25.00%) showed a significant improved after WM treatments. CH was higher than WM (OR=46.5; 95%

CI: 11.05, 195.7; P<0.00001). No heterogeneity presented in all the data synthesis and analysis (P=0.18).

By using the fixed effect model, Figure 1 (2.1.5, Section 3.1.3) showed a meta-analysis on the NIP of debility, 105 patients were involved from 2 included RCTs (0 HQT). The result indicated that 71 out of 74 patients (95.95%) were significantly improved after CH treatments; whereas 19 out of 31 patients (61.29%) showed a significant improved after WM treatments. CH was higher than WM (OR=14.95; 95% CI: 3.83, 58.42; P=0.0001). No heterogeneity presented in all the data synthesis and analysis (P=0.98).

By using the fixed effect model, Figure 2 (Section 3.1.3) showed a meta-analysis on the NIP of relapse rate, 269 patients were involved from 3 included RCTs (0 HQT). The result indicated that 89 out of 149 patients (59.73%) relapsed after CH treatments; whereas 102 out of 120 patients (85.00%) relapsed after WM treatments. CH was lower than WM (OR=0.17; 95% CI: 0.07, 0.38; P<0.0001). No heterogeneity presented in all the data synthesis and analysis (P=0.90).

By using the random effect model, Figure 3 (2.3.1, Section 3.1.3) showed a meta-analysis on the data of 3 included RCTs (0 HQT) that compared CH to WM on abstinent symptom scores. The result indicated that CH treatment was more effective to diminish abstinent symptom than that of WM treatments (SMD=-2.38, 95% CI: -4.07, -0.68; P=0.006). Heterogeneity presented in the data synthesis and analysis (P<0.00001).

By using the random effect model, Figure 3 (2.3.2, Section 3.1.3) showed a meta-analysis on the data of 2 included RCTs (0 HQT) that compared CH to WM on insomia. The result indicated that CH treatment showed similar effective to diminish insomia than that of WM treatments (SMD=-2.28, 95% CI: -7.16, 2.61; P=0.36). Heterogeneity presented in the data synthesis and analysis (P=<0.00001).

By using the random effect model, Figure 3 (2.3.3, Section 3.1.3) showed a meta-analysis on the data of 2 included RCTs (0 HQT) that compared CH to WM on pain. The result indicated that CH treatment was less effective to diminish pain than that of WM treatment (SMD=0.52, 95% CI: 0.02, 1.01; P=0.04).

By using the random effect model, Figure 3 (2.3.4, Section 3.1.3) showed a meta-analysis on the data of 2 included RCTs (0 HQT) that compared CH to WM on

inappetence. The result indicated that CH treatment was similar effective to diminish inappetence than that of WM treatment (SMD=-1.39, 95% CI: -5.34, 2.56; P=0.49). Heterogeneity presented in the data synthesis and analysis (P=<0.00001).

By using the random effect model, Figure 3 (2.3.5, Section 3.1.3) showed a meta-analysis on the data of 2 included RCTs (0 HQT) that compared CH to WM on palpitation. The result indicated that CH treatment was similar effective to diminish palpitation than that of WM treatment (SMD=-0.86, 95% CI: -3.63, 1.90; P=0.54). Heterogeneity presented in the data synthesis and analysis (P=<0.00001).

By using the random effect model, Figure 3 (2.3.6, Section 3.1.3) showed a meta-analysis on the data of 2 included RCTs (0 HQT) that compared CH to WM on dysphoria. The result indicated that CH treatment was similar effective to diminish dysphoria than that of WM treatment (SMD=-1.48, 95% CI: -5.43, 2.47; P=0.46). Heterogeneity presented in the data synthesis and analysis (P=<0.00001).

By using the random effect model, Figure 3 (2.3.7, Section 3.1.3) showed a meta-analysis on the data of 2 included RCTs (1 HQT) that compared CH to WM on anxiety. The result indicated that CH treatment was more effective to diminish anxiety than that of WM treatment (SMD=-3.42, 95% CI: -6.38, -0.46; P=0.02). Heterogeneity presented in the data synthesis and analysis (P=<0.00001).

**(2) CH vs. placebo**

For the NIP of relapse rate, Figure 4 (Section 3.1.3) showed 51 patients were involved from 1 included RCTs (1 HQT). The result indicated that 16 out of 28 patients (57.14%) relapsed after CH treatments; whereas 20 out of 23 patients (86.96%) relapsed after WM treatments. CH was lower than WM (OR=0.20; 95% CI: 0.05, 0.83; P=0.03).

By using the random effect model, Figure 5 (2.5.1, Section 3.1.3) showed a meta-analysis on the data of 5 included RCTs (2 HQT) that compared CH to placebo on abstinent symptom scores. The result indicated that CH treatment was more effective to diminish abstinent symptom than that of placebo treatments (SMD=-4.55, 95% CI: -7.12, -1.98; P=0.0005). Heterogeneity presented in the data synthesis and analysis (P<0.00001).

By using the random effect model, Figure 5 (2.5.2, Section 3.1.3) showed a

meta-analysis on the data of 3 included RCTs (1 HQT) that compared CH to placebo on insomina. The result indicated that CH treatment was more effective to diminish insomina than that of placebo treatments (SMD =-5.30, 95% CI: -8.60, -2.00; P=0.002). Heterogeneity presented in the data synthesis and analysis (P<0.00001).

By using the random effect model, Figure 5 (2.5.3, Section 3.1.3) showed a meta-analysis on the data of 3 included RCTs (1 HQT) that compared CH to placebo on muscle and joint pain. The result indicated that CH treatment was more effective to diminish pain than that of placebo treatments (SMD =-3.13, 95% CI: -4.29, -1.96; P<0.00001.) Heterogeneity presented in the data synthesis and analysis (P<0.0001).

In addition, Figure 5 (2.5.4, 2.5.5 and 2.5.6, Section 3.1.3) showed 1 included trial (0 HQT) that compared CH to placebo on inappetence, palpitation and dysphoria. The result indicated that CH treatment had similar effect to diminish inappetence than that of placebo treatments (SMD =0.19, 95% CI: -0.32, 0.70; P=0.47); but was more effective to diminish palpitation (SMD =-2.05, 95% CI: -2.68, -1.42; P<0.00001) and dysphoria (SMD=-2.65, 95% CI: -3.36, -1.95; P<0.00001) than placebo treatments.

#### 2.1.3.5 Meta-analysis on high-quality trials

Further meta-analysis on high-quality RCTs for protracted abstinent symptoms (CH vs. Placebo) was available. The result based on available high-quality RCTs was similar to that result from all included RCTs (Fig. 6 in the Section 3.1.3).

### 2.2.4 Summary

In long-term heroin detoxification (>10 days) CH was more effective to diminish protracted abstinent symptoms, anxiety and relapse rate when compared with WM (diazepam, oryzanol, tramadol, naltrexone, clonidine, etc.) or placebo. CH was more effective to improve NIP in all or single symptoms including insomnia, anxiety, pain, debility, palpitation and dysphoria. Also CH was safer than WM in long-term treatments, although available data could not be integrated in a meta-analysis. It suggests that CH may be a new way to treat protracted abstinent symptoms, and prevent relapse. However, owing to insufficient data and poor quality of the trials those baffle to document the results. Further trials with high quality of study design should be necessarily conducted in this field, and not only more category data but also

measurement data from clinical trials should be systematically assessed in a new meta-analysis.

## 2.3 Treating adverse symptoms of pscychtropic drugs

### 2.3.1 Introduction

Psychotropic drugs are drugs that affect the mental process e.g. cognition or affect and emotional state when administered into human body. There are certain categories in psychotropic drugs including neuroleptic drug, antidepressant, anxiolytic, hypnotic, mood stabilizer and psychostimulant that were used commonly in clinics. Psychotropic drugs have been abused for non-medical purpose and attrtact more and more attention. The term psychoactive drug and its equivalent, psychotropic substance, are the most neutral and descriptive term for the whole class of substances including licit and illicit. According to the Central Registry of Drug Abuse in Hong Kong, the number of reported psychotropic drug abusers increased significantly. In 2006, 7364 out of 13204 drug abusers reported were psychotropic drug abusers.

Other than psychoactive drug abuse, millions of people worldwide are affected by mental, behavioural, and neurological problems that need to be treated by psychotropic drugs. Estimates made by WHO showed that 154-million people globally suffer from depression and 25-million people from schizophrenia; 50-million people suffer from epilepsy and 24-million from Alzheimer and other dementias. Many other diseases affect the nervous system or produce neurological sequelae such as 326-million people suffer from migraine, 18-million from neuroinfections or neurological sequelae of infections. Number of people with neurological sequelae of nutritional disorders and neuropathies (352-million) and neurological sequelae secondary to injuries (170-million) also add substantially to the above amount. In addition, mental illnesses are affected by chronic conditions such as cancer, AIDS, cardiovascular diseases and diabetes. As patients with mental disorders increased, studies on cost and change of medical police in psychotropic drugs revealed the trend of increasing consumption of these drugs in recent years.

Psychotropic drugs may result in various adverse effects clinically. For example, their anti-dopamine effects may express as parkinsonism, dystonia, akathisia, tardive

dyskinesia, etc.; and anti-choline effects may express blurred version, dry mouth, constipation, urinary retention, etc.; whereas the manifestations of anti-adrenal effect may include orthostatic hypotension, reflex tachycardia, etc. Other adverse effects including depression, arrhythmia, sleepiness, fatigue, disturbance of consciousness, coma, leucopenia, etc. may occur in some patients. Up to now, a conventional way to deal with the adverse symptoms caused by psychotropic drugs is to stop the drug treatments even though it is necessary to control the illness in some patients. Some WM can be selected to relieve the adverse symptoms, but they may lead additional side effects secondarily. Searching for new approaches to help patients remains one of the hot research topics in this field.

CH has been traditionally applied to treat mental disorders for thousands of years since ancient time. Meanwhile, nature herbs and their preparations also have therapeutic effects to treat various adverse effects caused by psychotropic drugs. In the last decades more and more clinical studies including randomized controlled trials (RCTs), controlled clinical trials (CCTs), case studies, etc. have been conducted to examine CH in the treatment of adverse symptoms caused by pscychtropic drugs. It should be valuable to assess the data and quality of clinical trials with principles and measurements of EBM. The aims of this study were to assess the quality and data of eligible clinical trials, and compare the efficacy and safety of CH with WM in clinical treatments.

### 2.3.2 Method

#### 2.3.2.1 Criteria for considering study

All RCTs that compared the effects and/or adverse events of CH alone or CH plus WM vs. WM alone were included. Eligible participants were the patients with side effects caused by psychotropic drugs. There was no restriction on the gender, or age and race of patients. In the treatment group, interventions included any formulation types of CH and decoctions at any dosage, while patients in control groups were treated with WM alone. The outcome measurements were mainly based on the NIP, treatment emergent symptom scale (TESS) and adverse events incidence.

#### 2.3.2.2 Search strategy for identification of studies

A search strategy was designed to retrieve all the literatures of relevant clinical trials by electronic searching, hand searching and additional searching regardless of language and publication status (published, unpublished, in press, and in progress). The general structure of the search strategy was “adverse effect”, “psychotropic drug”, “antipsychotics”, “antidepressant”, “mood stabilizer”, “anxiolytic”, “hypnotic”, “psychostimulant”, “neuroleptic drug”, “clorazepate”, “valium”, “phenamine”, “clozapine”, “morphine”, “cocame”, “coca”, “cough remedy”, and their synonyms were applied as keywords. The following keywords as free-text search terms that involved combined terms such as mental disorders, drug dependence, drug addiction, drug abuse, drug detoxification, withdrawal symptoms, side effects, adverse events, adverse effect, herbal medicine, herbal therapy, Chinese herbs, plant medicine, plant drug, phytomedicine, phytotherapy, etc. were used.

### 2.3.3 Result

#### 2.3.3.1 Included and excluded trial

In literature searching, 68 trials published in China were retrieved, however 11 trials were excluded as they did not meet the inclusion criteria including (1) inappropriate comparisons in the study design such as CH compared to CH (3 trials), (2) insufficient outcomes (3 trials), and (3) duplicated data (5 trial). Finally, a total of 57 RCTs involving 4841 patients were included for further data analyses.

In 57 included RCTs, 4 trials were performed for treating constipation, 9 trials for sialorrhea, 3 trials for dry-mouth, 4 trials for abnormal ECG, 4 trials for amenorrhea, 3 trials for enuresis, 5 trials for leucopenia, 8 trials for coma, 2 trials for hepatic damage, 8 trials for total TESS, 2 trials for obesity, and other 5 trials for dysuria, neutropenia, intestinal obstruction, sexual dysfunction and withdrawal syndrome respectively. The group size in these included RCTs ranged from 20 to 124 participants. 2493 participants were treated with CH, while 1742 participants were treated with WM, and 606 participants did not treated with CH or WM.

#### 2.3.3.2 Outcome measurement

In the 57 included RCTs, NIP was reported by 40 trials, while TESS was reported by 2 trials. In these 42 trials, 1820 patients were treated with CH, and 1630 patients

were treated with WM. The data in other 15 trials could not be integrated in meta-analysis. Among them, the date of 4 trials reported TESS in different ways such as total score of TESS, NIP of TESS, etc., 3 trials reported different endpoints such as score of sialorrhea, ALT (alanine transarninase), AST (glutamic-oxal(o)acetic transaminase), FBG (fasting blood glucose), TC (total cholesterol), TG (Triglyceride), etc. and the data of 8 trials were removed because of significant heterogeneity.

#### 2.3.3.3 Quality assessment

The assessment by Jadad's scale showed that 10 included RCTs were classified as high-quality trials (3 or 5 points) [*57,*60,*61,*66,*70,*72,*81,*83,*92,*107], and the rest were low-quality trials (1-2 points) owing to poor descriptions on randomization, double-blind method and dropout rate. 2 high-quality trials [*57,*60] were not enrolled for meta-analysis as their outcome reports were different from other trials (Figure 2 in the Section 3.1.4, meta-analyses on TESS scores).

#### 2.3.3.4 Meta-analysis on efficacy and safety

**(1) NIP of adverse symptom**

By using the fixed-effect model, Figure 1 (3.1.1, Section 3.1.4) showed a meta-analysis on total NIP of adverse symptoms to compared CH groups with WM groups. 615 patients were involved from 8 included RCTs (0 HQT). The result indicated that 292 out of 322 patients treated with CH were significantly improved (90.68%), while 201 out of 293 patients treated with WM were significantly improved (68.60%) and lower than CH treatment (OR=5.67; 95% CI: 3.42, 9.41; P<0.00001). No heterogeneity presented in data synthesis and analysis (P=0.08).

By using the fixed-effect model, Figure 1 (3.1.2, Section 3.1.4) showed a meta-analysis on the NIP in the treatment of constipation, in which 418 patients were involved from 4 included RCTs (0 HQT). The result indicated that 131 out of 223 patients treated with CH were significantly improved (58.74%), while 84 out of 195 patients treated with WM were significantly improved (43.08%) and lower than CH treatment (OR=1.96; 95% CI: 1.31, 2.94; P=0.001). No heterogeneity presented in the data synthesis and analysis (P=0.18).

By using the fixed-effect model, Figure 1 (3.1.3, Section 3.1.4) showed a

meta-analysis on the NIP in the treatment of sialorrhea in which 670 patients were involved from 7 included RCTs (3 HQT) [*66,*70,*72]. The result indicated that 289 out of 342 patients (84.50%) were significantly improved after CH treatments, while 229 out of 328 patients treated with WM were significantly improved (69.82%) and lower than CH treatment (OR=2.59; 95% CI: 1.74, 3.85; P<0.00001). No heterogeneity presented in the data synthesis and analysis (P=0.06).

By using the fixed-effect model, Figure 1 (3.1.4, Section 3.1.4) showed a meta-analysis on the NIP in the treatment of dry mouth in which 173 patients were involved from 3 included RCTs (2 HQT) [*81,*83]. The result indicated that 84 out of 88 patients treated with CH were significantly improved (95.45%), while 18 out of 85 patients treated with WM were significantly improved (21.18%) and lower than CH treatment (OR=79.97; 95% CI: 24.94, 256.39; P<0.00001). No heterogeneity presented in data synthesis and analysis (P=0.55).

By using the fixed-effect model, Figure 1 (3.1.5, Section 3.1.4) showed a meta-analysis on the NIP in the treatment of abnormal ECG in which 464 patients were involved from 4 included RCTs (1 HQT) [*107]. The result indicated that 221 out of 243 patients treated with CH were significantly improved (90.95%), while 177 out of 221 patients treated with WM were significantly improved (80.09%) and lower than CH treatment (OR=2.46; 95% CI: 1.42, 4.27; P=0.001). No heterogeneity presented in data synthesis and analysis (P=0.07).

By using the fixed-effect model, Figure 1 (3.1.6, Section 3.1.4) showed a meta-analysis on the NIP in the treatment of amenorrhea in which 270 patients were involved from 4 included RCTs (1 HQT) [*92]. The result indicated that 108 out of 157 patients (68.79%) were significantly improved after CH treatments, while 58 out of 113 patients treated with WM were significantly improved (51.33%) and lower than CH treatment (OR=2.44; 95% CI: 1.44, 4.12; P=0.0009). No heterogeneity presented in the data synthesis and analysis (P=0.41).

By using a fixed-effect model, Figure 1 (3.1.7, Section 3.1.4) showed a meta-analysis on the NIP in the treatment of enuresis in which 228 patients were involved from 3 included RCTs (0 HQT). The result of indicated that 106 out of 114 patients treated with CH were significantly improved (92.98%), while 35 out of 114 patients treated with WM were significantly improved (30.70%) and lower than CH

treatment (OR=31.74; 95% CI: 13.48, 74.74; P<0.00001). No heterogeneity presented in data synthesis and analysis (P=0.33).

By using the fixed-effect model, Figure 1 (3.1.8, Section 3.1.4) showed a meta-analysis on the NIP in the treatment of leucopenia in which 286 patients were involved from 5 included RCTs (0 HQT). The result indicated that 131 out of 143 patients (91.61%) were significantly improved after CH treatments, while 97 out of 143 patients treated with WM were significantly improved (67.83%) and lower than CH treatment (OR=5.47; 95% CI: 2.72, 11.01; P<0.00001). No heterogeneity presented in the data synthesis and analysis (P=0.53).

By using the fixed-effect model, Figure 1 (3.1.9, Section 3.1.4) showed a meta-analysis on the NIP in the treatment of coma in which 228 patients were involved from 3 included RCTs (0 HQT). The result indicated that 127 out of 136 patients treated with CH were significantly improved (93.38%), while 76 out of 92 patients treated with WM were significantly improved (82.61%) and lower than CH treatment (OR=3.88; 95% CI: 1.57, 9.58; P=0.003). No heterogeneity presented in data synthesis and analysis (P=0.54).

**(2) TESS score**

By using the random-effect model, Figure 2 (3.2.1, 3.2.2 and 3.2.3, Section 3.1.4) showed meta-analyses on TESS scores of dry mouth, nausea and poor appetite in which 98 participants were involved from 2 included RCTs (1 HQT) [*60]. The results indicated that there was no difference of dry mouth between two groups (SMD= -0.24; 95% CI: -0.64, 0.16; P=0.23); whereas, TESS scores of nausea and poor appetite in the CH groups were significantly lower than WM groups (SMD=-1.41; 95% CI: -2.38, -0.44; P=0.005; or SMD=-0.49; 95% CI: -0.90, -0.08; P=0.02) respectively. No heterogeneity presented in the data synthesis and analysis for dry mouth and poor appetite (P=0.48), but heterogeneity presented in the data synthesis and analysis of nausea (P=0.03).

### 2.3.3.5 Meta-analysis on single herbal preparations

Further sub-group meta-analysis on herb Senna Tea vs. Glycerine Enema was done for more details of CH therapy in the treatment of neuroleptic-induced astriction

(Fig. 3 in the Section 3.1.4).

#### 2.3.3.6 Meta-analysis on high-quality trials

Further meta-analyses on high-quality RCTs for NIP of adverse symptoms (CH vs. WM) were available. The results based on available high-quality RCTs were similar to those results from all included RCTs (Fig. 4 in the Section 3.1.4).

### 2.3.4 Summary

In this systematic review and meta-analyses of 57 included RCTs, we at the first time evaluated CH in the treatment of adverse symptoms caused by psychotropic drugs. The current available randomized evidence indicated that CH was more effective and safer to treat psychotropic-drug induced dry mouth, sialorrhea, nausea, poor appetite, constipation, abnormal ECG, amenorrhea, enuresis, leucopenia, even coma in acute and severe cases. Based on the results of this meta-analysis the benefits of CH in decreasing adverse symptoms and improving patient's quality of life were ascertained when compared with WM or placebos. However, this study could not evaluate other adverse effects caused by psychotropic drugs due to insufficient quantity and quality of published trials. We suggest that standardized report data format should be designed, and multi-centered and high quality clinical trials should be conducted in the future research.

# CHAPTER 3

# **Appendix**

## 3.1 Forest plots

### 3.1.1 Short-term detoxification of heroin dependence (36 RCTs)

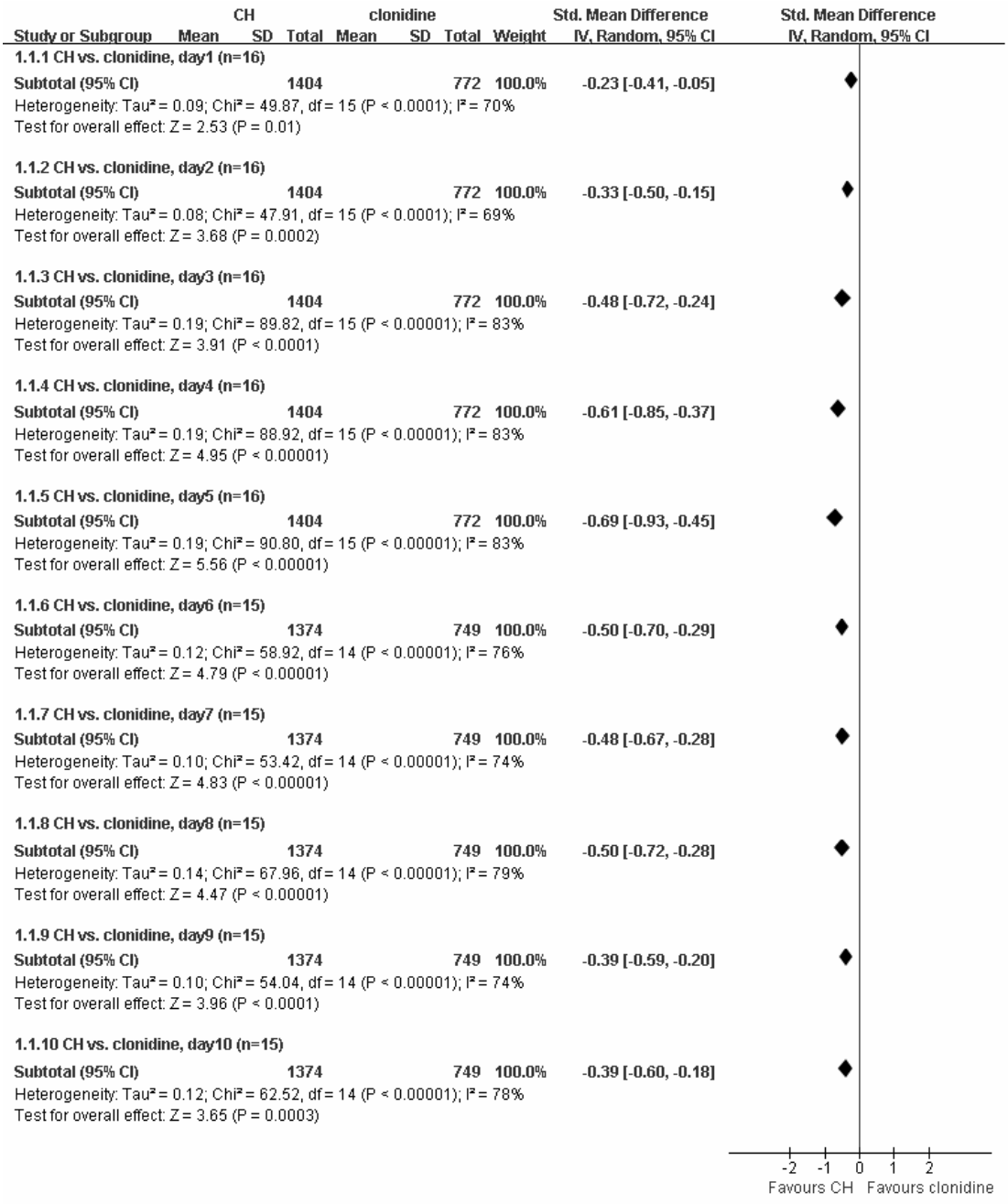



Fig 1. Meta-analyses of CINA scores for acute abstinent symptoms on the Day 1 to 10 (CH vs. clonidine)

Note: (1) Detail data and comparisons on the Day1 to 10 were attached (3.1.2).

(2) The CINA (Clinical Institute Narcotic Assessment) scale contains 10 opioid withdrawal signs (nausea, vomiting, gooseflesh, sweating, restlessness, tremor, larcrimation, nasal congestion, yawning, changes in heart rate and systolic blood pressure) and 3 opiate withdrawal symptoms (abdominal pain, muscle pain and feeling hot or cold).

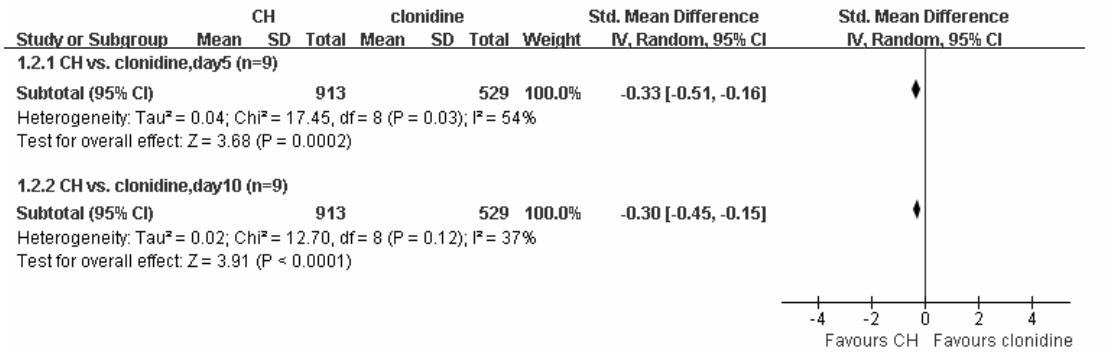



Fig 2. Meta-analyses of HAMA scores for acute anxiety symptoms on the Day 5 and 10 (CH vs. clonidine)
Note: Detail data and comparisons on the Day 5 and 10 were attached (3.1.2)

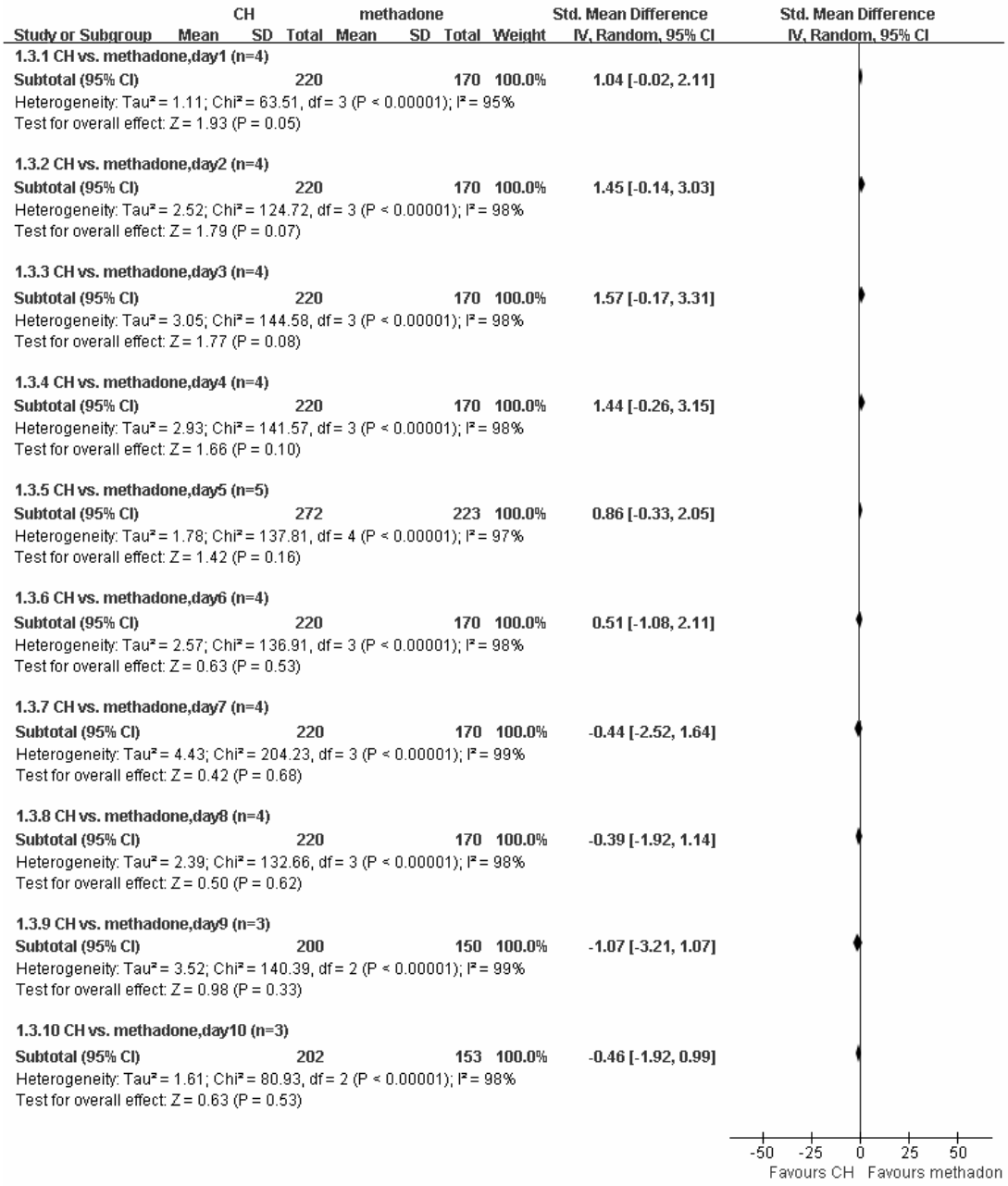



Fig 3. Meta-analyses of CINA scores for acute abstinent symptoms
on the Day 1 to 10 (CH vs. methadone)
Note: Detail data and comparisons on the Day 1 to 10 were attached (3.1.2)

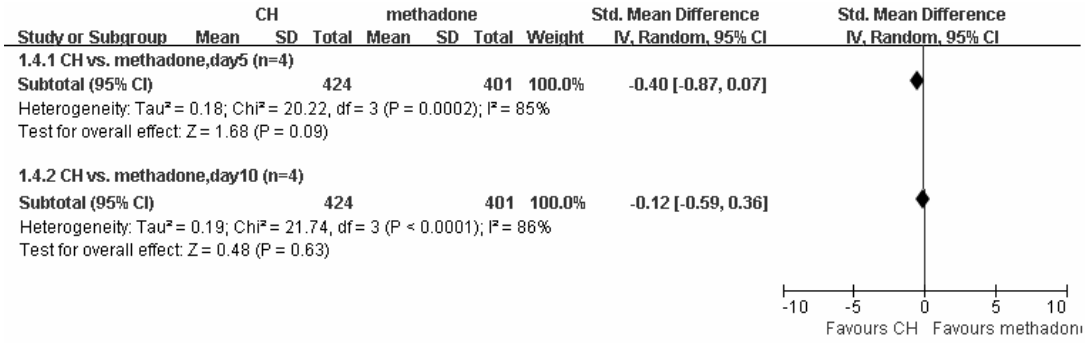



Fig 4. Meta-analyses of HAMA scores for acute anxiety symptoms on the Day 5 and 10 (CH vs. methadone)
Note: Detail data and comparisons on the Day 5 and 10 were attached (3.1.2)

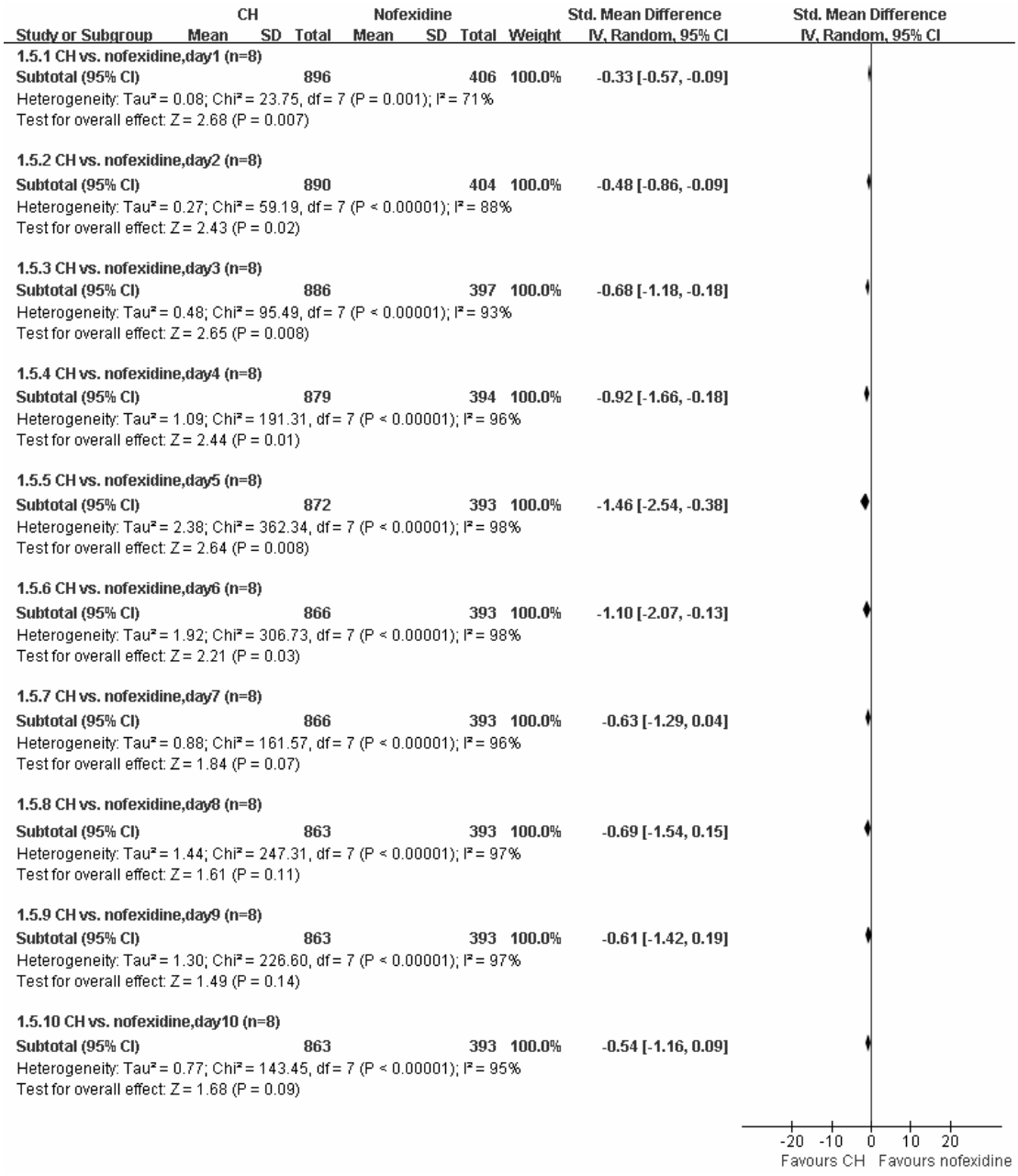



Fig 5. Meta-analyses of CINA scores for acute abstinent symptoms on the Day 1 to 10 (CH vs. nofexidine)

Note: Detail data and comparisons on the Day 1 to 10 were attached (3.1.2)

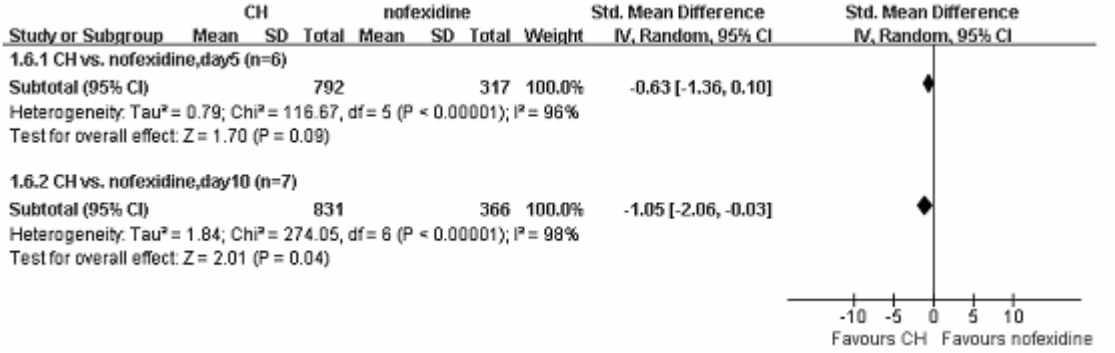



Fig 6. Meta-analyses of HAMA scores for acute anxiety symptoms
on the Day 5 and 10 (CH vs. nofexidine)
Note: Detail data and comparisons on the Day 5 and 10 were attached (3.1.2)

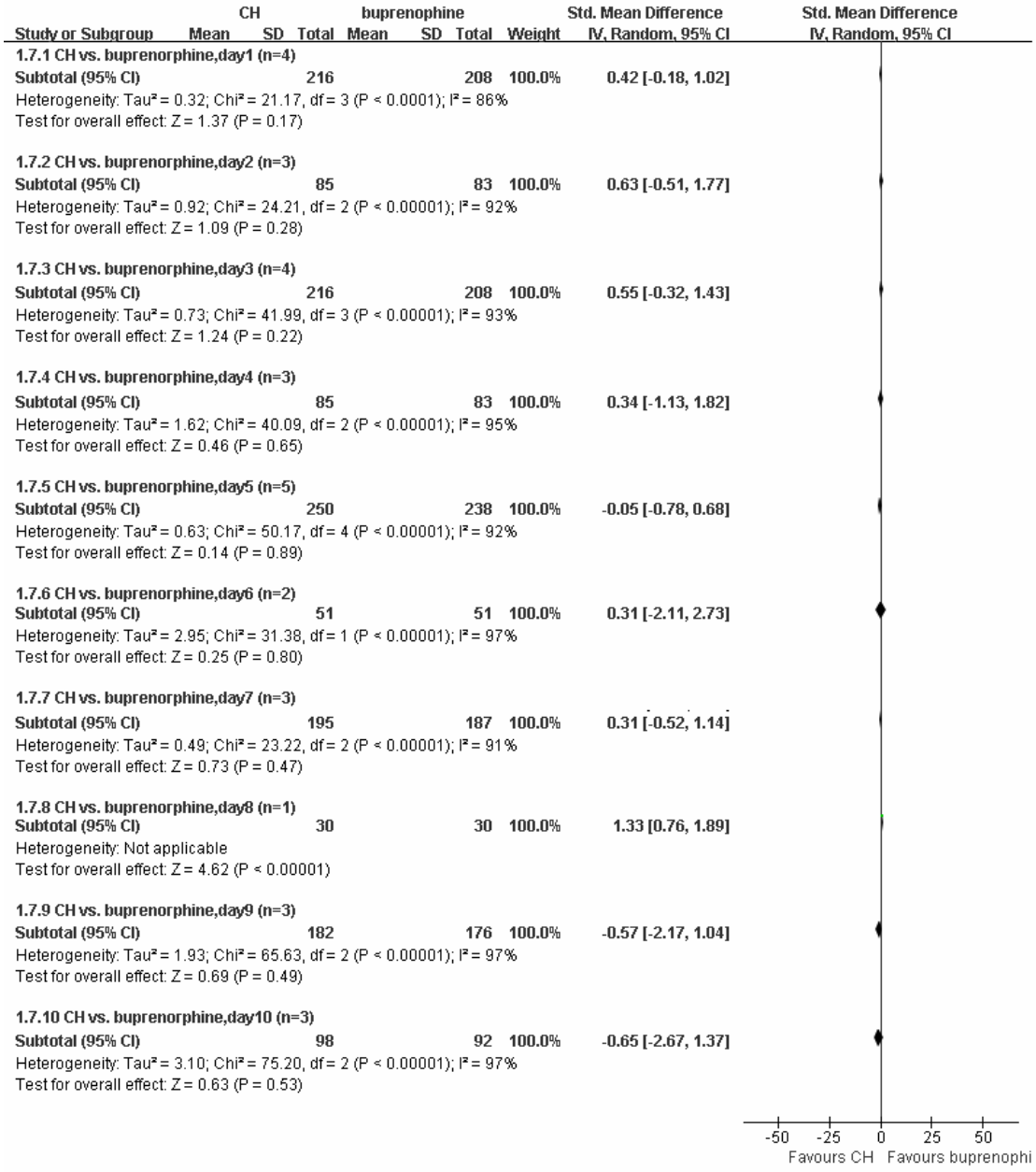



Fig 7. Meta-analyses of CINA scores for acute abstinent symptoms
on the Day 1 to 10 (CH vs. buprenorphine)
Note: Detail data and comparisons on the Day 1 to 10 were attached (3.1.2)

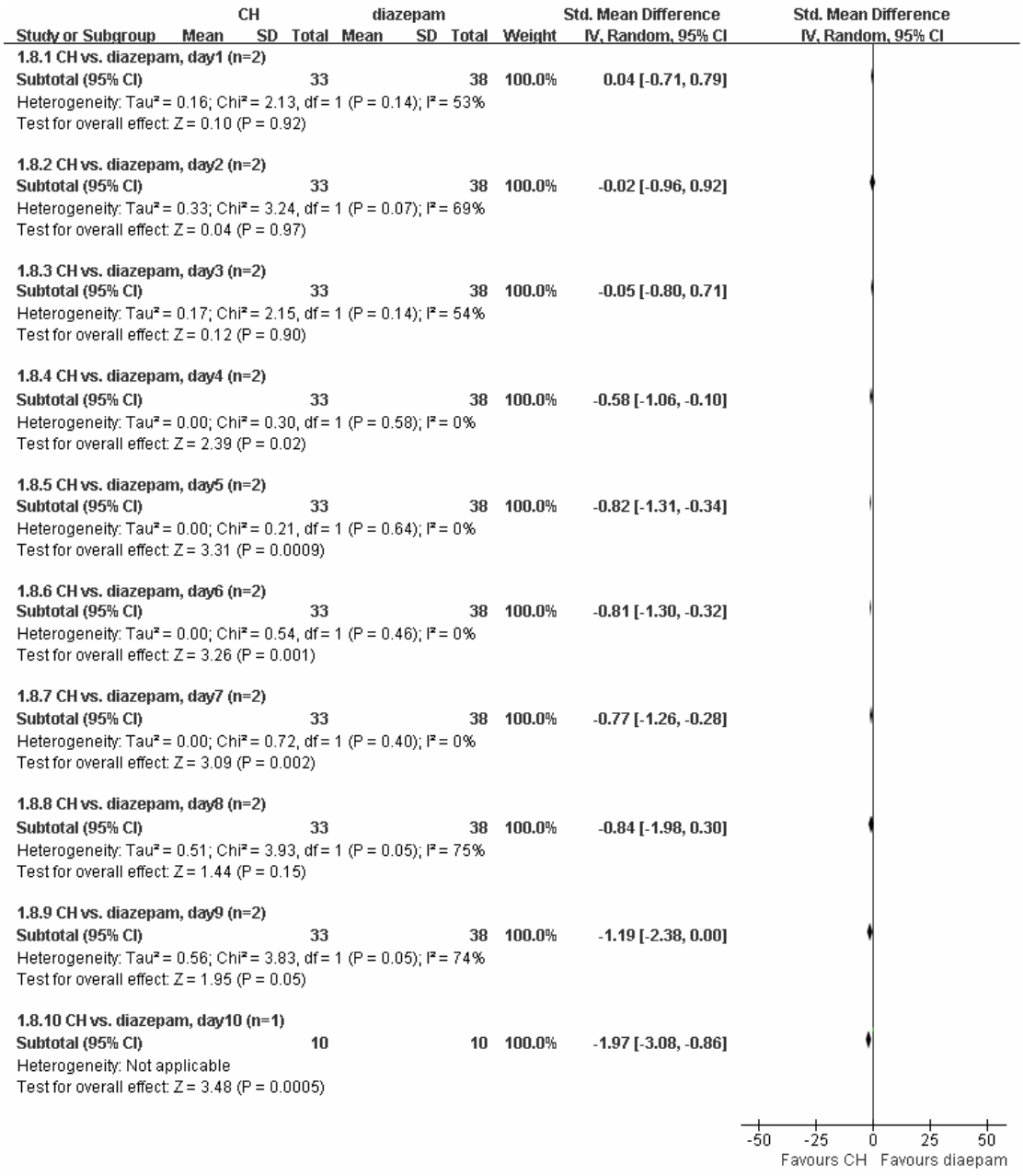



Fig 8. Meta-analyses of CINA scores for acute anxiety symptoms on the Day 1 to 10 (CH vs. diazepam)

Note: Detail data and comparisons on the Day 1 to 10 were attached (3.1.2)

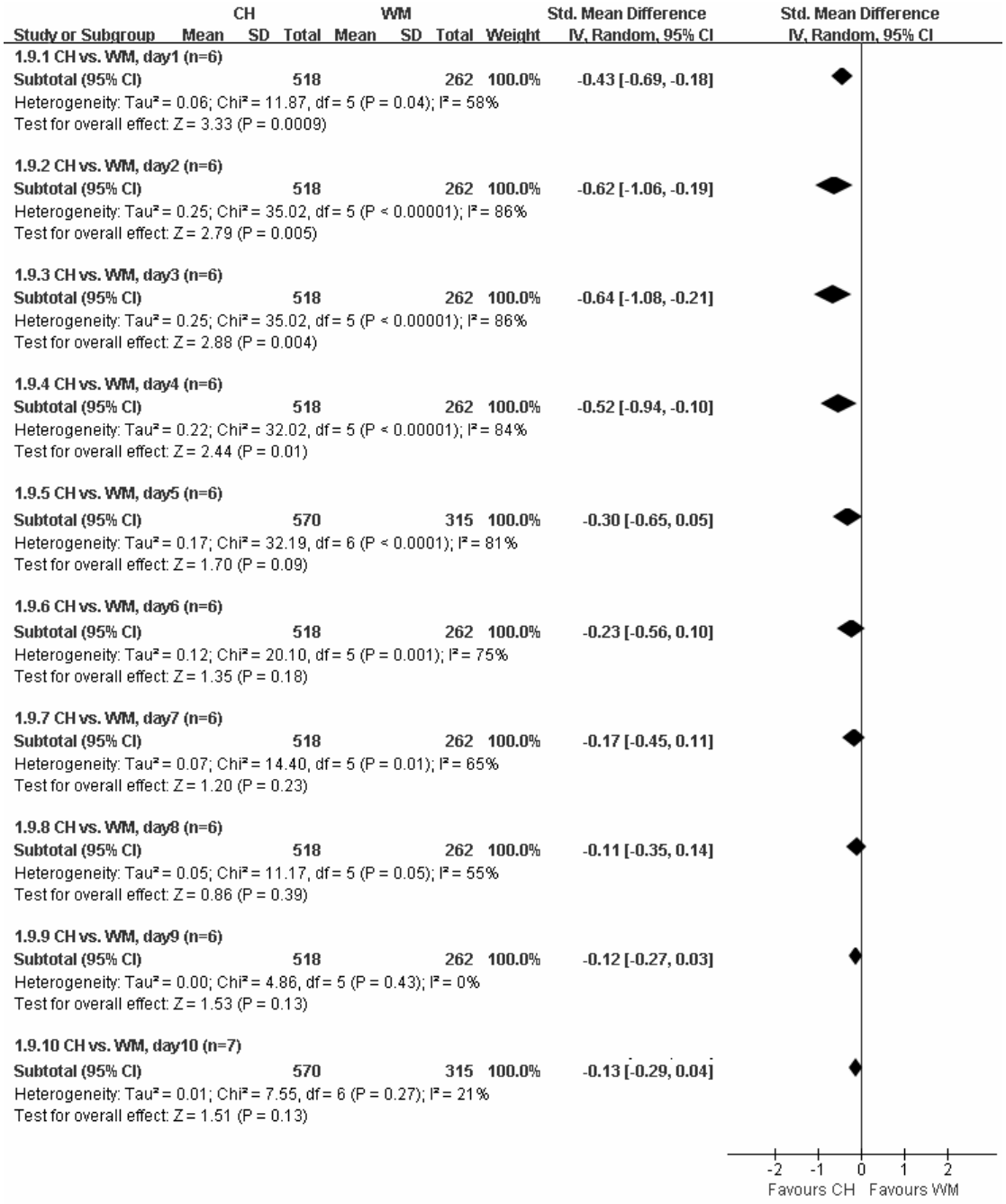



Fig 9. Meta-analyses of adverse-effect scores on the Day 1 to 10 (CH vs.WM)
Note: Detail data and comparisons on the Day 1 to 10 were attached (3.1.2)

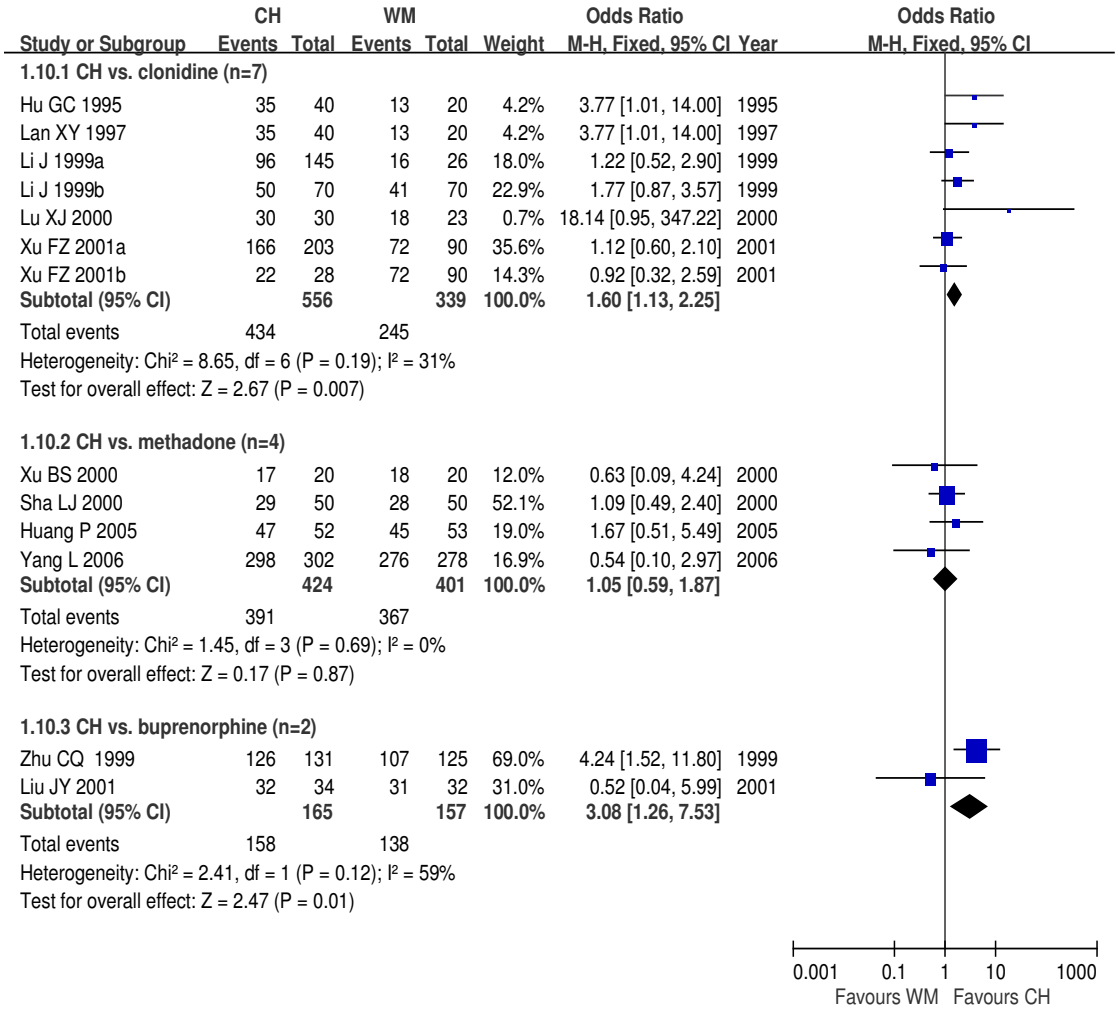



Fig 10. Meta-analyses of NIP of acute abstinent symptoms (CH vs.WM)

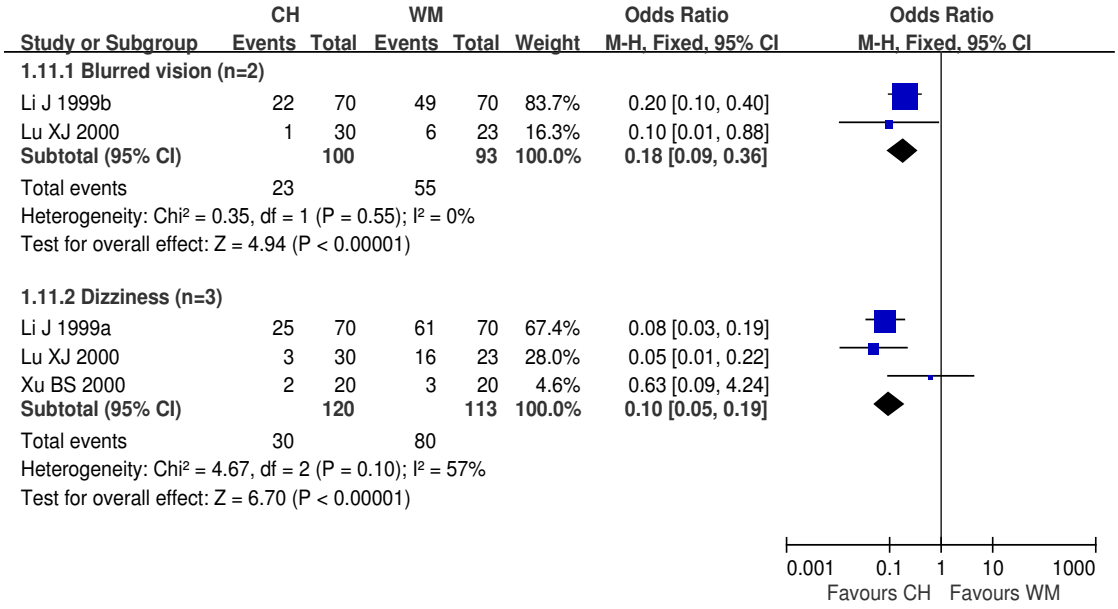
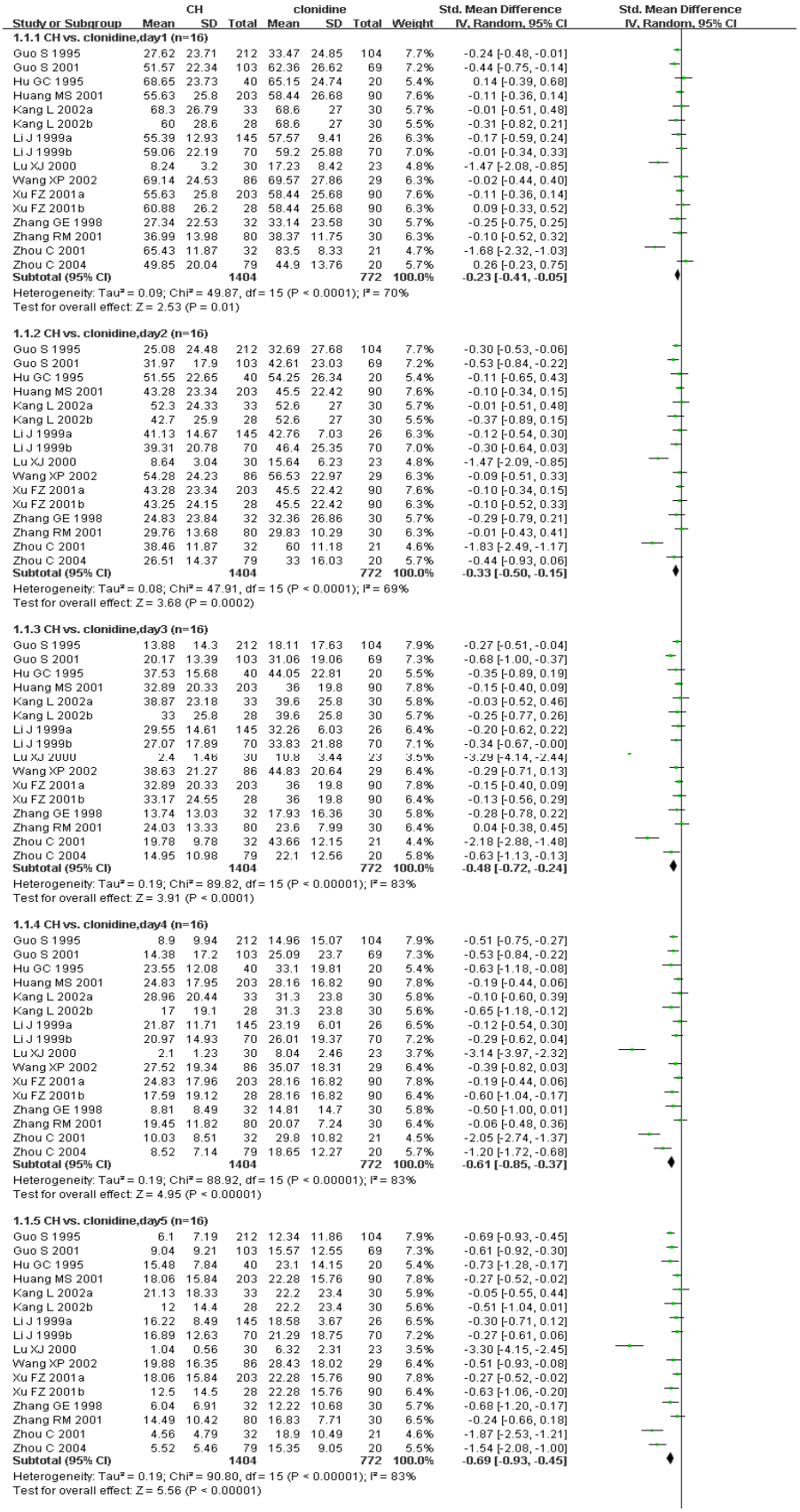



Fig 11. Meta-analyses of incidence of adverse symptoms (blurred vision and dizziness) (CH vs.WM)

## 3.1.2 Short-term detoxification of heroin dependence (Detail data)



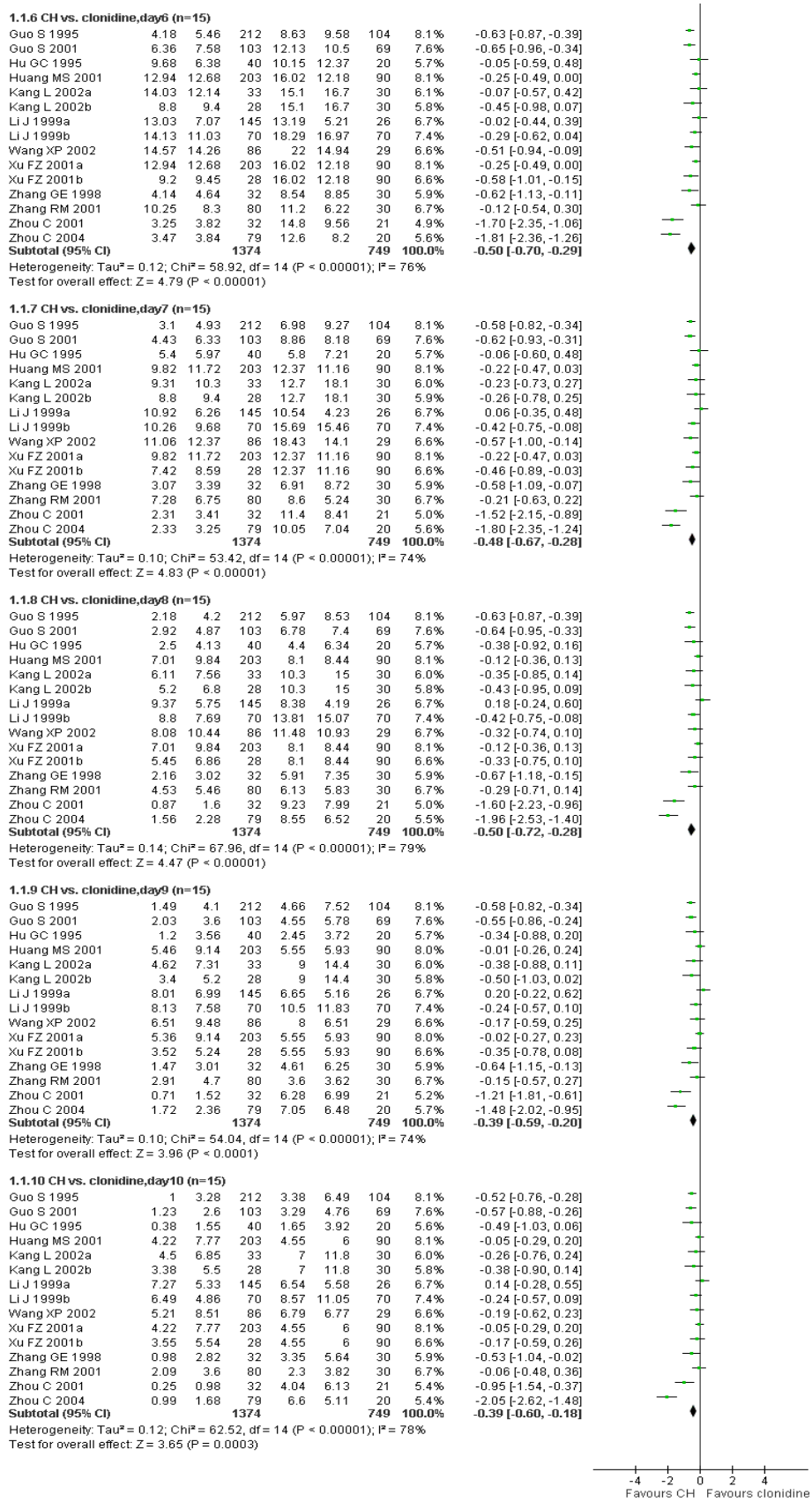



Fig 1. Meta-analyses of CINA scores for acute abstinent symptoms on the Day 1 to 10 (CH vs. clonidine)

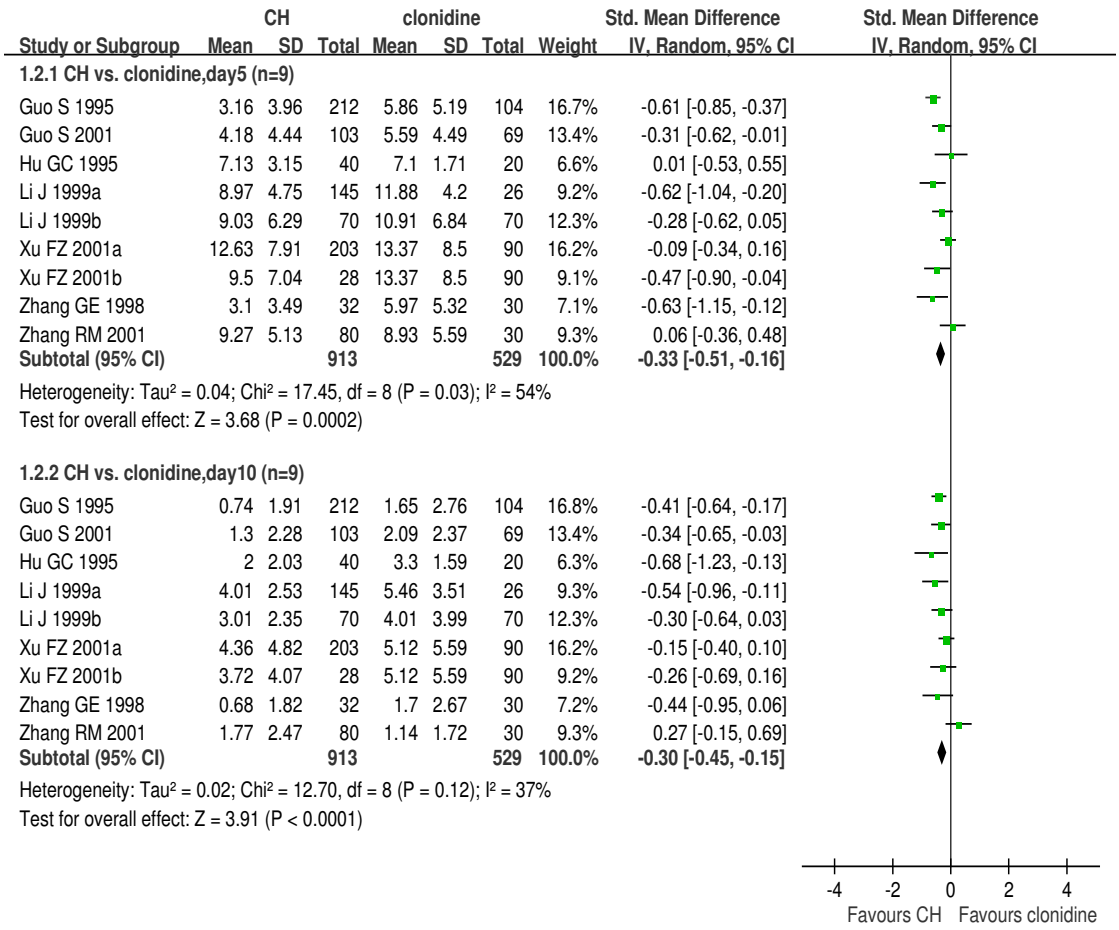



Fig 2. Meta-analyses of HAMA scores for anxiety symptoms on the Day 5 and 10 (CH vs. clonidine)

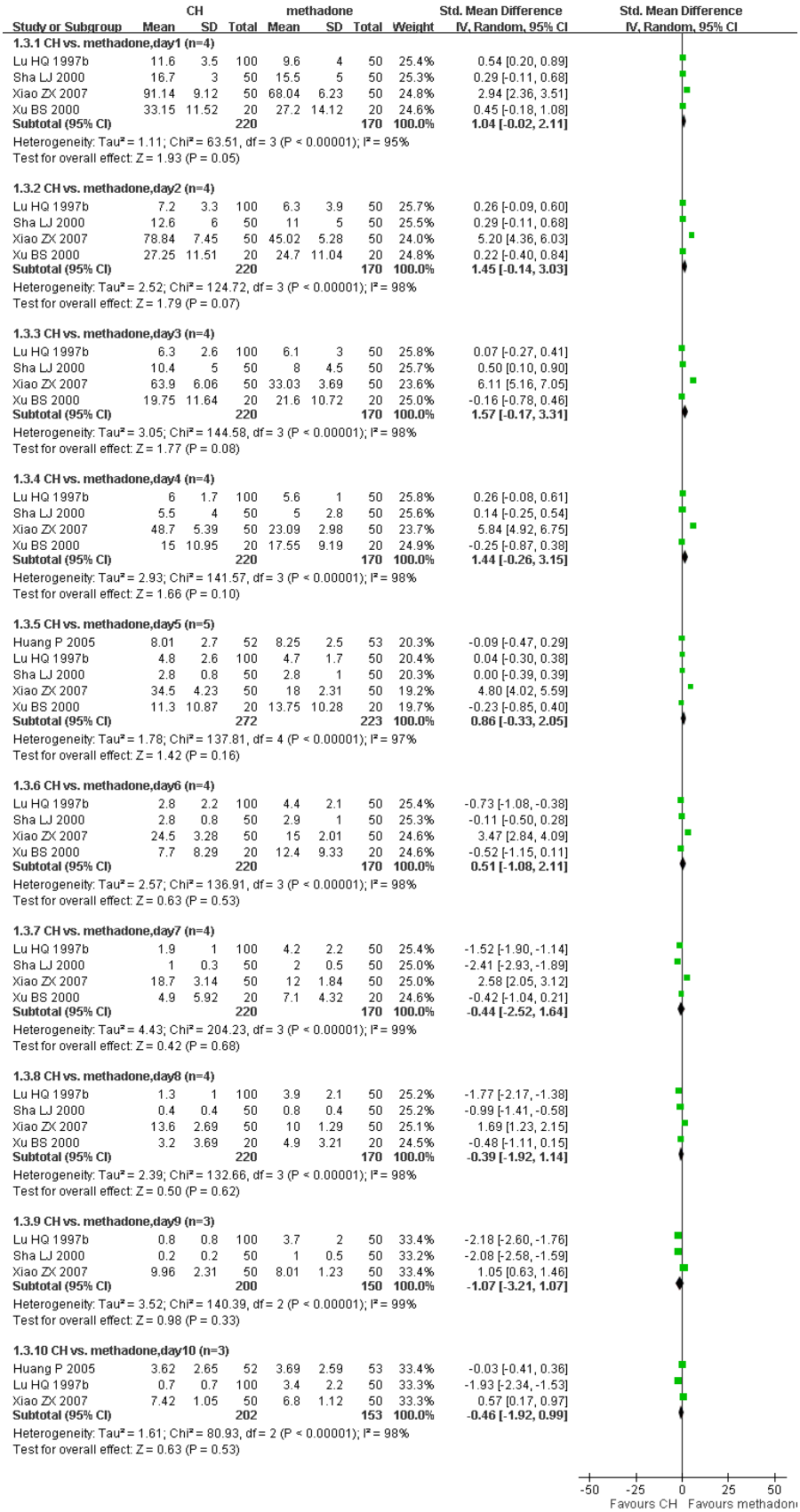



Fig 3. Meta-analyses of CINA scores for acute abstinent symptoms on the Day 1 to 10 (CH vs. methadone)

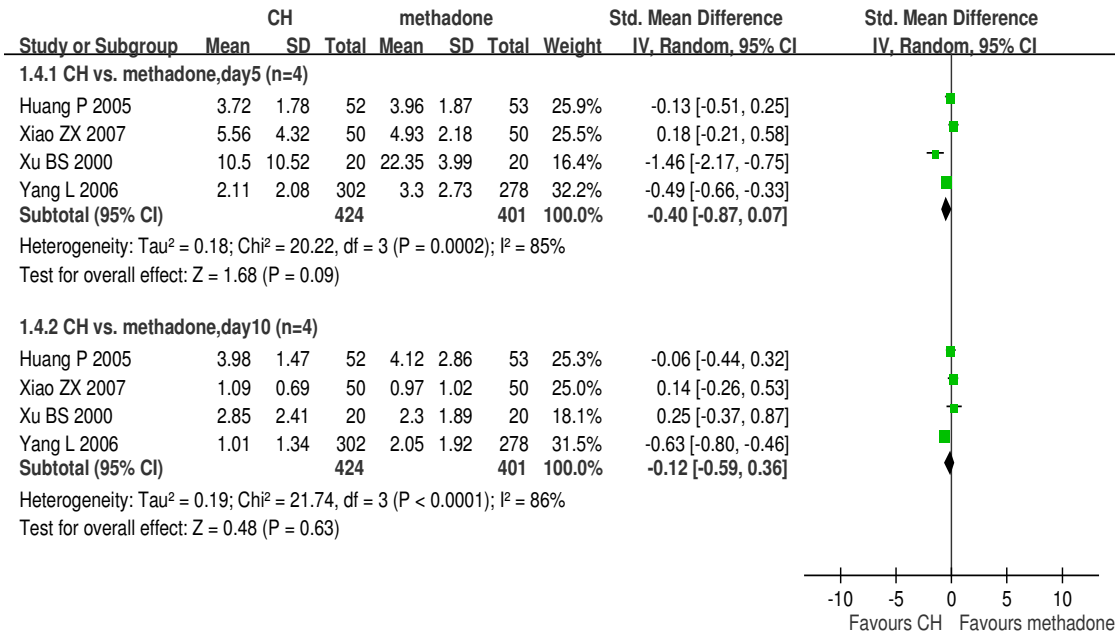
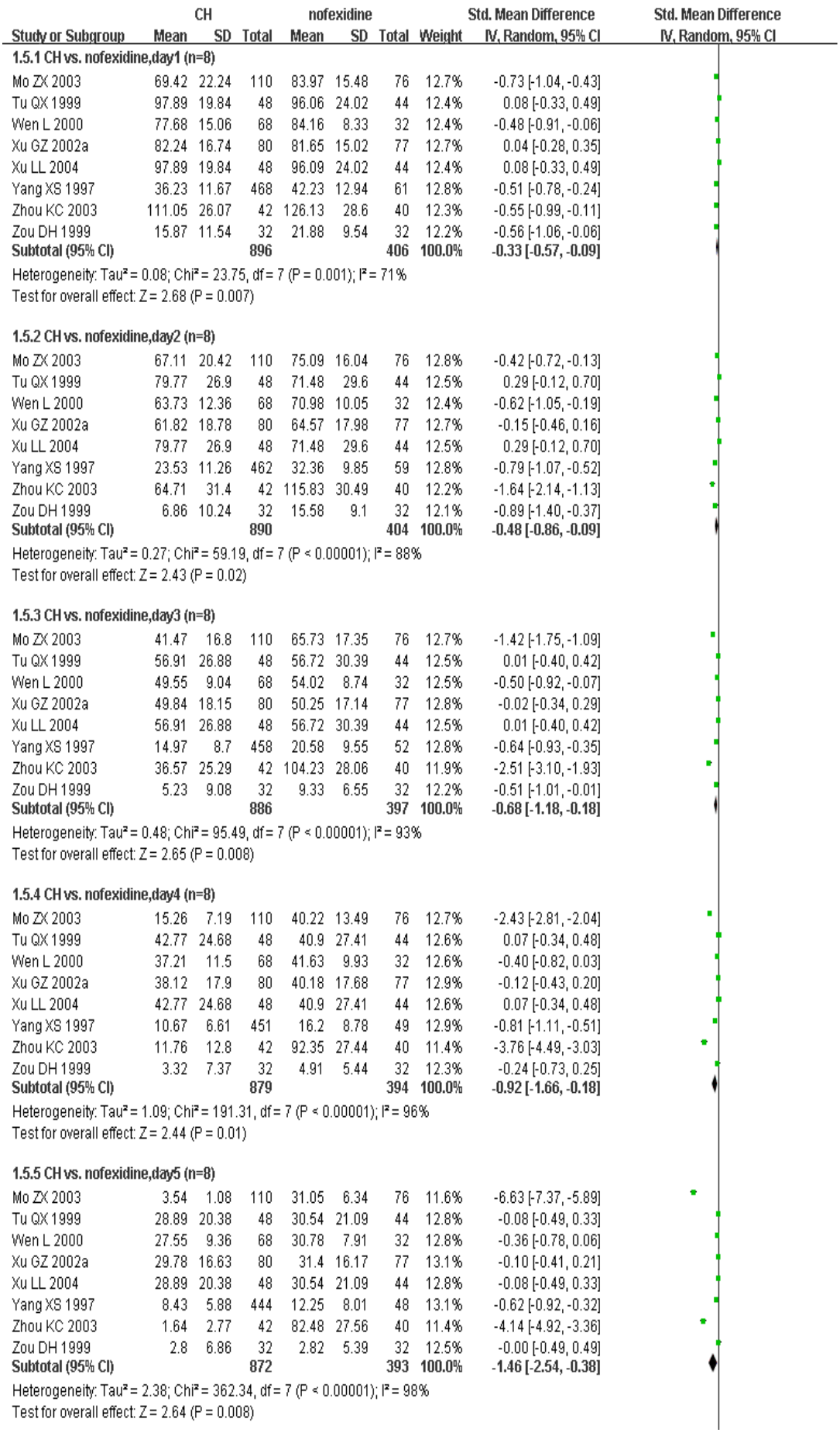



Fig 4. Meta-analyses of HAMA scores for anxiety symptoms on the Day 5 and 10 (CH vs. methadone)


CH
nofexidine
Std. Mean Difference
Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.5.1 CH vs. nofexidine,day1 (n=8)
Mo ZX 2003 69.42 22.24 110 83.97 15.48 76 12.7% -0.73 [-1.04, -0.43]
Tu QX 1999 97.89 19.84 48 96.06 24.02 44 12.4% 0.08 [-0.33, 0.49]
Wen L 2000 77.68 15.06 68 84.16 8.33 32 12.4% -0.48 [-0.91, -0.06]
Xu GZ 2002a 82.24 16.74 80 81.65 15.02 77 12.7% 0.04 [-0.28, 0.35]
Xu LL 2004 97.89 19.84 48 96.09 24.02 44 12.4% 0.08 [-0.33, 0.49]
Yang XS 1997 36.23 11.67 468 42.23 12.94 61 12.8% -0.51 [-0.78, -0.24]
Zhou KC 2003 111.05 26.07 42 126.13 28.6 40 12.3% -0.55 [-0.99, -0.11]
Zou DH 1999 15.87 11.54 32 21.88 9.54 32 12.2% -0.56 [-1.06, -0.06]
Subtotal (95% CI) 896 406 100.0% -0.33 [-0.57, -0.09]
Heterogeneity: Tau² = 0.08; Chi² = 23.75, df = 7 (P = 0.001); I² = 71%
Test for overall effect: Z = 2.68 (P = 0.007)
1.5.2 CH vs. nofexidine,day2 (n=8)
Mo ZX 2003 67.11 20.42 110 75.09 16.04 76 12.8% -0.42 [-0.72, -0.13]
Tu QX 1999 79.77 26.9 48 71.48 29.6 44 12.5% 0.29 [-0.12, 0.70]
Wen L 2000 63.73 12.36 68 70.98 10.05 32 12.4% -0.62 [-1.05, -0.19]
Xu GZ 2002a 61.82 18.78 80 64.57 17.98 77 12.7% -0.15 [-0.46, 0.16]
Xu LL 2004 79.77 26.9 48 71.48 29.6 44 12.5% 0.29 [-0.12, 0.70]
Yang XS 1997 23.53 11.26 462 32.36 9.85 59 12.8% -0.79 [-1.07, -0.52]
Zhou KC 2003 64.71 31.4 42 115.83 30.49 40 12.2% -1.64 [-2.14, -1.13]
Zou DH 1999 6.86 10.24 32 15.58 9.1 32 12.1% -0.89 [-1.40, -0.37]
Subtotal (95% CI) 890 404 100.0% -0.48 [-0.86, -0.09]
Heterogeneity: Tau² = 0.27; Chi² = 59.19, df = 7 (P < 0.00001); I² = 88%
Test for overall effect: Z = 2.43 (P = 0.02)
1.5.3 CH vs. nofexidine,day3 (n=8)
Mo ZX 2003 41.47 16.8 110 65.73 17.35 76 12.7% -1.42 [-1.75, -1.09]
Tu QX 1999 56.91 26.88 48 56.72 30.39 44 12.5% 0.01 [-0.40, 0.42]
Wen L 2000 49.55 9.04 68 54.02 8.74 32 12.5% -0.50 [-0.92, -0.07]
Xu GZ 2002a 49.84 18.15 80 50.25 17.14 77 12.8% -0.02 [-0.34, 0.29]
Xu LL 2004 56.91 26.88 48 56.72 30.39 44 12.5% 0.01 [-0.40, 0.42]
Yang XS 1997 14.97 8.7 458 20.58 9.55 52 12.8% -0.64 [-0.93, -0.35]
Zhou KC 2003 36.57 25.29 42 104.23 28.06 40 11.9% -2.51 [-3.10, -1.93]
Zou DH 1999 5.23 9.08 32 9.33 6.55 32 12.2% -0.51 [-1.01, -0.01]
Subtotal (95% CI) 886 397 100.0% -0.68 [-1.18, -0.18]
Heterogeneity: Tau² = 0.48; Chi² = 95.49, df = 7 (P < 0.00001); I² = 93%
Test for overall effect: Z = 2.65 (P = 0.008)
1.5.4 CH vs. nofexidine,day4 (n=8)
Mo ZX 2003 15.26 7.19 110 40.22 13.49 76 12.7% -2.43 [-2.81, -2.04]
Tu QX 1999 42.77 24.68 48 40.9 27.41 44 12.6% 0.07 [-0.34, 0.48]
Wen L 2000 37.21 11.5 68 41.63 9.93 32 12.6% -0.40 [-0.82, 0.03]
Xu GZ 2002a 38.12 17.9 80 40.18 17.68 77 12.9% -0.12 [-0.43, 0.20]
Xu LL 2004 42.77 24.68 48 40.9 27.41 44 12.6% 0.07 [-0.34, 0.48]
Yang XS 1997 10.67 6.61 451 16.2 8.78 49 12.9% -0.81 [-1.11, -0.51]
Zhou KC 2003 11.76 12.8 42 92.35 27.44 40 11.4% -3.76 [-4.49, -3.03]
Zou DH 1999 3.32 7.37 32 4.91 5.44 32 12.3% -0.24 [-0.73, 0.25]
Subtotal (95% CI) 879 394 100.0% -0.92 [-1.66, -0.18]
Heterogeneity: Tau² = 1.09; Chi² = 191.31, df = 7 (P < 0.00001); I² = 96%
Test for overall effect: Z = 2.44 (P = 0.01)
1.5.5 CH vs. nofexidine,day5 (n=8)
Mo ZX 2003 3.54 1.08 110 31.05 6.34 76 11.6% -6.63 [-7.37, -5.89]
Tu QX 1999 28.89 20.38 48 30.54 21.09 44 12.8% -0.08 [-0.49, 0.33]
Wen L 2000 27.55 9.36 68 30.78 7.91 32 12.8% -0.36 [-0.78, 0.06]
Xu GZ 2002a 29.78 16.63 80 31.4 16.17 77 13.1% -0.10 [-0.41, 0.21]
Xu LL 2004 28.89 20.38 48 30.54 21.09 44 12.8% -0.08 [-0.49, 0.33]
Yang XS 1997 8.43 5.88 444 12.25 8.01 48 13.1% -0.62 [-0.92, -0.32]
Zhou KC 2003 1.64 2.77 42 82.48 27.56 40 11.4% -4.14 [-4.92, -3.36]
Zou DH 1999 2.8 6.86 32 2.82 5.39 32 12.5% -0.00 [-0.49, 0.49]
Subtotal (95% CI) 872 393 100.0% -1.46 [-2.54, -0.38]
Heterogeneity: Tau² = 2.38; Chi² = 362.34, df = 7 (P < 0.00001); I² = 98%
Test for overall effect: Z = 2.64 (P = 0.008)

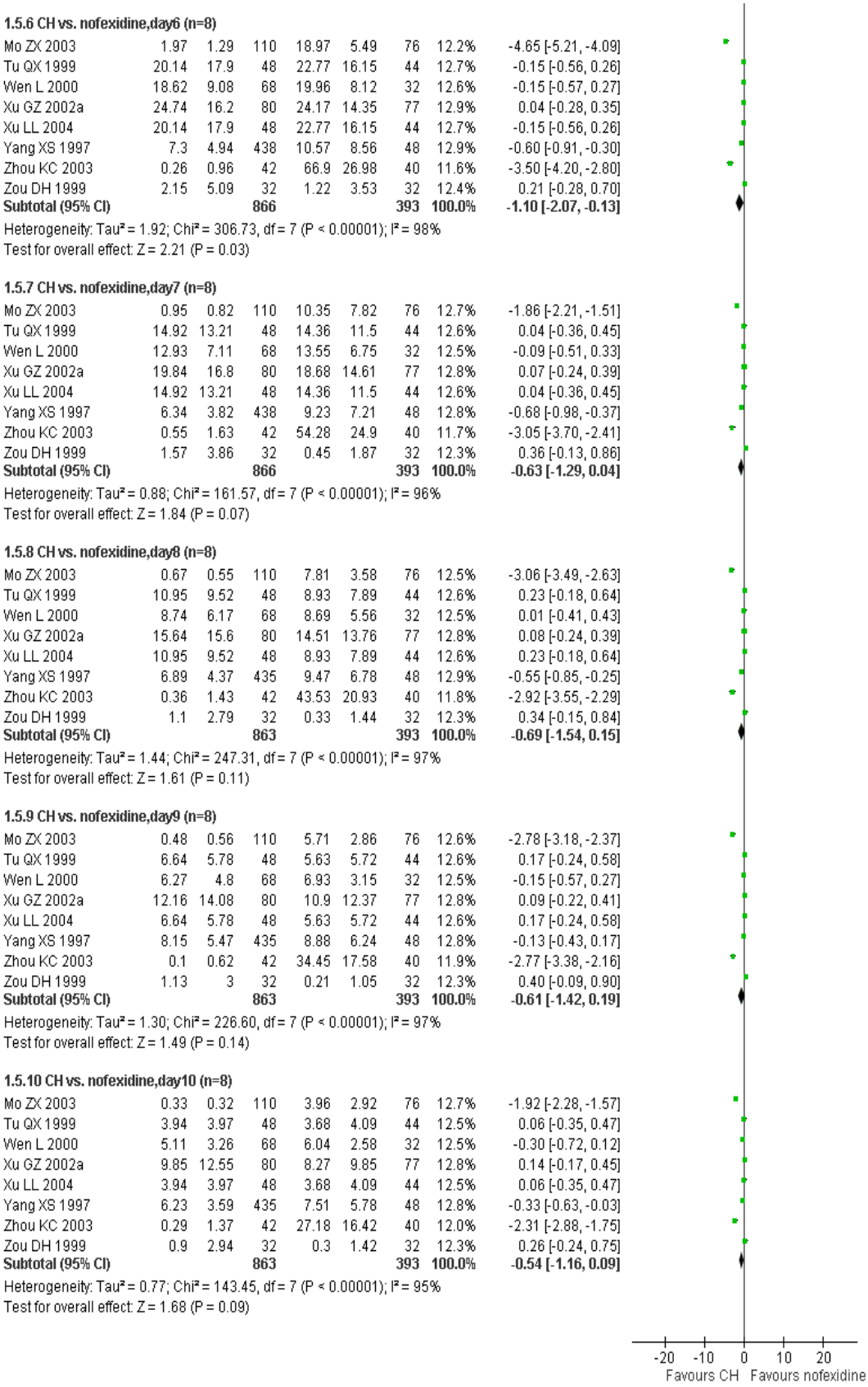



Fig 5. Meta-analyses of CINA scores for acute abstinent symptoms on the Day 1 to 10 (CH vs. nofexidine)

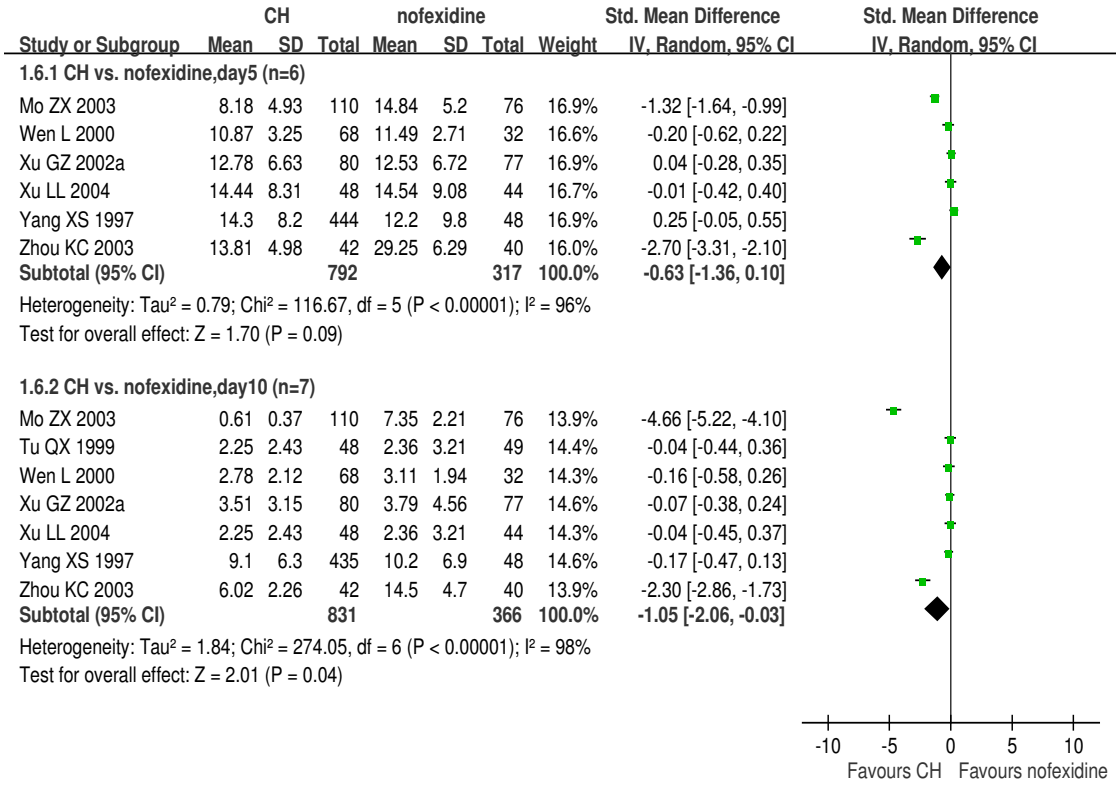



Fig 6. Meta-analyses of HAMA scores for anxiety symptoms on the Day 5 and 10 (CH vs. nofexidine)

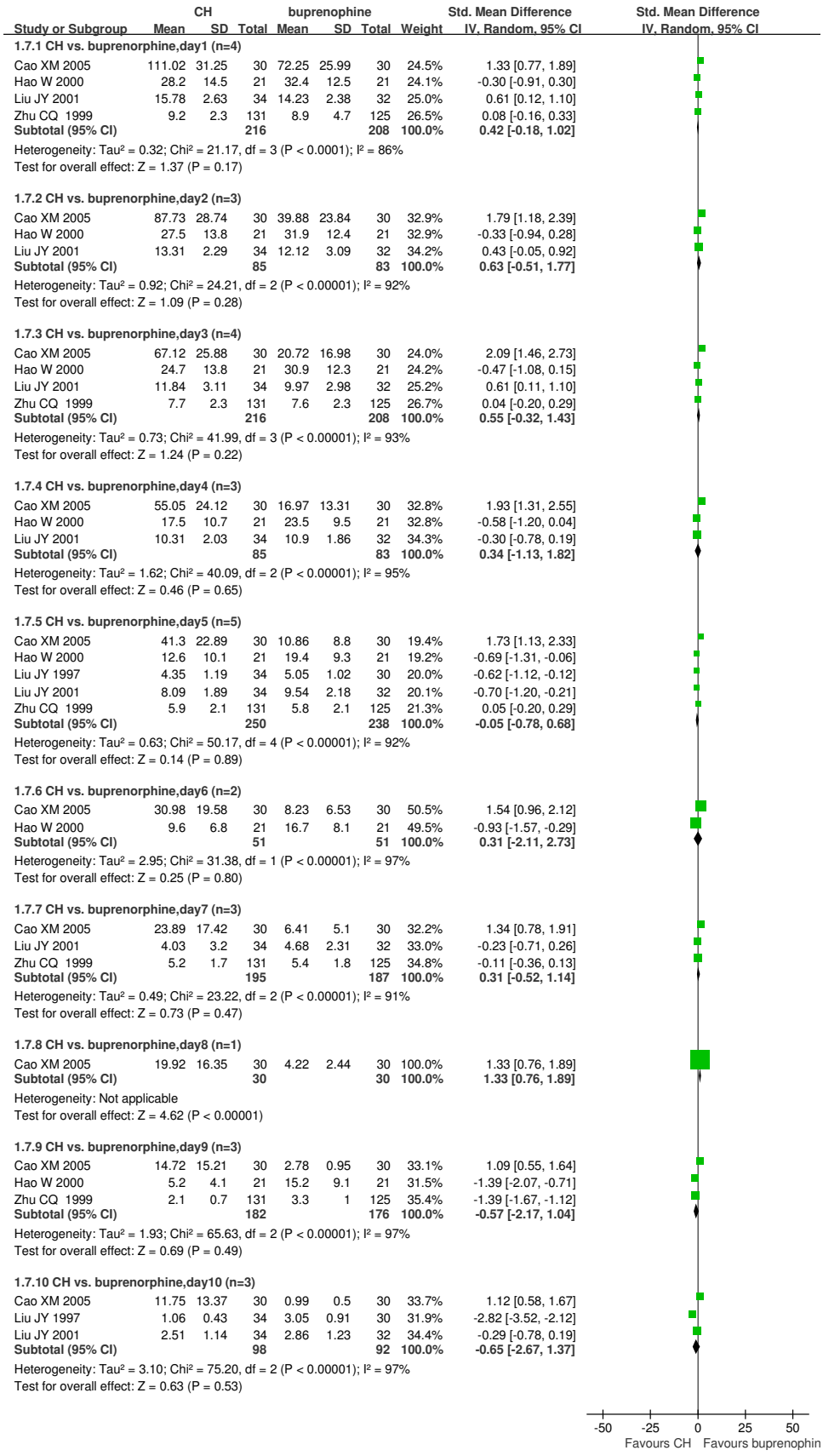



Fig 7. Meta-analyses of CINA scores for acute abstinent symptoms on the Day 1 to 10 (CH vs. buprenorphine)

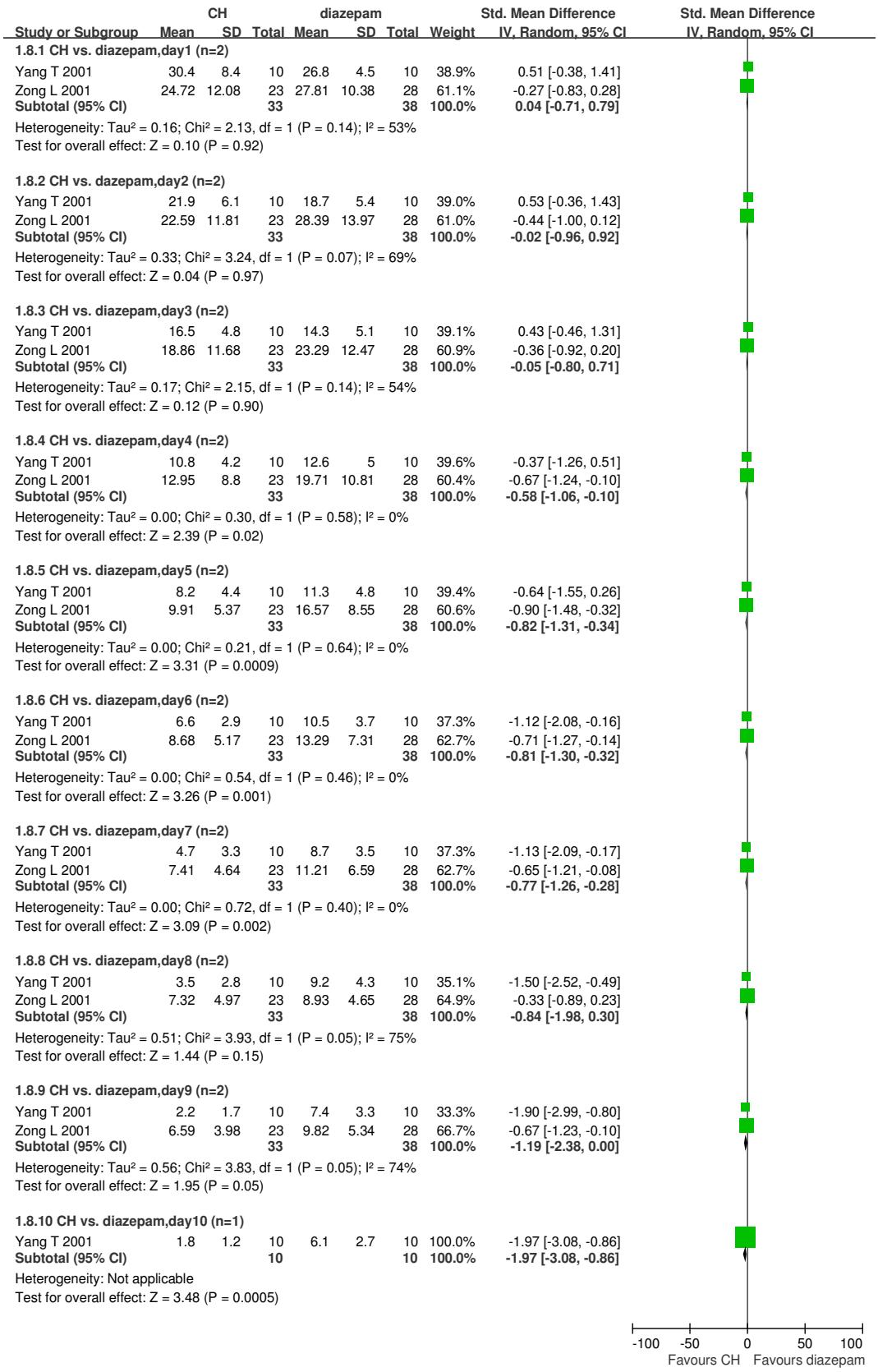
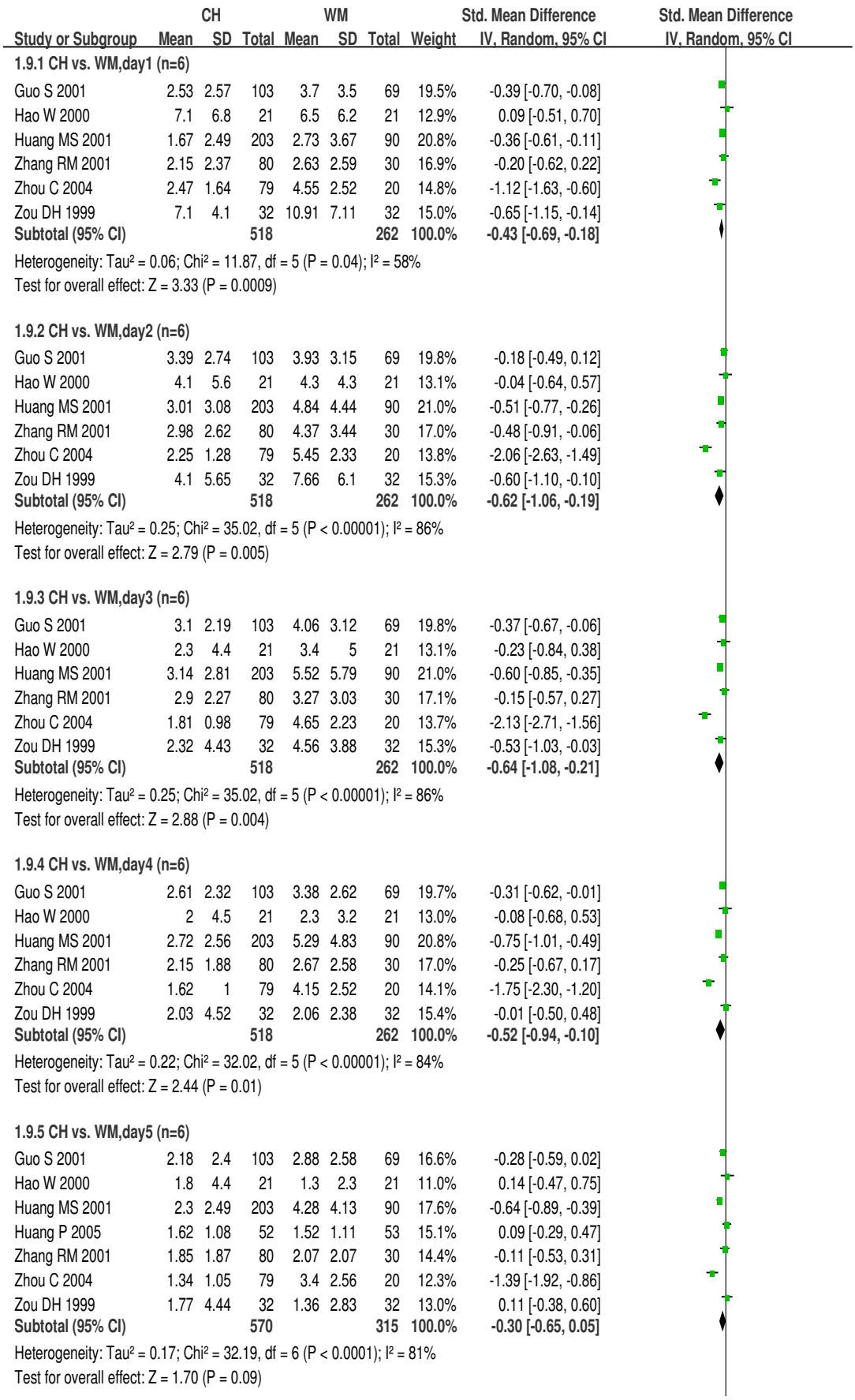



Fig 8. Meta-analyses of CINA scores for acute abstinent symptoms on the Day 1 to 10 (CH vs. diazepam)


CH
WM
Std. Mean Difference
Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.9.1 CH vs. WM,day1 (n=6)
Guo S 2001 2.53 2.57 103 3.7 3.5 69 19.5% -0.39 [-0.70, -0.08]
Hao W 2000 7.1 6.8 21 6.5 6.2 21 12.9% 0.09 [-0.51, 0.70]
Huang MS 2001 1.67 2.49 203 2.73 3.67 90 20.8% -0.36 [-0.61, -0.11]
Zhang RM 2001 2.15 2.37 80 2.63 2.59 30 16.9% -0.20 [-0.62, 0.22]
Zhou C 2004 2.47 1.64 79 4.55 2.52 20 14.8% -1.12 [-1.63, -0.60]
Zou DH 1999 7.1 4.1 32 10.91 7.11 32 15.0% -0.65 [-1.15, -0.14]
Subtotal (95% CI) 518 262 100.0% -0.43 [-0.69, -0.18]
Heterogeneity: Tau² = 0.06; Chi² = 11.87, df = 5 (P = 0.04); I² = 58%
Test for overall effect: Z = 3.33 (P = 0.0009)
1.9.2 CH vs. WM,day2 (n=6)
Guo S 2001 3.39 2.74 103 3.93 3.15 69 19.8% -0.18 [-0.49, 0.12]
Hao W 2000 4.1 5.6 21 4.3 4.3 21 13.1% -0.04 [-0.64, 0.57]
Huang MS 2001 3.01 3.08 203 4.84 4.44 90 21.0% -0.51 [-0.77, -0.26]
Zhang RM 2001 2.98 2.62 80 4.37 3.44 30 17.0% -0.48 [-0.91, -0.06]
Zhou C 2004 2.25 1.28 79 5.45 2.33 20 13.8% -2.06 [-2.63, -1.49]
Zou DH 1999 4.1 5.65 32 7.66 6.1 32 15.3% -0.60 [-1.10, -0.10]
Subtotal (95% CI) 518 262 100.0% -0.62 [-1.06, -0.19]
Heterogeneity: Tau² = 0.25; Chi² = 35.02, df = 5 (P < 0.00001); I² = 86%
Test for overall effect: Z = 2.79 (P = 0.005)
1.9.3 CH vs. WM,day3 (n=6)
Guo S 2001 3.1 2.19 103 4.06 3.12 69 19.8% -0.37 [-0.67, -0.06]
Hao W 2000 2.3 4.4 21 3.4 5 21 13.1% -0.23 [-0.84, 0.38]
Huang MS 2001 3.14 2.81 203 5.52 5.79 90 21.0% -0.60 [-0.85, -0.35]
Zhang RM 2001 2.9 2.27 80 3.27 3.03 30 17.1% -0.15 [-0.57, 0.27]
Zhou C 2004 1.81 0.98 79 4.65 2.23 20 13.7% -2.13 [-2.71, -1.56]
Zou DH 1999 2.32 4.43 32 4.56 3.88 32 15.3% -0.53 [-1.03, -0.03]
Subtotal (95% CI) 518 262 100.0% -0.64 [-1.08, -0.21]
Heterogeneity: Tau² = 0.25; Chi² = 35.02, df = 5 (P < 0.00001); I² = 86%
Test for overall effect: Z = 2.88 (P = 0.004)
1.9.4 CH vs. WM,day4 (n=6)
Guo S 2001 2.61 2.32 103 3.38 2.62 69 19.7% -0.31 [-0.62, -0.01]
Hao W 2000 2 4.5 21 2.3 3.2 21 13.0% -0.08 [-0.68, 0.53]
Huang MS 2001 2.72 2.56 203 5.29 4.83 90 20.8% -0.75 [-1.01, -0.49]
Zhang RM 2001 2.15 1.88 80 2.67 2.58 30 17.0% -0.25 [-0.67, 0.17]
Zhou C 2004 1.62 1 79 4.15 2.52 20 14.1% -1.75 [-2.30, -1.20]
Zou DH 1999 2.03 4.52 32 2.06 2.38 32 15.4% -0.01 [-0.50, 0.48]
Subtotal (95% CI) 518 262 100.0% -0.52 [-0.94, -0.10]
Heterogeneity: Tau² = 0.22; Chi² = 32.02, df = 5 (P < 0.00001); I² = 84%
Test for overall effect: Z = 2.44 (P = 0.01)
1.9.5 CH vs. WM,day5 (n=6)
Guo S 2001 2.18 2.4 103 2.88 2.58 69 16.6% -0.28 [-0.59, 0.02]
Hao W 2000 1.8 4.4 21 1.3 2.3 21 11.0% 0.14 [-0.47, 0.75]
Huang MS 2001 2.3 2.49 203 4.28 4.13 90 17.6% -0.64 [-0.89, -0.39]
Huang P 2005 1.62 1.08 52 1.52 1.11 53 15.1% 0.09 [-0.29, 0.47]
Zhang RM 2001 1.85 1.87 80 2.07 2.07 30 14.4% -0.11 [-0.53, 0.31]
Zhou C 2004 1.34 1.05 79 3.4 2.56 20 12.3% -1.39 [-1.92, -0.86]
Zou DH 1999 1.77 4.44 32 1.36 2.83 32 13.0% 0.11 [-0.38, 0.60]
Subtotal (95% CI) 570 315 100.0% -0.30 [-0.65, 0.05]
Heterogeneity: Tau² = 0.17; Chi² = 32.19, df = 6 (P < 0.0001); I² = 81%
Test for overall effect: Z = 1.70 (P = 0.09)

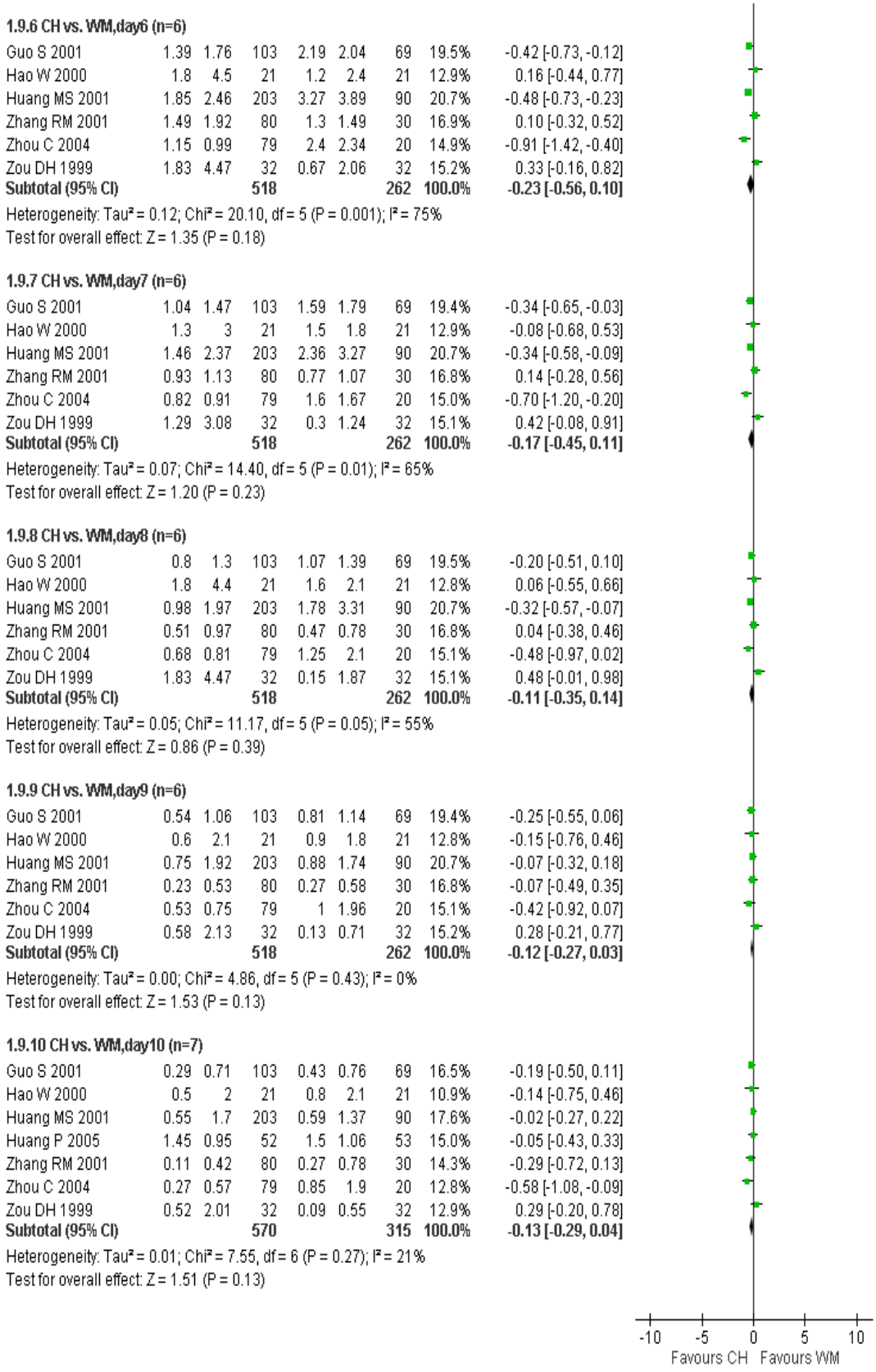
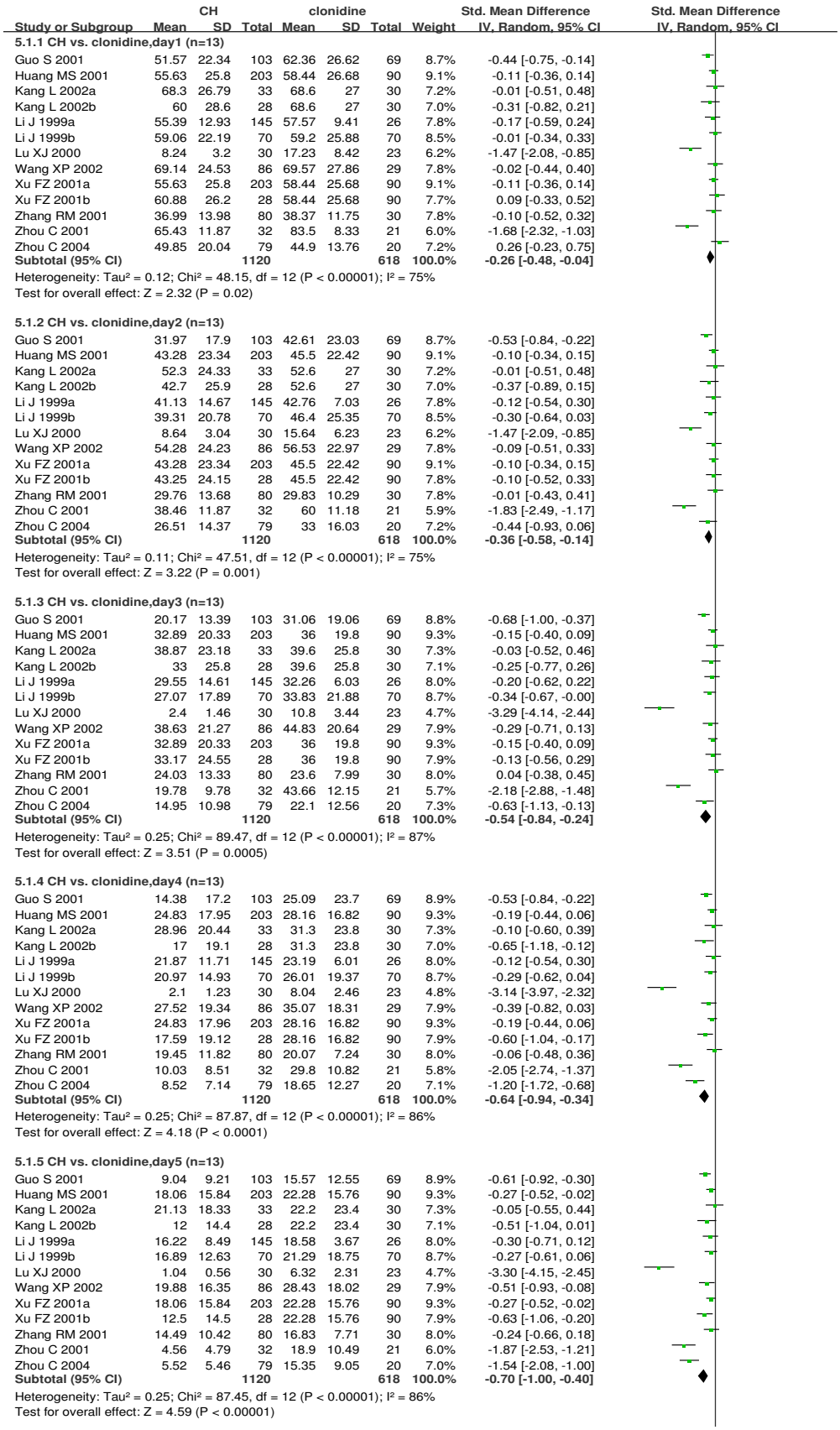



Fig 9. Meta-analyses of adverse-effect scores on the Day 1 to 10 (CH vs.WM)


CH
clonidine
Std. Mean Difference
Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
5.1.1 CH vs. clonidine,day1 (n=13)
Guo S 2001 51.57 22.34 103 62.36 26.62 69 8.7% -0.44 [-0.75, -0.14]
Huang MS 2001 55.63 25.8 203 58.44 26.68 90 9.1% -0.11 [-0.36, 0.14]
Kang L 2002a 68.3 26.79 33 68.6 27 30 7.2% -0.01 [-0.51, 0.48]
Kang L 2002b 60 28.6 28 68.6 27 30 7.0% -0.31 [-0.82, 0.21]
Li J 1999a 55.39 12.93 145 57.57 9.41 26 7.8% -0.17 [-0.59, 0.24]
Li J 1999b 59.06 22.19 70 59.2 25.88 70 8.5% -0.01 [-0.34, 0.33]
Lu XJ 2000 8.24 3.2 30 17.23 8.42 23 6.2% -1.47 [-2.08, -0.85]
Wang XP 2002 69.14 24.53 86 69.57 27.86 29 7.8% -0.02 [-0.44, 0.40]
Xu FZ 2001a 55.63 25.8 203 58.44 25.68 90 9.1% -0.11 [-0.36, 0.14]
Xu FZ 2001b 60.88 26.2 28 58.44 25.68 90 7.7% 0.09 [-0.33, 0.52]
Zhang RM 2001 36.99 13.98 80 38.37 11.75 30 7.8% -0.10 [-0.52, 0.32]
Zhou C 2001 65.43 11.87 32 83.5 8.33 21 6.0% -1.68 [-2.32, -1.03]
Zhou C 2004 49.85 20.04 79 44.9 13.76 20 7.2% 0.26 [-0.23, 0.75]
Subtotal (95% CI) 1120 618 100.0% -0.26 [-0.48, -0.04]
Heterogeneity: Tau² = 0.12; Chi² = 48.15, df = 12 (P < 0.00001); I² = 75%
Test for overall effect: Z = 2.32 (P = 0.02)
5.1.2 CH vs. clonidine,day2 (n=13)
Guo S 2001 31.97 17.9 103 42.61 23.03 69 8.7% -0.53 [-0.84, -0.22]
Huang MS 2001 43.28 23.34 203 45.5 22.42 90 9.1% -0.10 [-0.34, 0.15]
Kang L 2002a 52.3 24.33 33 52.6 27 30 7.2% -0.01 [-0.51, 0.48]
Kang L 2002b 42.7 25.9 28 52.6 27 30 7.0% -0.37 [-0.89, 0.15]
Li J 1999a 41.13 14.67 145 42.76 7.03 26 7.8% -0.12 [-0.54, 0.30]
Li J 1999b 39.31 20.78 70 46.4 25.35 70 8.5% -0.30 [-0.64, 0.03]
Lu XJ 2000 8.64 3.04 30 15.64 6.23 23 6.2% -1.47 [-2.09, -0.85]
Wang XP 2002 54.28 24.23 86 56.53 22.97 29 7.8% -0.09 [-0.51, 0.33]
Xu FZ 2001a 43.28 23.34 203 45.5 22.42 90 9.1% -0.10 [-0.34, 0.15]
Xu FZ 2001b 43.25 24.15 28 45.5 22.42 90 7.8% -0.10 [-0.52, 0.33]
Zhang RM 2001 29.76 13.68 80 29.83 10.29 30 7.8% -0.01 [-0.43, 0.41]
Zhou C 2001 38.46 11.87 32 60 11.18 21 5.9% -1.83 [-2.49, -1.17]
Zhou C 2004 26.51 14.37 79 33 16.03 20 7.2% -0.44 [-0.93, 0.06]
Subtotal (95% CI) 1120 618 100.0% -0.36 [-0.58, -0.14]
Heterogeneity: Tau² = 0.11; Chi² = 47.51, df = 12 (P < 0.00001); I² = 75%
Test for overall effect: Z = 3.22 (P = 0.001)
5.1.3 CH vs. clonidine,day3 (n=13)
Guo S 2001 20.17 13.39 103 31.06 19.06 69 8.8% -0.68 [-1.00, -0.37]
Huang MS 2001 32.89 20.33 203 36 19.8 90 9.3% -0.15 [-0.40, 0.09]
Kang L 2002a 38.87 23.18 33 39.6 25.8 30 7.3% -0.03 [-0.52, 0.46]
Kang L 2002b 33 25.8 28 39.6 25.8 30 7.1% -0.25 [-0.77, 0.26]
Li J 1999a 29.55 14.61 145 32.26 6.03 26 8.0% -0.20 [-0.62, 0.22]
Li J 1999b 27.07 17.89 70 33.83 21.88 70 8.7% -0.34 [-0.67, -0.00]
Lu XJ 2000 2.4 1.46 30 10.8 3.44 23 4.7% -3.29 [-4.14, -2.44]
Wang XP 2002 38.63 21.27 86 44.83 20.64 29 7.9% -0.29 [-0.71, 0.13]
Xu FZ 2001a 32.89 20.33 203 36 19.8 90 9.3% -0.15 [-0.40, 0.09]
Xu FZ 2001b 33.17 24.55 28 36 19.8 90 7.9% -0.13 [-0.56, 0.29]
Zhang RM 2001 24.03 13.33 80 23.6 7.99 30 8.0% 0.04 [-0.38, 0.45]
Zhou C 2001 19.78 9.78 32 43.66 12.15 21 5.7% -2.18 [-2.88, -1.48]
Zhou C 2004 14.95 10.98 79 22.1 12.56 20 7.3% -0.63 [-1.13, -0.13]
Subtotal (95% CI) 1120 618 100.0% -0.54 [-0.84, -0.24]
Heterogeneity: Tau² = 0.25; Chi² = 89.47, df = 12 (P < 0.00001); I² = 87%
Test for overall effect: Z = 3.51 (P = 0.0005)
5.1.4 CH vs. clonidine,day4 (n=13)
Guo S 2001 14.38 17.2 103 25.09 23.7 69 8.9% -0.53 [-0.84, -0.22]
Huang MS 2001 24.83 17.95 203 28.16 16.82 90 9.3% -0.19 [-0.44, 0.06]
Kang L 2002a 28.96 20.44 33 31.3 23.8 30 7.3% -0.10 [-0.60, 0.39]
Kang L 2002b 17 19.1 28 31.3 23.8 30 7.0% -0.65 [-1.18, -0.12]
Li J 1999a 21.87 11.71 145 23.19 6.01 26 8.0% -0.12 [-0.54, 0.30]
Li J 1999b 20.97 14.93 70 26.01 19.37 70 8.7% -0.29 [-0.62, 0.04]
Lu XJ 2000 2.1 1.23 30 8.04 2.46 23 4.8% -3.14 [-3.97, -2.32]
Wang XP 2002 27.52 19.34 86 35.07 18.31 29 7.9% -0.39 [-0.82, 0.03]
Xu FZ 2001a 24.83 17.96 203 28.16 16.82 90 9.3% -0.19 [-0.44, 0.06]
Xu FZ 2001b 17.59 19.12 28 28.16 16.82 90 7.9% -0.60 [-1.04, -0.17]
Zhang RM 2001 19.45 11.82 80 20.07 7.24 30 8.0% -0.06 [-0.48, 0.36]
Zhou C 2001 10.03 8.51 32 29.8 10.82 21 5.8% -2.05 [-2.74, -1.37]
Zhou C 2004 8.52 7.14 79 18.65 12.27 20 7.1% -1.20 [-1.72, -0.68]
Subtotal (95% CI) 1120 618 100.0% -0.64 [-0.94, -0.34]
Heterogeneity: Tau² = 0.25; Chi² = 87.87, df = 12 (P < 0.00001); I² = 86%
Test for overall effect: Z = 4.18 (P < 0.0001)
5.1.5 CH vs. clonidine,day5 (n=13)
Guo S 2001 9.04 9.21 103 15.57 12.55 69 8.9% -0.61 [-0.92, -0.30]
Huang MS 2001 18.06 15.84 203 22.28 15.76 90 9.3% -0.27 [-0.52, -0.02]
Kang L 2002a 21.13 18.33 33 22.2 23.4 30 7.3% -0.05 [-0.55, 0.44]
Kang L 2002b 12 14.4 28 22.2 23.4 30 7.1% -0.51 [-1.04, 0.01]
Li J 1999a 16.22 8.49 145 18.58 3.67 26 8.0% -0.30 [-0.71, 0.12]
Li J 1999b 16.89 12.63 70 21.29 18.75 70 8.7% -0.27 [-0.61, 0.06]
Lu XJ 2000 1.04 0.56 30 6.32 2.31 23 4.7% -3.30 [-4.15, -2.45]
Wang XP 2002 19.88 16.35 86 28.43 18.02 29 7.9% -0.51 [-0.93, -0.08]
Xu FZ 2001a 18.06 15.84 203 22.28 15.76 90 9.3% -0.27 [-0.52, -0.02]
Xu FZ 2001b 12.5 14.5 28 22.28 15.76 90 7.9% -0.63 [-1.06, -0.20]
Zhang RM 2001 14.49 10.42 80 16.83 7.71 30 8.0% -0.24 [-0.66, 0.18]
Zhou C 2001 4.56 4.79 32 18.9 10.49 21 6.0% -1.87 [-2.53, -1.21]
Zhou C 2004 5.52 5.46 79 15.35 9.05 20 7.0% -1.54 [-2.08, -1.00]
Subtotal (95% CI) 1120 618 100.0% -0.70 [-1.00, -0.40]
Heterogeneity: Tau² = 0.25; Chi² = 87.45, df = 12 (P < 0.00001); I² = 86%
Test for overall effect: Z = 4.59 (P < 0.00001)

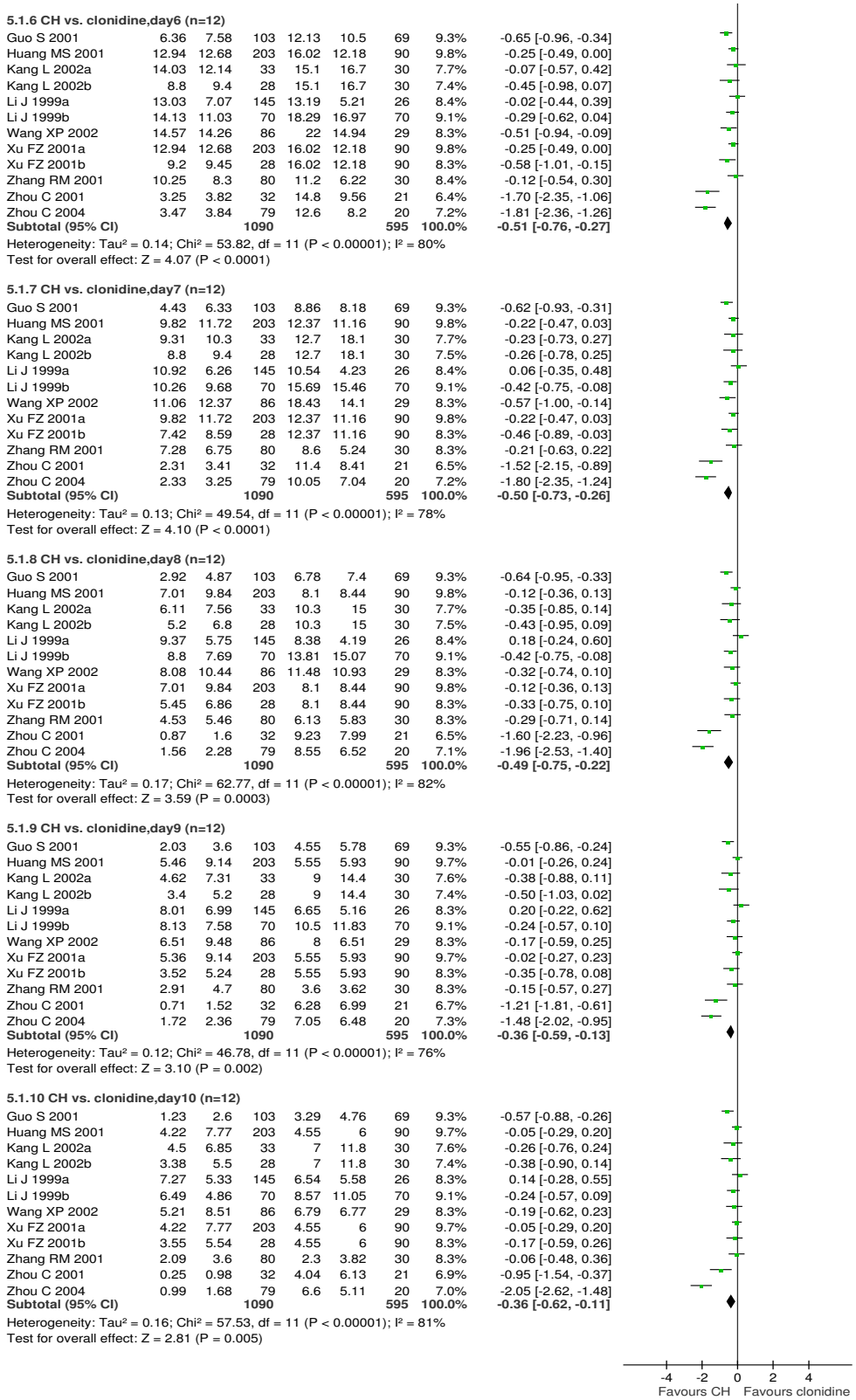



Fig 10. Meta-analysis on high-quality RCTs

Note: This was a subgroup meta-analysis of data in the Section 1.1.1 to 1.1.10 ( Fig.1).

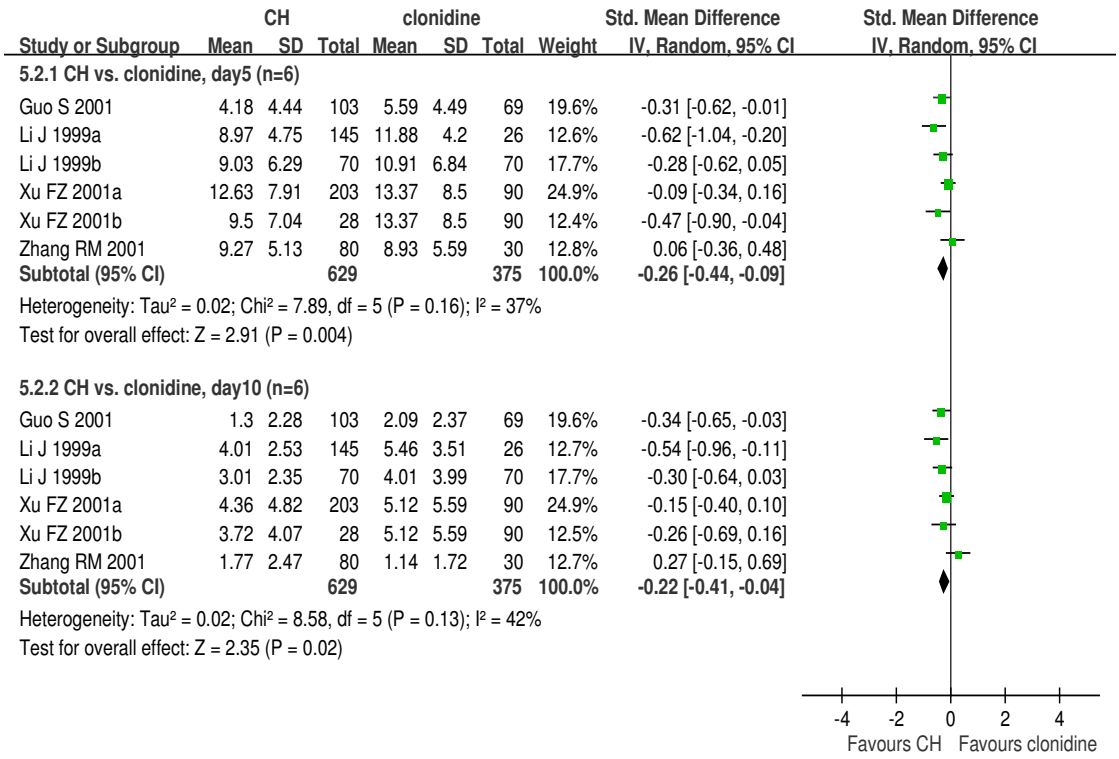



Fig 11. Meta-analysis on high-quality RCTs

Note: This was a subgroup meta-analysis of data in the Section 1.2.1 to 1.2.2 ( Fig.2).

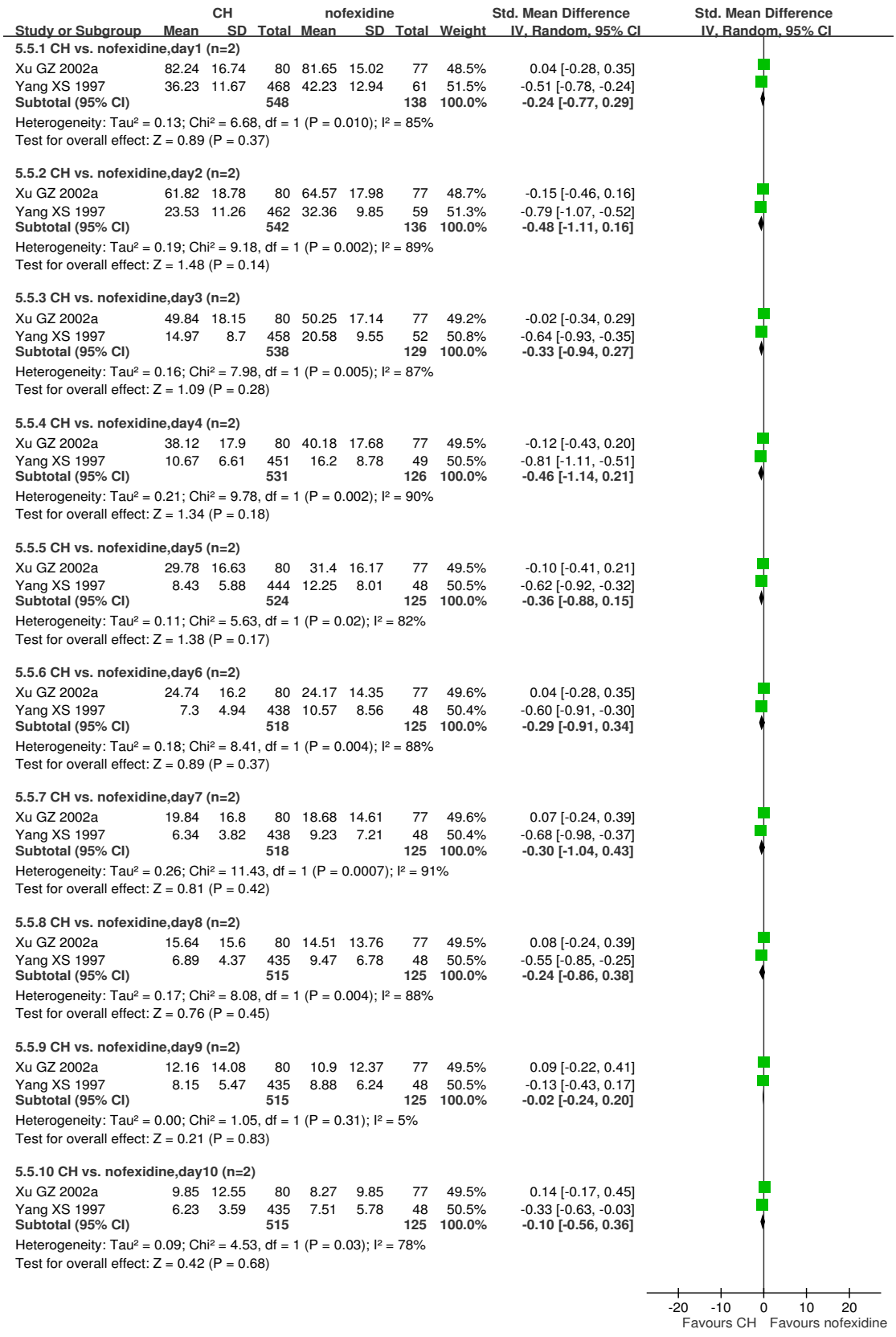



Fig 12. Meta-analysis on high-quality RCTs

Note: This was a subgroup meta-analysis of data in the Section 1.5.1 to 1.5.10 ( Fig.5).

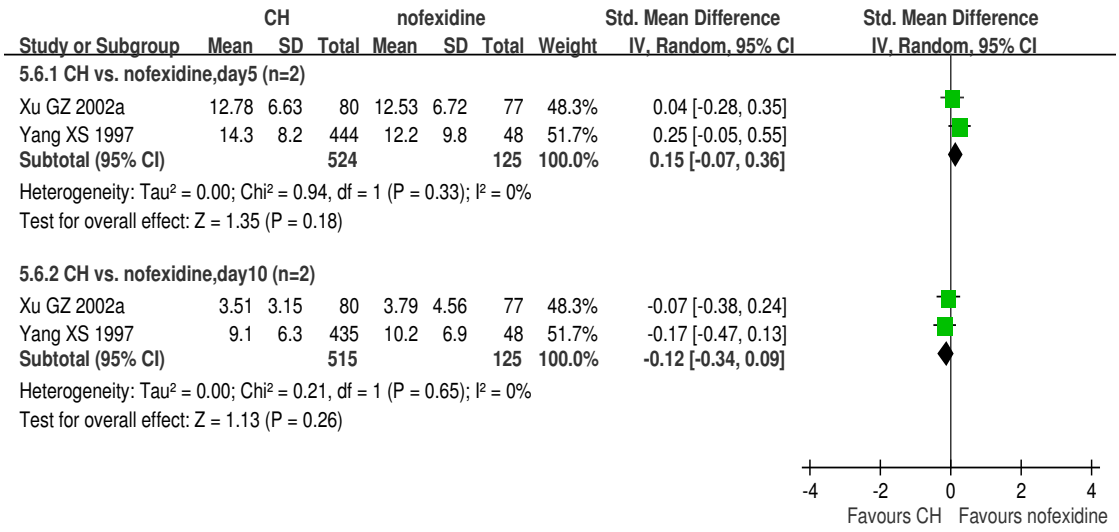



Fig 13. Meta-analysis on high-quality RCTs

Note: This was a subgroup meta-analysis of data in the Section 1.6.1 and 1.6.2 ( Fig.6).

### 3.1.3 Long-term detoxification of heroin dependence (14 RCTs)

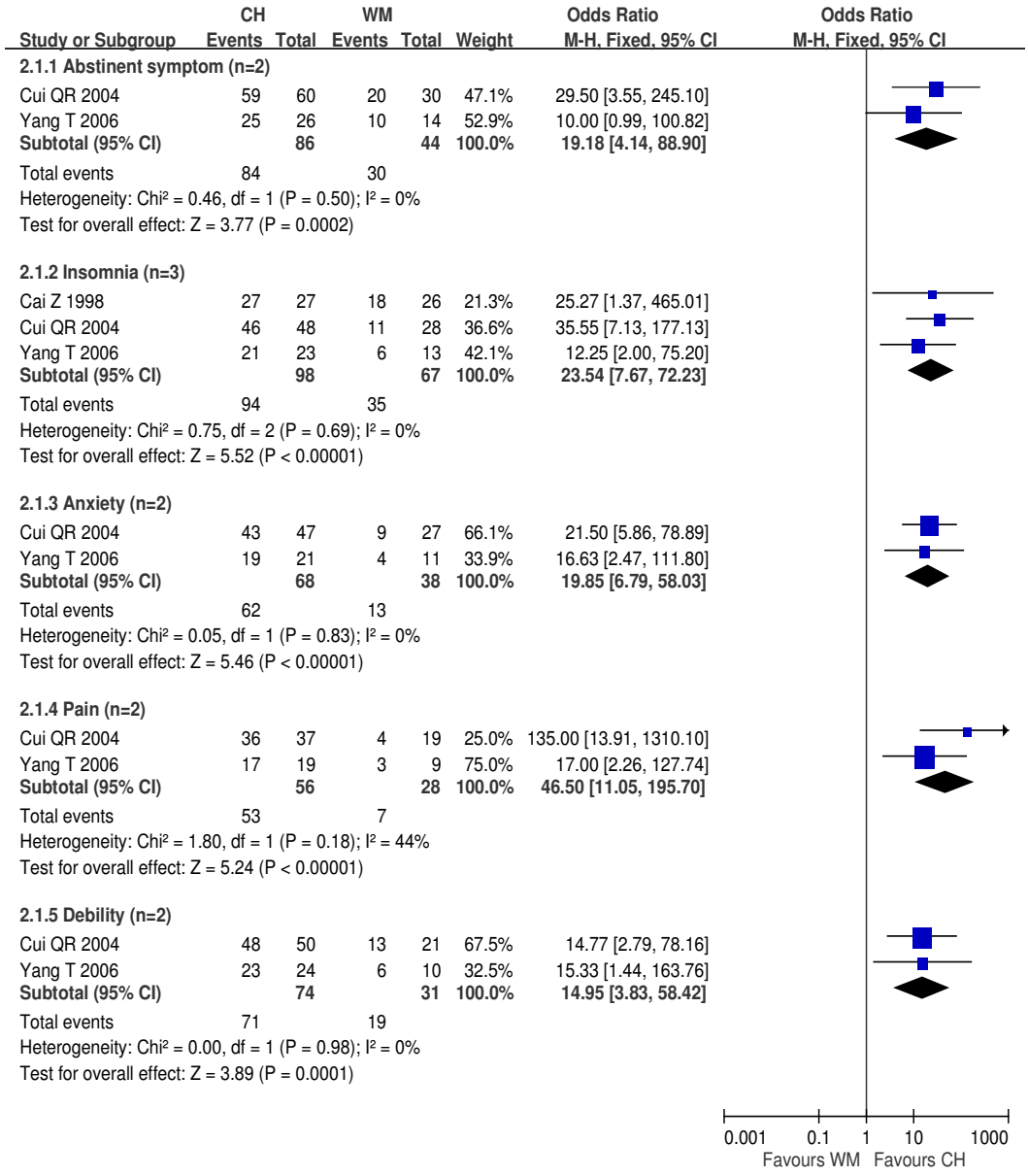



Fig 1. Meta-analyses of NIP of protracted abstinent symptoms (CH vs. WM)

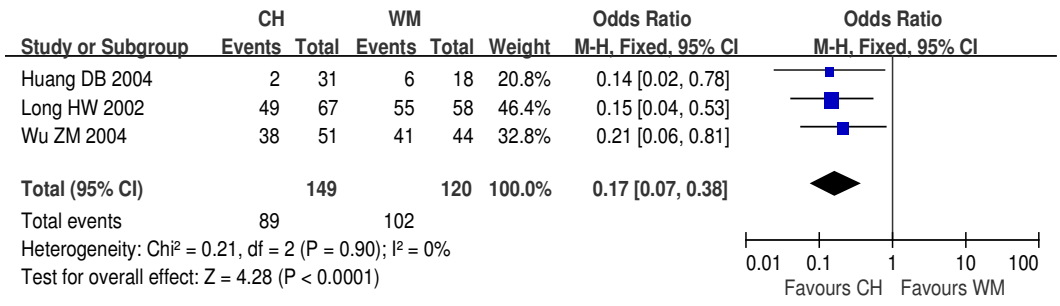



Fig 2. Meta-analyses of relapse rate (CH vs. WM)

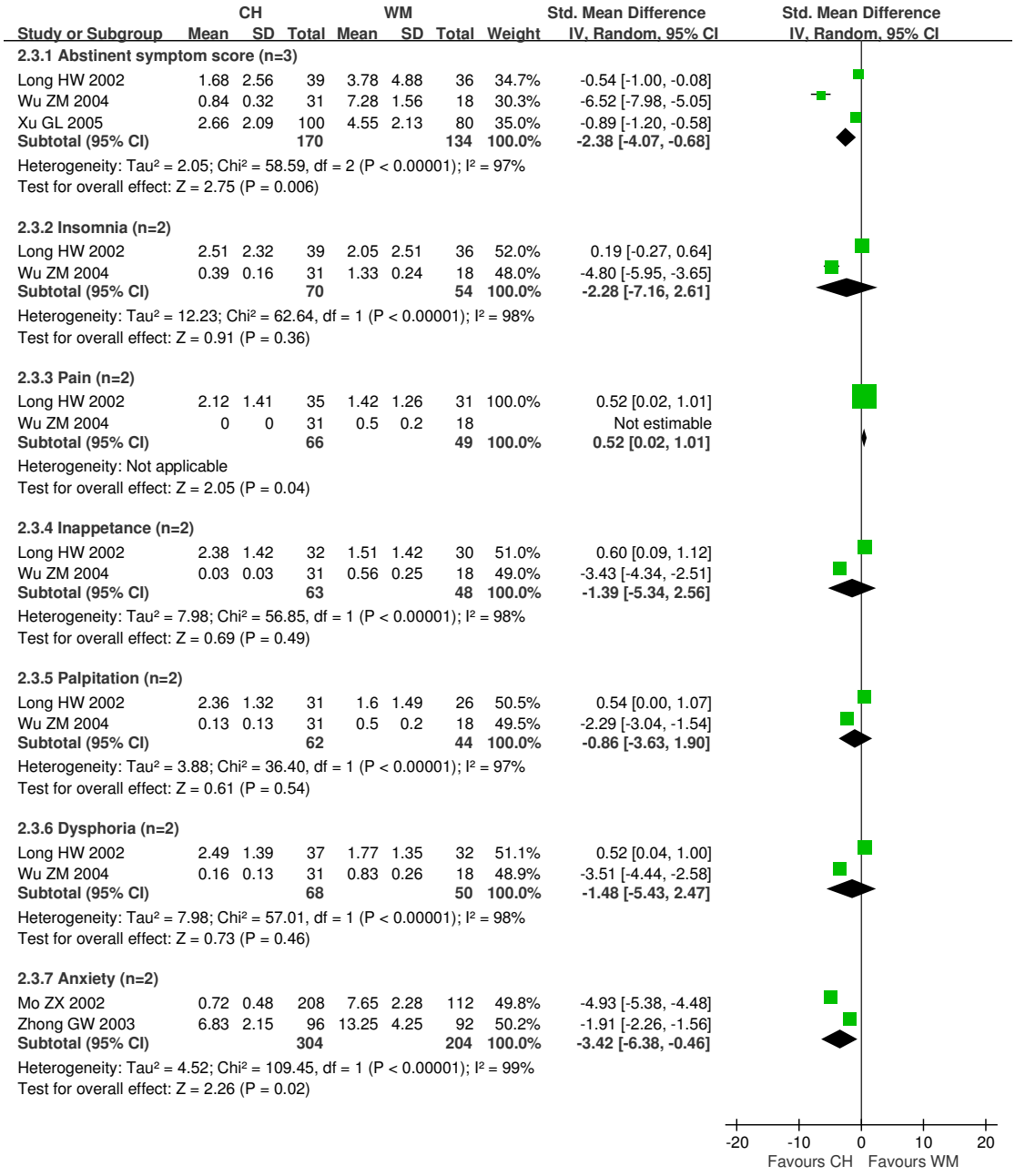



Fig 3. Meta-analyses of scores for protracted abstinent symptoms (CH vs. WM)

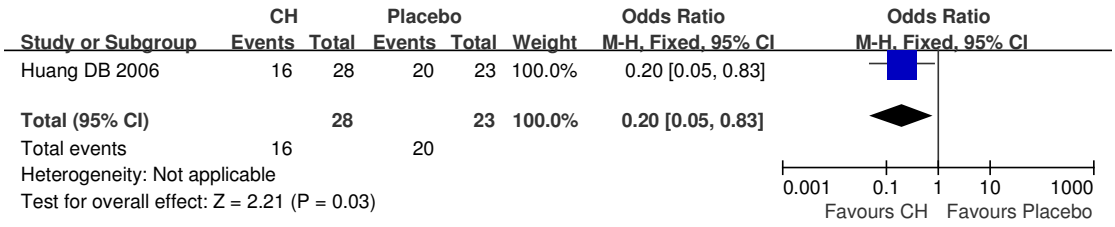



Fig 4. Meta-analyses of relapse rate (CH vs. Placebo)

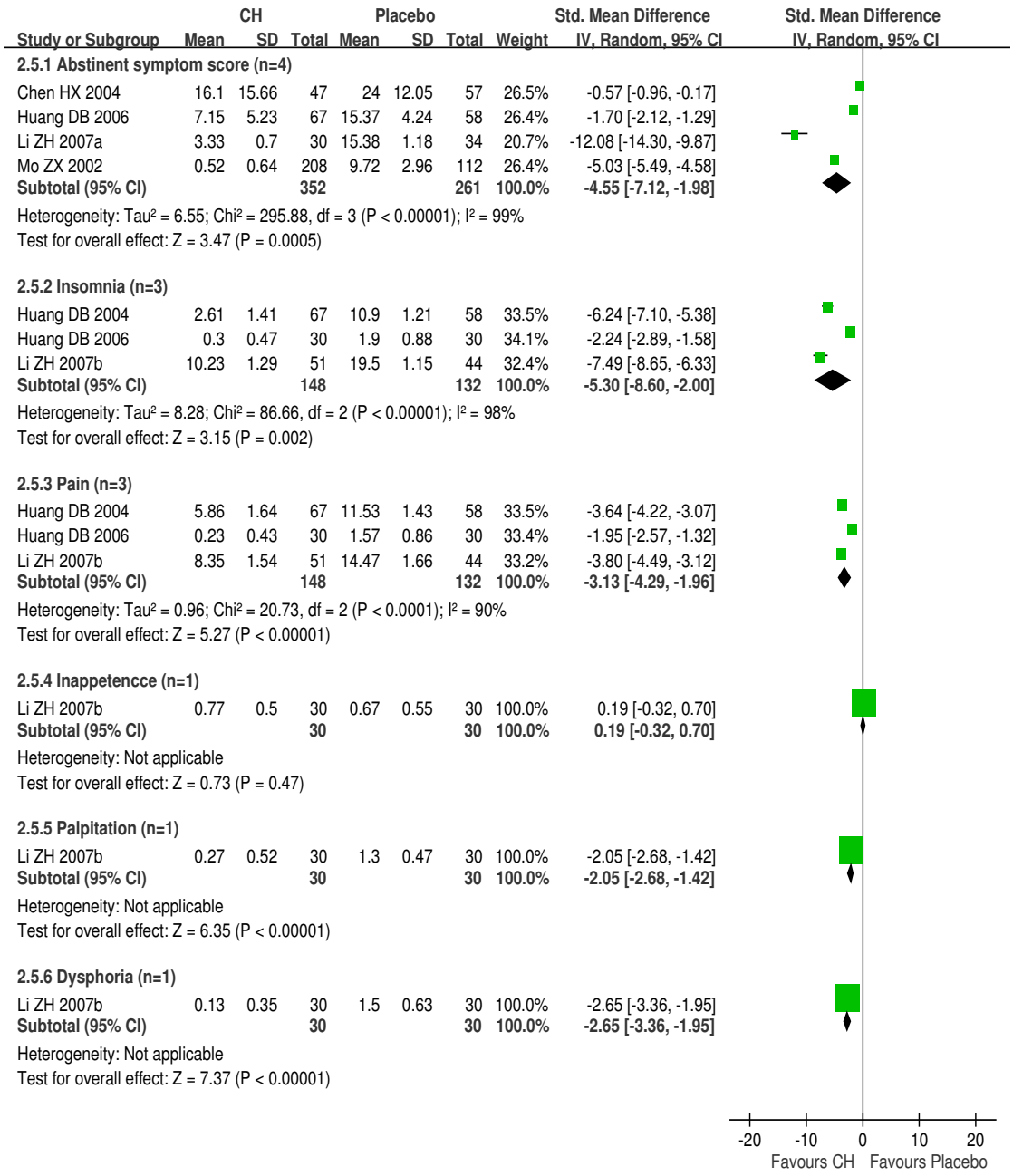



Fig 5. Meta-analyses of scores for protracted abstinent symptoms (CH vs. Placebo)

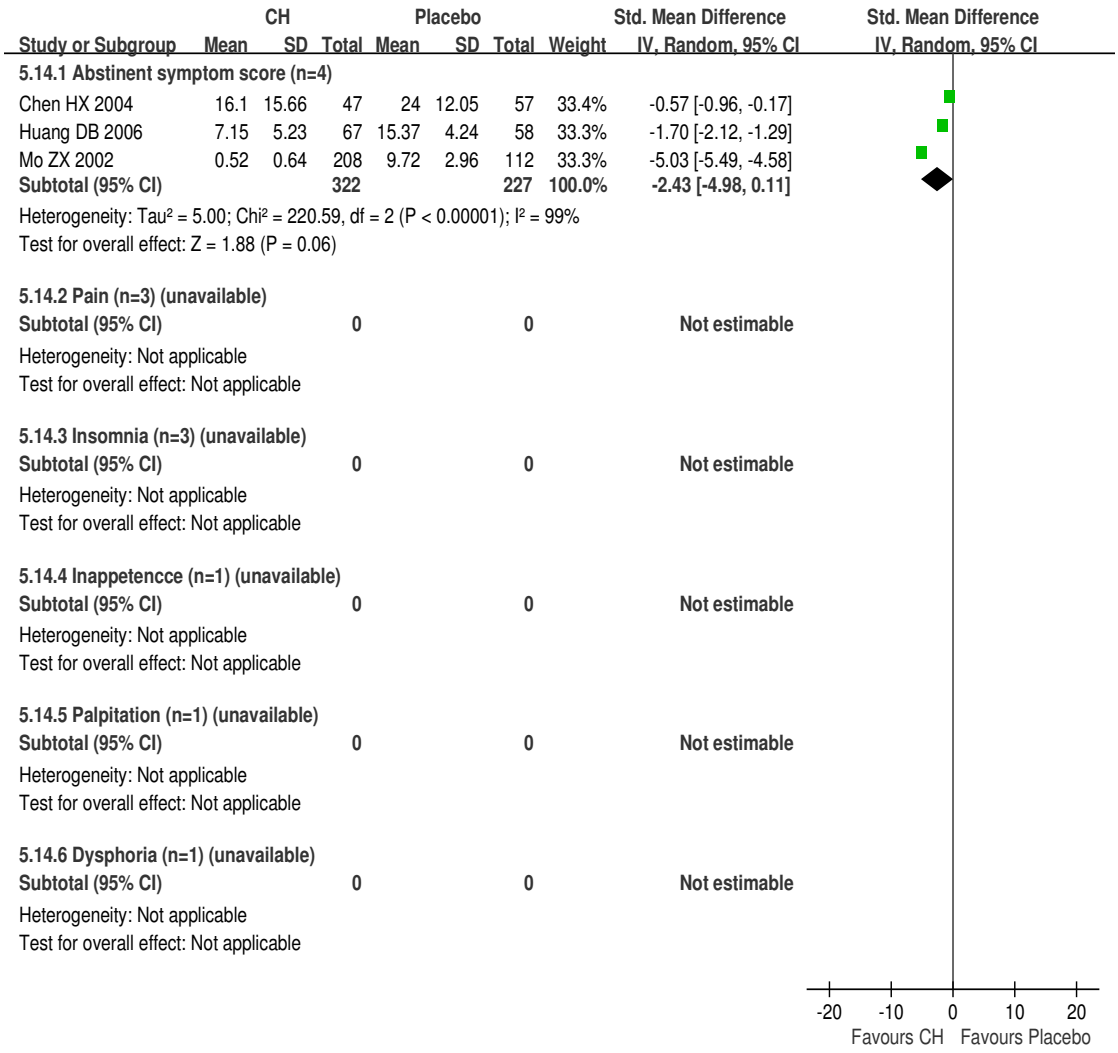
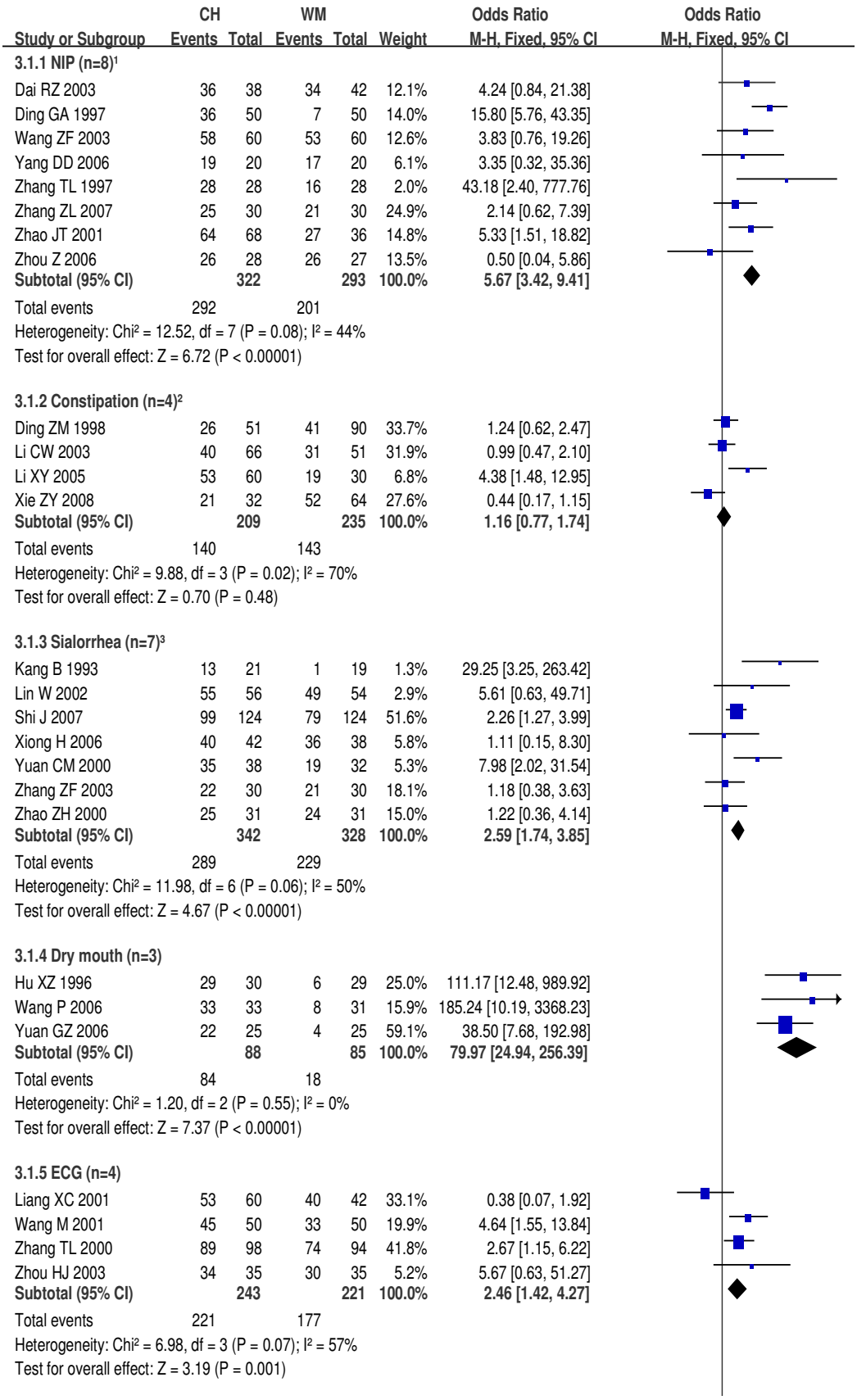



Fig 6. Meta-analysis on high-quality RCTs

Note: This was a subgroup meta-analysis of data in the Section 2.1.1 ( Fig.5).

### 3.1.4 Treating adverse symptoms of psychotropic drugs (57 RCTs)



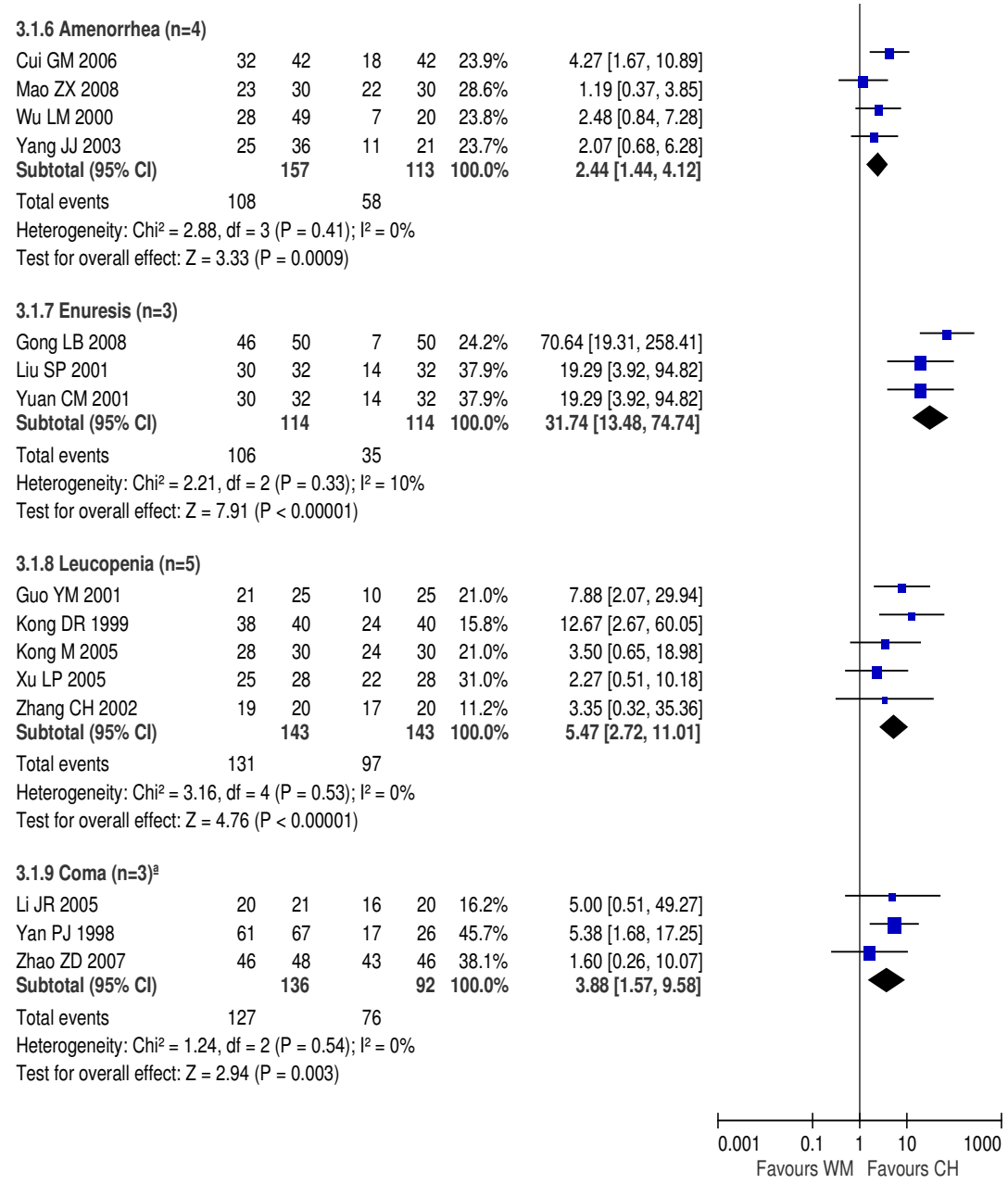



Fig 1. Meta-analyses of NIP of adverse symptoms (CH vs. WM)

Note: (1) Wang DH 2001 was deleted as heterogeneity (p=0.006, n=9, OR=6.43), and the result was in favor of the treatment group.

(2) Xie ZY 2008 was deleted as heterogeneity (P=0.02, n=5, OR=1.55).

(3) Wen YX 2008 was deleted as heterogeneity (P=0.005, n=8, OR=3.73), and the result was in favor of the treatment group.

(a) 6 trials (Zhao ZD 2007, Lin LS 2005, Li HJ 2004, Ding HT 2004, Lin XL 2003, Yuan ZQ 2001) reported resuscitation time (mean hrs) of patients with coma, but were not included because of heterogeneity (P=0.02, n=6, WMD=-1.90); and the result was in favor of the treatment group.

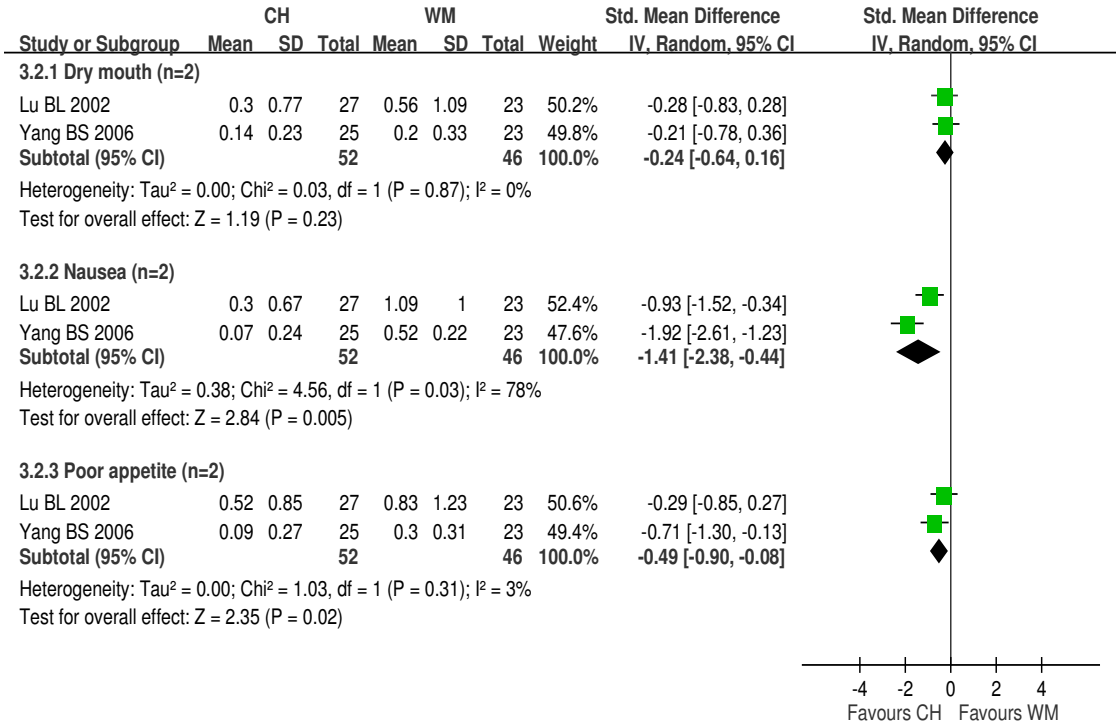



Fig 2. Meta-analyses of TESS of adverse symptoms (CH vs. WM)

Note: 7 trials (Zhang F 2005, Zhu YP 2005, Hu SH 2004, Li BJ 2002, Pan HM 2002, Yin CR 2000, Fan QZ 1996) were not included for meta-analysis. The date of other 4 trials reported TESS with different ways (total TESS, NIP, etc.) and 3 trials reported different endpoints (ALT, AST, score of sialorrhea, FBG, TC, TG, etc.)

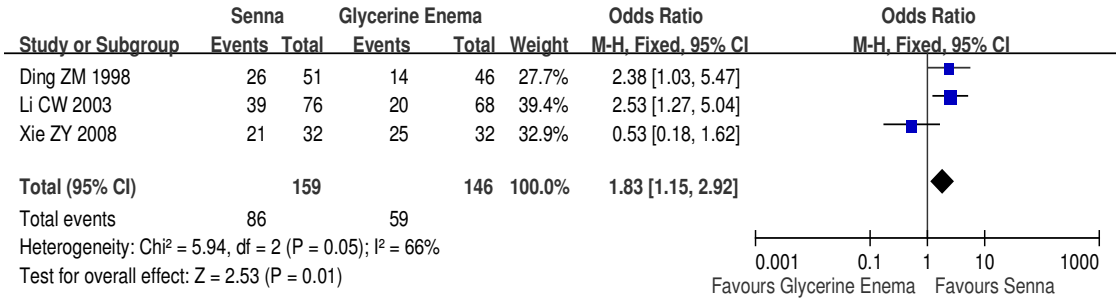



Fig 3. Meta-analysis on single herbal preparation (Senna vs. Glycerine Enema)

Note: This was a subgroup meta-analysis of data in the Section 3.1.2 Constipation ( Fig.1).

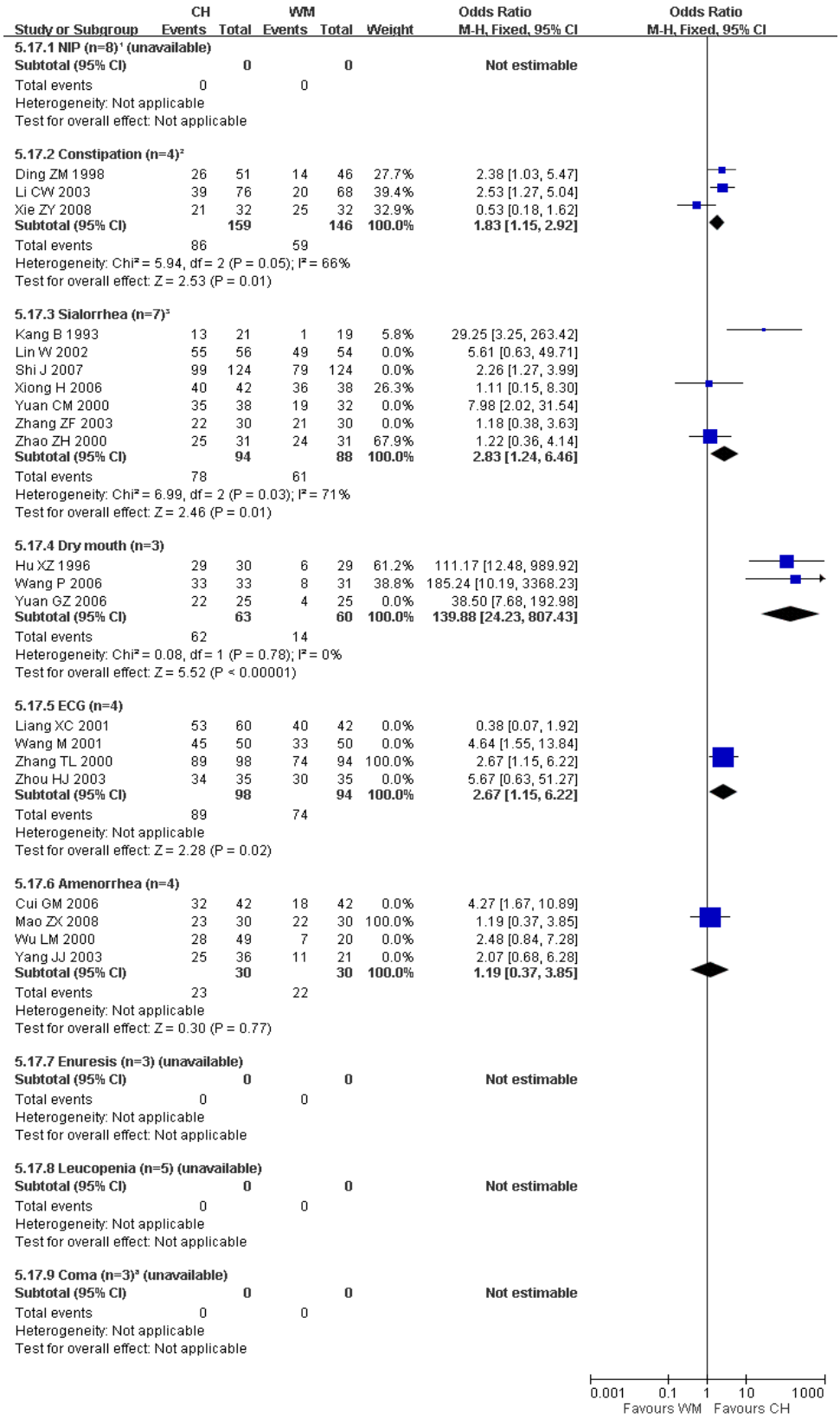



Fig 4. Meta-analysis on high-quality RCTs

Note: This was a subgroup meta-analysis of data in the Section 3.1.2 to 3.1.6 ( Fig.1).

## 3.2 Trial characteristics

### 3.2.1 Short-term detoxification of heroin dependence (36 RCTs)

| | |
|---|---|
| Trial 1 | Guo S, Jiang ZN, Wang Y, Hu G, Wu YM, Huang MS (1995) |
| Study eligibility | A comparative study of Chinese herbal medicine Fukang Pian with clonidine hydrochloride on opiate withdrawal symptoms |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria and positive urinary morphine analysis were enrolled, patients with serious physical and psychiatric diseases, or normal physical examinations were excluded. They were randomly allocated into treatment and control group. |
| Participant | N=316, 212 participants in the treatment group and 104 participants in the control group with the mean age 26.35 years old (treatment group) and 26.31 years old (control group). 71% males in the treatment group and 78.43% males in the control group. |
| Intervention | Treatment: Fukang Pian, 12-16 piece/day<br>Control: Clonidine, 1.0-1.5 mg/day<br>Dosage was gradually decreased during the Day 4-10. |
| Outcome | Abstinence symptom score for the Day 1-10, HAMA score on the D5 and 10, frequency of adverse effects, comparison of reduction rate of withdrawal syndrome scores after treatments were measured. |
| Trial duration | 10 days |
| Note | By using the CINA and HAMA score, the abstinence symptom and anxiety were recorded. Frequency of adverse reactions during treatment was reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 2 | Guo S, Jiang JY, Sheng LX (2001) |
| Study eligibility | A double-blinded randomized controlled trial of Zhengtongyin Decoction compared with clonidine in the treatment of heroin withdrawal symptoms |
| Method | Heroin addicts fulfilling the DSM-Ⅵ criteria with positive urinary morphine analysis and history of heroin addiction, aged between 16-45, were enrolled, and randomly allocated into the treatment, control and placebo groups by a ratio of 100:70:30. |
| Participant | N=216, 107 participants in the treatment group and 70 participants in the control group and 39 participants in the placebo group, with the mean age was 28.45, 29.20 and 29.46 years old in the treatment, control or placebo group respectively. 76.4% males and 23.4% females in the treatment group and 77.1% males and 22.9% females in the control group and 79.5% males and 20.5% females in the placebo group. |
| Intervention | Treatment: Zhengtongyin Decoction, 180 mg from D1-10 in a decrease dosage manner.<br>Control: Clonidine hydrochloride, 1 mg from D1-10 in a decrease dosage manner |
| Outcome | 10-day abstinence symptom score, HAMA score on D5 and 10, specific scores on shivering, yawning, insomnia, bone and muscle ache from Day 1 to 10, common adverse symptoms and adverse effect scores were reported. |
| Trial duration | 10 days |
| Note | By using the CINA and HAMA score, the abstinence symptom and anxiety were recorded. Common adverse symptoms and adverse-effect scores on the D1, 3, 6 and 7 were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 4 |

| | |
|---|---|
| Trial 3 | Huang MS, Li J, KW, Li JW, Wang XP, Zhang YM, Li JX, Liu TQ, Kang L, Li GH, Sun XL (2001) |
| Study eligibility | A multi-center clinical trial of Shengfutuodu Capsules to control heroin withdrawal symptoms |
| Method | Heroin addicts fulfilling the DSM-Ⅵ criteria with positive urinary morphine analysis and history of heroin addiction, aged between 18-45, were enrolled, and randomly allocated into the treatment or control groups. |
| Participant | N=293, 203 participants in the treatment group and 90 participants in the control group with the mean age 28.68 years old in treatment group and 28.64 years old in control group respectively, 83.7% males and 16.3% females in treatment group and 76.7% males and 23.3% females in control group. |
| Intervention | Treatment: Shengfutuodu Capsules, 2-4 pieces, t.i.d.<br>Control: Clonidine hydrochloride, 1-5 piece t.i.d. (0.075 mg/piece)<br>The dosage was gradually decreased from D1-10. |
| Outcomes | 10-day abstinence symptom score, HAMA score on D5 and 10, 10-day adverse-effect score and common adverse symptoms were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA and self-developed adverse-effect scoring system, the abstinence symptom, anxiety and adverse effect were recorded. 10-day adverse-effect score and common adverse symptoms were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 4 |

| | |
|---|---|
| Trial 4 | Hu GC, Huang MS (1995) |
| Study eligibility | A randomized controlled study on the detoxification effect of Fukang Pian in heroin addicts: Clinical report of 40 cases |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria and positive urinary morphine analysis with history of heroin addiction were enrolled and randomly allocated into treatment and control groups. |
| Participant | N=60, 40 participants in the treatment group and 20 participants in the control group, with the mean age 26.77 years old, 70% males and 30% females. |
| Intervention | Treatment: Fukang Pian, 3-6 g, t.i.d.<br>Control: Clonidine hydrochloride, 0.3-0.6 mg, t.i.d.<br>The doses in both groups were decreased after the D4. |
| Outcome | 10-day abstinence symptom score, HAMA score on D5 and 10, 10-day adverse-effect score, graph of daily change of adverse reaction and distribution of adverse reaction were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA and self-developed adverse-effect scoring system, the abstinence symptom, anxiety and adverse effects were recorded. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 5 | Kang L, Li J, Huang MS (2002) |
| Study eligibility | A randomized double-blind trial on effects of Kangfuxin, Fukangpian & clonidine hydrochloride for opiate withdrawal syndromes |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria with positive urinary morphine analysis, aged between 16-60 years old, were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=120 participants, 33 cases in the treatment group-1 (Kangfuxin), 28 cases in the treatment group-2 (Fukangpian), 30 cases in the clonidine group, and 29 cases in the placebo group. |
| Intervention | Treatment-1: Kangfuxin, 0.4 g/piece, t.i.d.<br>Treatment-2: Fukangpian, 10-13 pieces/day<br>Control-1: Clonidine, 0.075 mg/piece, t.i.d.<br>Control-2: Placebo, t.i.d. |
| Outcome | 10-day abstinence symptom score, HAMA score on D5 and 10, and 10-day adverse-effect score (graph) were reported. |
| Trial duration | 10 days |
| Note | Table of adverse effects according to the anti-opiate guide of Chinese government was used. By using the CINA, HAMA and self-developed adverse-effect scoring system, the scoring of abstinence symptoms, anxiety and adverse effects were recorded. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals/ drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 5 |

| | |
|---|---|
| Trial 6 | Li J, Wang MS, Liu W, Wan WP, Zhang B, Yang F, Tian WC, Liu B, Wang YL (1999) |
| Study eligibility | Evaluation of clinical efficacy of Lingyi Capsule in treating opiate withdrawal symptoms under a randomized controlled setting |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria with positive urinary morphine analysis and history of heroin addiction were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=330, 215 participants in the treatment group (70 cases in a double-blinded trial and 145 cases in an open trial) and 96 participants in the control group (70 cases in a double-blinded trial and 26 cases in an open trial), with the mean age 25.96 and 25.42 years old in the treatment and control group respectively. 92.2% males and 4.8% females in the treatment group and 46.2% males and 54.8% females in the control group. |
| Intervention | Treatment: Lingyi Capsule, 0.4 g/piece.<br>Control: Clonidine hydrochloride, 0.075 mg<br>The dose was gradually decreased during D4-10. |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, 10-day adverse-effect score, score of individual adverse effects (rhinorrhea, chilliness, myalgenia, abdominal pain, insomnia, spontaneous emission) were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA and self-developed adverse-effect score system, the abstinence symptom, anxiety and adverse effect were recorded. Self-developed tables for adverse effects, and body-weight changes were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 5 |

| | |
|---|---|
| Trial 7 | Lu XJ, Qin GC, Liang F, Ban CT, Li HX (2000) |
| Study eligibility | A randomized controlled study to compare effects of Baokangjiedu Chongji with clonidine in heroin addicts |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria, positive urinary morphine analysis were enrolled and randomly allocated into treatment and control groups by a computer generated random allocation table. |
| Participant | N=56, 30 participants in the treatment group and 26 participants in the control group with the mean age 23.5 years old, and 80% males and 20% females. |
| Intervention | Treatment: Baokangjiedu Chongji, 15 g, t.i.d.<br>Control: Clonidine, 0.075 mg/piece, 3 pieces/time, t.i.d. |
| Outcome | 5-day abstinence symptom score, incidence of adverse effects, urine morphine test results were reported. |
| Trial duration | 10 days |
| Note | By using the CINA scoring system, the abstinence symptom and incidence of adversee effects were recorded. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 5 |

| | |
|---|---|
| Trial 8 | Wang XP, Liu TQ, Ha W (2002) |
| Study eligibility | This was a double-blinded clinical controlled trial of Shengfutuodu Capsules to treat heroin withdrawal symptoms |
| Method | Heroin addicts fulfilling the DSM-Ⅵ criteria with positive TIC-test result, aged 18-45, were enrolled and were randomly allocated into treatment and control groups. |
| Participant | N=120, 90 participants in the treatment group and 30 participants in the control group, with the mean age 28.58 and 27.93 years old for treatment and control group respectively, 81% males and 19% females for treatment group and 80% males and 20% females for control group. |
| Intervention | Treatment: Shengfutuodu Capsules, 0.4g/piece<br>Control: clonidine hydrochloride, 0.075 g/piece<br>There was no mention of the dosage strategy. |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, scores for all withdrawal symptoms, 10-day comparisons of systolic and diastolic blood pressure, lab test results, incidence of adverse effects were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA and self-developed adverse-effect scoring system, the abstinence symptom, anxiety and adverse effect were recorded. Incidence of adverse effects was reported, and 5 drop-out cases were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| | |
|---|---|
| Trial 9 | Xu FZ, He Y L (2001) |
| Study eligibility | Clinical observation of 321 cases of opioid depencence treated with Sheungfu- tuodu Capsules under a randomized setting |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria with positive urinary morphine analysis, aged between 20-50 years old were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=321, 203 participants in the treatment group and 90 participants in the control group, with the mean age 32 years old, duration of heroin addiction from 5 months to 14 years. |
| Intervention | Treatment: Sheungfutuodu Capsule, 0.4g/piece, 3 pieces, t.i.d.<br>Control: Clonidine 0.075 mg/piece, 3 pieces, t.i.d. |
| Outcome | 10-day abstinence symptom score, HAMA score on day 5 and day 10, graph of adverse effect score were presented. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA, and a graph of adverse-effect score, the abstinence symptom, anxiety and adverse effect were recorded. Hb and WBC before and after treatment, and graph of adverse-effect scores were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| | |
|---|---|
| Trial 10 | Zhang RM, Li JX, Sun XH, Zheung L, Yang LP, Zhang J, Li JH, Ma KJ (2001) |
| Study eligibility | A double-blinded clinical trial of Shengfutuodu capsule in the treatment of heroin withdrawal symptoms |
| Method | Heroin addicts fulfilling the DSM-Ⅵ criteria were enrolled and randomly allocated into treatment and control groups. |
| Participant | N=110, 80 participants in the treatment group and 30 participants in the control group, with the mean age 28.19 years old in the treatment group and 28.03 years old in control group respectively, 91% males and 9% females in the treatment group and 97% males and 3% females in the control group. |
| Intervention | Treatment: Shengfutuodu Capsules, 1-4 piece, t.i.d.<br>Control: Clonidine hydrochloride, 0.075 mg/piece, 1-5 piece, t.i.d.<br>The dosage was in a decreased manner with days. |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, scores for insomnia and pain (bone and muscle) form D1-10, frequency of symptoms occurring percentage, 10-day adverse-effect score and incidence of common adverse effects were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA and self-developed adverse effect scoring system, the abstinence symptom, anxiety and adverse effect were assessed. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 3 |

| | |
|---|---|
| Trial 11 | Zhang GE, Li J, Hou JC, Xie LY, Bian RY, Chao YC (1998) |
| Study eligibility | A clinical observation of Tongdangduke Capsules to treat 32 cases of heroin dependents |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria with positive urinary morphine analysis and history of heroin addiction were enrolled, and randomly allocated into the treatment and control groups. |
| Participant | N=62, 32 participants in the treatment group and 30 participants in the control group. No mention of age and sex of the participants. |
| Intervention | Treatment: Tongdangduke Capsules, 8-13 pieces/day for a10-day program<br>Control: lonidine hydrochloride, 0.3-0.6 mg, t.i.d. |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5-10 were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA effect scoring system, the abstinence symptom and anxiety were recorded. There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 12 | Zhou C, Zhang DY, Bao HQ (2001) |
| Study eligibility | The comparative study of Tianchaokeli and clonidine for opiate withdrawal symptoms |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria with positive TIC test and aged 16-45 were enrolled, and were randomly allocated into the treatment and control groups. |
| Participant | N=106, 32 participants in the treatment group and 21 participants in the control group and 13 participants in the placebo group, other participants in an open-trial group, with the mean age 27.86 and 28.81 years old in the treatment and control group respectively, 80% males and 20% females in the treatment group and 82% males and 18% females in the control group. |
| Intervention | Treatment: Tianchaokeli, 15 g/U, D1-10: 12, 12, 12, 12, 8, 6, 5, 4, 2, 1U<br>Control: Clonidine hydrochloride: 0.075 g/piece, D1-10: 10, 10, 10, 7, 7, 7, 4, 4, 2, 2 pieces |
| Outcome | 10-day abstinence symptom score, common adverse effects with percentage were reported. |
| Trial duration | 10 days |
| Note | By using the CINA scoring system, the abstinence symptoms were assessed. Common adverse effects with percentage were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 3 |

| | |
|---|---|
| Trial 13 | Zhou C, Zhong D, Wang L (2004) |
| Study eligibility | The effect of treating opium withdrawal syndrome by TCM formula Yian Decoction and clonidine under a randomized controlled setting |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria and positive urinary morphine analysis were enrolled and randomly allocated into treatment and control groups. |
| Participant | N=99, 79 participants in the treatment group and 20 participants in the control group, with the mean age 6.9 years old, 71% males and 29% females. |
| Intervention | Treatment: Yian Decoction, 16 mg, b.i.d.<br>Control: Clonidine, 0.975 mg, t.i.d. |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, 10-day adverse-effect score, incidence of adverse effects were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA and self-developed adverse effect scoring system, the abstinence symptom, anxiety and adverse effect were recorded. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 3 |

| | |
|---|---|
| Trial 14 | Lan XY, Deng HC, Guo RQ, Liu BC, Chen ZQ, Bao CY (1997) |
| Study eligibility | Primary studies on Jieduqing for heroin detoxification |
| Method | Heroin addicts were enrolled and randomly allocated into 2 groups. |
| Participant | N=60, 40 participants in the treatment group and 20 participants in the control group. Participants' age and sex were not reported. |
| Intervention | Treatment: Jieduqing Capsules, 12-16 pieces/day<br>Control: onidine, 1-1.5 mg/day |
| Outcome | The number of improved patients whose heroin withdrawal syndrome was treated effectively. |
| Trial duration | 10 days |
| Note | The number of improved patients was recorded. Common adverse effects were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 15 | Mo ZX, Wang CY, Luo XY, Zhang XF (2003) |
| Study eligibility | Clinical observation of Qingfeng Capsules in the treatment of heroin addicts |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria with positive TIC-test results and history of heroin addiction were enrolled, and randomly allocated into the treatment and control groups. |
| Participant | N=186, 110 participants in the treatment group and 76 participants in the control group, with the mean age 30.67 years old in the treatment group and 30.12 years old in the control group respectively. 63% males and 37% females in the treatment group and 62% males and 38% females in the control group. |
| Intervention | Treatment: Qingfeng Capsules, 4 pieces, t.i.d.<br>Control: Nofexidine, 0.2 mg/day |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, urine morphine test before and after treatments, common adverse effects were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA score system, the abstinence symptom and anxiety were recorded. Common adverse symptoms were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 16 | Tu QX, Zhao HG, Chen YP, Chen YM, Wang XP, Hang M (1999) |
| Study eligibility | A randomized double-blind control trial of Jitai Capsule and nofexidine to treat opioid withdrawal syndrome |
| Method | The study enrolled heroin addicts fulfilling the DSM-Ⅲ-R criteria with aged 15-45 and positive urinary morphine analysis, and randomly allocated into treatment and control groups. |
| Participant | N=97, 48 participants (34 males & 14 females) in the treatment group and 49 participants (34 males & 15 females) in the control group, with the mean age 29.20 and 29.48 years old for the treatment and control group respectively. |
| Intervention | Treatment: Jitai Capsule, 0.5 g/capsule, 7.5 g/day<br>Control: Nofexidine: 3 piece (0.6 mg), t.i.d.<br>Dosage was gradually decreased after the D4. |
| Outcome | 10-day abstinence symptom score, NIP in abstinence symptom, Hama score on the D5 and 10, blood pressure, pulse variation before and after treatments were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA score system, the abstinence symptom and anxiety were recorded. The incidence of adverse effect was reported in detail. 5 drop-out cases in nofexidine group due to bradycardia (<50 beat/minute) were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 17 | Wen L, Zheng YS, Yu LZ, Mo ZX, Qu JW (2000) |
| Study eligibility | A clinical study of modified Shenfu Decoction in 68 heroin addicts |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria with positive urinary morphine analysis and history of heroin addiction, aged 16-45 years old, were enrolled and randomly allocated into treatment and control groups. |
| Participant | N=100, 68 participants in the treatment group and 32 participants in the control group, with the mean age 28.6 and 30.4 years old in the treatment and control groups respectively, 81% males and 19% females in the treatment group and 84% males and 16% females in the control group. |
| Intervention | Treatment: Shenfu Decoction, 10 ml/U, D1-3: 20 ml t.i.d.; D4-10: 10 ml, t.i.d.<br>Control: Nofexidine: D1-3: 0.4-0.6 mg, t.i.d.; D4-10: 0.2 mg, t.i.d. |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, blood pressure and heart rate variation before and after treatments, and incidence of adverse effects were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA score, abstinence symptom and anxiety were assessed. Incidence of adverse effects was reported (4 cases in control group had faint). |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 18 | Xu GZ, Duan LX, Liu C, Gao WY, Wang ZF, Xu BZ, Cai ZJ (2002) |
| Study eligibility | Randomised double-blind clinical research of Fuzhengkang Decoction for detoxification of heroin dependence |
| Method | Heroin addicts fulfilling the DSM-Ⅲ criteria with history of heroin addiction, aged 16-50 years old, were enrolled and randomly allocated into treatment and control groups. |
| Participant | N=421, 312 participants in the treatment group and 79 participants in the control group, 30 participants in the placebo group, with the mean age was 30.20, 29.60 and 29.93 years old respectively. 83% males and 17% females in the treatment group and 77% males and 23% females in the control group and 70% males and 30% females in the placebo group. |
| Intervention | Treatment: Fuzhengkang Decoction, 10 g/U, D1: 5U, q.i.d.; D2-3: 6U, t.i.d.; D4-6: 4U, t.i.d; D7-8: 3U, t.i.d.; D9: 2U, b.i.d.; D10: 1U, b.i.d.<br>Control-1: Nofexidine, 0.2 mg/piece; D1: 2 pieces, b.i.d.; D2-4: 3 pieces, t.i.d.; D5-7: 2 pieces, t.i.d.; D8: 1 piece, t.i.d.; D9: 1 piece, b.i.d.; D10: 1 piece.<br>Control-2: Placebo |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, and craving score, anxiety score, bone and muscle ache score, insomnia score, and common adverse effects were reported. |
| Trial duration | 10 days |
| Note | The abstinence symptom and anxiety were recorded by using CINA and HAMA scores. Common adverse effects were observed, and 2 drop-out cases were reported in control group as bradycardia. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 4 |

| | |
|---|---|
| Trial 19 | Xu LL, Zhu HT (2004) |
| Study eligibility | A randomized double-blinded control clinical trial on treating opiate withdrawal syndrome by Jitai Capsule and nofexidine |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria with history of heroin addiction and positive TIC test, aged 18-50, were enrolled and randomly allocated into treatment and control groups. |
| Participant | N=97, 48 participants in the treatment group and 49 participants in the control group, with the mean age 29.20, 29.48 years old in the treatment and control group respectively. 71% males and 29% females in the treatment group and 69% males and 31% females in the control group. |
| Intervention | Treatment: Jitai Capsule (洋金花，川芎，延胡索，丹參，當歸，0.5 g/capsule), 7.5 g/day<br>Control: Nofexidine, 0.2 mg, t.i.d. |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, incidence of adverse effects were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA score system, the abstinence symptom and anxiety were recorded. Incidence of adverse effects was reported. 5 drop-out cases were repoted due to bradycardia. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 20 | Yang XS, Mao C, Jing FB, Chu GY, Yang J (1997) |
| Study eligibility | Clinical research of Duyinxiao capsule to treat heroin withdrawal syndrome |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria were enrolled and randomly allocated into treatment and control groups. |
| Participant | N=483, 435 participants in the treatment group and 48 participants in the control group, with the mean age 23.4 years old, 88% males and 12% females<br>In the treatment group, and 22.7 years old, 85% males and 15% females in the control group. |
| Intervention | Treatment: Duyinxiao Capsule (栀子, 木香, 大黄, 元胡) 300 mg/capsule, D1-3: 10 capsules; D4-5: 6 capsules; D6-7: 3 capsules; D8-10: 1-2 capsules, b.i.d.<br>Control: Nofexidine, 0.2 mg/piece, 2-3 pieces, b.i.d. |
| Outcome | A 10-day abstinence symptom score, and Hama score on day 5 and 10 were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA score, the abstinence symptom and anxiety were recorded. Adverse effects were recorded and 4 drop-out cases in the control group were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 3 |

| | |
|---|---|
| Trial 21 | Zhou KC, Liu JG, Xie RQ (2003) |
| Study eligibility | An observation on clinical efficacy of Tuoduling Capsule in the treatment of heroin dependence |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria with history of heroin addiction and positive TIC-test result, aged 16-50, were enrolled, and randomly allocated into treatment and control groups. |
| Participant | N=182, 42 participants in the treatment group and 40 participants in the control group, with the mean age 32.38 and 31.73 years old in treatment and control group respectively. 78% males and 22% females in treatment group and 75% males and 25% females in the control group. |
| Intervention | Treatment: Tuoduling Capsule, 0.5g/U, 7 g, t.i.d, daily dosage was gradually decreased after D5.<br>Control: Nofexidine: 0.2 mg/U, D1: 0.4 mg t.i.d., D2-6: 0.4 mg t.i.d., D7-8: 0.2 mg b.i.d., D10: 0.2 mg q.d. |
| Outcome | 10-day abstinence symptom score, HAMA score on the D5 and 10, systolic and diastolic pressure, pulse score change, craving the D5 and 10, graph of 10-day adverse effect score. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA score system, the abstinence symptom and anxiety were recorded. A graph of 10-day adverse effect score was presented. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. is the blindness adequately described? | 0 |
| Total scores | 1 |

| | |
|---|---|
| Trial 22 | Zou DH, Liu TQ, Kuo W (1999) |
| Study eligibility | A randomized controlled study of Keyinning Capsules and nofexidine to treat opiate withdrawal syndromes |
| Method | The study enrolled heroin addicts fulfilling the DSM-Ⅵ criteria and randomly allocated them into the treatment and control groups. |
| Participant | N=65, the mean age was 32.1 years old, 83% males and 17% females. |
| Intervention | Treatment: Keyinning Capsule, D1-5: 10 piece/time, q.i.d.; D6-10: 8 piece/time, q.i.d.<br>Control: nofexidine, D1-5: 0.2-0.4 mg, t.i.d.; D5-10: 0.8-1 mg, t.i.d.<br>Dosage was grudually decreased after the D7. |
| Outcome | 10-day abstinence symptom score, changes of adverse scores during 10 days were reported. |
| Trial duration | 10 days |
| Note | Reported the adverse effect score in 10 days in a conclusive manner. 1 case drop-out due to incorporation. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 23 | Huang P, Wu G, Zhou PL, Wu HJ, Tang YM (2005) |
| Study eligibility | A clinical observation of Yian Decoction in treatment of heroin dependence |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria with positive urinary morphine analysis and 6 months or more additive history without serious disease were enrolled. They were randomly allocated into the treatment and control groups. |
| Participant | N=105, 53 participants in the treatment group and 52 participants in the control group, with the mean age 30.8 and 29.3 years old in the treatment and control group respectively, 75% males and 25% females. |
| Intervention | Treatment: Yian Decoction: 10 ml/unit, D1-3: 2-3 unit/time, t.i.d.; D4-10: 1 unit/time, t.i.d.<br>Control: Methadone: D1: 10-30 mg/day; D2: 20-40 mg; D3: 16-32 mg; D4: 12-26 mg; D5: 8-20 mg; D6: 6-16 mg; D7: 4-12 mg; D8: 2-8 mg; D9: 1-6 mg; D10: 1-4 mg; b.i.d. |
| Outcome | 10-day abstinence symptom score, HAMA scores on the D5 and 10, and adverse effects on the D5 and 10 were reported. |
| Trial duration | 10 days |
| Note | By using the OWS, HAMA scoring system, the abstinence symptom, anxiety and adverse effect were reported. Follow up for 1 month and TIC test. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 24 | Lu HQ, Wang G, Lan SM, Yuan TF, Jin ZM (1997) |
| Study eligibility | Clinical study on effects of Qingjunyin in the heroin detoxification |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria with positive urinary morphine analysis and history of heroin addiction, aged 18-35 years old, were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=200, 100 participants in the treatment group and 100 participants in the control group (50 methadone) and (50 clonidine), with the mean age was 23.5 years old, 77% males and 23% females. |
| Intervention | Treatment: Qingjunyin, 10 ml<br>Control: Methaodone, 5 mg/10 mg; Clonidine, 0.1 mg<br>The author did not mention the dosage strategy. |
| Outcome | 10-day abstinence symptom score |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA and self-developed adverse effect scoring system, the abstinence symptom, anxiety and adverse effect were recorded. There was no report on adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 25 | Sha LJ, Zhang ZX, Cheng LX, Liu J, Zhang ZM (2000) |
| Study eligibility | Treatment of Heroin abstinence syndrome by Xinxheng Oral-liquid: A clinical investigation of 424 cases |
| Method | Heroin addicts fulfilling the DSM-Ⅲ criteria with positive urinary morphine analysis and history of heroin addiction were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=100, 50 participants in the treatment group and 50 participants in the control group, with the mean age 30 years old, 70% males and 30% females. |
| Intervention | Treatment: Xinxheng Oral-liquid (党參, 元胡, 杜仲, 白花蛇舌草, 陳皮). D1-3: 100-150 ml, q4-6h; D4-5: 100-150 ml, q6-8h; D6-7: 50-100 ml, q6-8h; D8: 50-100 ml, q12h; D9: 50-100 ml, q12-24h; D10: observation only.<br>Control: Methadone, D1-3: 30 mg/d; D4-5: 120 mg/d; D6-7: 10-15 mg/d; D8: 10 mg/d; D9: 5 mg/d; D10: observation only. |
| Outcome | 9-day abstinence symptom score, withdrawal symptom score before and after treatments were reported. |
| Trial duration | 10 days |
| Note | By using the CINA score system, the abstinence symptoms were recorded. There was no report of adverse effects. There were 9 withdrawal cases with serious withdrawal symptoms that could not be controlled satisfactorily. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 26 | Xu BS, Tie EG, Wang PX, Lu QL, Sun ZW, Jin J, Sun ZT (2000) |
| Study eligibility | A controlled clinical trial using Qingdubuzheng Decoction to treat heroin dependence |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria with positive urinary morphine analysis and history of heroin addiction were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=40, 20 participants in the treatment group and 20 participants in the control group, with the mean age 31.35 and 29.25 years old in the treatment and control groups respectively, 100% males in the treatment group and 85% males and 15% females in control group. |
| Intervention | Treatment: Qingdubuzheng Decoction (夏天無, 人參, 甘草, 制附片, 羌活, 當歸, 徐長卿, 細辛, 姜黃, 金銀花), D1: 60 ml, q2h; D2-3: 60 ml, q3h; D4-5: 50 ml, q4h; D6-7: 40 ml, q6h; D8: stop treatment (10-15 ml for drug history over 5 years).<br>Control: methaodone, D1-3: 20-40 mg/day, decrease 10 mg per day after D4 |
| Outcome | 10-day abstinence symptom score, HAMA score from the D1 to 8, frequency of adverse effects were reported. |
| Trial duration | 10 days |
| Note | By using the CINA, HAMA and self-developed adverse-effect scoring system, the abstinence symptom, anxiety and adverse effect were recorded. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 27 | Yang L, Xu X, Chen J, Li LJ, Weng PX, Zhang XL (2006) |
| Study eligibility | Controlled clinical study on Paiduyangsheng Capsule in detoxification of heroin abuse |
| Method | Heroin addicts fulfilling the DSM-IV-R criteria with positive urinary morphine analysis and history of heroin addiction over 9 months were enrolled, and randomly allocated into the treatment and control groups. |
| Participant | N=580, with 302 participants (196 male & 106 female) in the treatment group and 278 participants in the control group (185 male & 93 female). The mean age was 23.4 years old. |
| Intervention | Treatment: Paiduyangsheng Capsule (紅參, 三七, 兩面針, 元胡, 天麻, 龍膽草, 大黃), D1-3: 3-5 capsules/12h; D4-6: 2-4 capsules/12h; D7-10: 1-2 capsules/12h<br>Control: Methaodone: D1-3: 40-50 mg/24h; then 20% decrease per day after the D4; and D10: 1-2 mg. |
| Outcome | 10-day abstinence symptom score, Hama score and NIP on the D2, 4, 9 and 10 were reported. |
| Trial duration | 10 days |
| Note | By using the OWS, HAMA score, the abstinence symptom and anxiety were recorded. There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 3 |

| | |
|---|---|
| Trial 28 | Chao XM, Hu WJ (2005) |
| Study eligibility | A clinical research of Yian Decoction in treating heroin dependence |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria with history of heroin addiction and positive TIC-test result, aged 15-45, were enrolledand and randomly allocated into the treatment and control groups. |
| Participant | N=90, 60 participants in the treatment group and 30 participants in the control group, with the mean age was 28.9 years old, 79% males and 21% females. |
| Intervention | Treatment: Yian Decoction, 10 ml/U, D1-3: 3U, t.i.d.; D4-7: 2U, b.i.d.; D8-10: 1U, b.i.d.<br>Control: Buprenorphine, D1-2: 2.2 mg, q8h; D3: 1.6 mg, q8h; D4: 1 mg q8h; D5: 0.8 mg q8h; D6: 1mg, b.i.d.; D7: 0.6 mg b.i.d.; D8: 0.4 mg, b.i.d.; D9: 0.3 mg, b.i.d.; D10: 0.4 mg, q.d. |
| Outcome | 10-day abstinence symptom score |
| Trial duration | 10 days |
| Note | By using the OWS score system, the abstinence symptoms were recorded. There was no report on adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 29 | Hao W, Zhao M (2000) |
| Study eligibility | A comparative study on the effect of WeiniCom, a Chinese herbal compound, in alleviation of heroin withdrawal symptom and craving |
| Method | Heroin addicts fulfilling the DSM-Ⅵ criteria with history of heroin addiction and positive TIC-test result were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=42, 21 participants in the treatment group and 21 participants in the control group, with the mean age 26.2 years old, 88% males and 12% females in the study. |
| Intervention | Treatment: WeiniCom, 10 capsules, 4-5 times per day.<br>Control: Buprenorphine, 0.9-1.2 mg b.i.d. |
| Outcome | 10-day abstinence symptom score, craving rating score, side-effect rating score, urine test, etc. were reported. |
| Trial duration | 10 days |
| Note | By using the WSRS, craving rating score system, side effects rating scale, the abstinence symptom, craving and side effect was recorded. Adverse-effect scores over 10 days were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 30 | Liu Jy, Gu Q, Wu XW, Zhou JY (1997) |
| Study eligibility | A clinical study of Yijienin Decoction to treat opiate dependence |
| Method | Heroin addicts fulfilling the DSM-ⅢⅠ-R criteria with history of heroin addiction and positive TIC-test results, aged 15-45, were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=64, 48 participants in the treatment group and 49 participants in the control group, with the mean age 28.94 years old. 70% males and 30% females. |
| Intervention | Treatment: Yijienin (川烏 15g, 細辛 30g, 乾姜 15g, 紅參 15g, 黃連 10g, 黃柏 30g), 1.5 g/ml, 20 ml t.i.d<br>Control: Buprenorphine, 3, 4, 6 mg/day for mild, mediate and severe patients.<br>The dosage was decreased after the D5. |
| Outcome | 10-day abstinence symptom score on the D5 and 10, serum FSH, E2, PRL, etc. were reported. |
| Trial duration | 10 days |
| Note | By using the CINA score system, the abstinence symptom was recorded. There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 31 | Liu JY, Yang QH, Wu XW (2001) |
| Study eligibility | A clinical study on the treatment of heroin abstinence syndrome by compound *yang*-warming, *qi*-invigorating and blood-activating prescription |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria with history of heroin addiction and positive TIC-test results, aged 15-45, were enrolled and randomly allocated into the treatment and control groups. |
| Participant | N=66, 34 participants in the treatment group and 32 participants in the control group, with the mean age 29.7 and 19.32 years old in the treatment and control group respectively. 65% males and 35% females in the treatment group and 69% males and 31% females in control group. |
| Intervention | Treatment: Herbal Prescription (附子, 紅參, 元胡, 等), Mild: 20 ml t.i.d. Mediate: 30 ml q.i.d., Severe: 40 ml q.i.d.<br>Control: Buprenorphine, 3, 4, 6 mg/day for mild, mediate and severe patients.<br>Dosage was gradually decreased after the D7. |
| Outcome | 10-day abstinence symptom score on the D1, 2, 3, 4, 5, 7, 10 only, Serum FSH, E2, PRL, LH, etc. were reported. |
| Trial duration | 10 days |
| Note | By using the OWS score system, the abstinence symptom was recorded. There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 32 | Zhu CQ, Zhang HS, Fan XC, Chen DM (1999) |
| Study eligibility | Treatment of heroinism by Jiedutuoyin Capsule in 131 cases |
| Method | Heroin addicts fulfilling the DSM-Ⅲ criteria with history of heroin addiction, positive TIC-test results, were enrolled and randomly allocated into the treatment and control group. |
| Participant | N=256, 131 participants in the treatment group and 125 participants in the control group, with the mean age 27.2 and 19.32 years old in the treatment and control group respectively, 87% males and 13% females in the treatment group and 82% males and 18% females in control group. |
| Intervention | Treatment: Jiedutuoyin Capsule (川烏, 黃耆, 鈎藤, 党參, 元胡, 細辛, 梔子, 雞血藤, 黃連, 黃柏, 生地, 山茲, 茯苓, 丹皮), 3.0 g, t.i.d. for mild patients, or 4.8 g, q.i.d. for mediate and severe patients. Observation was conducted during and after 8 days.<br>Control: Buprenorphine 3, 4, 6 mg/day for mild, mediate, severe patients Dosage was decreased after the D5 and treatment was stopped on the D8. |
| Outcomes | 10-day abstinence symptom score (Data on D1, 3, 5, 7, 9 only) was reported. |
| Trial duration | 10 day |
| Note | By using the self-developed core system, the abstinence symptoms was recorded. There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 33 | Yang T, Ma JQ, Sun XJ, Lin Z (2001) |
| Study eligibility | The clinical study on the efficacy of acupuncture for heroin detoxification was performed. However, the Chinese herbal medicines were also studied |
| Method | Heroin addicts fulfilling the DSM-ⅢI-R criteria with history of heroin addiction, positive TIC-test results, were enrolled, and randomly allocated into the treatment and control group. |
| Participant | N=25, 15 participants in the treatment group and 10 participants in the control group, with the mean age 28.9 years old, 60% males and 40% females. |
| Intervention | Treatment: Herbal decoction (黃連, 白朮, 枳壳, 熟地, 等 9 味中藥), D1-3: 150 ml, q.i.d.; D4-10: 150 ml, t.i.d.<br>Control: Valium, 10 mg/day |
| Outcome | 10-day abstinence symptom score. |
| Trial duration | 10 days |
| Note | By using the Himmelsbach score, the abstinence symptoms were recorded. There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 34 | Zong L, Hu J, Li Yu, Lu Ying, Xin YF (2001) |
| Study eligibility | The effects of acupuncture and Chinese medicine in the treatment of heroin addiction |
| Method | Heroin addicts fulfilling the DSM-Ⅲ-R criteria with history of heroin addiction, positive TIC-test results, were enrolled, and randomly allocate into the treatment or control group. |
| Participant | N=51, 23 participants in the treatment group and 28 participants in the control group, with the mean age was 30.4 years old, 45.8% males and 54.2% females. |
| Intervention | Treatment: Qiedu Capsule-1, 4 capsules b.i.d., D1-3<br>Qiedu Capsule-2, 4 capsules b.i.d., D4-10<br>Control: Valium, 10 mg/day, D1-10 |
| Outcome | 10-day abstinence symptom score |
| Trial duration | 20 days |
| Note | There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 35 | Xiao ZX, Qin DS, Li J, Min MS, Ren GH, Yang JH (2007) |
| Study eligibility | The observation of curative effect of methadone and Yianhuisheng Oral-liquid for treating heroin addicts |
| Method | Heroin addicts fulfilling the DSM-Ⅳ criteria with opium withdrawal syndromes, positive urine morphine-test results were enrolled, and randomly allocated into 3 group. |
| Participant | N=150, 50 participants in each group. The mean age was 33.3 years old. 85.38% males and 14.70% females. |
| Intervention | Treatment: Yianhuisheng Oral-liquid, 20-80ml/day<br>Control-1: Methadone, 0-40 ml/day<br>Control-2: Methadone, 40-32-25 ml on the D1-3; 20-16 ml on D4-6 and Yianhuisheng Oral-liquid, 10-80 ml on D4-10. |
| Outcome | 10-day abstinence symptom score, anxiety score, and pupilla change were recorded. |
| Trial duration | 10 days |
| Note | There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 36 | Xiong JG, Li J (2000) |
| Study eligibility | Clinical observation of treating heroin dependence with the combination of traditional Chinese medicine and Western medicine |
| Method | Heroin addicts with positive urine morphine-test result were enrolled, and randomly allocated into 3 groups. |
| Participant | N=240, 80 participants in each group with the mean age 27.4 years old; 62.67% males and 37.33% females. |
| Intervention | Treatment: Jitai Capsule, 4 pieces in the D1-3, 3 pieces in the D4-6, 2 pieces in the D7-8, 1 piece in the D9-10.<br>Control-1: Tramadol 100 mg/day.<br>Control-2: Jitai Capsule and Tramadol |
| Outcome | The number of improved patients whose heroin withdrawal syndrome treated effectively was recorded. |
| Trial duration | 10 days |
| Note | Common adverse effects were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

### 3.2.2 Long-term detoxification of heroin dependence (14 RCTs)

| | |
|---|---|
| Trial 1 | Cai Z, Xu SH (1998) |
| Study eligibility | Clinical observation of 50 cases for treatment of protracted abstinent syndrome by using Guipi Decoction |
| Method | 100 heroin addicts who met the dependence criteria made by Chinese National Institute on Drug Dependence were randomly assigned to two treatment groups. Subjects of each group were treated for 6 days with Guipi Decoction and Oryzanol after 10 days' detoxification, and were assessed with improvement of 3 protracted abstinent syndromes. |
| Participant | N=100, 50 patients in each group. |
| Intervention | Treatment: Guipi Decoction (白術, 茯苓, 黃芪, 龍眼肉, 酸棗仁, 黨參, 木香, 當歸, 遠志, 大棗, 甘草), b.i.d.<br>Control: Oryzanol, 20 mg, t.i.d. |
| Outcome | Patients' number of improvement of anorexy, spontaneous perspiration and insomnia were recorded after treatments. |
| Trial duration | 6 days |
| Note | There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 2 | Chen HX, Hao W, Liu TQ (2004) |
| Study eligibility | A controlled study on clinical efficacy of Chinese herbal compounds, Anjunning and Kanfuxin on alleviating opioid protracted abstinent symptoms |
| Method | 166 heroin addicts for compulsive detoxification who met the DSM-IV criteria were randomly assigned to three treatment groups. Subjects of each group were treated for one month with Anjunning, Kanfuxin and placebo according to the principle of parallel-control and double blindness, and were assessed with self-rating scale of protracted abstinence symptoms on the D7, 14, 21, 28, 35, 42, 56 and 70 after admission. |
| Participant | N=166, Anjunning group (n=47), Kanfuxin group (n=58), and Placebo group (n=61), with age 18-55. |
| Intervention | Treatment-1: Anjunning, 6 g, b.i.d.<br>Treatment-2: Kanfuxin, 2 capsules, b.i.d.<br>Control: Placebo, 2 capsules, b.i.d. |
| Outcome | Self-rating scale of protracted abstinence symptoms on the D7, 14, 21, 28, 35, 42, 56 and 70 after admission, the total score of the self-rating scale on emotional symptoms factor, sleeping factor, physical symptoms factor and craving factor were rassessed. |
| Trial duration | 56 days |
| Note | There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| | |
|---|---|
| Trial 3 | Cui QR, Li H, Li CP, et al (2004) |
| Study eligibility | The practical research on the treatment of protracted opioid abstinence syndrome by Corydalisyanhusuo Capsules |
| Method | The addicts were divided into two groups randomly, i.e. the treatment group treated with Corydalisyanhusuo Capsules; and the control group adopted support treatments. Then the effects of treatments between two groups were compared. |
| Participant | N=90, treatment group (n=60), aged 26-36; control group (n=30), aged 27-37. |
| Intervention | Treatment: Corydalisyanhusuo Capsule, 5 capsules, t.i.d.<br>Control: 10% Glucose 500 ml + ATP 40 mg + Coenzyme A 100U + Vitamin C 2.0 g + Vitamin B6 0.2 mg + 10% Glucose Gluconate, i.v. daily; and Lannaconitine 4 ml, i.m. for pain; Atropine p.o. for abdominal pain and salivation; Diazepam 10 mg p.o. or i.m. for insomnia and anxiety. |
| Outcome | Protracted opioid abstinence syndrome was observed. |
| Trial duration | 21 days |
| Note | There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 4 | Huang DB, Liu XL, Yu ZF, Fu L (2004) |
| Study eligibility | Efficacy of Huoxiangzhengqi Oral-liquid and tablet of Radix et Caulis Acanthopanacis Senticosi for heroin withdrawal symptoms |
| Method | 137 heroin addicts were randomly divided into three groups, i.e. control group, treatment group A and B. They were detoxified by using Lofexidine Hydrochloride Tablet (LFX) for 12d, and then, the control group was treated with an imitate preparation, the treatment group A was treated with Huoxiangzhengqi Oral-liquid and Tablet of Radix et Caulis Acanthopanacis Senticosi (HOL+TRCAS) for 60 days, but group B took HOL+TRCAS from the beginning of detoxification. |
| Participant | N=137, Treating group A (n=42), Treating group B (n=51), Control group (n=44), aged 18-45. |
| Intervention | (LFX treatment for 12 days from the beginning of detoxification)<br>Control: Placebo (starch tablets)<br>Treatment A: HOL+TRCAS 4 tablets, b.i.d. for 60 days.<br>Treatment B: HOL+TRCAS 4 tablets, b.i.d. for 72 days from the beginning of detoxification. |
| Outcome | The protracted abstinent syndromes for the three groups were observed and scored for 7 days, and the drug re-abusing cases of the three groups were investigated by urinoscopy one year later. |
| Trial duration | 72 days |
| Note | There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 0 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 5 | Huang DB, Yu ZF, Fu L (2006) |
| Study eligibility | Efficacy of modified Banxiahoupu Decoction on protracted abstinence syndrome and 1-year relapse rate after heroin-dependence detoxification |
| Method | 187 cases were randomly divided into three groups, namely control group, treatment group A and B. They were detoxified by using Lofexidine Hydrochloride Tablet (LFX) for 12 days, and then, the control group took an imitate preparation, the treatment group A took Banxiahoupu Decoction for 60 days, while treatment group B took Banxiahoupu Decoction for 72 days. |
| Participant | N=187, Control group (n=58), Treatment group A (n=62), Treatment group B (n=67), aged 18-44. |
| Intervention | (LFX treatment for 12 days from the beginning of detoxification)<br>Control: Placebo<br>Treatment A: Banxiahoupu Decoction for 60 days<br>Treatment B: Banxiahoupu Decoction for 72 days |
| Outcome | The protracted abstinent syndrome of the three groups was observed before and after treatments. 5 protected abstinent syndromes were scored after treatment. The drug re-abusing cases of the three groups were investigated through urinoscopy one year later. |
| Trial duration | 72 days |
| Note | There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 3 |

| | |
|---|---|
| Trial 6 | Jian YP, Wang DM, Nie RC (2007) |
| Study eligibility | Clinical observation of 91 cases for the treatment of protracted abstinent headache based on differential treatment of Jueyin |
| Method | 181 heroin addicts who met the CCMD-3 criteria and VAS score their headache was assessed by. They were randomly assigned to two treatment groups. Subjects of each group were treated for 14 days with Dangguisini Decoction etc. and Somedon etc. after Methadone detoxification, and were assessed with number of improved patients and VAS score after treatments. |
| Participant | N=181, 91 patients in the treatment group and 90 in control group. |
| Intervention | Treatment: Dangguisini (or Sini or Longdanxiegan) decoction<br>Control: Somedon, 2-4 tablets/4-6 hours or Bucinperazine, 60-120 mg/4-6 hours |
| Outcome | Number of improvement of VAS score, the change of VAS score after treatment, clinical global impression score and efficacy index were recorded. |
| Trial duration | 6 days |
| Note | TESS score and adverse-effect severity index were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 7 | Li ZH, Lv Q, Du Q, Wang Y (2007) |
| Study eligibility | The clinical efficacy of Chinese herbs for heroin addicts with *qi* and *yin* deficiency |
| Method | 100 addicts who met the DSM-Ⅳ criteria with positive TIC-test result were randomly assigned to 2 groups. Subjects in the treatment group were treated with Yiqiziyinanshen Decoction for 10 days, and were assessed with total protracted abstinent-syndrome score on the D0, 5 and 10, and compared with that of the blank-control group |
| Participant | N=100, 50 patients in each group. |
| Intervention | Treatment: Yiqiziyinanshen decoction (黃芪, 人參, 川芎, 當歸, 延胡索, 麥冬, 沙參, 珍珠母, 柏子仁，酸棗仁, 等) b.i.d<br>Control: blank |
| Outcome | Protracted abstinent-syndrome score was assessed. |
| Trial duration | 10 days |
| Note | There was no report of adverse effects. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 8 | Li ZH, Tang YX, Hua SZ, Wang Y (2007) |
| Study eligibility | Efficacy of Jitai for protracted withdraw symptoms of heroin dependence |
| Method | 60 heroin addicts who met the DSM-Ⅳ criteria with positive TIC-test result were randomly assigned to the treatment group and black control group. Subjects in the treatment group were treated with Jitai tablets for 5 days after methadone-detoxification progam, and were assessed with protracted abstinent-syndrome score after treatment; and compared with that of blank control group. |
| Participant | N=60, 30 patients were divided into each group. |
| Intervention | Treatment: Jitai tablets, 2 tablets, t.i.d.<br>Control: Blank |
| Outcome | Protracted abstinent-syndrome score was recorded before and after treatments. |
| Trial duration | 5 days |
| Note | Hydrodipsia, dry mouth, nausea, vomit, dizzy, discomfort after eating, etc. were observed. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 9 | Long HW, Mei ZL, Den CL (2002) |
| Study eligibility | Treatment of heroin protracted abstinent-syndrome by herbal detoxification and nourishing *qi* -- Clinical observation of 39 cases |
| Method | Patients were randomly divided into herb-treatment group and clonidine-control group. Marks were calculated by using designed questionnaire. |
| Participant | N=75, Chinese medicine observation group n=39, clonidine control group n=36. Aged 16-43. |
| Intervention | Herb-treatment group: Chinese medicine observation group:<br>Clonidine-control group: 2-3 tablets t.i.d, for the D1-3, 654-2 and benzodiazepines were given when necessary. |
| Outcome | The scale of protracted abstinent syndrome and adverse effect were recorded. |
| Trial duration | 15 days |
| Note | Two cases with sinus bradycardia and shock, and 1 case with Adams' stoke were reported, and dropped out from the study. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 10 | Mo ZX, Wang CY, Luo XY, et al. (2002) |
| Study eligibility | A study on the efficacy of Qingfeng Capsules for protracted withdrawal syndrome of heroin addicts |
| Method | 320 heroin addicts after detoxification over 10 days were randomly divided into placebo group and Qingfeng Capsule group for 30-day treatments. The efficacy of two groups were compared. |
| Participant | N=320. Qingfeng Capsule group (n=208), placebo group (n=112), aged 17-46. |
| Intervention | Treatment: Qingfeng Capsules, 2 capsules, b.i.d. for 30 days.<br>Control: Placebo (starch), 0.2 g/capsule, 2 capsules, b.i.d. for 30 days. |
| Outcome | History of each case, score of protracted withdrawal symptom and anxiety were recorded. Adverse reactions were also reported. |
| Trial duration | 30 days |
| Note | 9 cases treated by anti-allergy drug and disappeared in 2-3 days had skin allergy. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| | |
|---|---|
| Trial 11 | Wu ZM, Jia SWi, Luo HE, Wu P, Xie XJ, Ou HH, Yin SG (2004) |
| Study eligibility | Clinical observation on U'finertm Capsules for the treatment of heroin induced prolonged withdrawal symptoms |
| Method | 70 heroin addicts with prolonged withdrawal symptoms were randomly divided into two groups, and one group treated with U'finertm Capsules, another group treated with Naltrexone as control. |
| Participant | N=70, Treatment group (n=40), Control group (n=30), aged 17-36. |
| Intervention | Treatment: U'finertm Capsule 1.5 mg, p.o. t.i.d. for 6 months<br>Control: Naltrexone 15 mg, p.o. daily for 6 months |
| Outcome | Revised scale for heroin prolonged withdrawal symptoms. SPECT DAT imaging was used in the study. |
| Trial duration | 6 months |
| Note | |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 0 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 12 | Xu GL, Wang CS, Song XZ, Yang F, Wang Z, Tang ZL (2005) |
| Study eligibility | Clinical study on treating protracted abstinence syndrome in heroin addicts by Yiyinningsheng Decotion (YYNSD) |
| Method | 180 heroin addicts with protracted abstinence syndrome were randomly divided into the treatment group and control group. |
| Participant | N=180, treatment group (n=100), aged 16-42, control group (n=80), aged 16-39. |
| Intervention | Treatment: Concentrated pill of YYNSD, 10 g b.i.d. for 20 days<br>Control: Blank |
| Outcome | Scores of protracted abstinence syndrome was recorded. |
| Trial duration | 20 days |
| Note | |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 0 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 13 | Yang T, Yang Y, Huang ZF (2006) |
| Study eligibility | The effects of Yianhuisheng Oral-liquid in the treatment of heroin protracted abstinent syndrome -- Observation of 40 cases |
| Method | Heroin addicts were randomly separated into the treatment group and control group. Patients in the treatment group were treated Yianhuisheng Oral-liquid, while control group were treated by support therapy and heteropathy. |
| Participant | N=40, 26 cases in the treatment group and 14 cases in the control group, aged 22-48. |
| Intervention | Treatment: Yianhuisheng Oral-liquid, daily.<br>Control: For support therapy: Gamma Oryzanol 20 mg, t.i.d., Vitamin B6 20 mg t.i.d.; For heteropathy: Ibuprofen 0.2 mg p.o. for pain, Diazepam 7.5 mg for insomnia and anxiety, Metoclopramide 10 mg i.m. for nausea and vomiting. |
| Outcome | Score for protracted abstinent syndrome were recorded. |
| Trial duration | 10 days |
| Note | |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 14 | Zhong GW (2003) |
| Study eligibility | The treatment of protracted withdrawal-syndrome of heroin dependence in 96 cases |
| Method | 188 heroin addicts were treated by detoxifying herbs and herbs for nourishing *qi* and regulating blood, and were compared the results with the Naltrexone-control group. |
| Participant | N=188, treatment group (n=96), control group (n=92), aged 15-45. |
| Intervention | Treatment: Herbal decoction<br>Control: Naltrexone, 25 mg for the first dose, if no serious adverse reaction then continue to give until 50 mg, afterwards for each Monday and Wednesday, 100 mg of Naltrexone was given, for each Friday, 150 mg of Naltrexone was given. |
| Outcome | Scores of CINA, HAMA, and HAMD were recorded. Pain scale was also measured. |
| Trial duration | 42 days |
| Note | Main adverse reactions including lymphocyte increase, ALT increase, ECG disoder, constipation, skin irritation, blurred sight and others were recorded |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrwals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

### 3.2.3 Treating adverse symptoms of psychotropic drugs (57 RCTs)

| | |
|---|---|
| Trial 1 | Li XY, Wang XL (2005) |
| Study eligibility | A comparative study on the effect of Rhubarb Mirabilis and Magnolia Officinalis Rehd et Wils in treating neuroleptic-induced astriction |
| Method | Psychotics fulfilling the CCMD-2-R criteria and suffering from neuroleptic -induced astriction, aged 21-72, were enrolled, and were randomly allocated into the treatment and control groups. By observing patient's defecation conditions, the effects of Rhubarb Mirabilite and Magnolia Officinalis Rehd et Wils or Senna Tea were recorded. Adverse effects were also recorded. |
| Participant | N=90, 30 participants in the treatment-1 group (Jiangjuntongyou Powder), 30 participants in the Treatment-2 group (Senna Tea), and 30 participants in the control group, with the mean age 41.3 years old. |
| Intervention | Treatment-1: Jiangjuntongyou Powder, 6-8 g/time, after breakfast<br>Treatment-2: Senna Tea, 400 ml/time<br>Control: Phenolphthalein, 2 tablets/time |
| Outcome | Effect scores of treating narcoleptic-induced astriction |
| Trial duration | 1 day |
| Note | Adverse effects during treatment were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 2 | Xie ZY, Yao XF, Su M, Zhao YH (2008) |
| Study eligibility | A comparative study on the therapeutic effects of 3 different approaches in treating neuroleptic-induced astriction |
| Method | Psychotics fulfilling the CCMD-3 criteria and suffering from neuroleptic -induced astriction, aged 16-59, were enrolled, and were randomly allocated into 3 groups. By observing the defecation conditions of the patients, efficacy and adverse effect were recorded. |
| Participant | N=96, 32 participants in the treatment group (Senna), 32 participants in the control-1 group (Mannitol) and 32 participants in the control-2 group (Glycerine Enema). |
| Intervention | Treatment: Senna tea, 500 ml/day<br>Control-1: 20 % Mannitol, 125 ml/day<br>Control-2: Glycerine Enema, 80 ml/time |
| Outcome | Clinical results |
| Trial duration | 1 day |
| Note | Common adverse effects and adverse-effect scores were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 3 | Ding ZM (1998) |
| Study eligibility | A comparative randomized controlled clinical study of different approaches in treating neuroleptic-induced astriction |
| Method | Psychotics fulfilling the CCMD-II criteria and suffering from neuroleptic -induced astriction, aged 17-60, were enrolled, and were randomly allocated into 4 treatment groups. By observing the defecation conditions of the patient, effects of drugs were recorded. Adverse effect was also recorded. |
| Participant | N=174, 51 participants in the treatment group, 46 participants in the Control-1 group (Glycerine Enema), 44 participants in the Control-2 group (Vitamin $B_1$) and 33 participants in the control-3 group (Warm salt water). Age and gender of the participants did not be mentioned. |
| Intervention | Treatment: Senna mixture, 20 ml/day<br>Control-1: Glycerine Enema<br>Control-2: Vitamin $B_1$, 20 mg/day<br>Control-3: 1.5% Warm salt water, 500 ml/day |
| Outcome | Clinical results |
| Trial duration | 23 days |
| Note | Common adverse effects and adverse-effect scores were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 4 | Li CW (2003) |
| Study eligibility | A comparative study of different approaches in treating neuroleptic-induced astriction |
| Method | Psychotics fulfilling the CCMD-II criteria and suffering from neuroleptic -induced astriction, aged 17-60, were enrolled, and were randomly allocated into 4 groups. By observing the defecation conditions of the patients, effects of interventions were compared. |
| Participant | N=261, 66 participants in the treatment-1 group (Maziren Pill), 76 participants in the treatment-2 group (Senna mixture), 68 participants in the control-1 group (Glycerine Enema) and 51 participants in the control-2 group (Warm salt water), with 83% males involved in the study. The participants' age did not be mentioned. |
| Intervention | Treatment-1: Maziren Pill, 6 g/day<br>Treatment-2: Senna mixture, 20 ml/ay<br>Control-1: Glycerine Enema<br>Control-2: 1.5% Warm salt water, 500 ml/day |
| Outcome | Clinical results |
| Trial duration | 25 days |
| Note | Self-developed scale of adverse effect was used. Common adverse effects and adverse-effect scores were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 5 | Pan HM, Li JW (2002) |
| Study eligibility | A randomized controlled clinical trial on Shenqiwuweizi Tablet in treating side effects induced by antipsychotics |
| Method | Psychotics fulfilling the CCMD-3 criteria and suffering from neuroleptic -induced heart, liver and renal impairments, aged 24-74, were enrolled, and were randomly allocated into treatment group and control group. By TESS scoring system, effects of interventions were compared. |
| Participant | N=76, 46 participants in the treatment group (Shenqiwuweizi Tablet), 30 participants in the control group, with the mean age 37.5 years old (treatment group) and 35.2 years old (control group) respectively, and 65.2% males in the treatment group, and 66.7% males in the control groups. |
| Intervention | Treatment: Shenqiwuweizi Tablet, 3 tablets, t.i.d<br>Control: Vitamins or other drugs |
| Outcome | TESS score |
| Trial duration | 6 weeks |
| Note | No adverse effect caused by interventions was reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 1 |

| | |
|---|---|
| Trial 6 | Yang BS (2006) |
| Study eligibility | A randomized controlled clinical study of Wendan decoction in treating neuroleptic-induced adverse effects |
| Method | Psychotics fulfilling the CCMD-3 criteria and suffering from neuroleptic -induced dyspepsia, aged 22-54, were enrolled, and of cases with serious diseases were excluded. They were randomly allocated into the treatment group and control groups. By TESS scoring system, effects were assessed. |
| Participant | N=140, 70 participants in the treatment group, 70 participants in the control group, with the mean age 29.97 years old, and there was 100% males in the study. 45 and 25 participants were treated with chlorpromazine and clozapine in the treatment group, while 47 and 23 participants were treated with chlorpromazine and clozapine in the control group. |
| Intervention | Treatment: Wendan Decoction, 400 ml/day, 6 days/week and Chlorpromazine, max. dosage 500 mg/day or Clozapine, max. dosage 450 mg/day<br>Control: Chlorpromazine, max. dosage 500 mg/day or Clozapine, max. dosage 450 mg/day |
| Outcome | TESS score was reported. |
| Trial duration | 6 weeks |
| Note | No adverse effect was reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 2 |

| | |
|---|---|
| Trial 7 | Zhang F, Fei JF, Lu GH, Lu SL (2005) |
| Study eligibility | A comparative study of randomized controlled clinical trials of the efficacy of Chinese medicine decoction in the prevention of hyperglycemia hyperlipemia and other adverse events caused by antipsychotic |
| Method | Psychotics fulfilling the CCMD-3 criteria and exclusion of serious physical and other cardiac, liver, endocrine and nervous system linked disease, normal physical examination, aged 17-59, were enrolled, and were randomly allocated into treatment group and control group. By TESS scoring system, effects of drugs were recorded. |
| Participant | N=110, 53 participants in the treatment group, 57 participants in the control group with the mean age 31.1 years old (treatment group) and 32.0 years old (control group) respectively, and there was 100% males in the study. |
| Intervention | Treatment: Self-prepared herbal decoction, b.i.d.<br>Control: antipsychotic drugs.<br>Decreasing dosage every 2 days after the first month in the treatment group. |
| Outcome | Comparison of difference in TESS scales between 2 groups |
| Trial duration | 60 days |
| Note | Self-developted scale, blood sugar, cholesterol and triglyceride levels were reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| | |
|---|---|
| Trial 8 | Hu SH, Xu SQ (2004) |
| Study eligibility | A comparative study of randomized controlled clinical trials of the efficacy of self prepared Chinese medicine decoction in treating anticholinergic effect caused by antipsychotics |
| Method | Psychotics fulfilling the CCMD-3 criteria aged 18-65, were enrolled, and were randomly allocated into treatment group and control group. By TESS scoring system, effects of drugs were recorded. |
| Participant | N=100, 50 participants in the treatment group, 50 participants in the control group, with the mean age 37 years old (treatment group) and 36 years old (control group) respectively, and there was 74% males in the treatment group and 78% males in the control group. |
| Intervention | Treatment: Self-prepared herbal decoction, 1000 ml/day<br>Control: Anethol trithione tablet, 25 mg/time, q.i.d. |
| Outcome | Comparison of difference in TESS scales between 2 groups |
| Trial duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 9 | Li BJ, Fang M, Fan CL, Wu B (2002) |
| Study eligibility | A randomized controlled clinical study of the efficacy of Fuan Decoction in the prevention of adverse effect caused by antipsychotics |
| Method | Psychotics fulfilling the CCMD-II-R criteria aged 16-56, were enrolled, and were randomly allocated into the treatment group and control group. By TESS scoring system, effects of drugs were recorded. |
| Participant | N=40, 21 participants in the treatment group, 19 participants in the control group, with the mean age 31 years old (treatment group) and 29 years old (control group) respectively, and there was 66.7% males in the treatment group and 63.2% males in the control group. |
| Intervention | Treatment: Fuan Decoction, b.i.d.<br>Control: No drug was prescribed. |
| Outcome | Comparison of difference in TESS scales between 2 groups |
| Trial duration | 7 days |
| Note | Self-developed scale to compare adverse effects caused by antipsychotic before and after treatment. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 10 | Lu BL, Chen CP (2002) |
| Study eligibility | A comparative randomized controlled clinical study of the effectiveness of anshenjianpi syrup in the treatment of antipsychotic-induced side reactions of digestion tract |
| Method | Psychotics fulfilling the CCMD-2-R criteria and suffering from neuroleptic -induced digestion impairment, aged 16-54, were enrolled, and were randomly allocated into the treatment group and control group. By TESS scoring system, effects of drugs were recorded. |
| Participant | N=143, 71 participants in the treatment group, 72 participants in the control group, with the mean age of all participants 29.97 years old, and there was 100% males in the study. 45 participants and 27 participants were prescribed chlorpromazine and clozapine in the treatment group respectively, while 49 participants and 23 participants were prescribed chlorpromazine and clozapine in the control group. |
| Intervention | Treatment: Anshenjianpi syrup, 50 ml, t.i.d and Chlorpromazine, max. dosage 700 mg/day or Clozapine, max. dosage 400 mg/day<br>Control: Chlorpromazine, max. dosage 700 mg/day or Clozapine, max. dosage 400 mg/day |
| Outcome | TESS score was measured, and the first TESS scores on day 10 and the rest on every 2 weeks were reported. |
| Trial duration | 6 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 3 |

| | |
|---|---|
| Trial 11 | Yin CR (2000) |
| Study eligibility | A comparative randomized controlled clinical study of the preventive and curative effect of Shengmai Yin on the adverse drug reactions of antipsychotics |
| Method | Psychotics fulfilling the CCMD-2-R criteria and suffering adverse effect induced by antipsychotic, aged 19-66, were enrolled, and were randomly allocated into treatment group, prevention group and control group. By TESS scoring system, effects of drugs were recorded. |
| Participant | N=180, 60 participants in the treatment group, 60 participants in the prevention group and 60 participants in the control group, and there were 58.89% males in the study. There was no mention on the mean age of the participants. |
| Intervention | Treatment: Shengmai Yin,10 ml, q.i.d.<br>Prevention: Shengmai Yin, 10 ml, q.i.d. and Antipsychotics<br>Control: Antipsychotics |
| Outcome | TESS score was measured, and TESS scores of every 2 weeks were reported. |
| Trial duration | 6 weeks |
| Note | No adverse effect was reported. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| | |
|---|---|
| Trial 12 | Zhu YP (2005) |
| Study eligibility | A comparative randomized controlled clinical study of the efficiency and possible mechanism of liver ferment resulted from Composite Salviae Dropping Pill (CSDP) together with Clozapine |
| Method | Psychotics fulfilling the CCMD-3 criteria and exclusion of serious physical and other cardiac, liver, endocrine and nervous system linked disease, normal physical examination, aged 18-60, were enrolled, and were randomly allocated into treatment group and control group. By ALT, AST and U/L rating system, effects of drugs were recorded. |
| Participant | N=99, 51 participants in the treatment group and 48 participants in the control group, with the mean age 24.1 years old (treatment group) and 24.8 years old (control group), and 62.75% males in the treatment group and 62.50% males in control group. |
| Intervention | Treatment: CSDP, 10 pills, q.i.d.<br>Clozapine (dose ?) was used in both group, t.i.d. |
| Outcome | ALT, AST and U/L scores were measured. |
| Trial duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 13 | Fan QZ, Zhang LY, Dan H, Yu SW, Bo CG, Zhao HQ (1996) |
| Study eligibility | A randomized controlled clinical comparative study of Huangyuan powder in reducing antipsychotic induced salivation |
| Method | Psychotics fulfilling the CCMD-II criteria aged 16-55, were enrolled, and were randomly allocated into treatment group and control group. Reduction of antipsychotic induced salivation was recorded. |
| Participant | N=62, 31 participants in the treatment group and 31 participants in the control group, with the mean age 26.8 years old (treatment group) and 27.0 years old (control group). There was no mention of participants' gender. |
| Intervention | Treatment: Huangyuan Powder, 2.5-5 g/time, t.i.d / q.i.d<br>Both treatment and control group: Clozapine, 50-75 mg, in the beginning, and dosage was increased to 150-500 mg within 2 weeks. |
| Outcome | The rate of salivation was measured every 2 weeks. |
| Trial duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 2 |

| | |
|---|---|
| Trial 14 | Wen YW, Huang YW, Gan JX, Mao YW, Zhou ZJ, Liang YR, Luo GC (2008) |
| Study eligibility | A randomized controlled clinical comparative study of Lianziqingxin syrup in reducing antipsychotics induced salivation |
| Method | Psychotics fulfilling the CCMD-3 criteria were enrolled, and were randomly allocated into treatment group and control group. By TESS and PANSS score, reduction of antipsychotics induced salivation was recorded. |
| Participant | N=72, 35 participants in the treatment group and 35 participants in the control group, with the mean age 29.3 years old (treatment group) and 29.8 years old (control group), and 62.5% males involved in both groups. There was no mention of the age range of the participants. |
| Intervention | Treatment: Lianziqingxin syrup, 150 ml, t.i.d<br>Both treatment and control group: Clozapine, 25 mg, b.i.d. in the beginning, and dosage was increased to 200-400 mg within 2 weeks. |
| Outcome | TESS and PANSS scores were measured, and TESS scores on week 1, 2, 4 and 6 were reported. |
| Trial duration | 6 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 15 | Shi J, Qi JN, Tao JQ, Zeng Q (2007) |
| Study eligibility | A randomized controlled clinical comparative study of Liujunzi decoction or Xiehuang decoction in reducing antipsychotics induced salivation |
| Method | Psychotics aged 16-58, were enrolled, and were randomly allocated into treatment group and control group. Reduction of antipsychotics induced salivation was recorded. |
| Participant | N=248, 124 participants in the treatment group and 124 participants in the control group, with the mean age was 33.5 years old (treatment group) and 32.5 years old (control group), and 66.13% males in the treatment group and 67.74% males in the control group. |
| Intervention | Treatment: Liujunzi Decoction or Xiehuang Decoction, t.i.d.<br>Control: Artane, 2-4 mg, t.i.d.; Promethazine, 25-50 mg, t.i.d.<br>Antipsychotics were used in both treatment and control groups. |
| Outcome | Numbers of improved patients |
| Trial duration | 1 month |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 16 | Xiong H, Xu SQ (2006) |
| Study eligibility | A randomized controlled clinical comparative study of Xiangshaliujun pill in reducing antipsychotics induced salivation |
| Method | Psychotics fulfilling the CCMD-3 criteria were enrolled, and were randomly allocated them into treatment group and control group. Reduction of antipsychotic induced salivation was recorded. |
| Participant | N=80, 42 participants in the treatment group and 38 participants in the control group. There was no mention on the age and the sex of the participants. |
| Intervention | Treatment: Xiangshaliujun pill, 6 g, t.i.d.<br>Control : Doxepin, 25 mg, t.i.d. |
| Outcome | Clinical results |
| Trial duration | There was no mention on the trial duration. |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 1 |
| Total scores | 3 |

| | |
|---|---|
| Trial 17 | Zhang ZF (2003) |
| Study eligibility | A randomized controlled clinical comparative study of Lizhong decoction in reducing neuroleptic salivation |
| Method | Psychotics fulfilling the CCMD-3 criteria were enrolled, and were randomly allocated into treatment group and control group. By TESS score, effectiveness in reduction of antipsychotics induced salivation was recorded. |
| Participant | N=60, 30 participants in the treatment group and 30 participants in the control group, with the mean age 34.2 years old (treatment group) and 35.7 years old (control group), and 50% males involved in both groups. |
| Intervention | Treatment: Lizhong decoction, 250 ml, t.i.d.<br>Control: Doxipin, from 50 mg/day to100 mg/day (increased dosage) |
| Outcome | By TESS score, the rate of salivation was measured every week, contrasting with that of other regular drugs. |
| Trial duration | 2 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 2 |

| | |
|---|---|
| Trial 18 | Lin W, Peng XX (2002) |
| Study eligibility | A randomized controlled clinical comparative study of the therapeutic effect of Chenxia Liujunzi Pill for neuroleptics salivation |
| Method | Psychotics aged 15-54, were enrolled, and were randomly allocated into the treatment group and control group. Salivation induced by antipsychotic was recorded. |
| Participant | N=110, 56 participants in the treatment group and 54 participants in the control group, with the mean age 32.62 years old (treatment group) and 33.13 years old (control group), and 67.86% males in the treatment group and 59.26% males in the control group. |
| Intervention | Treatment: Chenxialiujunzi Pill, 6-12 g, t.i.d or q.i.d.<br>Control: Artane, 1-4 mg, or Promethazine, 25-50 mg, b.i.d.<br>Regular antipsychotic drugs were used in both groups. |
| Outcome | Clinical results |
| Trial duration | 1 week |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 2 |

| | |
|---|---|
| Trial 19 | Yuan CM, Zhao XY, Han QY (2000) |
| Study eligibility | A randomized controlled clinical comparative study of Suoquan Pill in reducing antipsychotic induced salivation |
| Methods | Psychotics suffering from antipsychotic induced salivation, aged 16-52, were enrolled, and were randomly allocated into treatment group and control group. Reduction of antipsychotic induced salivation was recorded. Physical body check up (ECG, EEG, blood pressure, liver function, kidney function etc.) before, during and after the treatment. |
| Participants | N=70, 38 participants in the treatment group and 32 participants in the control group, with the mean age was 33 years old (treatment group) and 32 years old (control group). 60.53% male in the treatment group and 62.5% male in the control group. |
| Interventions | Treatment: Suoquan Pill, 9 g/pill, t.i.d.<br>Control: Clozapine, 25-50 mg, t.i.d. |
| Outcomes | The rate of salivation was measured after the treatment, contrasting with that of other regular drugs. |
| Trial Duration | 7 days |
| Notes | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 2 |

| | |
|---|---|
| Trial 20 | Zhao ZH, Chen HM, Xie BY, Sun SG, Wu HY, Ma QM, Guo JM, Liu HY, Zhang RJ, Qu JX, Wang JM, Geng B (2000) |
| Study eligibility | A randomized controlled clinical comparative study of Zhixian Capsule in reducing antipsychotics induced salivation |
| Method | Male psychotics fulfilling the CCMD-II-R criteria aged 21-59, were enrolled, and were randomly allocated into treatment group and control group and placebo group. Reduction of antipsychotic induced salivation was recorded. |
| Participant | N=93, 31 participants in the treatment group, 31 participants in the control group, and 31 participants in the placebo group, with the mean age 37.2 years old (treatment group), 42.3 years old (control group) and 41.0 years old (placebo group). All the participants were male. |
| Intervention | Treatment: Shaman Capsule, 0.4 g/capsule, 4 capsule, q.d.<br>Control: Benzamine, 0.4 g/capsule, 4 capsule, q.d.<br>Placebo: Vatamin $B_1$, 0.4 g/capsule, 4 capsule, q.d. |
| Outcome | The rate of salivation was measured after 2 weeks. |
| Trial duration | 2 weeks |
| Note | There was no report on adverse effect. |

| Jade's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 1 |
| Total score | 5 |

| | |
|---|---|
| Trial 21 | Kang B, Liu YC, Zhang YP, Han Y, Fan LZ, Zhou J (1993) |
| Study eligibility | A randomized controlled clinical comparative study of Siouan Pill in reducing antipsychotic induced salivation |
| Method | Psychotics suffering from antipsychotic induced salivation, aged 16-50, were enrolled, and were randomly allocated into treatment group and control group. Reduction of antipsychotic induced salivation was recorded. Physical body check up (ECG, EEG, blood pressure, liver function, kidney function etc.) before, during and after the treatment. |
| Participant | N=40, with 20 participants in the treatment group and 19 participants in the control group. The mean age was 32.40 years old (treatment group) and 28.99 years old (control group). 38.10% males in the treatment group and 26.32% males in the control group. |
| Intervention | Treatment: Suoquan Pill, 9 g, t.i.d.<br>Control: placebo, 9 g, t.i.d.<br>Regular Clozapine was used in both groups. |
| Outcome | The rate of salivation was measured 3 times per night, contrasting with that of other regular drugs. Table comparing the therapeutic effect in the end of each week. |
| Trial duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 1 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 3 |

| | |
|---|---|
| Trial 22 | Zhou Z, Fu R, Huang P (2006) |
| Study eligibility | A randomized controlled clinical study of Hugan Decoction in treating hepatic damage induced by antipsychotic |
| Method | Psychotics fulfilling the CCMD-III criteria with hepatic damage induced by antipsychotic, aged 21-68, were enrolled, and were randomly allocated into treatment group and control group. Clinical symptoms, AST, ALT as well as the recovery rates were recorded in order to obtain the effectiveness of Hugan decoction. |
| Participant | N=55, 28 participants in the treatment group and 27 participants in the control group, with the mean age 23.6 years old (treatment group) and 26.4 years old (control group). 64.29% males in the treatment group and 59.26% males in the control group. |
| Intervention | Treatment: Hugan Decoction, 100 ml, t.i.d.<br>Control: Tioproni 0.2 g, q.i.d. |
| Outcome | Clinical results, and AST, ALT levels were reported. |
| Trial Duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 23 | Dai RZ, Xu WL, Qiao HL (2003) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine in treating side effects induced by antipsychotic |
| Method | Psychotics fulfilling the CCMD-3 criteria with diseases induced by antipsychotic, aged 17-65, were enrolled, and were randomly allocated into treatment group and control group. TESS scores were recorded in order to obtain the effectiveness of the Chinese medicine after 2 weeks. |
| Participant | N=80, 38 participants in the treatment group and 42 participants in the control group, with the mean age was 46.2 years old (treatment group) and 47.3 years old (control group). 65.79% males in the treatment group and 66.67% males in the control group. |
| Intervention | Treatment: Longdanxiegan Decoction or Zengyechengqi Decoction or Zhenganxifeng Decoction or Ganmaidazao Decoction, t.i.d.<br>Control: Benzodiazepine or Clonazepam, 2 mg/day or Benzhexol HCL, 6 mg/day, or Phenolphthalein, 2 tablets/time<br>Regular antipsychotics were used in both groups. |
| Outcome | TESS scores after the treatment in both groups were reported. |
| Trial duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 24 | Wang ZF (2003) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Tongfuqingyu Decoction in treating paralytic ileus induced by antipsychotics |
| Method | Psychotics with paralytic ileus induced by antipsychotic, aged 16-69, were enrolled, and were randomly allocated into treatment group and control group. Efficacy of the drug in both groups was recorded. |
| Participant | N=120, with 60 participants in the treatment group and 60 participants in the control group. The mean age was 39 years old (treatment group) and 43 years old (control group). 80.00% males in the treatment group and 83.33% males in the control group. |
| Intervention | Treatment: Tongfuqingyu Decoction, 100 ml, t.i.d.<br>Control: Neostigmine, 0.5 mg, inj. t.i.d.; Motilium, 10 mg, q.i.d. |
| Outcome | Table showing the efficacy of drugs in both groups |
| Trial Duration | 1-3 days |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 25 | Zhao JT, Cheng ZC, Wang JL, Wang LH (2001) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Dahuangjiegeng Decoction in treating dysuria induced by antipsychotics |
| Methods | Psychotics with dysuria induced by antipsychotics, aged 18-56, were enrolled, and were randomly allocated into treatment group and control group. Efficacy of the drug in both groups was recorded. |
| Participants | N=104, 68 participants in the treatment group and 36 participants in the control group, with the mean age was 35.20 years old (treatment group) and 34.40 years old (control group). 41.18% males in the treatment group and 52.78% males in the control group. |
| Interventions | Treatment: Dahuangjiegeng Decoction, t.i.d.<br>Control : Neostigmine, 1 mg, i.m. |
| Outcomes | Clinical results |
| Trial Duration | 4 days |
| Notes | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 2 |

| | |
|---|---|
| Trial 26 | Zhang ZL (2007) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine in treating sexual dysfunction induced by antipsychotics |
| Methods | Male psychotics with sexual dysfunction induced by antipsychotics, aged between27-53, were enrolled, and were randomly allocated into treatment group and control group. Efficacy of the drug in both groups was recorded. |
| Participants | N=60, 30 participants in the treatment group and 30 participants in the control group, with the mean age was 36.3 years old (treatment group) and 34.1 years old (control group). Only males were involved in the study. |
| Interventions | Treatment: Self-prepared herbal decoction, t.i.d. and Antipsychotics<br>Control: Antipsychotics |
| Outcomes | Clinical results |
| Trial Duration | 6 weeks |
| Notes | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 27 | Zhang TL, Cao BY (1997) |
| Study eligibility | A randomized crossover controlled clinical study of Chinese medicine in treating granulocytopenia induced by antipsychotics |
| Method | Psychotics with WBC and PMN level decreased to $4.0x10^9$/L and $1.8x10^9$/L, aged between14-60, were enrolled, and were randomly allocated into treatment group and control group. The participants were switched to the opposite group after 4 weeks. Both groups were treated by Chinese medicine after 8 weeks. Efficacy of the drug in both groups was recorded. |
| Participant | N=56, 28 participants in the treatment group and 28 participants in the control group, with the mean age 30.28 years old (treatment group) and 25.66 years old (control group). 28.57% males in the treatment group and 32.14% males in the control group. |
| Intervention | Treatment: Quangui Capsule, 0.5 g/capsule, 2 capsules, t.i.d.<br>Control: Vitamin $B_4$, 20 mg, q.i.d.<br>Batilol, 50 mg, q.i.d.<br>Regular antipsychotics were used in both groups. |
| Outcome | Clinical results |
| Trial duration | 12 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 28 | Ding GA, Yu GH, Zhang JD, Liang XC, Liu LQ, Huang P, Chen WJ, Qiao AX, Li XF, Cai YL (1997) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Lingguizhugan Decoction in treating obesity induced by antipsychotics |
| Method | Obese psychotics were enrolled, and were randomly allocated into treatment group and control group. By BPPS and TESS scores, efficacy of the drug in both groups was recorded. |
| Participant | N=100, 50 participants in the treatment group and 50 participants in the control group, with the mean age was 38.1 years old (treatment group) and 38.1 years old (control group). 32% males in the treatment group and 38% males in the control group. |
| Intervention | Treatment: Lingguizhugan Decoction, 0.9 g/ml, 30 ml, t.i.d. and regular Antipsychotics<br>Control: Regular Antipsychotics |
| Outcome | Body weight, BPPS and TESS scores were reported. |
| Trial duration | 8 weeks |
| Note | TESS scores were reported on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 29 | Wang DH, Yang BS, Lu XP (2001) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine decoction in treating clozapine induced increase in body weight |
| Method | Psychotics fulfilling the CCMD-2-R criteria, and was found significantly increase in weight after treated with clozapine for 2 months,were enrolled, and were randomly allocated into treatment group and control group. By observing the weight difference of the patients, efficacy of the drug in both groups was recorded. |
| Participant | N=82, 42 participants in the treatment group and 40 participants in the control group, with the mean age 25.8 years old (treatment group) and 25.8 years old (control group). 47.62% males in the treatment group and 45.00% males in the control group. |
| Intervention | Treatment: Self-prepared Chinese medicine decoction,<br>and regular Clozapine<br>Control: Regular Clozapine |
| Outcome | Body weight |
| Trial duration | 8 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| Trial 30 | Yang DD (2006) |
|---|---|
| Study eligibility | A randomized controlled clinical study of Chinese medicine in treating Benzodiazepine induced insomnia and other adverse effect |
| Method | Psychotics fulfilling the CCMD-III criteria, with insomnia induced by Benzodiazepine, were enrolled, and were randomly allocated into treatment group and control group. By observing the PSQI, ZUNG score of the patients, efficacy of the drug in both groups was recorded. |
| Participant | N=40, 20 participants in the treatment group and 20 participants in the control group. There was no mention of the sex and age of the participants. |
| Intervention | Treatment: Self-prepared Chinese medicine decoction, q.i.d.<br>Control: Zopiclone<br>Decreasing Zopiclone every 3 days |
| Outcome | By PSQI and Zung scores, the therapeutic effect of the drug was recorded every 5 days. |
| Trial duration | 2 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 31 | Wang P, Duan DX, Wang XF, Wang YX, Wang YT (2006) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine in treating dry mouth induced by antipsychotics |
| Method | Psychotics with antipsychotics induced dry mouth, aged from 18-54, were enrolled, and were randomly allocated into treatment group and control group. By observing the degree of dry mouth before and after the treatment, therapeutic effect of the drug in both groups was recorded. Physical body check up (ECG, EEG, blood pressure, liver function, kidney function etc.) before, during and after the treatment. |
| Participant | N=64, 33 participants in the treatment group and 31 participants in the control group, with the mean age 32.6 years old (treatment group) and 33.7 years old (control group). 57.58% males in the treatment group and 51.61% males in the control group. |
| Intervention | Treatment: Yuyinshengjin Decoction and regular antipsychotics<br>Control: Regular antipsychotics |
| Outcome | Self-developed scale of dry mouth before and after 1, 2 and 4 weeks treated with Chinese medicine decoction. |
| Trial duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| | |
|---|---|
| Trial 32 | Yuan GZ, Huang YP, Zhao JF, Gong JX (2006) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine in treating dry mouth induced by antipsychotics |
| Method | Psychotics with antipsychotics induced dry mouth were enrolled, and were randomly allocated into treatment group and control group. By observing dry mouth before and after the treatment, therapeutic effects of the drug in both groups were recorded. |
| Participant | N=50, with 25 participants in the treatment group and 25 participants in the control group. The mean age was 36.8 years old (treatment group) and 39.8 years old (control group). 52% male in the treatment group and 68% male in the control group. |
| Intervention | Treatment: Shengjinrunzao decoction, 20 ml, q.i.d.<br>Control: Stop prescription of antipsychotic drug. |
| Outcome | Self-developed scale of dry mouth before and after treatment in week 1, 2, 4 and 6. ECG, EEG, blood pressure, liver function, kidney function etc. were recorded before and after the treatment. |
| Trial duration | 6 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 33 | Hu XZ, Wu XF (1996) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Longdanxiegan Pill in treating dry mouth induced by antipsychotics |
| Method | Psychotics with antipsychotics induced dry mouth, aged 17-68, were enrolled, and were randomly allocated into the treatment group and control group. By observing dry mouth before and after treatment, therapeutic effect of both groups was recorded. |
| Participant | N=59, 30 participants in the treatment group and 29 participants in the control group, with the mean age 34.7 years old. 61.02% males was involved in the study. |
| Intervention | Treatment: Longdanxiegan Pill, 6 g, t.i.d.<br>Control: Placebo, 6 g, t.i.d. |
| Outcome | Self-developed scale of dry mouth and other adverse effects. ECG, EEG, blood pressure, liver function, kidney function etc. were recorded before and after the treatment. |
| Trial duration | 2 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| Trial 34 | Kong M, Gao XM, Gong H (2005) |
|---|---|
| Study eligibility | A randomized controlled clinical study of Chinese medicine Dangguibuxue Decoction (DBD) in treating leucopenia induced by clozapine |
| Method | Psychotics fulfilling the CCMD-3 criteria and BPRS score (=/> 36), aged 18-50, were enrolled, and were randomly allocated into the treatment group and control group. By checking the WBC level, efficacy of the drug in both groups was recorded. |
| Participant | N=60, 30 participants in the treatment group and 30 participants in the control group, with the mean age 40 years old (treatment group) and 38.3 years old (control group). There was no mention on the sex of participants. |
| Intervention | Treatment: Dangguibuxue Decoction, 250 ml, t.i.d.<br>Control: Vitamin $B_4$ 30 mg/day; Batilol 150 mg/day<br>Regular clozapine were used in both groups. |
| Outcome | Scale of the drug efficacy, WBC level of 2 groups before and after treated on the D15, 30 and 45. |
| Trial duration | 6 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 35 | Xu LP, Ji JY, Chen FB, Shao YQ (2005) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Diyushengbai Tablet in treating leucopenia induced by clozapine |
| Method | Psychotics fulfilling the CCMD-3 criteria, aged 17-58, were enrolled, and were randomly allocated into the treatment group and control group. By checking the WBC level in the patients, efficacy of both groups was recorded. |
| Participant | N=56, 28 participants in the treatment group and 28 participants in the control group, with the mean age 24.3 years old (treatment group) and 21.3 years old (control group). 35.71% males in the treatment group and 32.14% males in the control group. |
| Intervention | Treatment: Diyushengbai Tablet, 4 tablet, q.i.d.<br>Control: Vitamin $B_4$, 60 mg/day; Leucogen tablet, 120 mg/day |
| Outcome | Clinical results, WBC level of 2 groups before and after treatment D3, 7 and 14 were reported. |
| Trial duration | 2 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 36 | Zhan CH, Wang HJ, Zhang ZH (2002) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Donkey-hide gelatin syrup (DHGS) compared with batiol and vitamin $B_4$ in treating leucopenia caused by clozapine |
| Method | Psychotics fulfilling the CCMD-2-R criteria, WBC level < $4.0x10^9$/L, aged 18-50, were enrolled, and were randomly allocated into treatment group and control group. By checking the WBC level in the patients, efficacy of both groups was recorded. |
| Participant | N=40, 20 participants in the treatment group and 20 participants in the control group, with the mean age was 40 years old (treatment group) and 38.3 years old (control group). There was no mention of the sex of the participants. |
| Intervention | Treatment: DHGS, 60 ml/day<br>Control: Vitamin $B_4$, 30 mg/day; Batilol, 150 mg/day<br>Regular clozapine were used in both groups. |
| Outcome | Clinical results, WBC level before and after treatment for 15, 30 and 45 days were reported. |
| Trial duration | 6 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 37 | Guo YM, Liu CF, Wang QX (2001) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Shengbai Decoction compared with batiol and vitamin $B_4$ in treating leucopenia caused by clozapine |
| Method | Psychotics fulfilling the CCMD-2-R criteria with leucopenia induced by clozapine, were enrolled, and were randomly allocated into treatment group and control group. By checking the WBC level in the patients, efficacy of the drug in both groups was recorded. |
| Participant | N=50, 25 participants in the treatment group and 25 participants in the control group, with the mean age 31.56 years old (treatment group) and 31.28 years old (control group). 80% males in the treatment group and 84% males in the control group. |
| Intervention | Treatment: Shengbai Decoction, t.i.d.<br>Control: Vitamin $B_4$, 20 mg, q.i.d.; Batilol, 100 mg, q.i.d.<br>Regular clozapine were used in both groups. |
| Outcome | Clinical results, WBC level before and after treatment werereported. |
| Trial duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 38 | Kong DR (1999) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Guipi Decoction compared with Leucogen in treating leucopenia caused by clozapine |
| Method | Psychotics fulfilling the CCMD-2-R criteria, WBC level < $3.5x10^9$/L, aged 16-54, were enrolled, and were randomly allocated into treatment group and control group. |
| Participant | N=80, 40 participants in the treatment group and 40 participants in the control group, with the mean age 27 years old. 55.0% males in the treatment group and 47.5% males in the control group. |
| Intervention | Treatment: Guipi Decoction, t.i.d.<br>Control: Leucogen, 60 mg, q.i.d.<br>Regular clozapine (400 ± 50 mg) were used in both groups. |
| Outcome | Patients' WBC level |
| Trial duration | 4 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 39 | Gong LB (2008) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Liuweidihuang Pill in treating antipsychotics induced enuresis |
| Method | Psychotics fulfilling the CCMD-3 criteria, with enuresis induced by antipsychotics, aged 18-45, were enrolled, and were randomly allocated into treatment group and control group. By comparing the BPRS and TESS scores as well as the enuresis condition, efficacy of the drug in both groups was recorded. |
| Participant | N=100, 50 participants in the treatment group and 50 participants in the control group. 30% males in the treatment group and 34% males in the control group. There was no mention of the mean age of the participants. |
| Intervention | Treatment: Liuweidihuang Pill, 8 pills, q.i.d.<br>Control: Regular antipsychotics |
| Outcome | The BPRS and TESS scores before and after treatment for 2, 4, 6 and 8 weeks. Meanwhile, ECG, EEG, blood pressure, liver function, kidney function, etc. were recorded. |
| Trial duration | 8 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 40 | Liu SP (2001) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Suoquan Pill in treating clozapine induced enuresis |
| Method | Psychotics fulfilling the CCMD-2-R criteria with enuresis induced by clozapine, were enrolled,and were randomly allocated into treatment group and control group. Observation of enuresis condition every morning. |
| Participant | N=64, with 32 participants in the treatment group and 32 participants in the control group. No mention of the mean age and the sex of the participants. |
| Intervention | Treatment: Suoquan Pill, 1 pill, q.i.d<br>Control: Benzhexol, 1 tablet, t.i.d.<br>Regular clozapine was used in both groups. |
| Outcome | Scores of enuresis before and after the treatment were reported. |
| Trial duration | 3 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 41 | Yuan CM, Lu SC, Han QY (2001) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Suoquan Pill in treating clozapine induced enuresis |
| Method | Psychotics fulfilling the CCMD-2-R criteria with enuresis induced by clozapine, were enrolled, and were randomly allocated into treatment group and control group. Observation of enuresis condition every morning. |
| Participant | N=64, 32 participants in the treatment group and 32 participants in the control group. There was no mention of participants' mean-age and the sex. |
| Intervention | Treatment: Suoquan Pill, 1 pill, q.i.d<br>Control: Benzhexol, 1 tablet, t.i.d.<br>Regular clozapine was used in both groups. |
| Outcome | Scores of enuresis before and after the treatment were reported. |
| Trial duration | 3 weeks |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 42 | Mao ZX, Zhang JH, Cheng J (2008) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Xuefuzhuyu Capsule in treating antipsychotics induced amenorrhea |
| Method | Female psychotics fulfilling the CCMD-3 criteria with amenorrhea induced by antipsychotics for more than 6 months and diagnosed with stagnation of *qi* and blood stasis, aged 18-40, were enrolled, and were randomly allocated into treatment group and control group. |
| Participant | N=60, 30 participants in the treatment group and 30 participants in the control group. No mention of the mean age of the participants. |
| Intervention | Treatment: Xuefuzhuyu Capsule, 6 capsules, t.i.d (D1-30)<br>Control: Diethylstilbestrol, 0.5 mg/night (D1-30)<br>Medroxyprogesterone acetate, 8 mg/night (D16-30)<br>Secondary treatment cycle began on the D5 of the menstruation; and regular dosage of antipsychotics was used in both groups. |
| Outcome | Observation of recovery of menstruation. ECG, EEG, blood pressure, liver function, kidney function etc. were recorded before and after the treatment. |
| Trial duration | 3 months |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

| | |
|---|---|
| Trial 43 | Cui GM, Zhang RL, Duan DX (2006) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Xuefuzhuyu Decoction in treating antipsychotics induced amenorrhea |
| Method | Female psychotics fulfilling the CCMD-3 criteria with amenorrhea induced by antipsychotics for more than 6 months and diagnosed with stagnation of *qi* and blood stasis, aged 17-42, were enrolled, and were randomly allocated into treatment group and control group. |
| Participant | N=84, 42 participants in the treatment group and 42 participants in the control group, with the mean age 28.3 year old (treatment group) and 27.9 years old (control group). |
| Intervention | Treatment: Xuefuzhuyu Decoction, 75-100 ml, t.i.d (D1-21)<br>Diethylstilbestrol, 1 mg/day (D1-21)<br>Control: Diethylstilbestrol, 1 mg/day (D1-21)<br>Medroxyprogesterone acetate, 10 mg/day (D16-20)<br>Stopping dosage on the D21-30, and secondary treatment cycle began on the D7 of menstruation, and regular antipsychotics were used in both groups. |
| Outcome | Observation of recovery of menstruation. ECG, EEG, blood pressure, liver function, kidney function etc. were recorded before and after the treatment. |
| Trial duration | 3 menstrual cycles. |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 44 | Yang JJ (2003) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine in treating antipsychotics with amenorrhea |
| Method | Female psychotics fulfilling the CCMD-2-R criteria with amenorrhea induced by antipsychotics for more than 3 months, aged 17-40, were enrolled, and were randomly allocated into treatment group and control group. |
| Participant | N=57, 36 participants in the treatment group and 21 participants in the control group, with the mean age 26.2 year old (treatment group) and 26.8 years old (control group). |
| Intervention | Treatment: Self-developed Chinese medicine decoction, t.i.d (D1-15)<br>Control: Diethylstilbestrol, 0.5 mg/day (D1-21)<br>Medroxyprogesterone acetate, 10 mg/day i.m. (D16-20)<br>Stopping dosage from the D21-30. Secondary treatment cycle began on the D5 of the menstruation, regular dosage of antipsychotics was used in both groups. |
| Outcome | The recovery of menstruation in each month for 3-6 months. Observe the recovery of menstruation. ECG, EEG, blood pressure, liver function, kidney function, lipids level in blood, blood viscosity etc. were recorded before and after the treatment. |
| Trial duration | 3 menstrual cycles |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 45 | Wu LM, Xie CP (2000) |
| Study eligibility | A randomized controlled clinical study of Chinese medicine Xuefuzhuyu Decoction in treating antipsychotics induced amenorrhea |
| Method | Female psychotics with amenorrhea induced by antipsychotics for more than 3 months, aged 16-42, were enrolled, and were randomly allocated into treatment group and control group. Observe the recovery of menstruation. |
| Participant | N=69, 49 participants in the treatment group and 20 participants in the control group. There was no mention of the mean age of the participants. |
| Intervention | Treatment: Xuefuzhuyu Decoction, t.i.d<br>(5-7 days before menstrual cycle, for 7 days)<br>Control: Medroxyprogesterone acetate, 20 mg/day i.m.<br>(5 days before menstrual cycle, for 4 days) |
| Outcome | Observation of the recovery of menstruation after 3 months |
| Trial duration | 3 menstrual cycles |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 46 | Yuan ZQ, Gao JJ, Ouyang X, Zhou YG (2001) |
| Study eligibility | A randomized controlled clinical study of the therapeutic efficacy of Composite Salvia Miltiorrhiza Injection (CSMI) and naloxone in the treatment of acute severe diazepam poisoning |
| Method | Psychotics with acute severe diazepam poisoned, aged from 14-50, were enrolled, and were randomly allocated into treatment group and control group. Consciousness restoration time and subjective symptoms eliminated time were evaluated. The initial-improvement time, marked-effective time and curative time was recorded. |
| Participant | N=70, 36 participants in the treatment group and 34 participants in the control group, with the mean age 27.4 years old (treatment group) and 25.6 years old (control group). 13.9% males in the treatment group and 11.76% males in the control group. |
| Intervention | Treatment: CSMI 10 ml + 10% glucose solution 250 ml, i.v. (gt); Naloxone Hydrochloride Injection 0.8 mg + 10% glucose solution 20 ml, i.v. (gt.)<br>Both groups were treated with 20% mannitic acid 250 ml, i.v. (gt.); Frusemide 20 mg i.v.; Bemegride 50 mg + l5% glucose solution 250 ml, i.v. (gt.) |
| Outcome | Consciousness restoration time, subjective symptoms eliminated time, therapeutic efficacy was reported. |
| Trial duration | There was no mentioned on trial duration. |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total scores | 2 |

| | |
|---|---|
| Trial 47 | Lin XL, Zhang XY (2003) |
| Study eligibility | A randomized controlled clinical study of the therapeutic efficacy of Xingnaojing injection and naloxone in the treatment of acute severe diazepam poisoning |
| Method | Psychotics with acute and severe diazepam poisoning, aged 15-70, were enrolled, and were randomly allocated into treatment group and control groups. Consciousness-restoration time and symptom-eliminated time were evaluated. The initial improvement time, marked effective time and curative time were recorded. |
| Participant | N=98, with 33 participants in the Xingnaojing-treatment group, 33 participants in the naloxone-treatment group and 32 participants in the control group. 26.53% males involved in the study. Participants' mean age did not be mentioned. |
| Intervention | Treatment-1: Xingnaojing 10 ml + 50% glucose solution 20 ml i.v. and<br>Xingnaojing 20 ml + 10% glucose solution 250 ml i.v. (gt.)<br>Treatment-2: Naloxone 0.4-1.2/hr i.v.<br>Control: Gastrolavage, diuretics etc. |
| Outcome | By consciousness restoration time, subjective symptoms eliminated time, therapeutic efficacy of Xingnaojing injection and naloxone were shown. |
| Trial duration | There was no mentioned on trial duration. |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 48 | Li HJ, Chen Y, Gao GP (2004) |
| Study eligibility | A randomized clinical study on the efficacy of Xingnaojing Injection and Bemegride in the treatment of acute and severe diazepam poisoning |
| Method | Psychotics with acute and severe diazepam poisoning, aged 14-46, were enrolled, and were randomly allocated into 2 groups. Consciousness-restoration time and symptom-eliminated time were evaluated. The initial improvement time, marked effective time and curative time was recorded. |
| Participant | N=64, 34 participants in the treatment group (Xingnaojing), 30 participants in the control group (Bemegride), with 6.25% males involved in the study. Participants' mean age did not be mentioned. |
| Intervention | Treatment: Xingnaojing Injection 20 ml + 5% glucose solution 500 ml, i.v. (gt.)<br>Control: Bemegride 200 mg + 5% glucose solution 500 ml, i.v. (gt.)<br>Both groups were treated with Frusemide 20 mg i.v., Vitamin C 5.0 g, ATP 40 mg, CoA 100 u, CDPC 0.5, q.d. |
| Outcome | By consciousness restoration time, subjective symptoms eliminated time, therapeutic efficacy of Xingnao injection and naloxone were shown. |
| Trial duration | There was no mentioned on trial duration. |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 49 | Ding HT (2004) |
| Study eligibility | A randomized clinical study on the efficacy of Fufangshexiang Injection and Naloxone in treatment of acute severe diazepam poisoning |
| Methods | Psychotics with acute and severe diazepam poisoning were enrolled, and were randomly allocated into 3 groups. Consciousness-restoration time was evaluated. |
| Participants | N=95, 35 participants in the treatment-1 group (Fufangshexiang Injection + Naloxone), 30 participants in the treatment-2 group (Fufangshexiang Injection) and 30 participants in the treatment-3 group (Naloxone), with 6.25% males involved in the study. Participants' mean age did not be mentioned. |
| Interventions | Treatment-1:<br>Fufangshexiang Injection 10 ml + 10% glucose solution 250-500 ml, i.v. (gt.), and Naloxone 1.2 mg + 10% glucose solution 250-500 ml i.v. (gt.), and Naloxone 0.4-0.8 mg, i.v.<br>Treatment-2:<br>Fufangshexiang Injection 20 ml + 10% glucose solution 250-500 ml, i.v. (gt.)<br>Treatment-3:<br>Naloxone 1.2 mg + 10% glucose solution 250-500 ml, i.v. (gt.), and Naloxone 0.4-0.8 mg, i.v.<br>Gastrolavage, diuretics, etc. were performed for all groups. |
| Outcomes | By consciousness-restoration time, symptom-eliminated time was shown. |
| Trial Duration | There was no mentioned on rial duration. |
| Notes | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 50 | Lin LS, Guo S (2005) |
| Study eligibility | A randomized controlled clinical study of the therapeutic efficacy of Daoxie decoction compared with naloxone in treatment of acute severe diazepam poisoning |
| Method | Psychotics with acute and severe diazepam poisonng, aged 16-52, were enrolled, and were randomly allocated into the treatment group and control group. Consciousness-restoration time and symptom-eliminated time were evaluated. The consciousness-restoration time, symptoms eliminated time was recorded. |
| Participant | N=56, 30 participants in the treatment group and 26 participants in the control group, with the mean age 32 years old (treatment group) and 35 years old (control group), and 20.00% males in the treatment group and 15.38% males in the control group. |
| Intervention | Treatment: Daoxie Decoction 200 ml, p.o.<br>Control: 33% Magnesium Sulfate 20-30 ml, p.o.<br>Frusemide 20-60 mg, i.v.<br>Gastrolavage, diuretics, etc. were performed in both two groups. |
| Outcome | By consciousness-restoration time, symptom-eliminated time was shown. |
| Trial duration | There was no mention on trial duration. |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 51 | Yan PJ (1998) |
| Study eligibility | A randomized controlled clinical study on the efficacy of Xingnaojing in treatment of acute and severe diazepam poisoning |
| Method | Psychotics with acute and severe diazepam poisoning, aged 16-65, were enrolled, and were randomly allocated into the treatment group and control group. Consciousness-restoration time and symptom-eliminated time were evaluated. |
| Participant | N=93, 67 participants in the treatment group and 26 participants in the control group, with 35.82% males in the treatment group and 42.31% males in the control group. |
| Intervention | Treatment: Xingnaojing 20 ml, i.v. or 40 ml, i.v. (gt.)<br>Control: Frusemide 40 mg + Vitamin C 5.0 g + Vitamin $B_6$ 200 mg + ATP 40 mg + $C_OA$ 100 u + Inosine 0.4 g, i.v.<br>Gastrolavage, diuretics, etc. were performed in both two groups. |
| Outcome | By Consciousness-restoration time, symptom-eliminated time was shown. |
| Trial duration | 1 hour |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 52 | Li JR, Rong K (2005) |
| Study eligibility | A randomized controlled clinical study of the therapeutic efficacy of Qingkailing Injection combined with Naloxone to treat acute and severe antipsychotics poisoning |
| Method | Psychotics with acute and severe antipsychotics poisoning, aged 18-50, were enrolled, and were randomly allocated into the treatment group and control group. Consciousness-restoration time and symptom-eliminated time were evaluated. The initial improvement time, marked effective time and curative time were analyzed. |
| Participant | N=41, 21 participants in the treatment group and 20 participants in the control group, with the mean age 30 years old (treatment group) and 32 years old (control group), and 52.38% males in the treatment group and 45.00% males in the control group. |
| Intervention | Treatment: Qingkailing Injection 50 ml + Naloxone Injection 0.8 mg + 5% glucose solution 250 ml, i.v. (gt.); and Naloxone Injection 0.8 mg, i.v. every 4 hours.<br>Control: Naloxone Injection 0.8 mg + 5% glucose solution 250 ml, i.v. (gt.); and Naloxone Injection 0.8 mg, i.v. every 4 hours. |
| Outcome | Consciousness-restoration time, symptom-eliminated time, etc. were recorded. |
| Trial duration | 3 days |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 53 | Zhao ZD, Wang Z (2007) |
| Study eligibility | A randomized controlled clinical study of the therapeutic efficacy of Xingnaojing Injection in the treatment of acute diazepam poisoning |
| Method | Psychotics with acute and severe diazepam poisoned were enrolled, and were randomly allocated into the treatment group and control group. Consciousness-restoration time and symptom-eliminated time were evaluated. |
| Participant | N=94, 48 participants in the treatment group and 46 participants in the control group. Participants' mean age and gender did not be mentioned. |
| Intervention | Treatment: Xingnaijing Injection, 20 ml + 5% glucose solution 250 ml, i.v. (gt.)<br>Control: No prescription of other drugs<br>Gastrolavage, diuretics, etc. were used in both groups. |
| Outcome | Consciousness restoration time, symptom eliminated time, etc. were recorded. |
| Trial duration | 12 hours |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 54 | Zhou HJ, Zhu YP (2003) |
| Study eligibility | A randomized controlled clinical study of Fufangdanshen Pill in the treatment of abnormal ST-T in ECG induced by clozapine |
| Method | Psychotics fulfilling the CCMD-3 criteria with changes in ST-T in ECG induced by clozapine, aged 18-40, were enrolled, and were randomly allocated into the treatment group and control group. ECG was checked up every week. |
| Participant | N=100, 50 participants in the treatment group and 50 participants in the control group, with the mean age 25.3 years old (treatment group) and 25.8 years old (control group), and 54.29% males in the treatment group and 54.29% in control group. |
| Intervention | Treatment: Fufangdanshen Pill, 10 pills, t.i.d.<br>Control: Potassium chloride, 1 g, q.d.<br>Clozapine were used in both groups. |
| Outcome | ECG, blood concentration of potassium, heart rate in the D7, 14 and 21 were recorded. |
| Trial duration | 21 days |
| Note | There was no report on adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 55 | Liang XC, Mou M (2001) |
| Study eligibility | A randomized controlled clinical trial on the effect of Tianhuangbuxin Pill in the treatment of abnormal ST-T in ECG induced by antipsychotics |
| Method | Psychotics with changes of ST-T in ECG induced by antipsychotics, aged 17-58, were enrolled, but patients with serious cardiovascular and other diseases were excluded. They were randomly allocated into the treatment group and control group. ECG was checked up every week. |
| Participant | N=102, 60 participants in the treatment group and 42 participants in the control group, with 58.33% males in the treatment group and 64.28% males in the control group. There was no mention of the mean age of the participants. |
| Intervention | Treatment: Tianwangbuxin Pill, 1 pill, q.i.d.<br>Control: Propranolol, 10-20 mg, q.i.d.<br>Dosage of antipsychotics was regulated in both groups. |
| Outcome | ECG every week was recorded. |
| Trial duration | 2 weeks |
| Note | There was no obvious adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 56 | Wang M, Yu C (2001) |
| Study eligibility | The effect of Tongxinluo Capsules in the treatment of abnormal ST-T in ECG induced by antipsychotics -- A randomized controlled clinical study |
| Method | Psychotics fulfilling the CCMD-2-R criteria with changes of ST-T in ECG induced by antipsychotics, aged 32-67, were enrolled, and were randomly allocated into treatment group and control group. ECG was checked up every week. |
| Participant | N=100, 50 participants in the treatment group and 50 participants in the control group, with the mean age 45.3 years old (treatment group) and 47.3 years old (control group). 22% males in the treatment group and 26% males in the control group. |
| Intervention | Treatment: Tongxinluo Capsule, 4 capsules, q.i.d.<br>Control: Coenzyme $Q_{10}$, 20 mg, q.i.d. |
| Outcome | ECG for every week was recorded. |
| Trial duration | 2 weeks |
| Note | There was no obvious adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 0 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 2 |

| | |
|---|---|
| Trial 57 | Zhang TL, Wang RF, Sun LL, Wang SB (2000) |
| Study eligibility | A randomized controlled clinical study on Tongxinluo Capsule in the treatment of abnormal ST-T in ECG induced by antipsychotics |
| Method | Psychotics fulfilling the ICD-10 criteria with abnormal ST-T in ECG induced by antipsychotics, aged 17-60, were enrolled, and were randomly allocated into the treatment group (Tongxinluo) and control group (ATP). ECG was checked up every 2 weeks. |
| Participant | N=205, 98 participants in the treatment group and 94 participants in the control group, with the mean age 2.02 years old (treatment group) and 29.3 years old (control group). 82.65% males in the treatment group and 81.91% males in the control group. |
| Intervention | Treatment: Tongxinluo Capsul, 0.38 g/capsule, 2 capsules, t.i.d.<br>Control: ATP, 40 mg, q.i.d.; Inosine, 0.2 g, q.d. |
| Outcome | Patient's ECG was checked up every 2 weeks. |
| Trial duration | 8 weeks |
| Note | There was no obvious adverse effect. |

| Jadad's scale (Yes=1, No=0) | |
|---|---|
| 1. Is the study randomized? | 1 |
| 2. Is the study double blinded? | 0 |
| 3. Is there a description of withdrawals / drop out? | 1 |
| 4. Is the randomization adequately described? | 1 |
| 5. Is the blindness adequately described? | 0 |
| Total score | 3 |

## 3.3 Included-trial list

### 3.3.1 Short-term detoxification of heroin dependence

| (A) | CH vs. clonidine |
|---|---|
| *1 | Guo S, Jiang ZN, Wang Y, Hu G., Wu YM, Huang MS. (1995) A study of Chinese herbal medicine Fukang Pian with clonidine hydrochloride in the treatment of opiate withdrawal symptoms. Chinese Bulletin of Drug Dependence 4(4):210-216. |
| *2 | Guo S, Jiang JY, Sheng LX. (2001) A double-blinded randomized controlled trial of Zhengtongyin Decoction compared with clonidine in the treatment of heroin withdrawal symptoms. Chinese Journal of Drug Dependence 10(2): 111-115. |
| *3 | Huang MS, Li J, K W, Li JW, Wang XP, Zhang YM, Li JX, Liu TQ, Kang L, Li GH, Sun XL. (2001) A multi-center clinical research of Shengfutuodu Capsules to control heroin withdrawal symptoms. Chinese Journal of Drug Dependence 10(3):193-196. |
| *4 | Hu GC, Huang MS. (1995) Preliminary study on Fukang Pian in heroin detoxification -- Clinical investigation of 40 cases. Chinese Bulletin of Drug Dependence 4(4):217-222. |
| *5 | Kang L, Li J, Huang MS. (2002) Randomized double-blinded study of Kangfuxin, Fukangpian & clonidine hydrochloride for opiate withdrawal syndrome. Chinese Journal of Clinical Rehabilitation 6(23):3586-3587. |
| *6 | Li J, Wang MS, Liu W, Wan WP, Zhang B, Yang F, Tian WC, Liu B, Wang YL. (1999) Evaluation of clinical efficacy of Ningyi capsule on controlling opiate withdrawal symptoms. Chinese Journal of Treatment and Prevention of Drugs Abuse (6):8-13. |
| *7 | Lu XJ, Qin GC, Liang F, Ban CT, Li HX. (2000) Random control study of comparing detoxicated effects of Baokang Jiedu Chongji and clonidine on heroin addicts. Zhoungguo Yao wu langyong Yufang Zhazi 2(2):37-40. |
| *8 | Wang XP, Liu TQ, Ha W. (2002) Clinical controlled study of Shengfutuodu Capsules to treat heroin withdrawal symptoms. Chinese Journal of Drug Dependence 11(2):120-124. |
| *9 | Xu FZ, He Y. (2001) Clinical observation on 324 cases of opioid depencence treated with Sheungfutuodu capsules. Journal of Chengdu University of TCM 24(3):14-17. |
| *10 | Zhang RM, Li JX, Sun XH, Zheung L, Yang LP, Zhang J, Li JH, Ma KJ. (2001) A double-blinded clinical trial of Shengfutuodu capsule in the treatment of heroin withdrawal symptoms. Chinese Journal of Drug Dependence 10(3):197-201. |
| *11 | Zhang GE, Li J, Hou JC, Xie LY, Bian RY, Chao YC. (1998). A clinical observation of Tongdangduke capsules to treat 32 cases of heroin dependents. Chinese Medicine Journal 19(6): 357-358. |
| *12 | Zhou C, Zhang DY, Bao HQ. (2001) A comparative study of TianChaoKeli and clonidine for opiate withdrawal symptoms. Journal of Guiyang Medical College 26(1):65-67. |

| | |
|---|---|
| *13 | Zhou C, Zhong D, Wang L. et. al. (2004) The compared clinical researches on treating opium withdrawal syndrome by Yian Decoction and clonidine. Chinese Magazine of Drug Abuse Prevention and Treatment 10(2):68-71. |
| *14 | Lan XY, Deng HC, Guo RQ, Liu BC, Chen ZQ, Bao CY. (1997) Primary research on Jieduqing for heroin detoxification. J Health Toxicol 11:69. |
| **(B)** | **CH vs. nofexidine** |
| *15 | Mo ZX, Wang CY, Luo XY, Zhang XF (2003) Clinical observation of Qingfeng Capsules in the treatment of heroin addicts. Journal of Chinese Medicinal Materials 26(7):531-533. |
| *16 | Tu QX, Zhao HG, Chen YP, Chen YM, Wang XP, Hang M. (1999) A randomized double-blind control comparison of Ji Tai Capsule and lofexidine to treat opioid withdrawal syndrome. Chinese Journal of Drug Dependence 8(4):285-288. |
| *17 | Wen L, Zheng YS, Yu LZ, Mo ZX, Qu JW. (2000) A clinical study of Modified Shen Fu Decoction on 68 cases of heroin addicts. Pharmacology and Clinics of Chinese Materia Medica 16(4):40-42. |
| *18 | Xu GZ, Duan LX, Liu C, Gao WY, Wang ZF, Xu BZ, Cai ZJ. (2002) Randomised double-blind clinical research of Fuzhengkang Decoction for detoxification of heroin dependence. Chinese Magazine of Treatment and Prevention of Drugs Abuse 4 (39):2-8. |
| *19 | Xu LL, Zhu HT. (2004) A randomized double-blinded controlled clinical research on treating opiate withdrawal syndrome by Jitai Capsule and lofexidine. Hubei Journal of Traditional Chinese Medicine 26(2):23-25. |
| *20 | Yang XS, Mao C, Jing FB, Chu GY, Yang J. (1997) Clinical research of Duyinxiao capsule to treat heroin withdrawal syndrome. Zhongyi Zhazi 38(8):483-484. |
| *21 | Zhou KC, Liu JG, Xie RQ. (2003) An observation on clinical efficacy of Tuoduling Capsule in the treatment of heroin dependence. Chinese Magazine of Drug Abuse Prevention and Treatment 9(4):17-19. |
| *22 | Zou DH, Liu TQ, Kuo W. (1999) A study of Keyinning Capsule and lofexidine to treat opiate withdrawal syndromes. Hunan Medical Journal 16(2):27-28. |
| **(C)** | **CH vs. methadone** |
| *23 | Huang P, Wu G, Zhou PL, Wu HJ, Tang YM. (2005) A clinical observation of Yian Decoction in the treatment of heroin dependence. Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine 5(3):15-16. |
| *24 | Lu HQ, Wang G, Lan SM, Yuan TF, Jin ZM. (1997) Clinical study of Qingjunyin for the treatment of heroin addicts. Clinical Journal of Medical Officer 25(3):1-3. |
| *25 | Sha LJ, Zhang ZX, Cheng LX, Liu J, Zhang ZM. (2000) Treatment of Heroinism Abstinence by Xinxheng Koufuye: Clinical Investigation of 424 cases. Zhongguo Zhongxiyijiehe Zhazi 20(4):267-268. |
| *26 | Xu BS, Tie EG, Wang PX, Lu QL, Sun ZW, Jin J, Sun ZT. (2000) A controlled trial using Qingdubuzheng decoction to treat heroin dependence. Chinese Magazine of Treatment and Prevention of Drugs Abuse (1):6-9. |

| | |
|---|---|
| *27 | Yang L, Xu X, Chen J, Li LJ, Weng PX, Zhang XL. (2006) Controlled Clinical Study on Paiduyangsheng Capsule in Detoxification of heroin abuse . Chinese Journal of Drug Abuse Prevention and Treatment 12(2):86-89. |
| *28 | Xiao ZX, Qin DS, Li J, Min MS, Ren GH, Yang JH. (2007) The observation of curative effect of methadone and Yian Huisheng oral liquid for treating heroin addict. Chinese Magazine of Drug Abuse Prevention and treatment 13(4):196-198, 233. |
| **(D)** | **CH vs. buprenorphine** |
| *29 | Chao XM, Hu WJ. (2005) A clinical research of Yi An Decoction in treating heroin dependence. Chinese Magazine of Drug Abuse Prevention and Treatment 11(5):295-296. |
| *30 | Hao W, Zhao M. (2000) A clinical study on the effect of WeiniCom, a Chinese herbal compound, in alleviation of heroin withdrawal symptoms. Journal of Psychoactive Drugs 32(3):277-284. |
| *31 | Liu JY, Gu Q, Wu XW, Zhou JY. (1997) A clinical research of Yijienin Decoction to treat opiate dependence. Journal of Nanjing University of Traditional Chinese Medicine (Natural Science) 13(4):204-206. |
| *32 | Liu JY, Yang QH, Wu XW. (2001) A clinical study on the treatment of heroin abstinence syndrome by *yang*-warming, *qi*- and blood-invigorating prescriptions. New Chinese Medicine 33(1):19-22. |
| *33 | Zhu CQ, Zhang HS, Fan XC, Chen DM. (1999) Treatment of heroin dependence by Jiedutuoyin Capsule in 131 cases. Shiyoung Zhongyi Zhazi 15(11):3-5. |
| **(E)** | **CH vs. valium or tramadol** |
| *34 | Yang T, Ma JQ, Sun XJ, Lin Z. (2001) Clinical study of acupuncture for heroin detoxification. Journal of Guiyang College of TCM 23(4):56-59. |
| *35 | Zong L., Hu J., Li Yu, Lu Ying, Xin YF. (2001) Comparison of the breaking effects of acupuncture, Chinese Medicine and their combination on heroin addiction. Shanghai Journal of acupuncture 20(2):1-3. |
| *36 | Xiong J.G, Li J. (2000) Clinical observation of treating heroin dependence with the combination of traditional Chinese and Western medicine. Chinese Magazine of Drug Abuse Prevention and Treatment 6:46-8. |

### 3.3.2 Long-term detoxification of heroin dependence

| | |
|---|---|
| *37 | Cai Z, Xu SH. (1998) Clinical observation of 50 cases in the treatment of protracted abstinent syndrome by using Guipi decoction. Hunan Journal of Trational Chinese Medicine 14(3):25. |
| *38 | Chen HX, Hao W, Liu TQ. (2004) A controlled study on clinical efficacy of Chinese herbal compounds, Anjunning and Kanfuxin on alleviating opioid protracted abstinent symptoms. Chinese Journal of Clinical Psychology 12(1):38-40. |

| | |
|---|---|
| *39 | Cui QR, Li H, Li CP, et al. (2004) The Practical Research on the Treatment of protracted opioid abstinence syndrome by Corydalis Yanhusuo Capsule. Chinese Magazine of Drug Abuse Prevention and Treatment 10(2):74-76. |
| *40 | Huang DB, Liu XL, Yu ZF, Fu L. (2004) Efficacy of Huoxiangzhengqi Oral Liquid and tablet of Radix et Caulis Acanthopanacis Senticosi on withdrawal symptoms from heroin. Chinese Traditional Patent Medicine 26(5):382-385. |
| *41 | Huang DB, Yu ZF, Fu L. (2006) Efficacy of modified banxia houpu decoction on protracted abstinence syndrome and one-year relapse rate after heroin-detoxification. Chinese Journal of Clinical Rehabilitation 10(11):165-167. |
| *42 | Jian YP, Wang DM, Nie RC. (2007) Clinical Observation of 91 cases in treatment of protracted abstinent headache based on differential treatment of Jueyin. Journal of Chinese Emergency Medicine 16(7):801-802. |
| *43 | Li ZH, Li Q, Du Q, Wang Y. (2007) The efficacy of Chinese herbs for treating heroin addicts with *qi* and *yin* deficiency. Herald of Medicine 26(7):766-767. |
| *44 | Li ZH, Tang YX, Hua SZ, Wang Y. (2007) Efficacy of Jitai for protracted withdraw symptoms in heroin addicts. Chinese Journal of Drug Dependence 16(4):284-287. |
| *45 | Long HW, Mei ZL, Den CL. (2002). The treatment of protracted abstinent syndrome by herbal detoxification and nourishing *qi* -- Clinical observation of 39 heroin addicts. Chinese Magazine of Drug Abuse Prevention and Treatment (4):20-22. |
| *46 | Mo ZX, Wang CY, Luo XY, et al. (2002) The efficacy of Qingfeng capsules in treatment of protracted withdrawal syndrome of heroin addicts. Chinese Journal of Clinical Rehabilitation 6(23):3588-3589. |
| *47 | Wu ZM, Jia SWi, Luo HE, Wu P, Xie XJ, Ou HH, Yin SG. (2004) Clinical observation on U'finertm capsules for treating heroin induced prolonged withdrawal symptoms. Chinese Journal of Drug Dependence 13(1):50-54. |
| *48 | Xu GL, Wang CS, Song XZ, Yang F, Wang Z, Tang ZL. (2005) Clinical observation of treating protracted abstinence syndrome from heroin dependent by Yiyinningsheng Decotion. Journal of Anhui TCM College 24(1):5-6. |
| *49 | Yang T, Yang Y, Huang ZF (2006) Yianhuisheng Oral-liquid in the treatment of protracted abstinent syndrome after heroin detoxification: observation of 40 heroin addicts. Chinese Journal of Drug Abuse Prevention and Treatment 12(4):214-215. |
| *50 | Zhong GW. (2003) Clinical Observation of 96 Cases of Heroin Dependent User on Protracted Withdrawal Syndrome. Treatment.Journal of Traditional Chinese Medicine 44(6):437-438. |

### 3.3.3 Treating adverse symptoms of psychotropic drugs

| | |
|---|---|
| *51 | Li XY, Wang XL. (2005) A comparative clinical study of the therapeutic effect of Rhubarb Mirabilite and Magnolia Officinalis Rehd et Wils in treating neuroleptic-induced astriction. Journal of Nursing Science 20(13):43-44. |
| *52 | Xie ZY, Yao XF, Su M, Zhao YH. (2008) A comparative clinical study of the therapeutic effect of 3 different approaches in treating neuroleptic-induced astriction. International Medicine & Health Guidance News 14(9):52-55. |
| *53 | Ding ZM. (1998) A comparative randomized controlled clinical study of different approaches in treating neuroleptic-induced astriction. Journal of Nursing Science 13(4):197-199. |
| *54 | Li CW. (2003) A comparative therapeutic study of randomized controlled clinical trials of different approaches in treating neuroleptic-induced astriction. Chinese Journal of Geriatric Care 1(3):33-34. |
| *55 | Pan HM, Li JW. (2002) A comparative study of randomized controlled clinical trials of Shen Qi Wu Wei Zi tablets in treating side effects induced by antipsychotics. China Synthesis Medicine 3(10):888-889. |
| *56 | Yang BS. (2006) A comparative randomized controlled clinical study of Wendan decoction in treating neuroleptic-induced impaired digestion. Journal of Shanxi Traditional Chinese Medicine University 7(6):30. |
| *57 | Zhang F, Fei JF, Lu GH, Lu SL. (2005) A comparative study of randomized controlled clinical trials of the efficacy of traditional chinese medicine decoction in the prevention of hyperglycemia hyperlipemia and other adverse events caused by antipsychotics. Journal of Practical Traditional Chinese Medicine 21(12):717-718. |
| *58 | Hu SH, Xu SQ. (2004) A comparative study of randomized controlled clinical trials of the efficacy of self enacted traditional chinese medicine decoction in treating anticholinergic effect caused by antipsychotics. Journal of Hubei Traditional Chinese Medicine 26(6):43. |
| *59 | Li BJ, Fang M, Fan CL, Wu B. (2002) A randomized controlled clinical study of the efficacy of Fuan decoction in the prevention of adverse effect caused by antipsychotics. Journal of Shanxi Traditional Chinese Medicine 23(8):706-707. |
| *60 | Lu BL, Chen CP. (2002) A comparative randomized controlled clinical study of the effectiveness of anshenjianpi syrup in the treatment of antipsychotic-induced side reactions of digestion tract. Journal of Nursing Science 17(5):361-363. |

| | |
|---|---|
| *61 | Yin CR. (2000) A comparative randomized controlled clinical study of the preventive and curative effect of Shengmai Yin on the adverse drug reactions of antipsychotics. Journal of Anhui Traditional Chinese Medicine College 19(1):13-15. |
| *62 | Zhu YP. (2005) A comparative randomized controlled clinical study of the efficiency and possible mechanism of liver ferment resulted from Composite Salviae dropping pill together with Clozapine. Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine 5(2):5-6. |
| *63 | Fan QZ, Zhang LY, Dan H, Yu SW, Bo CG, Zhao HQ. (1996) A randomized controlled clinical comparative study of Huangyuan powder in reducing antipsychotics induced salivation. Shandong Archives of Psychiatry (2):17-19. |
| *64 | Wen YW, Huang YW, Gan JX, Mao YW, Zhou ZJ, Liang YR, Luo GC. (2008) A randomized controlled clinical comparative study of Lianziqingxin syrup in reducing antipsychotics induced salivation. Journal of New Medicine 5(1):24-25. |
| *65 | Shi J, Qi JN, Tao JQ, Zeng Q. (2007) A randomized controlled clinical comparative study of Liujunzi decoction or Xiehuang decoction in reducing antipsychotics induced salivation. Journal of Shanxi Traditional Chinese Medicine 28(10):1318-1320. |
| *66 | Xiong H, Xu SQ. (2006) A randomized controlled clinical comparative study of Xiangshaliujun pill in reducing antipsychotics induced salivation. Medical Journal OF Chinese People's Health 18(10):898-899. |
| *67 | Zhang ZF. (2003) A randomized controlled clinical comparative study of Lizhong decoction in reducing neuroleptic salivation. Guangming Journal of Araditional Chinese Medicine 18(108):45-46. |
| *68 | Lin W, Peng XX. (2002) A randomized controlled clinical comparative study of the therapeutic effect of Chenxia Liujunzi pill for neuroleptic salivation. New Journal of Traditional Chinese Medicine 34(8):19-20. |
| *69 | Yuan CM, Zhao XY, Han QY. (2000) A randomized controlled clinical comparative study of Suoquan pill in reducing antipsychotics induced salivation. Chinese Journal of Psychiatry 33(4):206. |
| *70 | Zhao ZH, Chen HM, Xie BY, Sun SG, Wu HY, Ma QM, Guo JM, Liu HY, Zhang RJ, Qu JX, Wang JM, Geng B. (2000) A randomized controlled clinical comparative study of Zhiyan capsule in reducing antipsychotics induced salivation. Medical Journal of Chinese Civil Administration 12(2):95-96. |
| *71 | Kang B, Liu YC, Zhang YP, Han Y, Fan LZ, Zhou J. (1993) A randomized controlled clinical comparative study of Suoquan pill in reducing antipsychotics induced salivation. Chinese Journal of Integrative Medicine 13(6):347-348. |

| | |
|---|---|
| *72 | Zhou Z, Fu R, Huang P. (2006) A randomized controlled clinical study of Hugan decoction in treating hepatic damage induced by antipsychotics. Journal of Tianjin University of Traditional Chinese Medicine 25(3):172-174. |
| *73 | Dai RZ, Xu WL, Qiao HL. (2003) A randomized controlled clinical study of Chinese medicine in treating diseases induced by antipsychotics. Journal of Shanxi Traditional Chinese Medicine 24(2):142-144. |
| *74 | Wang ZF. (2003) A randomized controlled clinical study of Chinese medicine Tongfuqingyu decoction in treating paralytic ileus induced by antipsychotics. Chinese Journal of Misdiagnostics 7(28):6794-6795. |
| *75 | Zhao JT, Cheng ZC, Wang J, Wang LH. (2001) A randomized controlled clinical study of Chinese medicine Dahuangjugeng decoction in treating dysuria induced by antipsychotics. Chinese Journal of Behavioral Medical Science 10(1):50. |
| *76 | Zhang ZL. (2007) A randomized controlled clinical study of Chinese medicine in treating sexual dysfunction induced by antipsychotics. Journal of Practical Traditional Chinese Medicine 23(7):433-434. |
| *77 | Zhang TL, Cao BY. (1997) A randomized shifting controlled clinical study of Chinese medicine in treating decrease in WBC and PMN (polymorphonuclear leukocyte) induced by antipsychotics. Chinese Journal of Integrative Medicine 17(12):751. |
| *78 | Ding GA, Yu GH, Zhang JD, Liang XC, Liu LQ, Huang P, Chen WJ, Qiao AX, Li XF, Cai YL. (1997) A randomized controlled clinical study of Chinese medicine Lingguizhugan decoction in treating obesity induced by antipsychotics. Journal of Traditional Chinese Medicine 44(6):441-442. |
| *79 | Wang DH, Yang BS, Lu XP. (2001) A randomized controlled clinical study of Chinese medicine decoction in treating clozapine induced increase in body weight. Journal of Chinese Traditional Chinese Medicine 17(4):18-19. |
| *80 | Yang DD. (2006) A randomized controlled clinical study of Chinese medicine in treating Benzodiazepine induced insomnia and other adverse effect. Chinese Journal of information on TCM 13(10):60-61. |
| *81 | Wang P, Duan DX, Wang XF, Wang YT. (2006) A randomized controlled clinical study of Chinese medicine in treating dry mouth induced by antipsychotics. Journal of Sichuan Traditional Chinese Medicine 23(3):48-49. |
| *82 | Yuan GZ, Huang P, Zhao JF, Gong JX. (2006) A randomized controlled clinical study of Chinese medicine in treating dry mouth induced by antipsychotics. Journal of Clinical Psychological Medicine 10(3):189. |
| *83 | Hu XZ, Wu XF. (1996) A randomized controlled clinical study of Chinese medicine Longdanxiegan pill in treating dry mouth induced by antipsychotics. Journal of ZhongYuan Psychological Medicine 2(4):226-228. |

| | |
|---|---|
| *84 | Kong M, Gao XM, Gong H. (2005) A randomized controlled clinical study of Chinese medicine Dangguibuxue decoction (DBD) in treating leucopenia induced by clozapine. Journal of Shanxi Traditional Chinese Medicine 21(2):52-53. |
| *85 | Xu LP, Ji JY, Chen FB, Zhao YQ. (2005) A randomized controlled clinical study of Chinese medicine Dangguibuxue decoction (DBD) in treating leucopenia induced by clozapine. Clinical Focus 20(3):162-163. |
| *86 | Zhan CH, Wang HJ, Zhang ZH. (2002) A randomized controlled clinical study of Chinese medicine donkey-hide gelatin syrup compared with batiol and vitamin B4 in treating leucopenia caused by clozapine. Shangdong Archives of Psychiatry 15(3):147-148. |
| *87 | Guo YM, Liu CF, Wang QX. (2001) A randomized controlled clinical study of Chinese medicine Shengbai decoction compared with batiol and vitamin B4 in treating leucopenia caused by clozapine. Research of Traditional Chinese Medicine 17(2):12. |
| *88 | Kong DR. (1999) A randomized controlled clinical study of Chinese medicine Guipi decoction compared with Leucogen in treating leucopenia caused by clozapine. Journal of Traditional Chinese Medicine 40(6):377-378. |
| *89 | Gong LB. (2008) A randomized controlled clinical study of Chinese medicine Liuwedihuang pill in treating antipsychitics induced enuresis. Journal of Henan Traditional Chinese Medicine 28(7):96-97. |
| *90 | Liu SP. (2001) A randomized controlled clinical study of Chinese medicine Suochuan pill in treating clozapine induced enuresis. Chinese Journal of Traditional Medical Science and Technology 8(4):218. |
| *91 | Yuan CM, Lu SC, Han QY. (2001) A randomized controlled clinical study of Chinese medicine Suochuan pill in treating clozapine induced enuresis. Forum on Traditional Chinese Medicine 16(1):40. |
| *92 | Mao ZX, Zhang JH, Cheng J. (2008) A randomized controlled clinical study of Chinese medicine Xuefuzhuyu capsule in treating antipsychotics induced amenorrhea. Journal of Hebei Traditional Chinese Medicine 27(6):456-458. |
| *93 | Cui GM, Zhang RL, Duan DX. (2006) A randomized controlled clinical study of Chinese medicine Xuefuzhuyu decoction in treating antipsychotics induced amenorrhea. New Jouranl of Traditional Chinese Medicine 38(1):56-57. |
| *94 | Yang JJ. (2003) A randomized controlled clinical study of Chinese medicine self enacted chinese medicine decoction in treating antipsychotics induced amenorrhea. Chinese Journal of Information on Traditional Chinese Medicine 10(8):52-53. |

| | |
|---|---|
| *95 | Wu LM, Xie CP. (2000) A randomized controlled clinical study of Chinese medicine Xuefuzhuyu decoction in treating antipsychotics induced amenorrhea. Chinese Journal of Integrative Medicine 20(9):704-705. |
| *96 | Yuan ZQ, Gao JJ, Ouyang X, Zhou YG. (2001) A randomized controlled clinical study of the therapeutic efficacy of composite salvia miltiorrhiza injection and naloxone in treatment of acute severe diazepam poisoning. Practical Clinical Medicine 2(3):48-49. |
| *97 | Lin XL, Zhang XY. (2003) A randomized controlled clinical study of the therapeutic efficacy of Xingnaojing injection and naloxone in treatment of acute severe diazepam poisoning. Chinese Magazine of Clinical Medicinal Professional Research (80):13285 |
| *98 | Li HJ, Chen Y, Gao GP. (2004) A randomized clinical study of the therapeutic efficacy of Xingnao injection and naloxone in treatment of acute severe diazepam poisoning. Chinese Magazine of Clinical Medicinal Professional Research (130):13848 |
| *99 | Ding HT. (2004) A randomized clinical study of the therapeutic efficacy of Fufang Shexiang injection and naloxone in treatment of acute severe diazepam poisoning. Hubei Journal of Traditional Chinese Medicine 26(10):20-21. |
| *100 | Lin LS, Guo S. (2005) A randomized controlled clinical study of the therapeutic efficacy of Daoxie decoction compared with naloxone in treatment of acute severe diazepam poisoning. Journal of Emergency in Traditional Chinese 14(10):948. |
| *101 | Yan PJ. (1998) A randomized controlled clinical study of the therapeutic efficacy of Xingnaojing in treatment of acute severe diazepam poisoning. Journal of Henan Medical University 33(2):89. |
| *102 | Li JR, Rong K. (2005) A randomized controlled clinical study of the therapeutic efficacy of Qingkailing injection combined with naloxone in treatment of acute severe antipsychotics poisoning. Journal of Practical Nervous Diseases 8(2):73. |
| *103 | Zhao ZD, Wang Z. (2007) A randomized controlled clinical study of the therapeutic efficacy of Xingnaojing injection in treatment of acute severe diazepam poisoning. Journal of Practical Traditional Chinese Internal Medicine 21(9):79. |
| *104 | Zhou HJ, Zhu YP. (2003) A randomized controlled clinical study of Fufang Danshen pill in the treatment of change in ST-T in ECG induced by clozapine. Mordern Practical Medicine 15(2):100-101. |
| *105 | Liang XC, Mou M. (2001) A randomized controlled clinical study of Tianhuangbuxin pill in the treatment of change in ST-T in ECG induced by antipsychotics. New Journal of Traditional Chinese Medicine 33(11):30-31. |

| | |
|---|---|
| *106 | Wang M, Yu C. (2001) A randomized controlled clinical study of Tongxinluo capsule in the treatment of change in ST-T in ECG induced by antipsychotics. Journal of Hebei Traditional Chinese Medicine 23(7):544-545. |
| *107 | Zhang TL, Wang RF, Sun LL, Wang SB. (2000) A randomized controlled clinical study of Tongxinluo capsule in the treatment of change in ST-T in ECG induced by antipsychotics. Chinese Journal of Integrative Medicine 20(4):298. |

## 3.4 Excluded-trial list

| No. | Title of study | Author | Origin | Year | R |
|---|---|---|---|---|---|
| 1 | Efficacy of methadone combined with Yian decoction to treat hero dependence | Diao JH, Deng GF | Chinese Journal of Drug Dependence 16(5): 355-358 | 2007 | B |
| 2 | Effects of Xuefuzhuyu decoction combined with methadone in the treatment of 216 cases of heroin addicts | Deng XF, Zhang XF | Chinese Journal of Treatment and Prevention of Drug Abuse 13(5): 273-274,282 | | B |
| 3 | Efficacy of methadone combined with Shenfutuodu capsue for heroin detoxification | Gu N | Chinese Journal of Treatment and Prevention of Drug Abuse 13(4): 203-205 | | B |
| 4 | A clinical observation of Yianningsheng decoction to treat 100 cases of heroin addicts (protracted withdrawal symptoms) | Xu GL, Xu XG | Chinese Journal of Traditional Medical Science and Technology 13(1): 53-54 | 2006 | A |
| 5 | A clinical research of Banxiahoupu decoction for protracted symptoms of heroin withdrawal – one-year relapse rate analysis | Wang TB, Yu SF | Chinese Journal of Clinical Rehabilitation 10(11): 53-54 | | A |
| 6 | A clinical observation of "Shengshen injection" for heroin withdrawal | Cheng W, Song SL | International Medicine and Health guided news journal 12(7): 47-48 | | D |
| 7 | Yian decoction combined with buprenorphine for the treatment of heroin withdrawal symptoms | Li CC, Lin WP | Chinese Journal of Treatment and Prevention of Drug Abuse 12(4): 209-211 | | B |
| 8 | Combined Chinese and Western medicine to treat heroin dependence | Huang P, Wu G | Chinese Journal of Treatment and Prevention of Drug Abuse 12(5): 285-286 | | B |
| 9 | Combined Chinese and Western medicine to treat 250 cases of heroin dependence | Xu JX, Liu ZY | Chinese Journal of Treatment and Prevention of Drug Abuse 11(5): 293 | 2005 | B |
| 10 | Yiyin decoction to treat protracted withdrawal symptoms: a clinical observation of 115 cases | Wang J, Tang ZL | Journal of Anhui Traditional Chinese Medical College 24(1): 5-6 | | A |

| | | | | | |
|---|---|---|---|---|---|
| 11 | Banxiahoupu decoction for protracted symptoms of heroin withdrawal: clinical observation of 135 cases | Wang B, Liu SF | Journal of Traditional Chinese Medicine 24(6): 15-16 | | A |
| 12 | Clinical study of Anjunning and Kanfuxin in the treatment of heroin protracted withdrawal symptoms | Zheng HX, Kuo W | Chinese Journal of Clinical Psychiatry 12(1): 38-40 | 2004 | A |
| 13 | Clinical efficacy of Shengfu decoction and buprenorphine in the treatment of heroin withdrawal | Liu QW, Wang H | Chinese Journal of Drug Dependence 13(3): 121-123 | | B |
| 14 | Clinical observation of "Tuoyingfang" in the treatment of protracted withdrawal symptoms | Yuan J, Song XG | Chinese Journal of Information on Traditional Chinese Medicine 9(9): 26-27 | | A |
| 15 | Clinical observation of Jinjiawang decoction to treat 242 heroin addicts | Zhang CF | Chinese Journal of Treatment and Prevention of Drug Abuse 10(2): 106-107 | | D |
| 16 | Clinical observation of Fufang Yuanhu Capsules to treat heroin withdrawal symptoms | Chui QY, Li H | Chinese Journal of Treatment and Prevention of Drug Abuse 10(2): 74-76 | | B |
| 17 | A clinical observation of Jiufukang Capsules to treat protracted withdrawal symptoms | Lo W, Jia SM | Zhong Hua Xiandai Zhong Xi Yi Jiehe Zhazi 2(4): 296-297 | | A |
| 18 | A clinical observation of Chinese medicine combined with Western medicine in the treatment of heroin withdrawal symdrome | Zhang H, Song XG | Zhongguozhongxiyijiehe Zhazi 10(2): 23-25 | 2003 | B |
| 19 | Clinical observation of Yian decoction to treat 143 heroin addicts | Li ZB, Xu Z | Chinese Journal of Treatment and Prevention of Drug Abuse 9(3): 62-64 | | B |
| 20 | Clinical observation of Zheqingfengtongying pian to treat heroin addiction | Wang TQ, Yang ZJ | Zhongguo Zhongyi Xinxi Zhazi 10(2): 59 | | D |
| 21 | Zhengqingfengtongning Pian in treatment of in 100 heroin addicts | Wen TQ, Yang ZJ, Lei XL | Zhongguo Zhongyi Xinxi Zhazi 10(2): 59 | | D |
| 22 | Clinical observation of Yikangling for opiate detoxification | Wu JW, Su YP | Proceeding of Clinical Medicine Journal 12(5): 377-378 | | D |

| | | | | | |
|---|---|---|---|---|---|
| 23 | Detoxification with Zheng Qing Feng Tong Ling in 100 heroin addicts | Wen TQ, Yang SJ, Lei XL | Zhoungguo Zhongyiyao Xinxi Zhazi 10(2): 59 | | D |
| 24 | Treatment of 96 cases of protracted heroin abstinence symptoms by syndrome differentiation: clinical reserach | Zhong GW | Journal of Traditional Chinese Medical 12(1): 28-29 | | A |
| 25 | Clinical research of Chinese medicine Tuoyingfang combined with methadone for heroin detoxification | Yuan J, Song XG | Zhoungguo Zhongyiyao Xinxi Zhazi 9(9): 26-27 | 2002 | B |
| 26 | Clinical research of Qifeng Capsules to treat protracted withdrawal symptoms after heroin detoxification | Mo XY, Luo XY | Zhongyi Linchuan Kanfu Zhazhi 6(23): 3588-3589 | | A |
| 27 | Management of 56 cases of acute heroin intoxication with Xingaojing and naloxone | You SL, He XP | Journal of Practical Traditional Chinese Internal Medicine 16(4): 226 | | B |
| 28 | Clinical study of detoxification with Shifusheng capsules | Jin J, Zeng H | Chinese Journal of Treatment and Prevention of Drug Abuse (3): 37-38 | | B |
| 29 | Detoxification of 32 heroin addicts with Huakang Capsules | Han SF | Research of Traditional Chinese Medicine 18(2): 13-14 | | B |
| 30 | Buyang Huanwu Tang for preventing relapse of drug addiction after detoxification: A clinical observation of 60 cases | Jian BJ, Wang LM | New Journal of Traditional Chinese Medicine 34(5): 15-16 | | B |
| 31 | Detoxification with large dose of Chinese herbal medicine | Li CN | Journal of Hubei College of TCM 4: 50 | | C |
| 32 | Tonifying *qi* and detoxification herbs to treat protracted abstinence symptoms: clinical observation of 39 cases | Long HY, Li YX | Chinese Journal of Drug Dependence 4: 20-22 | | A |
| 33 | Treatment of 30 heroin addicts with combination of Rotundine, 654-2 and Alprazolam | Fang HM, Yang GX | Journal of Jianggsu Clinical Medicine 5(6): 594 | 2001 | B |
| 34 | Treatment of 120 drug addicts with a Chinese herbal pill (Case report) | Ou YM, Wu ZM | Hunan Journal of TCM 16(3): 37-38 | | C |

| | | | | | |
|---|---|---|---|---|---|
| 35 | Clinical observation of Combined Jitai Capsule and nofexidine to treat heroin dependence | Xiong JG, Xiao ZX | Chinese Journal of Drug Dependence 10(4): 290-294 | | B |
| 36 | Treatment of 445 opiate addicts with an experienced herbal detoxification formula | Tang XS | Zhongguo Mingjian Mingzu Yiyao Zazhi (6) 334-33 | | B |
| 37 | Clinical observation on 30 cases of heroin withdrawal syndrome treated with Huo Su Jun Wen Decoction | Li ZF | Journal of Traditional Chinese Medicine 42(4): 224-225 | | D |
| 38 | A case report of opiate detoxification with Sukunsang | Li MC | Chinese Journal of Treatment and Preventtion of Drug Abuse 15(2): 21 | | C |
| 39 | Clinical analysis of Yian Decoction in heroin detoxification | Liu RK, Xu GZ | Chinese Journal of Drug Dependence 10(3): 200-203 | | A |
| 40 | Clinical observation of Ketongyin in heroin detoxification | Zhang XD, et.al | Chinese Journal of Drug Abuse and Dependence 16(2): 45-47 | | D |
| 41 | Clinical observation of treating heroin dependence with the combination of traditional Chinese and Western medicine | Xiong JG, Li J | Chinese Journal of Drug Dependence 17(1): 46-48 | 2000 | D |
| 42 | Treatment of heroin abstinence syndrome by Xinxheng Koufuye: a clinical report of 424 cases | Sha LJ, Zhang ZX, Cheng LX, Liu J, Zhang ZM | Zhongguo Zhongxiyijiehe Zhazi 20(4): 267-268 | | D |
| 43 | A clinical trial on herbal preparation for drug withdrawal symptoms | Yu ZQ, Huang DB, Yu ZF | Journal of Hubei Institute for Nationalities 17(1): 15-18 | | D |
| 44 | Opiate detoxification with Sukun in addicts | Zhu YX, Sun JS | Journal of Drug Abuse 11(2): 19-2 | | C |
| 45 | Application of Radix Salviae Miltiorrhizae preparations in the treatment of drug withdrawal | Liu LJ, Xiao MM | Journal of Guiyang College of TCM 22(2): 13-14 | | D |

| | | | | | |
|---|---|---|---|---|---|
| 46 | Clinical observation of Xieyangkang capsules to treat heroin protracted abstinence symptoms | Wang XZ, Ma SL | Zhongguo Zhongxiyixingxi Zhazi 7(8): 53 | | D |
| 47 | Efficacy analysis of Zhetongying tablets to treat opiate withdrawal symptoms | Sheng LX, Jiang ZY | Chinese Magazine of Drug Abuse Prevention and Treatment (5): 39-42 | 1999 | B |
| 48 | 40 heroin addicts treated by Chinese medicine Taiji Tablet | Luan XM | Jiu Jiang Medical Journal 14(2): 120-121 | | D |
| 49 | Clinical study of Zhengtong Capsules to treat protracted withdrawal symptoms: a report of 100 cases | Zhang XS, Wang G | Zhongguo Zhongxiyijiehe Zhazi 19(5): 15-17 | | A |
| 50 | Case report: detoxification with Chinese herbal medicine in 68 drug addicts | Wang L | Zhejiang Zhongxiyi Jiehe Zazhi 10(5): 306 | | C |
| 51 | Keyinning Capsule and Lipofren in the treatment of opium withdrawal symptoms: a control trial | Zhou DH, Liu TQ | Hunan Medical Journal 16(2): 119-120 | | B |
| 52 | Preliminary observation on the effect of Yianhuisheng Oral-liquid | Shi X | Hainan Medical Journal 10(4): 263 | | B |
| 53 | Treating protracted withdrawal syndrome after heroin detoxification: a clinical observation of 300 cases | Liu LJ, Cheng GL | Chinese magazine of Drug Abuse Prevention and Treatment 8(3): 215-216 | | A |
| 54 | Influence of herbal preparations in heroin addicts' microcirculation | Liu JY, Guo Q | Journal of Nanjing University of TCM 15(6): 338-340 | | D |
| 55 | Treatment of 616 heroin addicts with Shuxiaojieduye | Qiao YH Zhang DQ | The Practical Journal of Integrated Chinese and Western Medicine 11(6): 494 | 1998 | B |
| 56 | The clinical effects of modified Mahuang Fuzhi Xixin Tang in 29 drug addicts | Shen HQ | Zhong Chen Yao 20(2): 22-23 | | D |
| 57 | Colonic dialysis therapy of Chinese herbal medicine in heroin detoxification: a report of 75 cases | Sha Lj, Ge WD | Chinese Journal of Integrative Medicine 17(2): 76-78 | | B |
| 58 | Primary research on Jie Du Qing for heroin detoxification | Lan XY, Deng HC | Weisheng Dulixue Zazhi 11(1): 69-71 | | D |

| | | | | | |
|---|---|---|---|---|---|
| 59 | A clinical report of Jieduanfang in the treatment of 60 heroin addicts | Yang DN, Rui XL | Chinese Journal of Traditional Medical Science and Technology 4(3): 178-180 | | D |
| 60 | Clinical observation of combined traditional Chinese and Western medicine to treat heroin dependence: 51 cases | Ge XM, Li DY | GuangxiYixue Zhazhi 18(5): 609-611 | 1997 | B |
| 61 | Clinical analysis of combined Chinese and Western medicine to treat heroin withdrawal symptoms | Wang JX | Guangdong Yixue Zhazi (4): 13-14 | | C |
| 62 | A clinical observation of Yinxiaoshu Mixture in drug detoxification | Qu QM, Li Z, Qu B, Zhang J, Jin YY | Henan Zhongyi Zhazhi 16(2): 39-40 | 1996 | B |
| 63 | Humen Mixture of TCM for heroin detoxification | Yang WY, Wang XZ, Li F | Journal of Beijing University of Traditional Chinese Medicine 19(4): 47-48 | | D |
| 64 | Jiawei Huangliangejiao decoction to treat heroin withdrawal symptoms | Liu AQ | Zhongguo Minjiang Liaofa Zhazi 4: 35-36 | | C |
| 65 | A case report: liver damage caused by drug abuse | Weng P | Zhongxiyi Jiehe Zazhi 6(4): 13 | | C |
| 66 | Clinical observation of Fuzhe Mixture and clonidine to treat opiate withdrawal | Wang XP Li CM | Chinese Magazine of Drug Abuse Prevention and Treatmen 7(2): 25-26 | | B |
| 67 | Treatment of heroin addicts with acupuncture and herbal medicine: an observation of 25 cases | Zhuang LX, Chen XH, Jian GH | Journal of Guangzhou University of TCM 12(1): 30-35 | 1995 | B |
| 68 | Primary observation on the treatment of 15 heroin addicts | Zhang C, Xu L, Fang L, | Yunnan Journal of Traditional Chinese Medicine 16(6): 5-8 | | C |
| 69 | Study of using Shennong suppository for opiate detoxification | YU LX | Zhongyi Hanshou Tongxun 14(4): 36-37 | | B |
| 70 | Observation of 131 heroin addicts treated with Jiedu Tuoying capsulas | Zhang HS, Zhu CQ, Fan XC | Shiyong Zhongyi Zazhi 15(11): 3-5 | | D |
| 71 | Clinical observation on efficacy of traditional Chinese | Li ZH, | Chinese Journal of Treatment and Prevention of Drug Abuse | 2007 | E |

| | | | | | |
|---|---|---|---|---|---|
| | medicine and methadone in heroin addicts | Li Q | 13(3): 137-138,162 | | |
| 72 | A clinical trial of Chinese medicine in the treatment of alcohol protracted withdrawal syndrome | Jian YP, Wang DM | Chinese Journal of Treatment and Prevention of Drug Abuse 12(5):265-267 | 2006 | A |
| 73 | Therapeutic effects of modified Banxiahoupu decoction for protracted abstinent syndrome in 135 heroin addicts | Huang DB, Yu SF | Journal of Traditional Chinese Medicine 46(6):130-132 | 2005 | E |
| 74 | Clinical observation of modified Banxiahoupu decoction in treating heroin addicts with protracted abstinence syndrome | Huang DB, Yu SF | Chinese Journal of Integrated Traditional and Western Medicine 24(3):216-218 | 2004 | E |
| 75 | Buyanghuanwu decoction for avoidance of narcotic retaking: a clinical observation of 60 cases | Jiang BJ, Wang LM | Journal of New Chinese Medicine 24(5):15-16 | 2002 | B |
| 76 | Therapeutic effects of Xingnaojing injection in the treatment of acute and severe poisoning of psychotropic drugs | Long YE | Journal of Shanxi Traditional Chinese Medicine 26(2): 125-126 | 2005 | D |
| 77 | Research of Danshen pill for treating abnormal liver function induced by clozapine | Zhu YP | Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine 5(2): 5-6 | 2005 | D |
| 78 | The efficacy of traditional Chinese medicine in the prevention of adverse events caused by antipsychotics | Lu GH, Lu SL | Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine 4(3): 5-6 | 2004 | E |
| 79 | The effects of aloe-paste in the treatment of constipation induced by antipsychotic agents | Zhang ZC | Journal of Qilu Nursing 10(6):419-420 | 2004 | B |
| 80 | Clinical observation of Lingguizhugan decoction in the treatment of psychotic medication-induced obesity | Ding GA, Yu GH | Journal of Traditional Chinese Medicine 44(6): 441-442 | 2003 | E |
| 81 | Oingkailing to treat acute-poisoning of valium: 30 cases | Zhu TQ, Dai YQ | Journal of Emergency in Traditional Chinese 12(4): 360 | 2003 | D |

| | | | | | |
|---|---|---|---|---|---|
| 82 | Therapeutic effects of rhubarb-powder in the treatment of antipsychotic constipation | Liang YM, Shuai SP | Journal of Nursing Science 17(1): 47-48. | 2002 | B |
| 83 | The effects of Syr Anshengjianpi for side effects caused by antipsychotic drugs in digestive system | Li KQ, He XJ | Medical Journal of Chinese Civil Administration 13(6): 326-330 | 2001 | E |
| 84 | Therapeutic effects of Guipi decoction for leucopenia induced by clozapine | Kong DR | Central Plains Medical Journal 25(4): 47-48 | 1998 | E |
| 85 | Oingkailing injection to treat 32 cases with acute valium poisoning | Jiang F | Chinese Journal of Integrated Traditional and Western Medicine in Intensive and Critical Care 5(5):215-216 | 1998 | D |
| 86 | A double-blind control trial of Longdanxiegan pill in the treatment of medication-induced bitter taste in mouth | Hu XZ, Li WH | Shanghai Archives of Psychiatry 8(1): 41-42 | 1996 | E |

**Note:**

| Code | Reason for exclusion | No. of trials |
|---|---|---|
| A | Non-treating acute or protracted withdrawal syndromes | 14 |
| B | Inappropriate comparisons | 31 |
| C | Incomplete data (reporting special case only) | 9 |
| D | Insufficient outcomes | 24 |
| E | Duplicated data | 8 |
| **Total** | | **86** |

### 3.5 Quality-assessment table

| RCTs | Total | High-quality | Low-quality |
|---|---|---|---|
| Short-term detoxification | 34 | 13 (38%) | 21 (62%) |
| Long-term detoxification | 14 | 3 (21%) | 11 (79%) |
| Treating adverse symptom | 57 | 18 (32%) | 39 (68%) |