Non-traditional Acupuncture Therapies for Smoking Cessation: A Systematic Review of Randomized Controlled Trials

Ying-Ying Zhang  
Beijing University of Chinese Medicine
Ze-Yu Yu  
Beijing University of Chinese Medicine
Hui-Di Lan  
GuangXi University of Chinese Medicine
Shi-Bing Liang  
Beijing University of Chinese Medicine
Min Fang  
Beijing University of Chinese Medicine
Nicola Robinson  
London South Bank University
Jian-Ping Liu (jianping_l@hotmail.com)  
Beijing University of Chinese Medicine  
https://orcid.org/0000-0002-0320-061X

Research

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Abstract

Background

Non-traditional acupuncture (NTA) therapies widely used for smoking cessation include acupressure, transcutaneous electrical acupoint stimulation (TEAS), laser acupuncture, intradermal needle, and acupoint catgut embedding (ACE). Our aim was to evaluate their therapeutic effects and safety for smoking cessation.

Methods

Randomized controlled trials (RCTs) comparing NTA therapies with sham NTA or conventional therapy for smoking cessation were included. Ten databases were searched from their inception to February 2021. Two review authors independently screened studies, extracted data, and assessed the risk of bias. Meta-analysis was conducted with RevMan 5.4 software. Grading of Recommendations Assessment, Development and Evaluation (GRADE) was applied to assess the quality of evidence. The primary outcome was abstinence rate at short-term (1-3 months), mid-term (3-6 months), and long-term (≥6 months).

Results

Twenty-five RCTs involving 2600 smokers were identified. Acupressure was found more effective than sham acupressure or conventional therapy in improving short-term (RR 1.41, 95% CI [1.04 to 1.91]; low certainty; 8 trials, n=637) and mid-term abstinence rate (RR 1.63, 95% CI [1.27 to 2.09]; low certainty; 8 trials, n=749). Intradermal needle was not superior to sham control or counseling for short-term (RR 1.62, 95% CI [0.85 to 3.08], low certainty; 5 trials, n=346) and mid-term abstinence rate (RR 1.49, 95% CI [0.68 to 3.27]; low certainty; 3 trials, n=187). TEAS failed to show a better effect than sham TEAS or counseling for short-term abstinence rate (RR 1.27, 95% CI [0.96 to 1.67]; moderate certainty; 5 trials, n=485). TEAS appeared more beneficial for mid-term abstinence (RR 1.58, 95% CI [1.10 to 2.27]; moderate certainty; 3 trials, n=325). Laser acupuncture was superior to sham control for long-term abstinence rate (RR 2.25, 95% CI [1.23 to 4.11]; moderate certainty; 2 trials, n=160). ACE was comparable to Bupropion for mid-term abstinence rate (RR 0.99, 95% CI [0.70 to 1.40]; low certainty; 2 trials, n=177). No serious adverse events were reported in the included trials.

Conclusions

Low to moderate certainty evidence suggests that acupressure, TEAS, laser acupuncture and ACE maybe effective in achieving short-term, middle-term or long-term smoking cessation. Further large, long-term follow-up RCTs are warranted to verify their benefits and safety.

Systematic review registration: INPLASY 202120054.

1. Background

Cigarette smoking is one of major public health issues worldwide, which is closely related to the onset and progression of many diseases. Reports suggest that about 480,000 people die prematurely every year, and one-fifth of the deaths are related to smoking [1]. The Global Burden of Diseases, Injuries, and Risk Factors Study reported that in 2019, out of 87 risk factors, smoking was the second leading risk factor for attributable deaths globally [2]. There were as many as 40 million adult smokers in the United States in 2017, and smokers accounted for 14% of the 15.8% adult population [3]. However, in 2019 more than 50.6 million US adults smoked (accounting for 20.8% of the adult population) [4]. Responses from the National Health Interview Survey in 2015 indicated that 68% smokers (a total of 33,672 adult smokers) wanted to quit smoking [5]. Currently, smoking cessation therapies recommended in guidelines and US Food and Drug Administration approved are pharmacological therapy, behavioral therapy, and complementary and alternative therapies [6]. However, studies have found that pharmacological therapy included nicotine replacement therapy (NRT), Varenicline and Bupropion have been limited for smoking cessation due to their high cost, side effects, tendency to relapse [7–9] as well as low popularity and being difficult access in China [10]. Additionally, withdrawal symptoms are hard to control with psychological and behavioral intervention alone. Acupuncture as a complementary and alternative therapy has been used for smoking cessation for nearly 50 years [11]. Clinical and experimental studies have found that acupuncture was effective for withdrawal symptoms through promoting the release of endogenous opioids [12–13] or suppressing the craving for cigarettes [14].

As acupuncture techniques have developed, various non-traditional acupuncture (NTA) techniques have been used to stop smoking. NTA therapies differ from traditional body acupuncture. Traditional body acupuncture generally using filiform needles inserted through the skin at acupoints. NTA therapies generally refer to acupressure, transcutaneous electrical acupoint stimulation (TEAS), laser acupuncture, intradermal needle, acupoint catgut embedding (ACE) or acupoint injection. These are also known as acupuncture or acupuncture related therapies. NTA therapies have been widely used for nicotine dependence in several trials worldwide due to convenience and acceptability. The majority of systematic reviews [15–17] aimed to evaluate the effectiveness of traditional body acupuncture for smoking cessation, one Cochrane systematic review [18] focused on the effectiveness of both traditional body acupuncture and some NTA therapies on smoking cessation. So far, we have not found any systematic reviews that comprehensively and individually evaluate common NTA therapies for smoking cessation. Therefore, this systematic review aims to collect all randomized controlled trials (RCTs) on NTA therapies for smoking cessation and to evaluate their therapeutic effect and safety.

2. Methods

This systematic review was reported following PRISMA 2020 [19] statement, and the protocol of this systematic review was registered on INPLASY (INPLASY 202120054) [20].
2.1 Eligibility criteria

Parallel group RCTs regardless of blinding were included. The study population comprised of smokers of any age who had no serious diseases or were pregnant and wanted to quit smoking. The study interventions were NTA therapies used alone or in combination with conventional therapy, which included medication or behavioral counseling. NTA therapies refer to acupressure, transcutaneous electrical acupoint stimulation (TEAS), laser acupuncture, intradermal needle, acupoint catgut embedding (ACE) or acupoint injection. Interventions with traditional inserted filiform needles on the body for smoking cessation were ineligible. The controls were medications (NRT, Bupropion or Varenicline), behavioral counseling, sham acupuncture or non-specific acupoint stimulation, or no treatment. The primary outcome was smoking cessation, defined as the abstinence rate. The secondary outcomes were nicotine withdrawal symptoms measured by Minnesota Nicotine Withdrawal Scale Score, daily cigarette consumption, the Fagerström test for nicotine dependence (FTND), the level of exhaled carbon monoxide (CO), relapse rate, craving for cigarettes and adverse events. Trials that failed to report at least one required outcome were excluded.

2.2 Search strategy

We systematically searched RCTs from PubMed, the Cochrane Library, EMBASE, Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), Sino-Med and Wanfang databases from their inception to February 10, 2021. Ongoing trials from Clinical Trials.gov and Chinese Clinical Trial Registry were also retrieved. An example of a search strategy for PubMed: (((((acupuncture[Title/Abstract]) OR (acupressure[Title/Abstract])) OR (transcutaneous OR [Title/Abstract])) OR (electric stimulation[Title/Abstract])) OR (auricular therapy[Title/Abstract])) OR (laser therapy[Title/Abstract])) OR (acupoint catgut embedding[Title/Abstract]) AND (smoking cessation[Title/Abstract])). Additionally, relevant reference lists from systematic reviews were also checked.

2.3 Study selection and data extraction

After removing duplicates, two authors (ZYY and HDL) independently screened studies by title and abstract, uncertainty was determined for eligibility through checking full texts. Reasons for excluding trials were recorded at the full-text screening stage, and any discrepancies were discussed by two review authors or arbitrated by third party (JPL). In the data extraction process, data were extracted by two authors (ZYY and HDL) independently using a pre-defined electronic data extraction form which included basic information of study design (study ID, setting, sample size, centers, and funding); participants characteristics; details of NTA therapies and controls; outcomes in different measuring time; follow ups; dropouts and adverse events.

2.4 Quality assessment

The methodological quality of each included trial was evaluated independently by two review authors (ZYY and HDL). Cochrane Risk of Bias tool (ROB) [21] was employed to assess the risk of bias of each trial based on its seven domains (the adequacy of sequence generation, allocation concealment, blinding of participants, blinding of outcome assessors, incomplete outcome data, selective reporting, and other bias). Grading of Recommendations Assessment, Development and Evaluation (GRADE) [22] was applied to evaluate the certainty of the body of evidence based on risk of bias, directness, precision, consistencies, and publication bias.

2.5 Data synthesis

For dichotomous data, data were presented as risk ratio (RR) with 95% confidence interval (CI). For continuous data, mean difference (MD) with 95% CI was estimated. Meta-analysis was conducted by Cochrane Review Manager 5.4 software when the trials have similarities in study design and clinical characteristics. Otherwise, data were synthesized qualitatively. The I^2 statistic was utilized to test the statistical heterogeneity. The heterogeneity [21] was considered as substantial when I^2 statistic value was greater than 50% [21,23]. The fixed effects model was used when I^2 ≤ 30%, otherwise the random effects model was applied in meta-analysis. To explain heterogeneity, subgroup analysis was predefined by the comparisons (active control and inactive control). Active controls referred to medication and/or behavioral counseling; inactive controls referred to sham acupuncture, non-specific acupoint stimulation, or no treatment. Sensitivity analysis was employed to explore the influence of the randomization concealment (clear or not) and blinding (blinded or not). Funnel plots were generated to detect possible publication bias if 10 or more trials were included in a meta-analysis.

3. Results

3.1 Screening

Initially 660 records were retrieved and 191 duplicates were removed. A total of 423 records were excluded in title and abstract screening process, remaining 46 records. In the full-text screening process, 21 trials were excluded because: not real RCTs, had only English abstracts, interventions were combined with traditional body acupuncture, ineligible controls, and ineligible or incomplete outcomes. Finally, 25 trials were identified and were all quantitatively synthesized. The flow chart of study selection was shown in (Fig. 1).

3.2 Characteristics of included trials

The identified 25 [24–48] trials were conducted in several countries, 11 [27,30–34,37,39,44,47–48] in China, five [28,36,41,43,45] in UK, two [38,40] in USA, three [24–26] in Korea, and one each in Canada [35], Australia [29], Turkey [42], and Singapore [46]. There were only two [33–34] multi-center trials, the rest were single center trials. Twelve trials [24–25,27–28,31–33,39–40,43,46,48] reported their funding source. The sample sizes varied from 18 to 500 and the ratio of males varied from 40–100%. The follow up ranged from 4 weeks to 18 months and the duration of treatment ranged from one week to 12 weeks. The dropout rates varied from 0 to 68.4%. Almost all treatment sites were in the ears except for 2 trials [47–48], the most commonly used auricular acupoints were "ear Lung (CO_{2})", "ear Shenmen (TF_{6})", and "ear Mouth (CO_{1})". Auricular acupressure was used alone or in combination with behavioral counseling or medication for smoking.
cessation in 11 trials [24–34]. Auricular intradermal needles were utilized alone or in combination with counseling in 5 trials [35–39]. TEAS was used in 6 trials [34, 40–44]. Two trials [45–46] focused on laser acupuncture and 2 trials [47–48] on ACE. There were two types of sham stimulation used controls, one was nonacupoint stimulation [26–27, 36, 38, 44], and the other one was real acupoints stimulation [24–25, 29, 31, 35, 38–39] (which were considered not specific acupoints for smoking cessation). Other controls included medications [28, 34, 47–48], behavioral counseling [24–25, 28, 30, 32, 36, 40–41], and no treatment [33, 37]. The outcomes reported at time-points varied from 4 weeks to 18 months. The smoking cessation was measured by biochemically verified abstinence rate in 6 trials, including cotinine test [24–25, 44] and exhaled carbon monoxide [27, 29, 47]. Smoking cessation was self-reported in the remaining trials. Secondary outcomes were not fully reported in the identified trials, and we combined all available outcomes. The details are shown in (Table 1).
Table 1: Characteristics of the included randomized controlled trials

| Study ID | Study population | Sample size T/C | Male (%) T/C | Intervention                          | Comparison                          | Treatment duration | Outcome measurement time | Outcome reported |
|----------|------------------|-----------------|--------------|---------------------------------------|-------------------------------------|--------------------|--------------------------|------------------|
| Lee 2019 [24] | 37 adults who have smoked for ≥ 6 months and wanted to quit smoking | 18/19 | 94.4/84.2 | auricular ACP + behavioral counseling | placebo ACP + behavioral counseling | 6w                 | 6w, 6m-1y, 1y           | 1, 2             |
| Lee 2019 [25] | 74 adults who have smoked for ≥ 6 months and wanted to quit smoking | 42/32 | 97.6/96.9 | auricular ACP + group counseling | placebo ACP + group counseling | 6w | 6w, 6m-1y, 1y | 1, 2, 3 |
| Lee 2016 [26] | 53 male smoking college students | 27/26 | 100/100 | auricular ACP | non-specific auricular acupoints ACP | 6w | 3w, 6w | 4, 5 |
| Wing 2010 [27] | 70 adults who wanted to quit smoking | 38/32 | 68.4/71.9 | auricular ACP + ACP (Hegu L14, Neiguan PC6) | non-acupoints ACP | 3w | 1w, 2w, 3w, 4w, 3m | 1, 3, 5, 6 |
| White 2007 [28] | 19 adults who smoked ≥ 10 cigarettes a day and wanted to quit smoking | 12/7 | 66.7/16.7 | auricular ACP + NRT + group counseling | NRT + group counseling | 5w | 5w | 1, 3, 7 |
| Zhang 2013 [29] | 43 adults who smoked ≥ 10 cigarettes a day and wanted to quit smoking | 20/23 | 40/43.5 | auricular acupoints ACP + counseling | non-specific auricular acupoints ACP + counseling | 8w | 8w, 3m | 1, 2 |
| Zhao 2017 [30] | 50 adult smokers | 25/25 | 92/84 | auricular acupoints ACP + behavioral counseling | behavioral counseling | 8w | 4w, 8w, 12w, 24w | 1, 3, 4, 5 |
| Li 2009 [31] | 140 adults who smoked ≥ 10 cigarettes a day and wanted to quit smoking | 70/70 | 74.3/78.6 | auricular acupoints ACP | non-specific auricular acupoints ACP | 3w | 3m | 1 |
| Jiang 2011 [32] | 47 soldiers who volunteered to quit smoking | 23/24 | 100/100 | auricular acupoints ACP + behavioral counseling | behavioral counseling | 1m | 1m, 3m, 6m, 1y | 1 |
| Li 2011 [33] | 150 adults who have smoked for ≥ 1 year and want to quit smoking | 75/75 | 98.4/98.5/98.4/98.2 | auricular ACP + behavioral counseling | behavioral counseling | 2m | 6m | 1, 2 |
| Chai 2019 [34] | 300 adults who smoked ≥ 10 cigarettes a day and wanted to quit smoking | 100/100/100 | 92/95/95 | T1. auricular acupoints ACP + behavioral counseling | NRT | 8w | 8w, 6m | 1, 5 |
| Gilbey 1977 [35] | 92 subjects who smoked ≥ 15 cigs/day for 3 years | 44/48 | NR | auricular acupoints intradermal needling | inactive auricular point ('Kidney') stimulation | 1w | 1m, 3m | 1 |
| Gillams 1984 [36] | 55 adults smoking ≥ 50 cigs/week for 5 years | 28/27 | NR | auricular acupoints intradermal needling | non-specific acupoints stimulation | 4w | 4w, 3m, 6m | 1 |

Notes: ACP, Acupressure; TEAS, Transcutaneous electrical acupoint stimulation; NR, Not reported; NRT, Nicotine replacement treatment; w, weeks; m, months; y, years. Outcomes: 1, Abstinence rate; 2, Daily cigarettes consumption; 3, Withdrawal symptoms; 4, The level of exhaled CO; 5, Nicotine dependence; 6, Craving for cigarettes; 7, Relapse rate.
| Study ID | Study population | Sample size T/C | Male (%) T/C | Intervention | Comparison | Treatment duration | Outcome measurement time | Outcome reported |
|----------|------------------|----------------|--------------|--------------|------------|-------------------|-------------------------|------------------|
| Leung 1991 [37] | 64 subjects who had smoked ≥ 1 year and were motivated to stop | 32/32 | NR | auricular acupoints | counseling | 2w | 1m, 3m, 6m | 1 |
| Parker 1977 [38] | 41 smokers, other characteristics unspecified | T1/C1:9/9, T2/C2:11/12 | NR | T1: auricular acupoints intradermal needling + counseling T2: auricular acupoints TEAS | C1: non-specific acupoints stimulation; C2: non-specific auricular acupoints TEAS | 3w | 6w | 1 |
| Wu 2007 [39] | 131 subjects who smoked > 10 cigs/day for 1 year | 64/67 | 81.4/88.1 | auricular acupoints intradermal needling + counseling | non-specific acupoints stimulation + counseling | 8w | 8w, 6M | 1, 2, 3 |
| Fritz 2013 [40] | 125 subjects who smoked > 10 cigs/day | 64/61 | 75.0/77.0 | auricular acupoints TEAS(0Hz) + counseling | sham TEAS (0Hz) + counseling | 5w | 3w, 6w | 1, 3 |
| White 1998 [41] | 76 adults who smoked > 10 cigs/day | 38/38 | 44.7/52.6 | TEAS + counseling | sham TEAS + counseling | 1w | 3d, 2w, 9m | 1 |
| Dinn 2011 [42] | 47 smokers who had a score of Fagerstrom ≥ 5 | 24/23 | 66.7/60.9 | auricular acupoints TEAS | sham TEAS | 3w | 3w, 7w, 3m, 6m | 1, 2, 3, 4, 5 |
| Yeh 2009 [44] | 79 subjects who had smoked for ≥ 1 year | 39/40 | NR | auricular acupoints TEAS + Tianmei acupoint TEAS | sham auricular acupoints TEAS + sham Tianmei acupoint TEAS | 6w | 6w | 1, 2, 4 |
| Waite 1998 [43] | 78 adults who smoked > 10 cigs/day | 40/38 | 55/55.3 | auricular acupoints TEAS + ACP | inactive TEAS + ACP | 2w | 2w, 2m, 4m, 6m | 1, 7 |
| Kerr 2008 [45] | 219 smokers who motivated to quit smoking | 130/89 | 56.5%(192/340) | laser acupuncture | sham laser acupuncture | 2w | 3m, 6m, 18m | 1 |
| Cai 2000 [46] | 330 adolescents who smoked > 5 cigs/day for 3 months | 160/170 | NR | laser acupuncture | sham laser acupuncture | 4w | 4w, 3m, 36m | 1 |
| Li 2019 [47] | 100 subjects who smoked > 10 cigs/day for 1 year | 50/50 | 83.7/83.3 | acupoint catgut embedding | Bupropion | 8w | 8w | 1 |
| Zeng 2019 [48] | 80 subjects who smoked > 10 cigs/day and wanted to quit smoking | 40/40 | 75/77.5 | acupoint catgut embedding | Varenicline | 12w | 4w, 8w, 12w | 1 |

**Notes:** ACP, Acupressure; TEAS, Transcutaneous electrical acupoint stimulation; NR, Not reported; NRT, Nicotine replacement treatment; w, weeks; m, months; y, years. Outcomes: 1, Abstinence rate; 2, Daily cigarettes consumption; 3, Withdrawal symptoms; 4, The level of exhaled CO; 5, Nicotine dependence; 6, Craving for cigarettes; 7, Relapse rate.

### 3.3 Risk of Bias assessment

The detailed methods of random sequence generation were reported in 14 trials [24–26, 28–30, 34–36, 39–41, 45–47], included random number tables [24–25, 28–29, 36, 39–41, 45–47], drawing lots [26], and the central randomization system [30, 34]. In terms of allocation concealment, ten trials [24–25, 28–30, 34–35, 40–41, 47] were judged as low risk of bias since the random number was kept in opaque envelopes. The blinding of the participants were reported and sham or placebo acupuncture was used in 13 trials [24, 26, 29, 35–36, 38, 40–46], hence these trials were assessed as low risk of performance bias. Blinding of the intervention was not successful in
one trial [25] as the participants were aware of treatments. The blinded outcome assessment was clearly reported in 7 trials [24, 29–30, 40–41, 45–46] and were rated as low risk of detection bias. In terms of attrition bias, 14 trials [24–26, 30, 32, 34, 36, 38–40, 42–43, 47–48] were assessed as low risk of bias due to the intention-to-treat analysis, and the dropouts rate was < 10%. Eight trials [27–29, 33, 41–44] were rated as high risk of attrition bias due to higher dropouts rates (>20%). Of the included 25 trials, only one trial [34] was assessed as low risk of reporting bias since the protocol was registered and the consistency between the outcomes described in protocol and actual outcomes in the results. One trial [29] was rated as 'high' due to the inconsistent outcomes between protocol and actual results. The protocols were not reported in the rest of the trials and were considered as unclear risk of reporting bias. In terms of the “other bias” domain, the funding was reported and the baseline data were comparable in 11 trials [24–25, 27, 29, 31–32, 34–35, 37, 40, 48]. There was potential conflicts of interest in one trial [43] and this was considered as high risk of bias. The remaining 13 trials were assessed as ‘unclear’ since either the funding or the baseline data was not reported. The risk of bias summary was shown in (Fig. 2).

3.4 Effects of interventions
Three time periods were employed to report each outcome to evaluate the therapeutic effects of interventions in short-term (1–3 months), mid-term (3–6 months), and long-term (≥6 months), when there was sufficient data for each outcome.

3.4.1 Acupressure versus sham acupressure or conventional therapy (counseling or NRT)

3.4.1.1 Primary outcome

Eight trials [24–25, 27–28, 30–32, 34] reported the short-term abstinence rate, with 126 of 328 (38.4%) smokers achieving smoking cessation in acupressure group versus 82 of 309 (26.5%) in the control group. Suggesting that acupressure was more effective (RR 1.41, 95% CI [1.04 to 1.91]; I² = 31%; low certainty; 8 trials, n = 637). Subgroup analysis by controls suggested that acupressure was still superior to inactive controls in improving short-term abstinence rate (RR 2.01, 95% CI [1.10 to 3.67]; low certainty; 2 trials, n = 210), but this effect was not observed in active controls (RR 1.30, 95% CI [0.93 to 1.82]; I² = 33%; low certainty; 6 trials, n = 427) (Fig. 3, Table 2). The mid-term abstinence rate was 29.9% in acupressure group and 18.9% in control group, suggesting that acupressure was still more effective in improving mid-term abstinence rate (RR 1.63, 95% CI [1.27 to 2.09]; low certainty; 8 trials [25, 34, 27, 29–33], n = 749). This effect was still observed regardless of the active controls (RR 1.52, 95% CI [1.17 to 1.98]; I² = 18%; low certainty; 6 trials, n = 539) and inactive controls (RR 2.44, 95% CI [1.13 to 5.25]; low certainty; 2 trials, n = 210) (Fig. 4, Table 2). However, the long-term abstinence effect was not significant between acupressure group and control group (RR 1.85, 95% CI [0.59 to 5.82]; I² = 14%; moderate certainty; 2 trials [24–25], n = 74) (Table 2, Additional file1: Table 1).
Table 2  
Evidence summary of smoking cessation: Acupressure versus sham acupressure or conventional therapy

| Certainty assessment          | Nº of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Nº of patients | Effect | Relative (95% CI) | Absolute (95% CI) |
|------------------------------|--------------|--------------|--------------|---------------|--------------|-------------|----------------------|----------------|--------|-------------------|--------------------|
| Short-term abstinence rate    | 8            | randomized   | serious a    | not serious   | not serious b| undetected  |                      | 126/328 (38.4%) | RR 1.40 | 106 more per 1,000 | (from 11 to 241 more) |
|                             |              | trials       |              |               |              |             |                      | 82/309 (26.5%) |        |                   |                    |
| Short-term abstinence rate in active controls | 6            | randomized   | serious a    | not serious   | not serious b| undetected  |                      | 98/220 (44.5%) | RR 1.30 | 100 more per 1,000 | (from 23 to 273 more) |
|                             |              | trials       |              |               |              |             |                      | 69/207 (33.3%) |        |                   |                    |
| Short-term abstinence rate in inactive controls | 2            | randomized   | serious a    | not serious   | not serious b| undetected  |                      | 28/108 (25.9%) | RR 2.01 | 129 more per 1,000 | (from 13 to 340 more) |
|                             |              | trials       |              |               |              |             |                      | 13/102 (12.7%) |        |                   |                    |
| Mid-term abstinence rate      | 8            | randomized   | serious a    | not serious   | not serious b| undetected  |                      | 114/381 (29.9%) | RR 1.63 | 118 more per 1,000 | (from 51 to 204 more) |
|                             |              | trials       |              |               |              |             |                      | 69/368 (18.8%) |        |                   |                    |
| Mid-term abstinence rate in active controls | 6            | randomized   | serious a    | not serious   | not serious b| undetected  |                      | 94/273 (34.4%) | RR 1.52 | 119 more per 1,000 | (from 39 to 225 more) |
|                             |              | trials       |              |               |              |             |                      | 61/266 (22.9%) |        |                   |                    |
| Mid-term abstinence rate in inactive controls | 2            | randomized   | serious a    | not serious   | not serious b| undetected  |                      | 20/108 (18.5%) | RR 2.44 | 113 more per 1,000 | (from 10 to 333 more) |
|                             |              | trials       |              |               |              |             |                      | 8/102 (7.8%)   |        |                   |                    |
| Long-term abstinence rate     |              |              |              |               |              |             |                      |                |        |                   |                    |

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention. GRADE Working Group grades of evidence: Moderate certainty (◯◯◯◯): We are moderately confident in the effect estimate. The true effect is likely to be similar to the estimate of the effect. Low certainty (◯◯◯◯): Our confidence in the effect estimate is limited. The true effect may differ from the estimate of the effect. Notes: ACP, Acupressure; CI, Confidence interval; RR, Risk ratio; a, The blinding method was not used; b, A small number of events were reported.
3.4.1.2 Secondary outcomes

Acupuncture was found to be more effective than sham acupuncture or counseling in relieving short-term withdrawal symptoms (MD -2.68, 95% CI [-5.34 to -0.03]; 83%; 4 trials [25, 27–29, 30], n = 180). Subgroup analysis suggested that acupuncture was still more effective than active control (MD -4.44, 95% CI [-5.40 to -3.48]; 3 trials, n = 115). In terms of daily cigarettes consumption, there was no significant difference between acupuncture and sham acupuncture in short-term (MD 1.27, 95% CI [-1.30 to 3.85]; 2 trials [24–25], n = 111) and long-term effect (MD -0.19, 95% CI [2.84 to 2.46]; 2 trials [24–25], n = 111) (Additional file1: Table 1). Acupuncture was also not superior to sham acupuncture in decreasing nicotine dependence score (FTND) in short-term (MD -0.32, 95% CI [-1.72 to 1.08]; 93%; 4 trials [26, 30–31, 34], n = 373), and mid-term FTND (MD -0.085, 95% CI [-4.00 to 2.29]; 97%; 2 trials [30, 34], n = 250). Subgroup analysis by controls did not change the result. The pooled data from 2 trials [26, 30] suggested that acupressure was more effective than sham acupressure in decreasing the level of short-term exhaled CO (MD -3.84, 95% CI [-5.03 to -2.66]; 2 trials, n = 103) (Additional file1: Table 1). However, acupressure failed to demonstrate a better effect than sham control in suppressing the short-term cravings for cigarettes (MD -0.13, 95% CI [-0.85 to 0.59]; 1 trial [27], n = 70).

3.4.2 Intradermal needle versus sham intradermal needle or counseling

3.4.2.1 Primary outcome

The short-term abstinence rate was reported in 5 trials [25–39], with 66 of 172 (38.4%) smokers achieving smoking cessation in intradermal needle group versus 40 of 174 (23%) smokers in control group. Suggesting that intradermal needle was not superior to sham control in improving abstinence rate (RR 1.62, 95% CI [0.85 to 3.08]; 64%; low certainty; 5 trials, n = 346) (Additional file1: Table 1–2). Subgroup analysis did not change the result, neither for active controls (RR 1.12, 95% CI [0.72 to 1.73]; moderate certainty; 3 trials, n = 165) nor for inactive controls (RR 3.49, 95% CI [0.40 to 30.59]; 88%; very low certainty; 2 trials, n = 181). The mid-term effect of quitting smoking was also not significant between two groups (RR 1.49, 95% CI [0.68 to 3.27]; low certainty; 3 trials [26–37, 39], n = 187) (Additional file1: Table 1–2).}

3.4.3 TEAS versus sham TEAS or counseling

3.4.3.1 Primary outcome

The short-term and mid-term abstinence rates were reported in five [34, 38, 40, 43–44] and three trials [34, 42–43] respectively. The pooled data indicated that TEAS failed to demonstrate a better effect than controls in achieving short-term smoking cessation (RR 1.27, 95% CI [0.96 to 1.67]; moderate certainty; 5 trials, n = 485) (Additional file1: Table 1, Table 3). However, TEAS maybe more beneficial for mid-term smoking cessation (RR 1.58, 95% CI [1.10 to 2.27]; 51%; moderate certainty; 3 trials, n = 325). TEAS failed to show a better effect on long-term abstinence rate (RR 0.50, 95% CI [0.05 to 5.28]; moderate certainty; 1 trial [41], n = 76) (Additional file1: Table 1, Table 3).

3.4.3.2 Secondary outcomes

Two trials [42, 44] reported the daily cigarettes consumption and the exhaled CO level in short-term. The pooled data showed that TEAS was not superior to sham TEAS in decreasing daily cigarettes consumption (MD -0.91, 95% CI [-3.55 to 1.73]; 2 trials, n = 126) and exhaled CO level (ppm) (MD -0.64, 95% CI [-6.59 to 5.31]; 66%; 2 trials, n = 124) (Additional file1: Table 1). The pooled data of FTND indicated that there was no significant difference between TEAS and controls in relieving nicotine dependence at mid-term follow-up (MD -0.30, 95% CI [0.90 to 1.49]; 51%; 2 trials [34, 42], n = 247) (Additional file1: Table 1). Only one trial [43] reported the short-term relapse rate and suggested that TEAS was not superior to sham TEAS in reducing relapse rate (RR 0.82, 95% CI [0.64 to 1.06]; 1 trial, n = 51) (Additional file1: Table 1).

3.4.4 Laser acupuncture versus sham laser acupuncture

3.4.4.1 Primary outcome

Only 2 trials [45–46] on laser acupuncture were identified, and which reported the mid-term and long-term abstinence rate. The pooled data suggested that laser acupuncture was not superior to sham laser acupuncture at mid-term follow-up (RR 2.98, 95% CI [0.24 to 37.81]; 96%; low certainty; 2 trials, n = 427) (Additional file1: Table 1, Table 4). However, laser acupuncture may be more effective in achieving long-term smoking cessation (RR 2.25, 95% CI [1.23 to 4.11]; moderate certainty; n = 160, 2 trials) (Additional file1: Table 1, Table 4).
3.4.5 ACE versus Bupropion or Varenicline

3.4.5.1 Primary outcome

Absorbable catgut was embedded in specific acupoints for continuous stimulation, usually one treatment every two weeks. Which was a new technique of acupuncture. Two trials \([47-48]\) comparing the effect of ACE with Bupropion or Varenicline on smoking cessation were identified. The pooled data suggested that ACE was comparable to medication in improving abstinence rate at mid-term follow-up (RR 0.99, 95% CI [0.70 to 1.40]; low certainty; 2 trials, n = 177) (Additional file 1: Table 1, Table 5).

3.4.6 Adverse events

Four trials \([24–26, 29]\) reported the transient and minor auricular adverse events both in the acupressure group (itching in 12 cases, mild tenderness in 13 cases, feeling hot in 4 cases) and in the control group (uncomfortable feeling in 5 cases, dizziness in 1 case), the pooled data suggested that there was no significant difference between acupressure and controls (RR 2.51, 95% CI [0.24 to 26.59]; \(I^2 = 70\%\); 4 trials, n = 240) (Additional file 1: Table 1). One trial \([43]\) reported adverse events both in TEAS group (pain in 2 cases, soreness in 3 cases) and sham TEAS (soreness in 2 cases, headache in 2 cases). One trial \([47]\) reported adverse events both in ACE group (pain and soreness in 2 cases, minor swelling in 1 case) and bupropion group (nausea in 5 cases, insomnia in 2 cases). No serious adverse events were reported in the included trials.

3.4.7 Publication bias

Funnel plots were not performed to detect publication bias since there was no meta-analysis combining more than ten trials at one time.

3.4.8 Additional analysis

Predefined subgroup analysis via the controls (active control and inactive control) was conducted for 3 outcomes under acupressure, and one outcome under intradermal needle. We were unable to conduct other meaningful subgroup analysis due to limited trials. Sensitivity analysis for allocation concealment for short-term abstinence rates suggested that clear allocation concealment may influence the results (RR 1.51, 95% CI [0.95 to 2.41]; \(I^2 = 44\%\); 5 trials \([24–25, 28, 30, 34]\), n = 520).

3.4.9 Certainty of evidence

GRADE approaches were employed to assess the certainty of evidence from primary outcomes. The quality of the evidence was downgraded to low or very low quality due to lack of blinding, imprecision, inconsistency or indirectness. The detailed evidence summary of outcomes is presented in (Table 2–3, Additional file 1: Table 2–5).

4. Discussion

4.1 Main findings

Twenty-five RCTs involving 2600 smokers were identified. The overall risk of bias was not serious. We downgraded the certainty of evidence to moderate or low due to small number of events or absence of blinding method. NTA therapies had different effects on smoking cessation at different time points. Compared with sham acupressure or conventional therapy, acupressure improved the short-term and mid-term abstinence rate by 11.9% and 11.0% respectively. Additionally, acupressure was also favorable to decrease the short-term withdrawal symptom score (2.68) and reduce the level of exhaled CO (-3.84 ppm). Intradermal needles failed to demonstrate a better effect than sham control or counseling in achieving both short-term and mid-term smoking cessation. TEAS was found superior to sham TEAS or counseling in improving mid-term abstinence rate by 11.2%. However, TEAS failed to show a better effect in reducing daily cigarettes consumption, the level of exhaled CO, FTND, and relapse rate. Two double blinded trials suggested that compared with sham laser acupuncture, laser acupuncture successfully improved abstinence rate by 20.6% at long-term follow-up. Two trials involving 180 smokers compared the effect of ACE with Bupropion or Varenicline, with 41.6% and 42.0% smokers achieving smoking cessation in the ACE group and control group respectively at 8–12 weeks follow-up suggesting that ACE maybe comparable with Bupropion or Varenicline in assisting smoking cessation. We have not found evidence of serious adverse events associated with the use of NTA therapies.

4.2 Relation to previous research

A Cochrane systematic review \([18]\) published in 2014 evaluated the effect of acupuncture and related interventions on smoking cessation. The interventions included some NTA therapies (e.g. acupressure, TEAS, laser acupuncture) used alone or in combination with traditional body acupuncture. In this systematic review, we identified NTA therapies (acupressure, TEAS, intradermal needles, laser acupuncture, ACE) and excluded any traditional body acupuncture interventions. We also focused on withdrawal symptoms, nicotine dependence, daily cigarettes consumption, the level of exhaled CO, relapse rate, and craving for cigarettes. We consistently found that acupressure was superior to sham acupressure in achieving short-term smoking cessation. Additionally, we found that acupressure was beneficial in improving mid-term abstinence rate, relieving withdrawal symptoms, and decreasing the level of exhaled CO. TEAS, laser acupuncture, and ACE were also potentially effective for mid-term or long-term smoking cessation.

4.3 Strengths and limitations

Several systematic reviews have been conducted to evaluate the effect of traditional body acupuncture on smoking cessation \([15, 18, 49]\). However, very few systematic reviews have focused on the potential benefits of NTA therapies on smoking cessation. NTA therapies are widely used for smoking cessation due to convenience and good compliance \([50]\). Therefore, this systematic review was a comprehensive and individual evaluation of NTA therapies for smoking.
cessation. Withdrawal symptoms, nicotine dependence, and other outcomes were also assessed. The protocol of this systematic review was registered on INPLASY. Predefined subgroup analysis via controls (active control and inactive control) was conducted. GRADE approaches were employed to assess the certainty of evidence. There were several limitations for this systematic review. Although, blinding of the participants was applied in more than 50% identified trials, it was difficult to confirm whether the participants were unaware of the interventions they received, since “sham acupuncture” can be easily identified. Additionally, the certainty of the evidence was downgraded to moderate or low certainty due to small number of participants and events.

### 4.4 Implications for practice

Quitting smoking is a process that requires long-term adherence to treatment if there are to be any beneficial effects to health. An in-depth interview study explored factors influencing participant compliance in acupuncture trials suggested that patient’s fear of traditional body acupuncture pain may reduce treatment compliance[51]. NTA therapies, such as acupressure was widely used for smoking cessation as it is painless, convenient and may be a self-administered procedure (every 2 or 3 days treatment cycle). It has been reported that withdrawal symptoms were the most serious after quitting for about one month but gradually die down over time, and relapse usually occurs at this stage[52]. Hence, it was important to control withdrawal symptoms to prevent relapse. Acupressure was found effective in relieving short-term withdrawal symptoms. We also found that TEAS, laser acupuncture and ACE were potentially effective in aiding cessation at mid-term or long-term follow up. Therefore, NTA therapies can play a complementary role in enhancing smoking cessation and relieving withdrawal symptoms.

### 4.5 Implications for research

The smoking cessation was measured by biochemically verification of abstinence rates in 6 trials[24–25, 27, 29, 44, 47], the remaining trials were self-reports. Therefore, cotinine or exhaled CO verifications of smoking cessation are warranted. Non-specific acupoints stimulation was used as sham or placebo acupuncture in many trials. However, it was uncertain whether this kind of sham control was really inactive for cessation, and participants may identify sham acupuncture easily. Hence, programmatic RCT may be more appropriate to evaluate the effect of NTA therapies for smoking cessation. Additionally, long-term follow up data was rarely reported in the included trials, and needs to be improved in future studies.

### Conclusion

Low to moderate certainty evidence suggests that acupressure, TEAS, laser acupuncture and ACE maybe effective in achieving short-term, middle-term or long-term smoking cessation. And acupressure was also beneficial to relieve withdrawal symptoms and decrease the level of exhaled CO. However, intradermal needle was found ineffective in aiding cessation at any time point. No serious adverse events were reported in the included trials. However, large sample size, fully reported and long-term follow up RCTs are warranted to confirm these effects.

### Abbreviations

ACE: Acupoint catgut embedding; ACP: Acupressure; CI: Confidence intervals; CNKI: China National Knowledge Infrastructure; CO: Carbon monoxide; FTND: Fagerström test for nicotine dependence; GRADE: Grading of Recommendations Assessment, Development and Evaluation; MD: Mean difference; NTA: Non-traditional acupuncture; NRT: Nicotine replacement therapy; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis; TEAS: transcutaneous electrical acupoint stimulation; RCTs: Randomized controlled trials; RR: Risk ratio; VIP: Chinese Scientific Journal Database.

### Declarations

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Not applicable

#### Authors’ contributions

YYZ and JPL had the idea for the study. YYZ and JPL contributed to study design. ZYY and HDL contributed to acquisition of data and quality assessment. YYZ contributed to analysis of data and drafted the manuscript. SBL, MF, NR and JPL revised and commented on the manuscript. All authors approved the final manuscript.

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#### Availability of data and materials

All data generated or analyzed during this study are included in this manuscript and its additional file.

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication
Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

1Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, No. 11 North Sanhuan East Road, Chaoyang District, Beijing 100029, China.  
2Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, Nanning, 530001, China.  
3Institute of Health and Social Care, London South Bank University, London, UK.

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**Figures**

![PRISMA flow diagram of study selection. RCT: randomized controlled trials](image-url)
Figure 2

Risk of bias summary

| Study or Subgroup     | ACP | Sham ACP or conventional therapy | Risk Ratio | Risk Ratio |
|-----------------------|-----|----------------------------------|------------|------------|
|                       | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI |
| 1.1.1 Active comparison |       |       |       |       |         |                      |                      |
| Chai 2019             | 56    | 100   | 39    | 100   | 31.6%  | 1.44 [1.06, 1.94]   |                      |
| Jiang 2011            | 17    | 23    | 15    | 24    | 25.9%  | 1.18 [0.60, 1.97]   |                      |
| Lee 2019 a            | 4     | 18    | 4     | 19    | 5.4%   | 1.06 [0.31, 3.60]   |                      |
| Lee 2019 b            | 4     | 42    | 5     | 32    | 5.4%   | 0.61 [0.18, 2.09]   |                      |
| White 2007            | 4     | 12    | 3     | 7     | 5.9%   | 0.78 [0.24, 2.51]   |                      |
| Zhao 2017             | 13    | 25    | 3     | 25    | 6.3%   | 4.33 [1.40, 13.37]  |                      |
| Subtotal (95% CI)     | 220   |       |       | 207   | 80.4%  | 1.30 [0.93, 1.82]   |                      |
| Total events          | 98    | 69    |       |       |         |                      |                      |
| Heterogeneity: $\text{Tau}^2 = 0.05$; $\text{Chi}^2 = 7.43$, df = 5 ($P = 0.19$); $I^2 = 33\%$ | | |                      |                      |
| Test for overall effect: $Z = 1.53$ ($P = 0.13$) | | |                      |                      |
| 1.1.2 Inactive comparison |     |       |       |       |         |                      |                      |
| Li 2009               | 20    | 70    | 8     | 70    | 12.1%  | 2.50 [1.18, 5.29]   |                      |
| Wing 2010             | 8     | 38    | 5     | 32    | 7.5%   | 1.35 [0.49, 3.71]   |                      |
| Subtotal (95% CI)     | 108   |       |       | 102   | 19.6%  | 2.01 [1.10, 3.67]   |                      |
| Total events          | 28    | 13    |       |       |         |                      |                      |
| Heterogeneity: $\text{Tau}^2 = 0.00$; $\text{Chi}^2 = 0.92$, df = 1 ($P = 0.34$); $I^2 = 0\%$ | | |                      |                      |
| Test for overall effect: $Z = 2.27$ ($P = 0.02$) | | |                      |                      |
| Total (95% CI)        | 328   |       |       | 309   | 100.0% | 1.41 [1.04, 1.91]   |                      |
| Total events          | 126   | 82    |       |       |         |                      |                      |
| Heterogeneity: $\text{Tau}^2 = 0.05$; $\text{Chi}^2 = 10.19$, df = 7 ($P = 0.18$); $I^2 = 31\%$ | | |                      |                      |
| Test for overall effect: $Z = 2.22$ ($P = 0.03$) | | |                      |                      |
| Test for subgroup differences: $\text{Chi}^2 = 1.62$, df = 1 ($P = 0.22$). $P = 34.2\%$ | | |                      |                      |

Figure 3

Acupressure for short-term smoking cessation. ACP: acupressure
Figure 4

Acupressure for mid-term smoking cessation. ACP: acupressure

| Study or Subgroup | ACP | Mean | SD | Total | Mean | SD | Total | Mean Difference | IV, Random, 95% CI | Mean Difference | IV, Random, 95% CI |
|-------------------|-----|------|----|-------|------|----|-------|-----------------|---------------------|-----------------|---------------------|
| **1.1.1 Active comparison** | | | | | | | | | | | |
| Lee 2019 b | 10.17 | 8.7 | 23 | 13.28 | 7.4 | 29 | 17.3% | -3.11 [-7.57, 1.35] | | | |
| White 2007 | 11.4 | 2.4 | 6 | 13.8 | 4 | 7 | 8.3% | -2.40 [-6.93, 0.0] | | | |
| Zhao 2017 | 5.24 | 1.67 | 25 | 9.92 | 1.82 | 25 | 32.1% | -4.66 [-5.70, -3.66] | | | |
| Subtotal (95% CI) | 54 | 61 | 70.4% | -4.44 [-5.40, -3.48] | | | | | | |
| **Heterogeneity:** | | | | | | | | | | | |
| Tau² = 0.00; Chi² = 1.64; df = 2 (P = 0.40); I² = 0% | | | | | | | | | | | |
| Test for overall effect: Z = 9.07 (P < 0.00001) | | | | | | | | | | | |

**1.1.2 Inactive comparison**

| Study or Subgroup | ACP | Mean | SD | Total | Mean | SD | Total | Mean Difference | IV, Random, 95% CI | Mean Difference | IV, Random, 95% CI |
|-------------------|-----|------|----|-------|------|----|-------|-----------------|---------------------|-----------------|---------------------|
| Wing 2010 | 8.79 | 2.91 | 32 | 9.25 | 4.05 | 33 | 29.6% | -0.46 [-2.17, 1.25] | | | |
| Subtotal (95% CI) | 32 | 33 | 29.6% | -0.46 [-2.17, 1.25] | | | | | | | |
| **Heterogeneity:** | | | | | | | | | | | |
| Not applicable | | | | | | | | | | | |
| Test for overall effect: Z = 0.53 (P = 0.60) | | | | | | | | | | | |
| **Total (95% CI)** | **86** | **94** | **100.0%** | **-2.68 [-5.34, -0.03]** | | | | | | | |
| **Heterogeneity:** | | | | | | | | | | | |
| Tau² = 5.45; Chi² = 17.65; df = 3 (P = 0.0005); I² = 83% | | | | | | | | | | | |
| Test for overall effect: Z = 1.96 (P = 0.05) | | | | | | | | | | | |
| Test for subgroup differences: Chi² = 15.81; df = 1 (P < 0.0001); I² = 93.7% | | | | | | | | | | | |

Figure 5

Acupressure for short-term withdrawal symptoms. ACP: Acupressure

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1.docx
- PRISMA2020abstractchecklist.docx
- PRISMA2020checklist.docx