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Patient-reported outcomes and acupuncture-related adverse events are overlooked in acupuncture randomised controlled trials: a cross-sectional meta-epidemiological study

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Abstract

Objectives To investigate the patient-reported outcomes (PROs) and acupuncture-related adverse events (A-AEs) in acupuncture randomised controlled trials (RCTs).

Design Cross-sectional meta-epidemiological study.

Data sources We comprehensively searched for eligible studies between 1 January 2014 and 1 May 2024, in MEDLINE, EMBASE, CENTRAL, CBM, CNKI, Wanfang Data and VIP Database.

Eligibility criteria RCTs that used acupuncture as the intervention group to obtain the efficacy and/or safety of acupuncture therapy. Acupuncture therapy should be based on Traditional Medicine theory.

Main outcome measures We assessed (1) the general characteristics of acupuncture RCTs; (2) the general characteristics of PROs; (3) the reporting scores of PROs by the Extension of Consolidated Standards of Reporting Trials of Patient-Reported Outcomes (CONSORT PRO Extension); (4) the general characteristic of A-AEs; (5) the incidence of A-AEs.

Results We included 476 studies in this study. 296 (62.2%) used PROs as study outcomes, 272 (57.1%) reported safety outcomes. The Visual Analogue Scale (149, 23.7%) and the Pittsburgh Sleep Quality Index (42, 6.7%) were the most common PROs reported. The reporting of PROs was incomplete, with sufficiently reporting scores ranging from 2.7% to 97.6% across the CONSORT PRO Extension. 164 studies reported A-AEs, of which 141 reported specific details, and we found that the OR for the incidence of AEs in the acupuncture group compared to the control group was 1.434 (95% CI 1.148 to 1.793). We identified 1277 reports of A-AEs in eligible studies, predominantly tissue injury (eg, haematoma, bleeding), irritation (eg, pain, post-acupuncture discomfort), with no reports of serious A-AEs. The reporting of A-AEs lacked details on the acquisition methods (15.5%), occurrence time (5.5%), A-AEs' treatment (18.1%) and A-AEs' recovery (19.7%). Studies that reported funding, registry information, acupuncturist qualifications and non-significant primary outcomes were associated with the A-AEs' reporting, and the difference was statistically significant ($p \leq 0.05$).

Conclusion This study found that the reporting of PROs and A-AEs was insufficient in acupuncture RCTs. Future studies should clarify the clinical significance of using PROs as outcomes and report AEs comprehensively to provide patients with sufficient information on the benefits and harms of acupuncture treatments.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patient-reported outcomes (PROs) and acupuncture-related adverse events (A-AEs) are valuable outcomes in acupuncture randomised controlled trials (RCTs), which provide the pros and cons of acupuncture treatment.

WHAT THIS STUDY ADDS

⇒ PROs are poorly reported in acupuncture RCTs (average sufficiently reporting rate is 38.7% across the Extension of Consolidated Standards of Reporting Trials of Patient-Reported Outcomes), and study outcomes may have limited guidance for clinical practice.

⇒ Of the 476 included studies, 204 omitted safety outcomes, and 108 claimed no adverse events, A-AEs in acupuncture RCTs may have been underestimated intentionally or unintentionally.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Before using PROs in acupuncture RCTs, researchers should undergo standardised training.

⇒ Future studies should predefine, accurately identify and completely report both patient-reported and investigator-reported A-AEs.

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Introduction

Acupuncture is one of the most popular complementary and integrative therapies globally, and has been recommended for treating 113 diseases by the WHO.[1] However, as in the case of other complementary therapies, acupuncture still faces dual scepticism about safety and efficacy.[2] Comprehensively synthesised high-quality acupuncture research evidence may explain this scepticism.[2] But evidence of study outcomes in clinical studies is often hampered by non-standardised selection and measurement of outcomes and incomplete reporting.[3] Randomised controlled trials (RCTs) are the gold standard for inferring causal relationships between interventions and outcomes[4] and have been widely used in acupuncture research, with over 4000 trials being published in the last 5 years.[5]

Patient-reported outcomes (PROs) are valuable outcomes in acupuncture RCTs that refer to health-related outcomes directly from patients without amendment by clinicians, caregivers or anyone else.[6] Using PROs in research can help assess patient-centred needs and select interventions that meet patient preferences,[7 8] as PROs capture the most intuitive perception of the treatment experience, illness and function for the patients themselves by a formal and systematic means.[9] To improve the inclusion and synthesis of PRO data in RCTs, the Extension of Consolidated Standards of Reporting Trials of Patient-Reported Outcomes (CONSORT PRO Extension) was published in 2013.[10] Studies have found that following the CONSORT PRO Extension can promote the adequate reporting of PROs in RCTs,[11] and accurately reporting can enhance the reproducibility of study results.[12] Nevertheless, the reporting of PROs in acupuncture RCTs has not been investigated to date.

In safety outcome assessment, despite widespread evidence showing that acupuncture is considerably safe when administered by qualified practitioners,[13] the evidence synthesis of acupuncture-related adverse events (A-AEs) is not convincing enough.[14] While more than 3000 acupuncture systematic reviews (SR) have been published,[15] the majority of SRs assessed safety outcomes as additional outcomes with poorly reported, and only a few case report SRs used A-AEs as the primary outcome.[14 16 17] Large-scale investigative studies (>10 000 cases) have found that the overall incidence of A-AEs is 6.71%–8.6% (generally mild and self-limiting),[13 18 19] and serious adverse events (SAEs) is 0%–0.047% (according to accepted criteria[20]).[13 19] Given that at least 100 million acupuncture treatments are performed globally each year,[20] and that case reports and investigative studies do not provide a definitive causal relationship between intervention and outcome.[17] There is an urgent need for a comprehensive, systematic synthesis of A-AEs in acupuncture RCTs.

This study explores the general characteristics and reporting of PROs and A-AEs of acupuncture RCTs. The findings will highlight whether published acupuncture RCTs reported sufficient information for patients to be well informed about the pros and cons of acupuncture treatment. Therefore, we assessed the reporting of PROs in acupuncture RCTs by the CONSORT PRO Extension and the A-AEs by the pre-specified A-AEs strategies.

Methods

We conducted a meta-epidemiological methodology for the general characteristics and reporting of PROs and A-AEs of acupuncture RCTs published from 2014 to 2024. Methods used in this study were prespecified and registered via Open Science Framework (OSF),[21 22] any inconsistencies with the protocol are available on the OSF.[23] The reporting of this study followed the guidelines for reporting meta-epidemiological methodology research.[24]

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans in this study.

Identification and selection of articles

The specific criteria for including studies are shown in table 1.

We comprehensively searched for eligible acupuncture RCTs between 1 January 2014 and 1 May 2024 in the following seven databases: MEDLINE, Excerpta Medica Database (EMBASE), Cochrane Central Register of Controlled Trials (CENTRAL) (three English datasets searched through OVID), Chinese Biomedical Literature Service System (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Data and VIP Chinese Medical Journal Database. The search strategy for all databases is available in online supplemental appendix 1.

We used EndNote (EndNote V.X7.1 for Chinese publications) and Rayyan (https://www.rayyan.ai/ for English publications) to screen and exclude studies. Two researchers (ZX and XL) independently screened the titles and abstracts according to the inclusion and exclusion criteria. Then two researchers (PZ and YDe) independently screened the full text. Two senior investigators (YDu and LY) addressed disagreements during the screening process.

For the specific PROs eligibility criteria: (1) we used outcomes defined as patient-reported outcomes as PROs, regardless of

Table 1 PICOS framework for eligibility criteria

Items	Criteria of exclusion and inclusion
Population	1. Studies published in peer-reviewed journals with no disease or journal type restrictions 2. Full text available 3. More than three authors 4. Published in English or Chinese language
Intervention	1. Acupuncture therapy only used in the intervention group 2. Acupuncture therapy based on Traditional Medicine 3. Needles should penetrate into the skin
Control	1. No intervention or waiting list 2. Sham acupuncture or placebo 3. Western medicine 4. Other interventions such as psychotherapy or rehabilitation and physical therapy guided by modern medical theory
Outcomes	All outcomes used to test the safety and efficacy of acupuncture therapy without specific limitations
Study Design	1. Randomised controlled trials with two parallel groups 2. Applied to humans 3. Sample size more than 20

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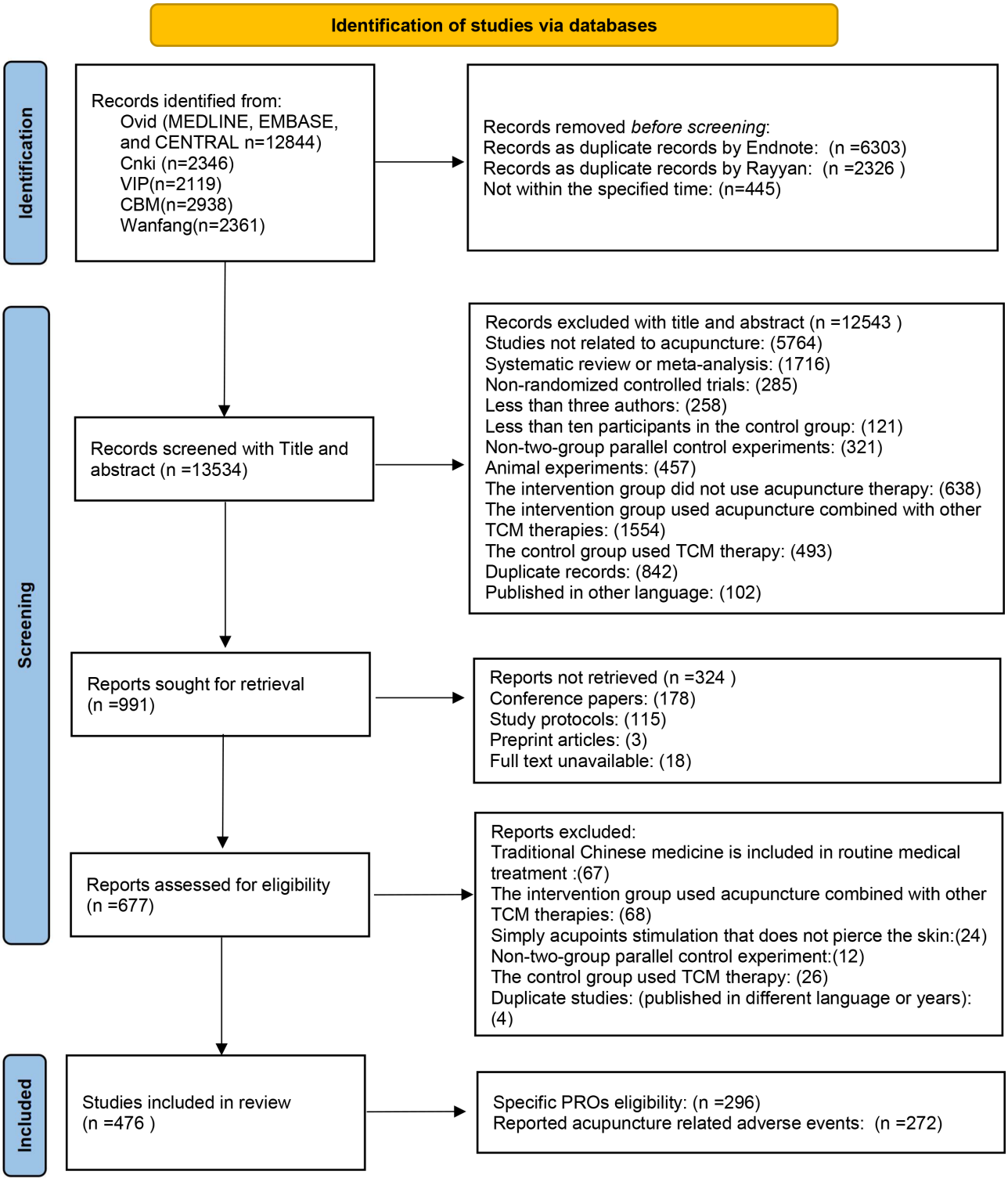


Figure 1 Identification of studies. PROs, patient-reported outcomes, TCM, Traditional Chinese Medicine.

whether they were reported by patients or not (as studies may not specify who reported scales); (2) studies that used PRO as primary and/or secondary outcomes.

For the identification of A-AEs: according to the Food and Drug Administration, the European Medicine Agency and the WHO, adverse events refer to any untoward medical occurrence after exposure to a medicine, which is not necessarily caused by that medicine[25–27] (online supplemental appendix 2). The purpose of our study was to explore any untoward safety outcomes caused by acupuncture therapy, thus, we used A-AEs in this study.

However, studies may not distinguish between AEs and A-AEs. Thus, we used a prespecified A-AEs identification to identify A-AEs based on previous knowledge as: (1) organ injury (pneumothorax, cardiac tamponade, etc); (2) tissue injury (bleeding, haematoma, bruise, etc); (3) tissue irritation (pain, post-acupuncture discomfort, etc); (4) systemic reactions (needle-sickness, abdominal

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Table 2 General characteristics of included studies

Characteristic	No. (%) (N=476)	No. (%) (N=296) Studies used PROs	No. (%) (N=272) Studies reported A-AEs
Publication language			
Chinese	258 (54.2)	153 (51.7)	129 (47.4)
English	218 (45.8)	143 (48.3)	143 (52.6)
Publication year			
2014–2015	47 (9.9)	26 (8.8)	21 (7.7)
2016–2017	71 (14.9)	42 (14.2)	32 (11.8)
2018–2019	70 (14.7)	43 (14.5)	39 (14.3)
2020–2021	89 (18.7)	61 (20.6)	49 (18.0)
2022–2024	199 (41.8)	124 (41.9)	131 (48.2)
Type of study centre			
Single-centre	121 (28.6)	114 (38.5)	115 (42.3)
Multi-centre	302 (71.4)	182 (61.5)	157 (57.7)
Acupuncture type			
Conventional acupuncture	276 (58.0)	173 (58.4)	160 (58.8)
Electro-acupuncture	163 (34.2)	96 (32.4)	90 (33.1)
Small needle-knife	12 (2.5)	9 (3.0)	8 (2.9)
Others	25 (5.3)	18 (6.1)	14 (5.1)
Registration			
Prospective registration	127 (26.7)	89 (30.1)	94 (34.6)
Retrospective registration	41 (8.6)	32 (10.8)	30 (11.0)
Unregistered	308 (64.7)	175 (59.1)	148 (54.4)
Funding			
Institutional funding	369 (77.5)	233 (78.7)	226 (83.1)
Individual funding	1 (0.2)	0	0
Mixed funding	1 (0.2)	0	1 (0.4)
None	105 (22.1)	63 (21.3)	45 (16.5)
Specific PRO items (n=629)			
PRO			
Visual Analogue Scale (VAS)		149 (23.7)	
Pittsburgh Sleep Quality Index (PSQI)		42 (6.7)	
Self-rating Depression Scale (SDS)		18 (2.9)	
Others		420 (66.8)	
Scale source			
Validated scales		553 (87.9)	
Validated scales for new population		31 (4.9)	
Non-validated scales		45 (7.2)	
Reliability and/or validity of PRO			
Reported		11 (1.7)	
Not reported		618 (98.3)	

A-AEs, acupuncture-related adverse events; PROs, patient-reported outcomes.

discomfort, allergic reaction, etc); (5) infections associated with acupuncture; (6) migration of broken acupuncture needles; (7) other complications associated with acupuncture (see online supplemental appendix 2). We also collect safety outcomes that are reported as A-AEs by authors.

Data extraction

We categorised data extraction into three categories: general characteristics extraction, PROs extraction and A-AEs. We created three standard data extraction tables in Microsoft Excel 2019 (Microsoft Excel 2019 MSO 2210 Build 16.0.15726.20188 32). Illustrations of the variables are available on the OSF.[23] To ensure the consistency and accuracy, we performed three rounds of pretests on a random sample of 10 studies.

Two researchers (SW and XZ) independently extracted the general characteristics, and a senior reviser (YDu) resolved any discrepancy in the data collected. The general characteristics included: (1) title, (2) authors, (3) language, (4) year, (5) sample size, (6) acupuncturist qualifications (reported and unreported), (7) type of study centre, (8) acupuncture practitioner qualifications, (9) source of funding, (10) conflict of interest, (11) registry, (12) disease system, (13) specific disease, (14) acupuncture types, (15) whether the primary outcome is significant and (16) sample size (or number of treatment sessions) in the acupuncture group and the control group for specific studies reported A-AEs (see online supplemental fappendix 3 for more details).

Two researchers (SL and YDe) independently extracted the PROs extraction, and a senior reviser (PZ) resolved any discrepancy in the data collected. The specific PRO information includes: (1) PRO scale name, (2) scale source (validated scales, validated scales for new populations and non-validated scales), (3) PRO scale number in each trial, (4) PROs as primary or secondary outcomes in each trial, (5) PROs acquisition methods, (6) PROs between-group significance. For the reporting scores of PROs, we used the CONSORT PRO Extension.[10] As the CONSORT PRO Extension item 6a contains questions about the reliability and validity of the PRO and how it was acquired, we categorised item 6a as item 6a1: evidence of PRO instrument validity and reliability should be provided or cited, if available; 6a2: details of the mode of PRO completion (see more details in online supplemental appendix 3). Specifically, a total of 15 items in six sections were scored in four possibilities: '0' for 'Unreported', '1' for 'Sufficiently reported', '2' for 'Insufficiently reported' and '3' for 'Not applicable'. The scoring details were made according to the explanatory notes for CONSORT PRO Extension, and shown in online supplemental appendix 3.

Two researchers (YC and YW) independently extracted the general characteristics, and a senior reviser (SW) resolved any discrepancy in the data collected. Which include: (1) did the study assess A-AEs? (2) if studies assessed AEs, was a between-group analysis done? (3) if studies omitted safety outcomes, did they claim acupuncture is safe? (4) in which arm did A-AEs happen (intervention or control sham acupuncture group)? (5) A-AEs events (total events and events in different types), (6) A-AEs type, (7) A-AEs acquisition (who reported A-AEs), (8) A-AEs occurrence, (9) A-AEs severity, (10) A-AEs treatment, (11) A-AEs recovery, (12) participant withdrawal due to A-AEs and (13) safety assessment in registry/protocol.

Confounders identification and adjusting

The potential confounders that may affect the reporting of AEs are identified based on prior knowledge by directed acyclic graphs (DAGitty V.3.1).[28] Potential confounders included: publication language, publication year, type of study centre, acupuncturist qualifications, funding, interest, acupuncture type, registry and whether the primary outcome is significant (online supplemental appendix 4).

Data analysis

We summarised the general characteristics and reporting of PROs and ARs of eligibility studies, and further explored the potential confounders that may affect the reporting of AEs and the prevalence estimates for A-AEs in acupuncture RCTs.

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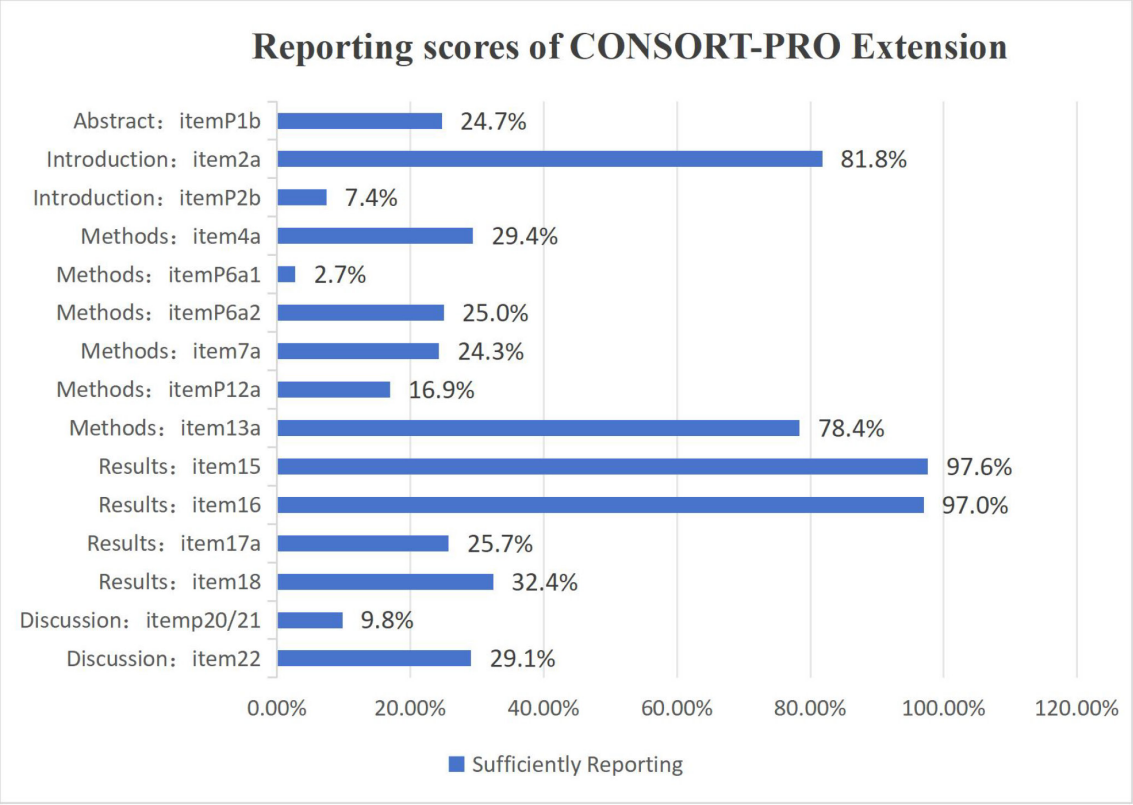


Figure 2 Reporting scores of the Extension of Consolidated Standards of Reporting Trials of Patient-Reported Outcomes.

For the general characteristics of PROs and ARs, we used descriptive statistics and presented as counts (n), percentages (%) in charts. We calculated and presented CONSORT PRO Extension scores for each item using bar chart (four scores for unreported, sufficiently reported, insufficiently reported and not applicable, more details in online supplemental appendix 3).

Binomial logistic regression analyses were used to estimate the ORs (aORs) and 95% CIs of the reporting of A-AEs with potential confounders. We used the reporting of A-AEs (reported and unreported) as the dependent variable, used publication language, publication year, type of study centre, acupuncturist qualifications, funding, interest, acupuncture type, registry and whether the primary outcome is significant as confounders.

We used random-effects meta-analysis to calculate the anticipated effects for A-AEs, and accounted for between-study heterogeneity.[29] We used sample sizes for studies that reported the number of participants who suffered AE (the same participants might suffer many AE) and used treatment sessions (used the specific treatment sessions reported in studies if reported or calculated by sample size×intervention counts) for studies that reported the number of AEs.

All statistical analyses were performed using the R software (R V.4.4.2), statistical significance was determined as p>0.05 (two-sided test), 95% (CI).

Results

In total, 476 studies were included in the final sample (figure 1). Among these studies, 296 used PROs as primary or secondary outcomes, and 272 reported A-AEs. All studies included in the review and the data extracted for each article are available on the OSF.[23]

General characteristics of eligibility studies

Table 2 presents the general characteristics of the included studies (the final kappa coefficient was 0.973, 95% CI 0.920 to 1.026) and the general characteristics of studies that used PROs and reported A-AEs. Specifically, the use of PROs and reporting of A-AEs in acupuncture RCTs increased over the years. For the specific PRO items, 47 (15.9%) studies used PROs as primary outcomes, 43 (15.5%) used PROs as secondary outcomes, but only 71 studies (24.0%) reported specific acquisition methods for PROs (online supplemental appendix 5 table 1). 629 PROs were identified in these studies, Visual Analogue Scale (149, 23.7%) was the most frequent scale. Most PROs (553, 87.9%) were validated scales, but only 11 scales (1.7%) reported the reliability and/or validity.

Reporting scores of the CONSORT PRO Extension

Figure 2 presents the reporting scores of the CONSORT PRO Extension (the final kappa coefficient was 0.95, 95% CI 0.882 to 1.018). Reporting scores ranged from 2.7% to 97.6% across the different items in the CONSORT PRO Extension, and 11 items (P1b, P2b, 4a, P6a1, P6a2, 7a, P12a, 17a, 18, P20/21, 22) had the sufficient reporting score of less than 50%. English publications have higher sufficiently reporting scores than Chinese publications (50.4% to 28.0%, online supplemental appendix 5 table 2). Registered studies significantly outperform than unregistered studies (50.4% to 30.8%, online supplemental appendix 5 table 3). Additionally, studies that reported A-AEs achieved higher reporting sufficient scores than those that did not report A-AEs (44.1% to 31.8%, online supplemental appendix 5 table 4).

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Table 3 General characteristics of A-AEs

Items	Details	No. (%) (n=476)
A-AEs assessment	Reported	164 (34.5)
	No A-AEs occurred	108 (22.7)
	Unreported	204 (42.9)
A-AEs acquisition	Reported by researchers	37 (7.8)
	Reported by patients	24 (5.0)
	Reported by researchers and patients	13 (2.7)
	Unreported	402 (84.5)
A-AEs occurrence	Immediately after acupuncture	26 (5.5)
	Unreported	450 (94.5)
A-AEs severity	AEs	97 (20.4)
	SAEs	0 (0)
	Undistinguished AEs	67 (14.1)
	Unreported	312 (65.6)
A-AEs treatment	No treatment required	38 (8.0)
	Described specific treatment details	48 (10.1)
	Unreported	390 (81.9)
A-AEs recovery	Recovered	91 (19.1)
	Recovered after treatment	3 (0.6)
	Irreversible injury	0 (0)
	Unreported	382 (80.3)
Participant withdrawal due to A-AEs	Reported	59 (12.4)
	Unreported	417 (87.6)
Safety outcome assessment in registry/protocol	Mentioned	30 (6.3)
	Unmentioned	446 (93.7)
Safety outcomes between-group analyses	Between-group analysis performed	157 (33.0)
	Between-group analysis not performed	119 (25.0)
Claim acupuncture is safe (for studies omitted safety outcomes)	Reported acupuncture is a safety therapy	41 (8.6)
	Not mentioned	163 (34.2)

A-AEs, acupuncture-related adverse events; AEs, adverse events; SAEs, serious adverse events.

General characteristics of A-AEs

Table 3 presents the characteristics of A-AEs (the final kappa coefficient was 0.962, 95% CI 0.887 to 1.036). 204 studies (42.9%) omitted safety outcomes, but among them 41 (8.6%) studies still claimed that acupuncture was safe. 164 studies reported details of A-AEs (34.5%) and 108 studies (22.7%) reported there were no AEs during intervention. However, among studies reported A-AEs, only 157 studies (33.0%) did between-group analyses.

The reporting of A-AEs is incomplete, 402 studies (84.5%) did not report who reported A-AEs, 450 (94.5%) did not report the time of occurrence of A-AEs, 312 (65.6%) did not differentiate the severity of A-AEs, 390 (81.9%) did not report the treatment of A-AEs, 382 (80.3%) did not report the recovery of A-AEs and 417 (87.6%) did not report the participant withdrawal due to A-AEs. Only 30 (6.3%) studies mentioned safety assessment in the registry/protocol.

Specific details of A-AEs

Table 4 presents the specific details of A-AEs in acupuncture RCTs. For studies reported A-AEs, no SAEs were reported, and a total of 1277 A-AEs were identified with a prevalence for A-AEs were 0%–76.6%. Tissue injury was the most frequent type of A-AEs in the acupuncture group, followed by tissue irritation and systemic reaction. For A-AEs in the sham acupuncture group, tissue irritation was the most frequent type, followed by tissue injury.

Subgroup meta-analysis based on the type of control group

Table 5 compared the ORs of adverse events between acupuncture and control groups, incorporating 141 studies which detailed reported adverse events. Significant heterogeneity was observed across subgroups (p<0.001). Acupuncture demonstrated a statistically higher odds of adverse events compared with sham acupuncture (OR=1.708, 95% CI 1.451 to 2.011; I^2=0%, p<0.001) and others (usual care, blank and placebo other than sham acupuncture) (OR=4.105, 95% CI 1.840 to 9.157; I^2=63.80%, <0.001). Conversely, no significant differences were observed against other active treatment (OR=0.992) or medicine (OR=0.713), though moderate heterogeneity existed (I^2=21.5%–50.8%).

Confounders that may affect the reporting of AEs

Table 6 presents potential confounders that may affect the reporting of AEs. We found that studies that reported funding, registry information, acupuncturist qualifications and non-significant primary outcomes were associated with a higher rate of reporting of A-AEs, and the difference was statistically significant (p<0.05). The publication language, year, type of study centre, acupuncture type and interest were not statistically significantly related to the reporting of A-AEs (p>0.05).

Discussion

This study investigated the reporting of PROs and A-AEs of 476 eligible acupuncture RCTs. Specifically, the reporting of PROs in acupuncture RCTs was insufficient (average sufficiently reporting score is 38.8%), especially in studies published in Chinese, without registry information. 1277 A-AEs were identified in eligible studies, and no serious A-AEs were reported. However, the reporting of A-AEs was inadequate, 204 studies (42.9%) omitted safety outcomes, 108 reported no AEs during the intervention, and studies that reported A-AEs rarely mentioned the treatment and recovery of A-AEs. The inadequate reporting of PROs and AEs in acupuncture RCTs may not provide sufficient information for acupuncture users to judge the benefits and harms of acupuncture, and it is essential to take approaches to address those problems.

Reporting of PROs in acupuncture RCTs

296 studies (62.2%) used PROs as study outcomes, which was much higher than that in other areas of health (diabetes, oncology and haematology studies),[3 8] indicated that researchers of acupuncture therapy may place greater importance on PROs. However, there are several problems with the reporting of PROs in acupuncture RCTs. First, the findings of PROs in acupuncture RCTs may have limited guidance for acupuncture clinical practice. The reporting of the rationale for selecting PROs and interpretation of PROs are poor, which may indicate that researchers may prefer to use PROs as outcome indicators to make the study appear more comprehensive rather than considering their implications for clinical practice. This may be attributed to the current absence of 'best evidence' guidelines for the use of PROs in clinical practice (heterogeneity between PRO selection, measurement and reporting for the same disease).[30] Second, the PROs reported in the included studies may not exclusively reflect patient perspectives. We found that the included studies did not provide sufficient information to allow us to judge whether the PRO scale was patient-reported. This may be related to the insufficient reporting or the unfamiliarity of

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Table 4 A-AEs in acupuncture group and sham acupuncture group

Items	A-AEs in acupuncture group	A-AEs in sham acupuncture group
Total number of A-AEs	998	279
Organ injury (pneumothorax, cardiac tamponade, etc)		
/	0	0
Tissue injury (bleeding, haematoma, bruise, etc)		
Haematoma	294 (20.0%)	61 (7.9%)
Bleeding	56 (11.3%)	5 (2.7%)
Bruise	108 (9.4%)	9 (4.2%)
Swelling	13	0
Tissue irritation (pain, post-acupuncture discomfort, etc)		
Pain	191 (19.4%)	57 (24.9%)
Post-acupuncture discomfort	66 (4.6%)	26 (4.2%)
Muscle convulsion	11 (1.3%)	
Systemic reactions (needle sickness, headache, etc)		
Needle-sickness	67 (20.8%)	30 (45.0%)
Drowsiness or insomnia	39 (4.6%)	16 (8.5%)
Headache	28 (0.1%)	31
Abdominal discomfort	33 (3.4%)	7 (2.1%)
Allergic reaction	42	9 (0.5%)
Others (tired, palpitation, etc)	3	3 (1.1%)
Infections associated with acupuncture		
Incision infection	2 (0.1%)	
Migration of broken acupuncture needles		
Stagnant or forget needle	3	1
Other complications associated with acupuncture		
Emotional issues	6 (5.3%)	1 (4.8%)
Aggravation of illness	2 (1.0%)	4
Others (hair loss, frequent urination)	8 (2.1%)	1

The above data are based on 141 studies, as 164 studies reported A-AEs, but 13 studies (study id: 3, 100, 110, 155, 254, 263, 328, 329, 340, 352, 385, 421, 453) did not report the specific number of A-AEs, 10 study (study id: 81, 85, 137, 144, 216, 239, 330, 349, 351, 392) did not differentiate A-AEs occurring in the acupuncture group or the control acupuncture group.

A-AEs, acupuncture-related adverse events.

the researchers with data collection methods for PROs. Third, the reporting of PROs in acupuncture RCTs had low compliance with the CONSORT PRO Extension. This may be related to the authors' unawareness of established reporting guidelines and the insufficient recommendations from peer reviewers regarding the use of the CONSORT PRO Extension.

A-AEs of acupuncture RCTs

Although serious acupuncture complications are rare, A-AEs such as pain and bleeding seem to be unavoidable.[16] However, 312 studies (65.5%) did not report any A-AEs during the intervention, which reveals a serious under-reporting of A-AEs in acupuncture RCTs. There are several possible reasons. First, reporting harms is more challenging than reporting benefits of interventions, as it may lead to trouble and discredit.[31] Second, A-AEs in acupuncture RCTs may be unintentionally omitted, as they may not be prospectively defined and monitored (only 30 studies mentioned safety assessment in registry/protocols). Third, several minor A-AEs (pain, blinding, haematoma, etc) may not be entirely identified in acupuncture RCTs, as acupuncturists/researchers consider such events are too trivial to be reported.[32] Fourth, A-AEs may also be confused with symptoms of the condition for which they are

Table 5 Subgroup meta-analysis based on the type of control group

Type of control group	Number of studies	OR (95% CI)	tau^2	I^2 (%)	Q-test p value
Sham acupuncture	58	1.738 (1.467 to 2.060)	0.000	0.00	‹0.001
Medicine	43	0.713 (0.448 to 1.136)	0.803	50.80	0.143
Other active treatment	19	0.992 (0.619 to 1.591)	0.162	21.50	0.972
Others (usual care, blank and placebo other than sham acupuncture)	21	4.105 (1.840 to 9.157)	2.170	63.80	‹ 0.001
Overall	141	1.434 (1.148 to 1.793)	0.767	50.00	0.002

(1) The above data are based on 141 studies; (2) 138 studies reported the number of participants who suffered A-AEs, and we used sample size, 3 studies (studies id: 83, 309, 316) reported the specific events of A-AEs, and we used treatment sessions (used the specific treatment sessions reported in studies if reported or calculated by sample size×intervention counts).

A-AEs, acupuncture-related adverse events.

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Table 6 Confounders that may affect the reporting of acupuncture-related adverse events

Variable	OR (95% CI)	P value
Publication language (Chinese vs English)	1.136 (0.627 to 2.058)	0.672
Publication year	1.043 (0.961 to 1.132)	0.315
Type of study centre (single vs multi)	1.077 (0.663 to 1.757)	0.764
Acupuncture type (conventional vs others)	1.033 (0.762 to 1.403)	0.834
Funding (unreported vs reported)	1.791 (1.107 to 2.914)	0.018*
Interest (unreported vs reported)	1.196 (0.64 to 2.231)	0.572
Registry (unreported vs reported)	1.712 (1.023 to 2.883)	0.041*
Significance of the primary outcomes (significant vs non-significant)	0.599 (0.384 to 0.927)	0.022*
Acupuncturist qualifications (unreported vs reported)	2.107 (1.354 to 3.296)	0.001*
(Intercept)	0 (0 to 1.409)	0.302

Data are based on 272 studies (reported safety outcomes).
*P<0.05.

being treated, leading to unrecognition. Fifth, possibly related to the insufficient reporting of acupuncture RCTs, we found that the reporting of A-AE was associated with studies that provided more study details (funding, registry, and acupuncturist qualifications).

The standardisation of RCT treatment and the short observation period may also contribute to the low A-AEs rate in acupuncture RCTs. First, acupuncture protocols in acupuncture RCTs were simplified and fixed, generally performed by qualified acupuncturists to stimulate fixed acupuncture points with specific depths, durations and techniques. Standardised acupuncture treatment procedures may have reduced A-AEs. Second, acupuncture RCTs may be limited in their ability to identify A-AEs due to the short duration of the intervention and the restricted study population.[33] In addition, only two cases of infection were identified as A-AE in the included studies, which may be due to the use of disposable sterile acupuncture needles and standardised acupuncture treatment procedures of included studies.

The elevated OR for sham acupuncture suggests that adverse events in acupuncture may arise from the physiological effects of needling itself, as sham procedures often mimic real acupuncture. The pronounced risk in usual care, and placebo other than acupuncture could reflect comparisons with less intensive interventions, where acupuncture's inherent risks become more apparent. Notably, the non-significant results for active treatment and medicine subgroups imply comparable safety profiles, possibly due to shared therapeutic mechanisms. Clinically, these results emphasise the importance of contextualising adverse event risks by control type. Future research should prioritise standardised reporting and larger samples for understudied controls like a placebo to refine safety assessments.

Strengths and limitations of the study

The strengths of this study are: (1) there were no limitations of disease types and journals of the included RCTs, allowing for a more comprehensive reflection of the reporting of PRO and A-AEs of acupuncture RCTs. (2) We explored the use and reporting of PROs in acupuncture RCTs and emphasised the ways of PRO data collection, which may be useful to promote the standardised use and reporting of PROs in future acupuncture RCTs. (3) This is the first study to comprehensively summarise A-AEs in acupuncture RCTs, and we provided a specific A-AEs identification from, which may benefit the identification of acupuncture-related AEs in future acupuncture RCTs. We further explored the reporting, management and potential impact of A-AEs in acupuncture RCTs.

The limitations of this study are: (1) A-AEs identification was specified based on previous studies, we may not be able to avoid subjective bias when assessing data. Analysis of A-AEs must be interpreted with caution. (2) We only included studies published in Chinese and English, study findings may not be generalisable to studies published in other languages. (3) We only included two parallel-group study designs and study results may not be generalised to multi-group designs.

Implications for future research

To ensure scientific progress and publication integrity, we recommend the following guidelines:

For the use of PROs in acupuncture RCTs we recommended that (1) emphasise the importance of PROs in clinical research and incorporate PROs into the Core Outcome Sets (COS) for outcome evaluation. COS is 'an agreed minimum collection of outcomes to measure in research studies'.[34] Incorporating the PROs into COS can address the lack of standardisation and comparability in the selection of PROs for studies and avoid selection bias.[30] Additionally, the inclusion of PROs into COS can promote it more responsive to patient interests; (2) researchers should be trained before using PROs in the study design, implementation, analysis and reporting phases to standardise the effective use of PROs and reduce research waste. Specifically, the Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols extension[35] provided the minimum elements required for PRO aspects in clinical trial protocols, the International Society for Quality of Life Research published minimum standards for PRO measures used in patientcentred research,[36] and the Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints Data Consortium provided recommendations on PRO analytical approaches.[37] The Patient Reported Outcomes Tools: Engaging Users and Stakeholders provided specific checklists, tutorials and other training resources for these three documents.[38] Researchers can use this website for training to standardise using PROs in research and clinical practice; (3) editors and peer reviewers strengthen the recommendation for using CONSORT PRO Extension to promote standardised reporting of PROs.

Acupuncture treatment is a therapy in which the patient has a strong subjective experience, thus, it is important to prospectively collect A-AEs to provide acupuncture users with a complete synthesis of evidence on the benefits and harms of acupuncture. We recommended that (1) in the study design, investigators should predefine A-AEs and develop a detailed monitoring scheme, with enrolment of the safety assessment protocol in the registry; (2) in the study implementation stage, A-AEs should be accurately identified and recorded; (3) in the study reporting, researchers are able to provide better reporting of A-AEs in acupuncture RCTs by adhering to reporting guidelines such as the CONSORT Harms 2022 statement.[33] (4) Both patient-reported A-AEs and investigator-reported A-AEs should be included. Studies have found that patient-reported adverse reactions were three times more than investigator-reported adverse reactions in acupuncture RCTs.[39] The combination of patient-reported and investigator-reported

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A-AEs systems allows for proper, comprehensive feedback on A-AEs and promotes the development of patient-centred treatments. Furthermore, clinical evidence has found that A-AEs can be prevented to some extent (eg, control the intensity and depth of the needle, avoid acupuncture when patients are hungry and tired),[14] and researchers should be aware of this prevention to protect patients.

Conclusion

This study found that PROs and A-AEs are insufficiently reported in acupuncture RCTs, particularly the rationale for PRO selection, the interpretation of PROs, and the identification and reporting of A-AEs. Our findings support the need to improve the reporting of acupuncture RCTs to provide patients with sufficient information on the benefits and harms of acupuncture treatments and make treatment choices more consistent with patient preferences.

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Contributors YDu and LY conceptualised and supervised the study, and are the guarantors of the study. ZX and PZ developed the search strategies and made the assessment standards. PZ, SL, SW, YDe, ZX, YW and YC screened, extracted and analysed data. YDu and PZ drafted the manuscript, and LY revised the manuscript. SL, SW, ZX, LS and FJ provided critical comments and substantially improved the quality of the manuscript. All authors provided detailed comments on earlier drafts and approved the final manuscript. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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