Comparison between Acupuncture and Nicotine Replacement Therapies for Smoking Cessation Based on Randomized Controlled Trials: A Systematic Review and Bayesian Network Meta-Analysis

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Objectives. To evaluate the efficacy and/or safety of acupuncture therapy (AT) in quitting smoking. Methods. Randomized controlled trials (RCTs) were searched in PubMed, Cochrane Library, Embase, Web of Science, and Chinese Biomedical Database (CBM). We used Cochrane Collaborative Quality Assessment to assess the risk of bias. Bayesian network meta-analysis was utilized to evaluate the efficacy and safety of different interventions. Data analyses were conducted using WinBUGS 1.4.3, Stata 14, and RevMan 5.3.5 software. Results. A total of 2706 patients from 23 studies were included, involving 6 treatment arms. Network meta-analysis demonstrated that there was no significant difference in short-term abstinence rates or changes in Fagerstrom test for nicotine dependence (FTND) scores and daily smoking among these groups (AT, sham acupuncture therapy (SAT), auricular acupressure (AA), sham auricular acupressure (SAA), acupuncture plus auricular acupressure (APAA), and nicotine replacement therapy (NRT)). However, there was a significant difference between SAA and AA with risk ratio (RR) of 2.49 (95% CI 1.14, 5.97) in long-term abstinence rate. The probabilistic ranking results showed that APAA and AA were superior to other interventions in the comparison of abstinence rates. There was no obvious inconsistency between the direct comparison and indirect comparison, using the consistency test. Conclusion. AA was superior to SAA in smoke quitting, but there was no difference among other interventions in long-term truncation rates. There was no difference in short-term abstinence rates among these selected groups. We need large sample RCTs to clarify the advantages of interventions such as APAA and AA. In addition, reporting of adverse events that may occur during treatment also should be enhanced to complement evidence-based medicine. The trial is registered with PROSPERO CRD42020164712.
1. Introduction

Tobacco dependence is one of the major public health problems [1], which is closely related to the development of lung cancers and cardiovascular diseases [2]. The information from WHO illustrates that mortality is >7 million or ~1.2 million people worldwide from direct tobacco or second-hand smoke [3]. Smoking not only contributes to the development of these chronic diseases but also is a huge economic burden [1]. Smoking, however, is a preventable cause of leading death and disability by smoking cessation to reduce the risk of illness and early death [4–6]. Therefore, quitting smoking is a great benefit from health and economic burden points of view [1].

The most internationally recognized standard therapy is nicotine replacement with the objective quantification of abstinence rate [7, 8]. However, there are a number of alternative approaches that have been tested for quitting smoke, including acupuncture, auricular acupressure, acupuncture plus auricular acupressure (APAA), and other traditional Chinese medicines [9–11]. It has been suggested that acupuncture and auricular acupressure (a traditional Chinese medicine) are effective on smoking cessation [12, 13], but their efficacy is still controversial. Meta-analysis on smoking cessation of acupuncture and auricular acupressure is different, which might be due to overlapping and redundancy of topics [8, 14]. El Bahri et al. extracted randomized and quasirandomized controlled trials (quasi-RCTs) to evaluate the effect of acupuncture and its derivatives on smoking cessation, showing that the effect of acupuncture on smoking cessation is affected by variation [15]. The advantages of nicotine replacement therapies are convenient with effect immediately, whereas the advantage of acupuncture therapy is diverse types, low price, and easier to be accepted by the public. On the other hand, there are some disadvantages for either nicotine replacement therapies or acupuncture therapy, such as dizziness, headache, or producing allergic phenomena in patients. Moreover, the efficacy of smoking quitting by acupuncture and other interventions is evaluated based on direct comparison, but the safety comparisons of different treatments are limited. Thus, in the current study, we aim to evaluate whether nicotine replacement therapies or acupuncture therapy is better than others, which could offer some evidence for the readers to understand the importance of this information.

2. Methods

2.1. Protocol and Registration. Our study has been registered on the International Prospective Register of Systematic Reviews (PROSPERO) and the registered number is CRD42020164712 which is available at https://www.crd.york.ac.uk/PROSPERO/.

2.2. Data Sources and Search Strategy. Five electronic databases were searched from inception to March 2021 for RCTs: PubMed, the Cochrane Library, Embase, Web of Science, and Chinese Biomedical Database (CBM). Forward and reverse citation screening through a systematic review of citation and bibliography were also conducted. We used the following search terms: smoking cessation, nicotine replacement therapy, acupuncture, and auricular acupressure, as well as synonyms and derivatives of these words. There are no language restrictions. Search strategies were demonstrated for searching the English and the Chinese e-libraries (Supplementary Table 1).

2.3. Eligibility Criteria. We included RCTs with acupuncture therapy (AT), auricular acupressure (AA), and acupuncture combined with auricular acupressure (APAA) as intervention measures for smokers who voluntarily quit smoking. The controls included in the study were sham acupuncture therapy (SAT), sham auricular acupressure (SAA), nicotine replacement therapy (NRT), or AA alone. The literature published in Chinese and/or English languages was included. To minimize heterogeneity, the smokers who received two or more treatment combinations (except auricular acupoint combination acupuncture) or any acupuncture with electrical or laser stimulation were excluded. Furthermore, articles with duplicate data, incomplete data, or no access to the full text were excluded.

2.4. Study Selection and Data Extraction. We imported the retrieved literature into Endnote X9. Two independent reviewers screened and included studies according to the eligibility criteria. For any disagreements between these two reviewers, a third senior researcher was consulted, and a conclusion was reached after the discussion. For articles with duplicate data, we only included one with a larger sample size or a longer follow-up period.

We used a predesigned Excel sheet to extract data from included studies. The main information includes the first author, year of publication, sample size, interventions, methods, and outcomes. When data were reported for multiple time periods, data at each time period were recorded.

2.5. Outcome Measures. We selected short-term and long-term abstinence rates as primary outcome measures. We preferred the sustained abstinence rates, and if the article did not report the results of sustained abstinence outcome, we chose the point abstinence rate. As stated above, the golden standard of abstinence rate is breath carbon monoxide, urinary cotinine, or both. We have adopted the principle of this standard in the current network meta-analysis accordingly [8]. Moreover, we chose the change of the scores of Fagerstrom test for nicotine dependence (FTND) and daily smoking prior to and after treatment as the secondary outcome measure.

2.6. Risk of Bias Assessment. Using the Cochrane Collaborative Quality Assessment tool, two independent reviewers evaluated the methodology quality of each included study [16]. Assessment tools included random sequence generation, allocation concealment, blinding of participants and
personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. For each study, the assessment criteria were defined in three levels of low risk, high risk, and unclear risk. Any disagreement between the reviewers was resolved through discussion with a third senior reviewer.

2.7. Date Synthesis and Analysis. Our study combined direct and indirect evidence from all available RCTs. Bayesian network meta-analysis was performed, using WinBUGS (V.1.4.3; MRC Biostatistics Unit, Cambridge University, UK) software, and Stata (V.14; StataCorp) was used to draw the network diagram, while the Review Manager Software (V.5.3.5; RevMan) was used to produce funnel plot to assess the risk of publication bias. We applied visual evaluation to evaluate the small size effect of test funnel plot asymmetry.

To measure the effects, weighted mean difference (WMD) was calculated for continuous data with 95% CI (confidence interval); risk ratio (RR) for short-term and long-term abstinence rates with 95% CI was calculated. We carried out a consistency model analysis on the main efficacy indicators. We calculated the probability of the lower surface of the cumulative sequencing curve (SUCRA) [17], ranked the optimal treatment measures, and performed node model analysis on the closed-loop network diagram to evaluate the consistency. Statistical heterogeneity [18, 19] was assessed by $\chi^2$ statistics and $I^2$ statistics. When the $P$ value was $\leq 0.05$ and $I^2$ was $\geq 50\%$, statistical heterogeneity existed, and the random effect model was adopted. The fitting degree of the model was judged by comparing the Deviance Information Criterion (DIC) values of the random effect model and the fixed effect model. When the difference value of DIC $< 5$, the fitting degree of the two models is consistent, and if DIC $> 5$, the model with a smaller DIC value is adopted. The model convergence was evaluated by the Potential Scale Reduction Factors (PSRF), and the closer the PSRF value was to 1, the better the convergence of the model was. Finally, two independent reviewers evaluated the quality of direct and indirect evidence using the recommended rating, development, and rating methods [20].

3. Results

3.1. Study Search. A total of 7,733 references were identified from the five electronic databases with 6 records from other sources. We retrieved 117 articles for further evaluation after screening them by title and abstract. Furthermore, 94 articles were excluded for the following reasons: unable to access full text ($n = 5$), not RCTs ($n = 28$), masters’ thesis ($n = 5$), not English or Chinese articles ($n = 1$), duplicate publications ($n = 4$), and laser/electroacupuncture interventions or control interventions not meeting inclusion criteria ($n = 51$). Finally, 23 RCTs [11, 13, 21–41] were included with 2706 patients. The details are shown in Figure 1.

3.2. Study Characteristic and Quality Assessment. Table 1 showed the characteristics of the 23 RCTs that met the criteria for our network meta-analysis. The studies have been published between 1978 and 2019, consisting of a total of 2706 patients from these studies and 6 treatment arms. The treatment period was between 10 days and 8 weeks, and the follow-up time was as short as 2 weeks and as long as 4 years. Among the 23 RCTs, 18 [11, 21, 23–32, 36–41] reported short-term abstinence rates, 8 [11, 21, 24, 30, 31, 36, 38, 41] reported long-term abstinence rates, 6 [11, 13, 21, 22, 29, 36] reported FTND scores, and 7 [13, 22, 25–27, 29, 41] reported daily smoking. Figure 2 graphically displays the networks of evidence for all outcomes.

All the studies mentioned “randomized,” but only 39.1% (9/23) [11, 13, 22, 26, 29, 33–36] of them were truly random, using random number table or computer randomization. Few studies showed low risk of bias. At least 18 studies (18/23) were at low risk of biases with incomplete outcome data. It was judged that all the studies were of low risk in selective reporting, according to the consistent evaluation between the main results of the study and the actual results reported. The overall quality of the evidence for all the results was low, because most of the studies are lacking details. The risk assessment of bias in the included studies is shown (Supplementary Figures 1 and 2).

3.3. Heterogeneity Analysis. We analyzed the consistency of the four outcome measures separately. The results show that the PSRF is 1, which indicates good data convergence. The heterogeneity test results showed that the heterogeneity was small in the short-term and long-term abstinence rates and daily smoking without significant difference. The random effect model was chosen because there was greater heterogeneity in the FTND score (Supplementary Table 2).

3.4. Model Fitting Degree Check. The results showed that the DIC values of short-term abstinence rate fixed effect model and random effect model were 97.3 and 70.36, the DIC values of long-term abstinence rate fixed effect model and random effect model were 97.27 and 29.38, the FTND scores of fixed effect model and random effect model were 34.23 and 27.69, and the DIC values of fixed effect model and random effect model of daily smoking amount were 34.23 and 28.34, respectively. The difference between the two models in each indicator is $> 5$, so the model with a smaller DIC value was selected (random effect model). We tested the model fitting degree of each outcome index under the random effect model, and the ratio value was all close to 1, which proved that the model fitting degree was good.

3.5. Network Meta-Analyses

3.5.1. Short-Term Abstinence Rates. We collected 18 RCTs on short-term abstinence rates. Direct pairwise randomized
Studies excluded because (n = 5289):
- Irrelevant to the topic (n = 3912)
- RCTs unrelated to the topic (n = 758)
- RCTs (NRT versus other interventions) (n = 619)

Studies excluded because (n = 37):
- Not RCTs (n = 28)
- Duplicated publications (n = 4)
- Unable to access full text (n = 5)

Studies excluded because (n = 609):
- Review or meta-analysis (n = 292)
- Protocol (n = 102)
- Observational study (n = 82)
- Clinical trials (n = 63)
- Retrospective study (n = 38)
- Case report (n = 15)

Studies included in quantitative synthesis (n = 23)

**Table 1:** The characteristics of 23 included trials.

<table>
<thead>
<tr>
<th>Study</th>
<th>Interventions</th>
<th>N</th>
<th>Proportion of females (%)</th>
<th>Mean age (year) (experimental group versus control group)</th>
<th>Dropout n (%)</th>
<th>Duration of treatment (T) and follow-up (F)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacHovec et al., 1978</td>
<td>AT versus SAT</td>
<td>24</td>
<td>0</td>
<td>37</td>
<td>Not reported</td>
<td>T: 1 month F: 6 months</td>
<td>Abstinence rate (short-term)</td>
</tr>
<tr>
<td>Lamontagne et al., 1980</td>
<td>AT versus SAT</td>
<td>65</td>
<td>Not reported</td>
<td>33.2 ± 7.9/35.1 ± 6.8</td>
<td>Not reported</td>
<td>T: 1 month F: 6 months</td>
<td>Abstinence rate (short-term and long-term)</td>
</tr>
<tr>
<td>Zhang et al., 2004</td>
<td>AT versus SAT</td>
<td>60</td>
<td>0</td>
<td>25.70 ± 4.40/25.43 ± 3.66</td>
<td>Not reported</td>
<td>T: 4 weeks F: 1 year</td>
<td>Abstinence rate (short-term)</td>
</tr>
<tr>
<td>Wu et al., 2007</td>
<td>AT versus SAT</td>
<td>118</td>
<td>15.25</td>
<td>54.3 ± 16.9/53.0 ± 16.9</td>
<td>Not reported</td>
<td>T: 8 weeks F: 6 months</td>
<td>Abstinence rate (short-term), mean daily smoking amount, FTND score</td>
</tr>
<tr>
<td>Hyun et al., 2010</td>
<td>AT versus SAT</td>
<td>80</td>
<td>6.25</td>
<td>40.0/42.0</td>
<td>Not reported</td>
<td>T: 2 weeks F: 2 weeks</td>
<td>MNWS score, BDI score, BAI score</td>
</tr>
<tr>
<td>Chae et al., 2011</td>
<td>AT versus SAT</td>
<td>29</td>
<td>0</td>
<td>24.9 ± 2.6/25.0 ± 3.4</td>
<td>Not reported</td>
<td>T: 3 weeks F: 8 months</td>
<td>Exhaled CO level, HRV during visual cues, distraction to smoking cues, belief in and credibility of acupuncture, blinding indices</td>
</tr>
<tr>
<td>Study</td>
<td>Interventions</td>
<td>N</td>
<td>Proportion of females (%)</td>
<td>Mean age (year) (experimental group versus control group)</td>
<td>Dropout n (%)</td>
<td>Duration of treatment (T) and follow-up (F)</td>
<td>Outcomes</td>
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<tr>
<td>Kang et al., 2013</td>
<td>AT versus SAT</td>
<td>25</td>
<td>0</td>
<td>25.2 ± 2.0/24.8 ± 1.6</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Exhaled CO level, craving scores to smoking-related visual cues</td>
</tr>
<tr>
<td>Ma et al., 2014</td>
<td>AT versus SAT</td>
<td>136</td>
<td>25.74</td>
<td>25.2 ± 2.0/24.8 ± 1.6</td>
<td>37–45</td>
<td>T: 8 weeks F: 6 months</td>
<td>Abstinence rate (short-term)</td>
</tr>
<tr>
<td>Wang et al., 2006</td>
<td>AA versus NRT</td>
<td>204</td>
<td>9.80</td>
<td>20–64</td>
<td>Not reported</td>
<td>T: 20 days F:/</td>
<td>Abstinence rate (short-term)</td>
</tr>
<tr>
<td>Li et al., 2009</td>
<td>AA versus SAA</td>
<td>140</td>
<td>23.57</td>
<td>38.23 ± 9.7/38.26 ± 9.56</td>
<td>4 weeks F: 3 months</td>
<td></td>
<td>Abstinence rate (short-term)</td>
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<tr>
<td>Yeh et al., 2009</td>
<td>AA versus SAA</td>
<td>79</td>
<td>Not reported</td>
<td>28 ± 7.79/27 ± 7.63</td>
<td>T: 6 weeks F:/</td>
<td>Abstinence rate (short-term), serum cotinine levels, cigarette consumption, exhaled CO level</td>
<td></td>
</tr>
<tr>
<td>Wing et al., 2010</td>
<td>AA versus SAA</td>
<td>70</td>
<td>30.00</td>
<td>46.5 ± 12.36/46.4 ± 11.36</td>
<td>Not reported</td>
<td>T: 3 weeks F: 3 months</td>
<td>Abstinence rate (short-term), exhaled CO level</td>
</tr>
<tr>
<td>Ayse A-D, 2011</td>
<td>AA versus SAA</td>
<td>47</td>
<td>36.17</td>
<td>33.8 ± 10.26/34.0 ± 10.43</td>
<td>Not reported</td>
<td>T: 1 month F: 6 months</td>
<td>Abstinence rate (short-term and long-term), exhaled CO level FTND score, BDI score</td>
</tr>
<tr>
<td>Zhang et al., 2013</td>
<td>AA versus SAA</td>
<td>43</td>
<td>58.14</td>
<td>50.4 ± 11.49/49.8 ± 8.53</td>
<td>Not reported</td>
<td>T: 8 weeks F: 3 months</td>
<td>Abstinence rate (short-term), cigarette consumption, daily smoking amount</td>
</tr>
<tr>
<td>Silva Rd.e et al., 2014</td>
<td>AA versus SAA</td>
<td>30</td>
<td>66.67</td>
<td>41</td>
<td>Not reported</td>
<td>T: 5 weeks F: 1 month</td>
<td>Exhaled CO level, FTND score, daily smoking amount</td>
</tr>
<tr>
<td>Lee et al., 2016</td>
<td>AA versus SAA</td>
<td>60</td>
<td>0</td>
<td>22.67 ± 2.02/22.19 ± 2.02</td>
<td>Not reported</td>
<td>T: 10 days F: 1 month</td>
<td>FTND score, exhaled CO level, self-efficacy for smoking cessation</td>
</tr>
<tr>
<td>Han, 2006</td>
<td>APAA versus AA</td>
<td>42</td>
<td>40.48</td>
<td>Not reported</td>
<td>T: 4 weeks F:/</td>
<td>Abstinence rate (short-term)</td>
<td></td>
</tr>
<tr>
<td>Liu et al., 2015</td>
<td>APAA versus AA</td>
<td>48</td>
<td>20.83</td>
<td>42 ± 8/40 ± 6</td>
<td>Not reported</td>
<td>T: 4 weeks F:/</td>
<td>Abstinence rate (short-term), daily smoking amount, FTND score, score of the tobacco dependence self-rating scale</td>
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<td>Abstinence rate (short-term), group mean change in daily cigarette consumption, Tehchi sensations reported by treatment group</td>
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<tr>
<td>Steiner et al., 1982</td>
<td>APAA versus SAT</td>
<td>32</td>
<td>34.38</td>
<td>Not reported</td>
<td>APAA:5 (31.25) SAT:4 (25.00)</td>
<td>T: 2 weeks F:/</td>
<td>Abstinence rate (short-term), daily smoking amount, FTND score, BDI score</td>
</tr>
<tr>
<td>Clavel F et al., 1985</td>
<td>AT versus NRT</td>
<td>429</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>T: 1 month F: 13 months</td>
<td>Abstinence rate (short-term and long-term)</td>
</tr>
<tr>
<td>Clavel F et al., 1997</td>
<td>AT versus NRT</td>
<td>485</td>
<td>55</td>
<td>All 34</td>
<td>Not reported</td>
<td>T: 6 months F: 4 years</td>
<td>Abstinence rate (short-term and long-term), exhaled CO level FTND score, BDI score</td>
</tr>
<tr>
<td>Zhang et al., 2017</td>
<td>AT versus NRT</td>
<td>60</td>
<td>Not reported</td>
<td>Not reported</td>
<td>T: 30 days F:/</td>
<td>Abstinence rate (short-term)</td>
<td></td>
</tr>
<tr>
<td>Chai et al., 2019</td>
<td>AT versus AA</td>
<td>400</td>
<td>6.5</td>
<td>43 ± 14/45 ± 14/46 ± 13/45 ± 14</td>
<td>Not reported</td>
<td>T: 8 weeks F: 16 weeks</td>
<td>Abstinence rate (short-term and long-term), FTND score, HIS score</td>
</tr>
</tbody>
</table>
Seven studies reported changes in daily smoking. A total of four interventions were involved, including APAA, AA, SAA, and SAT. No significant difference was observed among these four groups (Figure 3). In addition, network meta-analysis showed that there was no statistical difference between the four interventions. Among them, AA versus APAA RR was −6.8 (95% CI −16.01, 2.39), APAA versus SAA RR was 7.69 (95% CI −2.36, 17.66), and AA versus SAT RR was −11.5 (95% CI −24.23, 1.24) (Table 3).

3.5.2. Long-Term Abstinence Rates. Data on long-term abstinence rates were available from 8 RCTs, reporting a total of 696 participants with events. The results of the pairwise random effect meta-analyses showed that RRs were low and without a significant difference, showing that AA versus SAT was 2.57 (95% CI 0.78, 8.63), APAA versus SAT was 1.96 (95% CI 0.59, 6.63), NRT versus SAT was 1.80 (95% CI 0.61, 5.51), AT versus SAT was 1.44 (95% CI 0.54, 3.90), and SAA versus SAT was 1.03 (95% CI 0.23, 4.29) (Figure 3). Network meta-analysis showed that only AA versus SAA had a statistical difference in long-term abstinence rate and RR value was 2.49 (95% CI 1.14, 5.97), but not among other interventions. The results of the network meta-analysis are shown in Table 2.

3.5.3. FTND. Data on FTND scores were obtained from 6 RCTs; the direct meta-analysis showed that there was no significant difference in comparison between SAT and AA, APAA, AT, NRT, or SAA, showing that WMDs were −1.11 (95% CI −3.89, 4.20), 1.22 (95% CI −2.61, 5.23), 1.00 (95% CI −2.0, 3.99), 0.907 (95% CI −3.12, 4.90), or −0.324 (95% CI −4.49, 4.22) (Figure 3), respectively. Network meta-analysis showed that APAA versus AA was involved in two studies, and RR was 1.34 (95% CI −0.87, 3.16). Three studies involved SAA versus AA; RR was −0.19 (95% CI −1.9, 1.35). Comparisons between other interventions involved only one study, and none of the differences were statistically significant (Table 3).

3.5.4. Daily Smoking. Seven studies reported changes in daily smoking. A total of four interventions were involved, including APAA, AA, SAA, and SAT. No significant difference was observed among these four groups (Figure 3). In addition, network meta-analysis showed that there was no statistical difference between the four interventions. Among them, AA versus APAA RR was −6.8 (95% CI −16.01, 2.39), APAA versus SAA RR was 7.69 (95% CI −2.36, 17.66), and AA versus SAT RR was −11.5 (95% CI −24.23, 1.24) (Table 3).

3.6. Adverse Events. Of the 23 studies we included, 17 of them show [21–25, 28–33, 35, 37–41] no information on adverse events. Two studies report no adverse events [11, 34]. One reports adverse events such as minor bleeding, hematoma, dizziness, fainting, residual needle sensation, tenderness, and minor infection during treatment (AT: 41 subjects; SAT: 44 subjects) [36]. Another study reports that 1 person in the AA group and 4 people in the SAA group have local ear maladjustment and 1 person in the SAA group had dizziness [26]. Two other studies report adverse reactions such as local ear maladaptation and pain during treatment [13, 27].

3.7. Inconsistency Analyses. Because only the network graph with short-term abstinence rates became a closed loop, we only performed node-splitting analysis, and node-splitting analysis showed no inconsistency between APAA and AA (P = 0.75), AT and AA (P = 0.74), NRT and AA (P = 0.17), AT and APAA (P = 0.18), NRT and AT (P = 0.74), and SAT and AT (P = 0.92). The results of direct comparison and indirect comparison were consistent (Supplementary Table 3).

3.8. Rank Probability. Table 4 shows the ranking of the six interventions; the smaller the SU CRA, the better. Both AA and APAA had the best effects in terms of short-term and long-term abstinence rates, and AA also ranked high in terms of daily smoking. APAA and AT had good effects on FTND scores. The SAT had the worst effect on short-term abstinence rates. SAA was the least effective for long-term abstinence rates and FTND scores.

3.9. Sensitivity Analysis. We used short-term abstinence rates, long-term abstinence rates, and daily smoking as indicators of sensitivity analysis. The clinical similarity and methodological similarity of the included studies were good, and the analytical results were reliable. Thus, our data were robust and reliable.

3.10. Publication Bias. A funnel plot was performed for short-term abstinence rates, involving 18 studies, including a four arms study. It was divided into three separate studies. Funnel plots illustrated that scatters were almost visually symmetrical, and the result of Begg’s test was P = 0.82, meaning that publication bias was relatively low (Figure 4).

4. Discussion

It is well accepted that tobacco smoking is one of the most challenging public health problems nowadays, which also attracts enormous attention from the medical and social points of view [42]. Quitting smoking probably is an effective way to reduce such damage [43]. Bayesian network meta-analysis was used for comparing the relative safety and efficacy of traditional Chinese medicine such as AT, AA, APAA, and NRT in smoking cessation. Although there was no significant difference among these four groups, using network
meta-analysis, our data confirmed that the effects of smoking quit interventions among these four are similar, providing some useful information for smoking quitting. However, AA was superior to SAA in long-term abstinence rate comparison. The probability rankings of AA and APAA were also better than other interventions.

In addition to other sources of bias, most studies are not clear about whether the implementation of allocation concealment and blind method is correct, and the criteria are not clear, which may compromise the validity of the results. Particularly in the Chinese studies, most of them are subjective, which is more susceptible to affect the experimental outcomes objectively. We also consider that, due to the particularity of acupuncture and auricular acupressure, it may be difficult to treat blindness for doctors, but it is necessary to blind patients [26]. However, more than half of the studies have not performed blindness in this respect.

Most of the results of the Bayesian network meta-analysis were not statistically different, but the rank probability showed that AA and APAA were superior to other intervention indicators. It is worth noting that our estimates of the efficacy of these interventions are not accurate, which can be seen from the broad confidence interval. Moreover, the number of the included studies was relatively small. Some pairwise comparisons only involve one study. Therefore, more trials with a larger sample size are needed to establish more accurate efficient comparison. On the plus side, our paired meta-analysis results were consistent with the network meta-analysis results, which also improved the quality of our evidence. However, since most treatments do not have data on adverse events, the extent of their differences in safety is uncertain.

AT was not superior to other treatments such as SAT and NRT in the long-term abstinence rates, but there was a difference between AA and SAA, which was consistent with the previous research results. However, in terms of short-term abstinence rate, we did not conclude that AT or AA was superior to other therapies, which was consistent with the results of White et al., but different from those of Wang et al. [8, 44]. This may be related to the different interventions we have included. We excluded electroacupuncture and laser acupuncture only by incorporating pure acupuncture. Compared with previous studies, we may greatly reduce the heterogeneity between studies due to differences in intervention measures [8, 45]. Our research conclusions are not limited to the traditional acupuncture theory and are applicable to any therapy such as simple acupuncture and auricular acupressure. To our knowledge, there is no reticul-
Table 2: Network meta-analysis of the results on short-term abstinence rates and long-term abstinence rates (RR (95% CI)).

<table>
<thead>
<tr>
<th></th>
<th>Short-term abstinence rates</th>
<th>Long-term abstinence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AA</td>
<td>AA</td>
</tr>
<tr>
<td>AA</td>
<td>1.01 (0.54, 1.9)</td>
<td>0.66 (0.31, 1.42)</td>
</tr>
<tr>
<td>APAA</td>
<td>1.32 (0.62, 2.8)</td>
<td>0.65 (0.39, 1.46)</td>
</tr>
<tr>
<td>AT</td>
<td>1.78 (0.89, 3.65)</td>
<td>0.99 (0.56, 1.72)</td>
</tr>
<tr>
<td>NRT</td>
<td>1.43 (0.7, 2.85)</td>
<td>0.8 (0.48, 1.28)</td>
</tr>
<tr>
<td>SAA</td>
<td>2.49 (1.14, 5.97)</td>
<td>1.4 (0.49, 4.24)</td>
</tr>
<tr>
<td>SAT</td>
<td>2.57 (0.78, 8.63)</td>
<td>1.44 (0.54, 3.9)</td>
</tr>
</tbody>
</table>

Table 3: Network meta-analysis of the results on FTND scores and daily smoking (WMD (95% CI)).

<table>
<thead>
<tr>
<th></th>
<th>FTND scores</th>
<th>Daily smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AA</td>
<td>APAA</td>
</tr>
<tr>
<td>AA</td>
<td>1.34 (–0.87, 3.16)</td>
<td>1.13 (–1.88, 3.53)</td>
</tr>
<tr>
<td>APAA</td>
<td>–6.8 (–16.01, 2.39)</td>
<td>–0.19 (–2.84, 2.19)</td>
</tr>
<tr>
<td>AT</td>
<td>–3.05 (1.11, 6.16)</td>
<td>–0.19 (–2.75, 2.56)</td>
</tr>
<tr>
<td>NRT</td>
<td>–3.87 (–16.38, 9.64)</td>
<td>–1.25 (–4.17, 2.16)</td>
</tr>
<tr>
<td>SAA</td>
<td>0.88 (–3.16, 4.84)</td>
<td>7.69 (–2.36, 17.66)</td>
</tr>
<tr>
<td>SAT</td>
<td>–11.5 (–24.23, 1.24)</td>
<td>–4.68 (–13.52, 4.17)</td>
</tr>
</tbody>
</table>

Figure 3: Direct pairwise random effect meta-analyses of outcomes.
safer. Based on the existing knowledge of auricular point sticking for smoking cessation, we can strengthen the application of such intervention, which will benefit more smokers, especially for those who have strong desire to quit smoking but have no free time, which may be a more practical and applicable intervention method. Therefore, we suggest that RCTs with standardized intervention measures, long intervention duration, high quality, and large sample size should be carried out in future clinical trial studies to clarify the advantages of AA. In addition, our results are based on random evidence, and we also summarize the safety profile of interventions such as acupuncture when quitting, which makes our research more comprehensive than the previous ones to provide a reference for clinical decision-making.

There were some limitations to our network meta-analysis. First, the course of treatment in the RCTs we included varied from 10 days to 8 weeks and the follow-up time was also quite different. Thus, it would be best to determine the collected data from a similar period. However, it would reduce the power of significance if a specific treatment period was selected in the current study. We will collect the data from larger data based which probably will enable us to test a more specific period. If the later clinical study can unify the treatment cycle and follow-up time, it may have been more convincing. Second, although the selected points of the studies we included are almost the same, there are also subtle differences. Although existing studies have shown that there is no direct linkage between acupoint selection and curative effect [14], acupuncture is a complex process, and the difference in the needling manipulation may also lead to different research results [46]. Therefore, uniform acupuncture manipulation is also an important point in the design of RCTs on smoking cessation by acupuncture in the future. This issue may be solved by comparing different interventions with more repeated RCTs in the future. Finally, because of the small number of trials reporting valuable measures such as Minnesota Nicotine Withdrawal Scale (MNWS) [47], Beck Anxiety Inventory (BAI) [48], and Beck Depression Inventory (BDI) [49], there was no correlation between the intervention groups, which would affect the judgment of potential efficacy, so we did not analyze these indicators.

Our analysis shows that a larger sample size, more consistent intervention methods, and treatment follow-up time are needed for future RCTs of acupuncture, auricular acupressure, and other traditional Chinese medicine methods for smoking cessation, so as to improve the quality of research and clarify the advantages of such methods in smoking cessation effect. In addition, we should pay more attention to the possible adverse events of these intervention processes and strengthen the evidence-based medical evaluation of safety evaluation. However, there is a lack of sufficient data from the included studies in the current network meta-analysis to offer an objectively dose-dependent value. This will be performed in our future study.

5. Conclusions

AA was superior to SAA in long-term abstinence rate comparison. The probability rankings of AA and APAA were also better than other interventions. RCTs with larger sample size, more consistent intervention methods, and longer treatment follow-up time will be investigated in future to further clarify the advantages of treatment methods such as APAA and AA. In addition, more attention should also be paid to the possible adverse events during the treatment of TCM methods such as acupuncture, which should be reported to supplement the evidence-based medical evidence in this area.

Data Availability

All data analyzed during this study are included in this published article and the original study publications.
Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Runjing Dai and Yongchun Cao contributed equally to this work. Runjing Dai and Jingchun Fan designed the study. Runjing Dai drafted the protocol. Runjing Dai and Yongchun Cao conducted a literature search. Runjing Dai, Yongchun Cao, Hailiang Zhang, Na Zhao, and Guisen Zheng completed study screening, data extraction, and statistical analysis. Differences are finally determined through Jingchun Fan and Shisan Bao discussions. Runjing Dai and Yongchun Cao wrote the manuscript. Xingke Yan, Shisan Bao, and Jingchun Fan revised and polished the manuscript and approved the final version. All the authors agreed on the final manuscript.

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Supplementary Materials

Supplementary Table 1: search strategies. Supplementary Table 2: results of heterogeneity analysis. Supplementary Table 3: inconsistency analyses. Supplementary Figure 1: risk of bias summary, Supplementary Figure 2: risk of bias graph. (Supplementary Materials)

References


