

## Efficacy and safety of acupuncture in children: an overview of systematic reviews

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In recent years, acupuncture has increasingly being integrated into pediatric health care. It was used on ~150,000 children (0.2%). We aim to update the evidence for the efficacy and safety of acupuncture for children and evaluate the methodological qualities of these studies to improve future research in this area. We included 24 systematic reviews, comprising 142 randomized controlled trials (RCTs) with 12,787 participants. Only 25% (6/24) reviews were considered to be high quality (10.00±0.63). High-quality systematic reviews and Cochrane systematic reviews tend to yield neutral or negative results ( $P=0.052$ , 0.009 respectively). The efficacy of acupuncture for five diseases (Cerebral Palsy (CP), nocturnal enuresis, tic disorders, amblyopia, and pain reduction) is promising. It was unclear for hypoxic ischemic encephalopathy, attention deficit hyperactivity disorder, mumps, autism spectrum disorder (ASD), asthma, nausea/vomiting, and myopia. Acupuncture is not effective for epilepsy. Only six reviews reported adverse events (AEs) and no fatal side effects were reported. The efficacy of acupuncture for some diseases is promising and there have been no fatal side effects reported. Further high-quality studies are justified, with five diseases in particular as research priorities.

**A**cupuncture is one of the most popular forms of Traditional Chinese Medicine. It has been used to treat various diseases and relieve symptoms for more than 2,500 y and is growing in prominence in many parts of the world. Data from the United States suggests that the number of adults who used acupuncture increased from 2 million to 3 million between 2002 and 2007, and it was estimated that 4% of the United States population and 12% of the Canadian population had used acupuncture at any time in their lives (1–3). Acupuncture is used for a variety of conditions including stroke (4), anxiety and depression (5), irritable bowel syndrome (6), and pain (7).

In recent years, acupuncture has increasingly being integrated into pediatric health care. It was used on ~150,000 children (0.2%) and provided as a part of services in one-third of pediatric pain centers in the United States (7,8). Acupuncture in children has been widely used for asthma,

autism spectrum disorder (ASD), cerebral palsy, and complications of cancer (9–12).

Although the actual mechanisms of acupuncture are still unknown, Traditional Chinese acupuncture theory believes that health is achieved by maintaining an uninterrupted flow of Qi. Qi flows through a network of 14 channels, called “meridians”, which run along the surface of the human body. There are nearly 400 acupuncture points (acupoints) on the body surface, which linked through the 14 meridians to various organs or viscera (13). By stimulating various meridian points, acupuncture is thought to correct the imbalance of energy in the body and restore natural internal homeostasis (10,14–16).

Apart from traditional needle acupuncture, a wide variety of acupuncture types have been developed including acupressure (the application of pressure to acupoints with nonpenetrating needles or bands), moxibustion (a technique in which the Chinese herb mugwort or *Artemisia vulgaris* is burned to apply heat to an acupoint), laser acupuncture (the stimulation of traditional acupoints with low-intensity, nonthermal laser irradiation), electroacupuncture (acupuncture needles inserted at acupoints and then stimulated by a device that generates electric pulses), and auricular acupuncture (targets acupoints on the outer ear using manual stimulation or electroacupuncture) (17–19).

Hunt's study included six systematic reviews of acupuncture for children's conditions, with the search strategy updated in 2009 (20). Another review published in 2008 also evaluated the safety and efficacy of acupuncture for children, but again only included six systematic reviews (21). Although acupuncture originated from China and there are many studies published in China, neither of these reviews included systematic reviews published in China and so may have missed some important information. Recently, several systematic reviews and meta-analysis of acupuncture for different types of childhood diseases have been performed and the results were controversial. Therefore, we aim to update the evidence for the efficacy and safety of acupuncture for children and evaluate the methodological qualities of these studies to improve future research in this area.

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## RESULTS

## Results of the Search

Our searches initially identified a total of 828 potentially relevant articles. After the removal of duplicates, screening of titles and abstracts, and reading full texts, 24 systematic reviews were included in this overview (Figure 1). Of them, 18 reviews were published in English and the remaining were Chinese.

## The Characteristics of Included Studies

The overview included 24 systematic reviews, comprising 142 randomized controlled trials (RCTs) (median four RCTs) and 12,787 participants (median 279 participants) (Table 1). Eight of the 24 included reviews (33%) were Cochrane systematic reviews. The first authors originated from China ( $n = 16$ ), United States America ( $n = 2$ ), United Kingdom ( $n = 2$ ), Australia ( $n = 2$ ), Korea ( $n = 1$ ), and Austria ( $n = 1$ ).

The categories of disease included the nervous system ( $n = 13$ , four studies for cerebral palsy, three studies for nocturnal enuresis, two studies for ASD, one study for tic disorders, one study for hypoxic-ischemic encephalopathy, one study for attention deficit hyperactivity disorder, one study for epilepsy); the digestive system ( $n = 4$ , four for nausea/vomiting); the respiratory system ( $n = 3$ , three for asthma); and other disorders ( $n = 4$ , one for mumps, one for myopia, one for infantile colic and pain reduction, one for amblyopia).

## Quality Assessment

Only six out of the 24 reviews (25%) were considered to be high quality ( $10.00 \pm 0.63$ ), 17 out of 24 (72.8%) were medium quality ( $6.12 \pm 0.86$ ), and one review was low quality (AMSTAR score of 4). The average quality of Cochrane systematic reviews ( $n = 8$ ,  $9.13 \pm 1.73$ ) was significantly better than that of non-Cochrane systematic reviews ( $n = 16$ ,  $5.94 \pm 1.00$ ) ( $P = 0.000$ ). Compared with medium or low-quality systematic reviews, high-quality systematic reviews tended to yield significantly more neutral or negative results ( $P = 0.052$ ). Cochrane systematic reviews

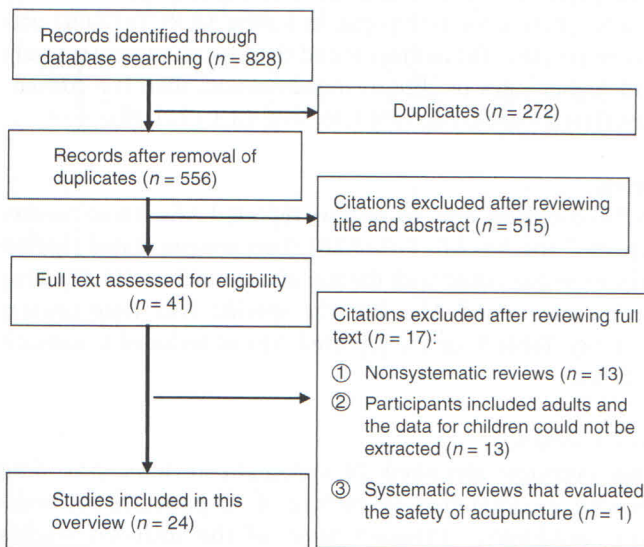


Figure 1. Flow chart of literature screening and selection process.

yielded significantly more neutral or negative results than non-Cochrane systematic reviews ( $P = 0.009$ ) (Table 2).

Eight out of the 24 systematic reviews (33.3%) did not register the study protocol before conducting the review. Eighteen out of 24 (75%) did not provide a list of the characteristics of included and excluded studies, with the six exceptions all being Cochrane reviews. Only nine out of 24 reviews (37.5%) conducted an assessment of publication bias. The status of publication (i.e., gray literature) was used as an inclusion criterion in 20.8% of reviews (5/24) stated and 54.2% of reviews (13/24) clearly acknowledged the potential sources of support (Table 3).

Non-Cochrane systematic reviews had the following issues: (i) no design protocol; (ii) did not consider publication status; (iii) did not provide a list of included and excluded studies; (iv) no assessment of the publication bias; (v) did not report conflicts of interest (Table 4).

## Efficacy and Safety Analysis

## Nervous System

**Cerebral palsy.** Our searches identified four non-Cochrane systematic reviews of cerebral palsy in children, comprising 47 RCTs (4,345 participants). All four reviews compared the efficacy of acupuncture plus conventional treatment with conventional treatment alone (i.e., rehabilitation therapy, drug treatment). The authors all conducted meta-analysis and concluded that acupuncture used as an adjunct to conventional treatment was beneficial for children with cerebral palsy, but further high-quality trials are warranted. Two reviews used the Activities of Daily Living (ADL) scale as an outcome measurement. Zhang *et al.* (11) found that acupuncture improved ADL in children with cerebral palsy (MD 6.38, 95% CI 5.15–7.61), but the heterogeneity was high ( $I^2 = 76.7\%$ ). Liao *et al.* (22) also reported improved ADL scores after acupuncture treatment of 3–4 mo (SMD 1.28, 95% CI 1.00–1.56). Another two reviews used rates of clinical improvements as an outcome measurement; both reviews found acupuncture to be associated with significantly greater improvements than the control group (RR 1.22, 95% CI 1.11–1.34, OR 3.19, 95% CI 2.31–4.38) (23,24).

**Nocturnal enuresis.** One Cochrane systematic review and two non-Cochrane systematic reviews comprising 18 RCTs (1,828 participants) focused on nocturnal enuresis, with two of these performing meta-analysis. One review meta-analyzed three RCTs and found a significant difference in the rate of self-defined clinical improvements after treatment of 10–30 d of acupuncture plus Traditional Chinese Medicine compared with Traditional Chinese Medicine alone (OR 5.75, 95% CI 1.88–17.54) (25). Another review showed that acupuncture was associated with significantly greater improvement in the reduction of the number of wet nights (OR 3.98, 95% CI 2.2–7.2) (26). Because the outcome measurements and interventions were different in included studies, the Cochrane review did not conduct meta-analysis and concluded that there was weak evidence to support the use of acupuncture for nocturnal enuresis (27).

**Autism spectrum disorder.** One Cochrane review and one non-Cochrane review assessed the efficacy of acupuncture for ASD, comprising 21 RCTs (888 participants). The Cochrane review showed no difference in primary outcome measurement of core autistic features Ritvo-Freeman Real Life Rating Scale total score between needle acupuncture and sham acupuncture (MD 0.09, 95% CI -0.03-0.21) (10). The non-Cochrane review did not conduct meta-analysis because of statistical and clinical heterogeneity, and concluded that the efficacy of acupuncture for ASD symptoms was mixed (28).

**Tic disorders.** One non-Cochrane review evaluated the efficacy of acupuncture for tic disorders, comprising five RCTs (434 participants) (29). The authors meta-analyzed four RCTs and found a significant difference in the rates of clinical improvements between acupuncture and medication (OR 3.39, 95% CI 1.73-6.65).

**Others.** Three Cochrane reviews focused on the efficacy of acupuncture for hypoxic-ischemic encephalopathy, attention deficit hyperactivity disorder, and epilepsy respectively, but there were no studies included in two reviews (30,31). Therefore, current evidence did not support acupuncture for treating hypoxic-ischemic encephalopathy and attention deficit hyperactivity disorder. Another review evaluating the efficacy of acupuncture for epilepsy, comprising four RCTs (293 participants), also concluded that the current evidence does not support acupuncture for treating epilepsy (32).

#### Digestive System

**Nausea/vomiting.** Four non-Cochrane reviews examined the efficacy of acupuncture for nausea and/or vomiting, comprising 20 RCTs (1,552 participants). One review determined the efficacy of acustimulation for postoperative nausea and vomiting in children by meta-analyzing 12 RCTs (33). The authors used 24-h postoperative nausea and vomiting as an outcome measurement and found that all acustimulation modalities reduced vomiting (RR 0.69, 95% CI 0.59-0.80) in 12 trials and reduced nausea (RR 0.59, 95% CI 0.46-0.76) in two trials compared with the control groups.

The second review examined acupuncture effects on prophylaxis of postoperative vomiting in children undergoing tonsillectomy (34). The authors meta-analyzed three RCTs and compared acupuncture plus conventional treatment with conventional treatment alone, and found no significant difference in the number of patients stopping vomiting (OR 0.83, 95% CI 0.45-1.4) (34).

The third review assessed the effects of acupuncture for nausea/vomiting but did not conduct meta-analysis (12). The authors concluded that there was a significant reduction in the need for antiemetics between the treatment group plus acupuncture and the treatment group alone, but there was no significant difference in reported nausea scores (12).

The fourth review examined the efficacy of acupuncture for preventing postoperative nausea and vomiting (35). We extracted the data for children, comprising four RCTs (249

participants). The authors did not perform meta-analysis and concluded that there was no significant benefit from acupuncture compared with placebo or conventional anti-emetics. Therefore, no sufficient evidence showed the effectiveness of acupuncture for nausea/vomiting in children.

#### Respiratory System

**Asthma.** One Cochrane review (36) and two non-Cochrane reviews (9,17) assessed the efficacy of acupuncture for asthma comprising six RCTs (275 participants) with no meta-analysis performed. The authors concluded that no robust evidence exists to support acupuncture as being effective for treating childhood asthma.

#### Others

**Pain.** One non-Cochrane review assessed the safety and efficacy of acupuncture in term and preterm infants and included four RCTs comprising 140 neonates (37). Neonates given acupuncture during heel prick showed significantly shorter crying duration (OR -65.30, 95% CI -101.60 to -29.00) and lower neonatal infant pain scale scores (OR -2.00, 95% CI -3.28 to -0.72) (37).

**Mumps.** One Cochrane review examined the efficacy of acupuncture for mumps and included only one RCT comprising 239 participants. The authors found that the acupuncture group had a higher recovery rate than the control group (RR 1.88, 95% CI 1.53-2.30), but took a longer time to recover (MD 0.42, 95% CI 0.31-0.53) (38).

**Myopia.** One Cochrane review assessed acupuncture for myopia and included two RCTs (131 participants) (39). The authors did not perform a meta-analysis and no conclusions can be drawn about the benefit of coacupressure for slowing the progress of myopia in children.

**Amblyopia.** One non-Cochrane review examined the efficacy of acupuncture for amblyopia, including 14 RCTs (2,662 participants) (40). The authors found that the acupuncture group had higher rates of clinical improvements than the conventional treatment group (RR 1.16, 95% CI 1.12-1.19).

#### Safety

In this overview, only six reviews reported AEs. Three reviews reported specific AEs (10,25,28). Two reviews stated that no AEs were associated with the use of acupuncture (11,17). One review mentioned AEs, but the specific AEs were unclear (27). See **Table 5** for the reported AEs of included systematic reviews.

#### DISCUSSION

This overview identified 24 systematic reviews, providing us with a comprehensive picture of acupuncture for pediatric conditions. Although most of the included studies could not draw firm conclusions because of the small size of the included trials or their low methodological quality,

**Table 1.** General characteristics of included studies

Reference	Country	Indication	Age (No. participants)	No. RCTs	Results	Overall conclusion (quote)	Comments	Quality
Zhang (11)	China	CP	3 mo to 16.8 y (n = 617)	Systematic review (n = 9) <sup>a</sup>	Acupuncture + CT vs. CT; ADL scale (two RCTs): MD 6.38, 95% CI 5.15–7.61, <i>P</i> = 76.7% Tongue acupuncture vs. sham tongue acupuncture; GMFM (one RCT): MD 1.86, 95% CI 0.07–3.66 Scalp acupuncture vs. PT+OT; ADL scale (one RCT): MD –0.18, 95% CI –0.69 to –0.32 Acupuncture vs. PT+OT; ADL scale (one RCT): MD –0.36, 95% CI –0.76 to –0.03	Acupuncture combined with CT may be beneficial in children with CP.	Due to the low methodological quality of studies, further high quality trials are warranted.	Moderate (7 scores)
Liao (22)	China	CP	<18 y (n = 570)	Systematic review (n = 8)	Acupuncture + CT vs. CT; WeeFIM (three RCTs): OR 3.61, 95% CI 1.78–7.34; Ashworth of Muscle spasm (three RCTs): WMD –0.67, 95% CI –1.05 to –0.30; ADL scale (three RCTs): SMD 1.28, 95% CI 1.00–1.56	Acupuncture is effective for CP	All included studies were published in chinese. EMBASE database was not searched	Moderate (5 scores)
Wang (23)	China	CP	<12 y (n = 2,087)	Systematic review (n = 18)	Acupuncture + rehabilitation therapy vs. rehabilitation therapy rates of clinical improvements (three RCTs): RR 1.22, 95% CI 1.11–1.34; handicapped children synthesis function measure in third month (two RCTs): RR 1.51, 95% CI 1.13–2.01; GMFM (one RCT): MD 4.94, 95% CI –2.60 to –12.48; GDS (one RCT): WMD 8.80, 95% CI 3.53–14.07	Acupuncture combined with rehabilitation is superior to rehabilitation therapy	All included RCTs were open control. Further high quality trials are warranted.	Moderate (6 scores)
Zhu (24)	China	CP	<18 y (n = 1,071)	Systematic review (n = 12)	Acupuncture + CT vs. CT or drug treatment rates of clinical improvements (12 RCTs): OR 3.19, 95% CI 2.31–4.38	The effect of acupuncture and CT are better than simple rehabilitation or medication	The authors only searched chinese database	Moderate (5 scores)
Wei (25)	China	Nocturnal enuresis	<18 y (n = 230)	Systematic review (n = 3) <sup>a</sup>	Acupuncture + TCM vs. TCM rates of clinical improvements (three RCTs): OR 5.75, 95% CI 1.88–17.54	TCM combined with acupuncture were effective for nocturnal enuresis	Only four Chinese databases were searched, publication bias may exist.	Moderate (5 scores)
Bower (26)	China	Nocturnal Enuresis	<18 y (n = 1,274)	Systematic review (n = 11)	Acupuncture + other therapy vs. other therapy reduction of the number of wet nights (three RCTs): OR 3.98, 95% CI 2.20–7.20; Laser acupuncture vs. antidiuretic medication reduction of the number of wet nights (1 RCT): OR 0.62, 95% CI 0.16–2.43	It provides tentative evidence for the efficacy of acupuncture for childhood nocturnal enuresis.	Due to the low methodological quality of studies; further high-quality trials are warranted	Moderate (6 scores)
Huang (27)	China	Nocturnal enuresis	>5 y (n = 324)	Cochrane review (n = 4) <sup>a</sup>	Laser acupuncture vs. desmopressin not cured (one RCT): RR 1.50, 95% CI 0.50–4.52; failure or relapse (one RCT): RR 1.40, 95% CI 0.53–3.68; Heat-producing needling vs. impiramine; not cured (one RCT): RR 0.76, 95% CI 0.47–1.24; not improved (1 RCT): RR 0.37, 95% CI 0.13–1.05; Acupuncture vs. sham acupuncture failure or relapse (one RCT): RR 0.67, 95% CI 0.48–0.94; Warm acupuncture vs. drugs (medlofenoxate, oryzanol, thiamine) failure or relapse (one RCT): RR 0.31, 95% CI 0.21–0.45	There was weak evidence to support the use of acupuncture for nocturnal enuresis.	Methodological quality of included studies was low.	Good (10 scores)
Cheuk (10)	China	ASD	3–18 y (n = 390)	Cochrane review (n = 10)	Needle acupuncture vs. sham acupuncture; RFLRS score (two RCTs): MD 0.09, 95% CI –0.03–0.21; Needle acupuncture + CT vs. CT; ABC (one RCT): RR 1.53, 95% CI 1.09–2.16; post-treatment total scores (one RCT): MD –5.53, 95% CI –10.76 to –0.31; ATEC (two RCTs): MD 6.28, 95% CI –1.05 to 13.61	Current evidence does not support the use of acupuncture for ASD.	The methodological quality of included trials was variable and six of the trials were at high risk.	Good (10 scores)
Lee (28)	Korea	ASD	2.1–14 y (n = 498)	Systematic review (n = 11)	Qualitative description only	The results provide mixed evidence of acupuncture's effectiveness for ASD symptoms	Total sample sizes and methodological quality of included studies were low	Moderate (7 scores)
Xiao (29)	China	Tic disorders	2.5–16 y (n = 434)	Systematic review (n = 5) <sup>a</sup>	Acupuncture vs. medication rates of clinical improvements (four RCTs): OR 3.39, 95% CI 1.73–6.65; YGTSS (one RCT): OR 3.18, 95% CI 1.00–10.07	Acupuncture had a better effect than the routine western drug group on improving clinical symptoms of tics. But the YGTSS evaluation showed no obvious therapeutic advantages.	The sample of included studies was small and the quality was not good.	Moderate (6 scores)
Wong (30)	China	HIE	Neonates (n = 0)	Cochrane review (n = 0)	Qualitative description only	The efficacy of acupuncture for HIE is unclear	No RCT was included	Moderate (6 scores)

Table 1. Continued on next page

**Table 1.** Continued

Reference	Country	Indication	Age (No. participants)	No. RCTs	Results	Overall conclusion (quote)	Comments	Quality
Li (31)	China	ADHD	<18 y (n=0)	Cochrane review (n=0)	Qualitative description only	The efficacy of acupuncture for ADHD is unclear	No RCT was included	Moderate (7 scores)
Cheuk (32)	China	Epilepsy	1-17 y (n=293)	Cochrane review (n=4) <sup>a</sup>	Needle acupuncture plus Chinese herbs vs. Chinese herbs alone; 50% or greater reduction in seizure frequency (two RCTs): RR 1.13, 95% CI 0.97-1.31; 75% or greater reduction in seizure frequency (two RCTs): RR 1.52, 95% CI 1.12-2.05; 25% or greater reduction in seizure frequency (two RCTs): RR 1.02, 95% CI 0.93-1.11; 75% or greater reduction in seizure duration (two RCTs): RR 1.90, 95% CI 0.97-3.74; 50% or greater reduction in seizure duration (two RCTs): RR 1.29, 95% CI 1.03-1.62	The current evidence does not support acupuncture for treating epilepsy. Comparability of groups at baseline was uncertain and the quality of included studies was poor	Good (11 scores)	
Rheingans (12)	USA	Nausea/vomiting	<18 y (n=11)	Systematic review (n=1) <sup>a</sup>	Qualitative description only	Added acupuncture can reduce need for antiemetics for cancer patients. There was no significant difference in reported nausea scores	Attrition rate is 45%.	Poor (4 scores)
Dune (33)	USA	Postoperative nausea and vomiting	1-18 y (n=1,027)	Systematic review (n=12)	Acustimulations vs. control group: The vomiting proportion (12 RCTs): RR 0.69, 95% CI 0.59-0.80; The nausea proportion (2 RCTs): RR 0.59, 95% CI 0.46-0.76; Acupressure vs. control group: The vomiting proportion (3 RCTs): RR 0.69, 95% CI 0.55-0.87; Acupuncture vs. control group: The vomiting proportion (6 RCTs): RR 0.42, 95% CI 0.29-0.67; ETS vs. control group: The vomiting proportion (2 RCTs): RR 0.81, 95% CI 0.62-1.01	Acupressure and acupuncture are effective to reduce postoperative vomiting, acupuncture had the greatest impact on reducing vomiting compared with acupressure and ETS	The control groups of included studies were mixed	Moderate (7 scores)
Bolton (34)	Australia	Postoperative vomiting	2-18 y (n=265)	Systematic review (n=3) <sup>a</sup>	Acupuncture + CT vs. CT the number of patients stopping vomiting: (3 RCTs): OR 0.83, 95% CI 0.45-1.40	There is currently insufficient evidence to suggest that acupuncture are clinically useful for prophylaxis of postoperative vomiting in children undergoing tonsillectomy	The quality of included RCTs was poor	Moderate (7 scores)
Lee (35)	Australia	Prevent postoperative nausea and vomiting	<18 y (n=249)	Systematic review (n=4) <sup>a</sup>	Qualitative description only	No significant benefit compared to placebo or conventional antiemetics	Three studies of good methodological quality although fourth was not placebo-controlled	Moderate (5 scores)
Martin (9)	UK	Asthma	8-13.5 y (n=35)	Systematic review (n=2) <sup>a</sup>	Qualitative description only	Evidence did not support the effect of acupuncture in reducing asthma.	Publication bias may exist in the included study.	Moderate (5 scores)
Zhang (17)	China	Asthma	7-17 y (n=176)	Systematic review (n=3)	Qualitative description only	No compelling evidence exists to suggest that laser acupuncture is not effective for childhood asthma	The quality of included RCTs was low.	Moderate (7 scores)
McCarney (36)	UK	Chronic asthma	5-17 y (n=64)	Cochrane review; (n=1) <sup>a</sup>	Qualitative description only	There is not enough evidence to make recommendations about the value of acupuncture in asthma treatment.	Only one RCT for children was included and the quality was poor.	Good (9 scores)
Raith (37)	Austria	Infantile colic (three RCTs)	Preterm and term infants. (n=140)	Systematic review (n=4)	Acupuncture+ breast milk vs. breast milk; crying time for heel prick procedure (1 RCT): OR -65.30, 95% CI -101.60 to -29.00; neonatal infant pain scale score (1 RCT): OR -2.00, 95% CI -3.28 to -0.72	Acupuncture is safe for pain reduction in term and preterm infants and a option to treat infantile colic.	Studies evaluating short- and long-term effects are urgently needed.	Moderate (7 scores)
He (38)	China	Mumps	3-12 y (n=239)	Cochrane review (n=1)	Acupuncture+moxibustion vs. medication recovery rate (1 RCT): RR 1.88, 95% CI 1.53-2.30; Time to cure (1 RCT): MD 0.42, 95% CI 0.31-0.53	Could not reach confident conclusions about the efficacy and safety of acupuncture	Only one RCT was included	Good (10 scores)
Wei (39)	China	Myopia	6-15 y (n=131)	Cochrane review; (n=2)	Qualitative description only	No conclusions can be drawn for the benefit of co-acupressure for slowing progress of myopia	Two RCTs were included	Moderate (10 scores)
Hu (40)	China	Amblyopia	<18 y (n=2,662)	Systematic review (n=14)	Acupuncture-moxibustion vs. CT rates of clinical improvements (14 RCTs): RR 1.16, 95% CI 1.12-1.19	Total rates of clinical efficacy of Acupuncture-moxibustion for amblyopia is superior to that of clinical routine treatment	Publication bias may exist in the included study and the quality was not good.	Moderate (6 scores)

ABC: autism behavior checklist; ADL: activities of daily living; ADHD: attention deficit hyperactivity disorder; ASD: autism spectrum disorders; ATEC: autism treatment evaluation checklist; CT: conventional treatment; CP: cerebral palsy; ETS: electrical stimulation; GDS: Gesell development schedules; GMFM: gross motor function measure; HLE: hypoxic-ischemic encephalopathy; OT: occupational therapy; PT: physical therapy; RCT: randomized controlled trial; RFLRS: Ritvo-Freeman Real-Life Rating Scale; TCM: traditional Chinese medicine; WeeFIM: The Functional Independence Measure; YGTSS: Yale Global Tic Severity Scale.

<sup>a</sup>Data were extracted from studies contained the data of adults and children or used traditional Chinese medicine containing acupuncture as interventions.

the efficacy of acupuncture for some pediatric conditions is promising, such as for cerebral palsy, nocturnal enuresis, tic disorders, amblyopia, and pain reduction. However, the efficacy of acupuncture for hypoxic-ischemic encephalopathy, attention deficit hyperactivity disorder, mumps, and myopia is unclear and the efficacy for ASD, asthma, and nausea/vomiting is controversial. Current evidence does not support the use of acupuncture for pediatric epilepsy. In this overview, we found that acupuncture was well tolerated and no fatal side effects were reported.

In general, the quality of systematic reviews was poor, and only one fifth of reviews were considered to be high quality. The quality of Cochrane systematic reviews was better than that of non-Cochrane systematic reviews. Most systematic reviews did not register the study protocol before conducting the review and did not provide a list of the characteristics of included and excluded studies, with the only exceptions being Cochrane reviews. Only nine out of 24 reviews (37.5%) of reviews conducted an assessment of publication bias, so we could not judge whether publication bias existed. The status of publication (i.e., gray literature) was used as an inclusion criterion was found in 20.8% of reviews, so the selecting bias may exist. The potential source of support of the systematic review was clearly acknowledged in 54% of reviews.

We also found that Cochrane systematic reviews tended to yield less positive results than non-Cochrane systematic reviews, and high-quality systematic reviews tended to yield neutral or negative results. So the poor quality of the systematic reviews makes analysis of the efficacy of acupuncture for children complex.

**Table 2.** The association between different systematic reviews and conclusions

Items	Neutral or negative results	Positive results	P
High-quality systematic reviews	6	0	0.052
Medium or low-quality systematic reviews	9	9	
Cochrane systematic reviews	8	0	0.009
Noncochrane systematic reviews	7	9	

**Table 3.** The quality assessment of included systematic reviews

AMSTAR question	Yes (n (%))	Partial or can't tell (n (%))	No (n (%))
1. Was an "a priori" design provided?	8 (33.3%)	0	16 (66.7%)
2. Was there duplicate study selection and data extraction?	19 (79.2%)	5 (20.8%)	0
3. Was a comprehensive literature search performed?	18 (75%)	0	6 (25%)
4. Was the status of publication (i.e., gray literature) used as an inclusion criterion?	5 (20.8%)	0	19 (79.2%)
5. Was a list of studies (included and excluded) provided?	6 (25%)	18 (75%)	0
6. Were the characteristics of the included studies provided?	22 (91.7%)	2 (8.3%)	0
7. Was the scientific quality of the included studies assessed and documented?	24 (100%)	0	0
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	24 (100%)	0	0
9. Were the methods used to combine the findings of studies appropriate?	21 (87.5%)	3 (12.5%)	0
10. Was the likelihood of publication bias assessed?	9 (37.5%)	2 (8.3%)	13 (54.2%)
11. Was the conflict of interest stated?	13 (54.2%)	0	11 (45.8%)

**Table 4.** The subgroup analysis of quality assessment according to type of systematic review

AMSTAR question	Cochrane systematic reviews			Non-cochrane systematic reviews			P value
	Yes	Unclear	No	Yes	Unclear	No	
1. Was an "a priori" design provided?	8	0	0	0	0	16	0.000
2. Was there duplicate study selection and data extraction?	8	0	0	11	5	0	0.130
3. Was a comprehensive literature search performed?	8	0	0	10	0	6	0.066
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	5	0	3	0	0	16	0.001
5. Was a list of studies (included and excluded) provided?	6	2	0	0	16	0	0.000
6. Were the characteristics of the included studies provided?	6	2	0	16	0	0	0.101
7. Was the scientific quality of the included studies assessed and documented?	8	0	0	16	0	0	—
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	8	0	0	16	0	0	—
9. Were the methods used to combine the findings of studies appropriate?	5	3	0	16	0	0	0.028
10. Was the likelihood of publication bias assessed?	4	2	2	5	0	11	0.041
11. Was the conflict of interest stated?	8	0	0	5	0	11	0.002

**Table 5.** The reported AEs in included studies

References	The type of ADR ( <i>n</i> = frequency)	Relevance between AEs and acupuncture
Lee (28)	27.3% (3/11) of included studies mentioned AEs. One RCT reported no adverse events, while two RCTs reported minor side effects (minor superficial bleeding crying, irritability during treatment, worsening hyperactivity and ritualistic behavior), the frequency of AEs was unclear	Unclear
Cheuk (10)	Worsening of sleeping pattern ( <i>n</i> = 1), superficial bleeding, crying due to fear or pain, irritability, worsening of hyperactivity and ritualistic behavior, the frequency of other AEs was unclear.	Unclear
Wei (25)	Painful bi-auricular stimulation ( <i>n</i> = 3), eczema ( <i>n</i> = 2), mild pain, heat or swelling while pressing, the frequency of other AEs was unclear	Unclear
Zhang (11)	Reported AEs, but the specific AEs were unclear	No relevance
Zhang (17)	Reported AEs, but the specific AEs were unclear	No relevance
Huang (27)	One trial report stated that there were no adverse effects and the remainder did not mention them.	Unclear

AE, adverse events; RCT, randomized controlled trials.

As to the safety of acupuncture in children, we found AEs were often ignored or not reported in included reviews. Only six reviews reported the occurrence of AEs, but some important data about the occurrence time, management of AEs, and the definite relationship between AEs and acupuncture was also inadequately reported; future studies should ideally pay more attention to the safety aspect of acupuncture. In general, acupuncture was well tolerated and no fatal side effects were reported, which was in accordance with some reviews evaluating the safety of acupuncture for children. One review included 37 reports and identified a total of 279 AEs, of which 25 AEs were serious, one was moderate, and 253 were mild (incidence 11.8% 95% CI: 10.1–13.5) (3). The authors found that many of the serious AEs might have been caused by substandard practice, and that acupuncture is safe when performed by appropriately trained practitioners. Another review included 22 RCTs involving 1,865 participants and reported that the risk of AEs and serious AEs occurring from acupuncture in pediatrics is estimated to be 1.55/100 and 5.36/10,000 treatments respectively (21).

Some limitations of this overview were identified: (i) A quantitative analysis of included reviews could not be conducted owing to statistical and clinical heterogeneity, (ii) The author(s) of included reviews were not contacted to enable judging of whether their methodological quality was assessed appropriately, (iii) Only reviews published in English or Chinese were included. Searches of non-English databases might have yielded further information, but it might be difficult to access local literature internationally as articles might not be indexed in conventional databases and access to local journals might be restricted. However, the priority for high-quality research is generally to be published in English journals, with Chinese databases also included in this review as acupuncture originated in China and there are many studies published in Chinese, (iv) Only systematic reviews were included, so some individual RCTs evaluating the efficacy of acupuncture may have been missed.

### Conclusion

The efficacy of acupuncture for some diseases is promising and there have been no fatal side effects reported. Further high-quality studies are justified, with five diseases in particular

(cerebral palsy, nocturnal enuresis, tic disorders, amblyopia, and pain reduction) as research priorities.

## METHODS

### Search Strategy

Electronic literature searches were carried out in the Cochrane Library (2014, Issue 7), PubMed (1966–2014.7), EMBASE (1974–2014, Issue 7), Chinese Biomedical Literature Database (CBM, 1978–2014.7), China National Knowledge Infrastructure (1980–2014.7), Chinese Science and Technique Journals Database (VIP, 1989–2014.7), Wanfang Data (<http://www.wanfangdata.com/>) (1990–2014.7), and the relevant reference lists. The search terms were “acupuncture”, “acupressure”, “auricular”, “moxibustion”, “acupoint”, “electric acupuncture”, “meridian”, “systematic review”, “meta-analysis”, “pediatrics”, “infant”, “neonate”, “newborn”, “child” and “adolescent”. The search was restricted to human studies, and the language was restricted to English and Chinese. The search was independently conducted by two investigators and discrepancies were resolved by discussion.

### Study Selection

Systematic reviews and meta-analysis of RCTs or quasi-RCTs evaluating any acupuncture modality (i.e., classical acupuncture, acupressure, moxibustion, scalp acupuncture, body acupuncture, auricular acupuncture, tongue acupuncture, injection acupuncture, electroacupuncture, or any combination of the above) for any type of childhood diseases were included.

We included all reviews including patients under the age of 18 y with any disease regardless of gender, nationality, or outpatient therapy or inpatient therapy.

Reviews were excluded if they: (i) were nonsystematic reviews, (ii) compared the efficacy of different acupuncture therapies, or (iii) included both children and adults and data of children could not be extracted separately.

### Data Extraction

Data were recorded using a standardized data collection form. The data extraction form included: (i) country of the first author, (ii) number of trials included, (iii) indication of included reviews, (iv) patient demographic and clinical data, (v) interventions, (vi) main outcomes and conclusions, and (vii) adverse events (AEs). Data extraction was independently conducted by two investigators and discrepancies were resolved by discussion.

### Assessment of Methodological Quality

Two reviewers independently assessed the methodological quality of all included systematic reviews using The Measurement Tool to Assess Systematic Reviews (AMSTAR). This tool is an 11-item questionnaire requiring assessors to answer “yes”, “no”, “partial or can't tell”. The scores range from 1 to 11. In our review, a score of 9–11 was considered as high quality, score of 5–8 as moderate quality, and

a score of 0–4 as low quality (41). Discrepancies in their evaluations were discussed and agreed upon through consensus.

### Statistical Methods

A quantitative analysis of included systematic reviews was not conducted owing to statistical and clinical heterogeneity. A narrative summary of included studies has been provided instead.

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C.Y. and Z.H. contributed equally to this study. C.Y.: designed the review, collected data, developed the search strategy, undertook searches, appraised the quality of papers, selected trials for inclusion, extracted data from papers. Data management: carried out analysis and interpretation of the data and wrote the review. Z.H.: collected data, undertook searches, appraised the quality of papers; selected trials for inclusion, extracted data from papers. Data management: checked the data and wrote the review. L.Z.: designed the review, collected data, undertook searches, appraised the quality of papers; selected trials for inclusion, extracted data from papers. Data management: checked the data and commented on drafts for previous version. Q.G.: collected data, undertook searches, appraised the quality of papers; selected trials for inclusion, extracted data from papers.

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