

SYSTEMATIC REVIEW

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Nonpharmacological interventions for decreasing anxiety during anesthesia induction in children: a systematic review and Bayesian network meta-analysis

Yuanyuan Li^{1†}, Shanshan Peng^{1†}, Xueqin Xia², Lin Yin³ and Limei Liao^{4*}

Abstract

Background Anxiety during anesthesia induction can lead to various negative outcomes and psychological burdens in children undergoing surgery. Nonpharmacological interventions are available for reducing anxiety in this context. However, due to a lack of evidence from head-to-head randomized controlled trials (RCTs), the specific effects of these methods on children with anxiety during anesthesia induction remain unclear.

Objective This network meta-analysis aimed to evaluate the comparative effects of all known nonpharmacological interventions for reducing anxiety in children during anesthesia induction and to rank these interventions based on their practical applicability.

Design Systematic review and Bayesian network meta-analysis.

Methods We searched PubMed, Embase, CINAHL, Cochrane Library, and Web of Science to identify articles published up to August 2024. Two reviewers independently assessed eligibility of potential studies and extracted data. Outcome measures of the meta-analysis were the anxiety levels of children during anesthesia induction, the anxiety levels of parents, and the child's compliance during anesthesia induction. A consistency model was selected to conduct a network meta-analysis to evaluate the relative effects and rank probabilities of different nonpharmacological interventions.

Results A total of 34 RCTs with 3,040 participants and six intervention methods were included. All trials confirmed the safety of the six intervention methods, with no significant adverse events reported. The network meta-analysis showed that the Passive Distraction Intervention (PDI)-Parental Presence at Induction of Anesthesia (PPIA), Interactive Distraction Intervention (IDI)-PPIA, IDI, PDI, and PPIA interventions were associated with more substantial reductions in anxiety than usual care. However, the studied interventions showed no statistically significant differences for reducing parental anxiety. The PPIA, IDI, and IDI-PPIA interventions also improved compliance during anesthesia induction.

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Conclusions Our study confirmed that some nonpharmacological interventions are effective at reducing anxiety in children and enhancing compliance during anesthesia induction. Therefore, we recommend several interventions for clinical practice, including the PDI-PPIA, IDI-PPIA, PDI, IDI, and PPIA when working with children undergoing anesthesia induction.

Registration We registered this network meta-analysis with PROSPERO (registration no. CRD42022262874).

Clinical trial number Not applicable.

Key messages

What is already known

- During anesthesia induction, higher anxiety levels in children can prolong the induction process and reduce compliance. Furthermore, children experiencing higher anxiety levels are at an increased risk of behavioral issues compared to those with lower anxiety levels during induction.
- Nonpharmacological methods are effective at reducing children's anxiety levels during anesthesia induction.
- Conventional meta-analyses can only provide direct comparative evidence; therefore, it is largely unknown which nonpharmacological interventions are most effective at reducing anxiety in children during anesthesia induction.

What this paper adds

- PDI-PPIA, IDI-PPIA, IDI, PDI, and PPIA showed statistically significant abilities to decrease anxiety during anesthesia induction.
- This review found that PDI-PPIA therapy was the most effective intervention for decreasing anxiety in children during anesthesia induction.

Keywords Nonpharmacological interventions, Children, Anxiety, Anesthesia induction, Bayesian network meta-analysis

Background

Over six million patients under 18 years of age undergo surgery with general anesthesia in America each year [1, 2]. About 50–67% of these youth experience perioperative anxiety [3–7], which typically peaks during anesthesia induction [8]. Children with higher anxiety levels face a 3.5-fold increased risk of behavioral problems during induction than those with lower anxiety levels [9]. Additionally, heightened anxiety during anesthesia induction can lead to prolonged induction times and reduced compliance with the process [10]. Therefore, reducing anxiety in children during anesthesia induction is essential.

Anesthesia induction is the process of transitioning a patient from a conscious to operable state, and it typically takes several minutes [11]. Both nonpharmacological and pharmacological methods can be employed to manage preoperative anxiety [3]. Premedication is an established method for alleviating anxiety in children, and midazolam, a rapid-acting benzodiazepine, is commonly administered. However, this medication is associated with several adverse effects, including opioid interactions, impaired psychomotor performance, paradoxical reactions, disorientation, and excessive sedation [12]. Additionally, routine sedative use before surgery can increase costs by necessitating more bed space and staffing, particularly for short outpatient procedures. Finally, excessive sedation in the post-anesthesia care unit may lead to delayed discharges [13].

Recent randomized controlled trials (RCTs) and meta-analyses have evaluated the effects of various non-pharmacological interventions for reducing perioperative anxiety, including preoperative tours; visiting the operating room before surgery; explaining anesthesia knowledge [14]; parental presence during induction of anesthesia [15–17]; virtual reality (VR); using the internet, smartphones, or tablets; web programs [18–25]; music therapy [26, 27]; clown doctors or clowns [28, 29]; psychological therapy [30]; interventions for parents [31]; and anesthesia mask interventions [10, 32]. However, the relative effects of these methods on children remain unclear due to a lack of evidence from head-to-head RCTs. Most RCTs have been usual-care controlled, and only a few have been head-to-head comparisons of different nonpharmacological interventions [21, 24, 33, 34]. Furthermore, most previous meta-analyses have only combined studies with the same pair of nonpharmacological interventions [35, 36].

The complexity of the various nonpharmacological interventions, along with the lack of head-to-head RCTs, complicates the identification of the most effective strategy for alleviating anxiety in children during anesthesia induction using traditional pairwise meta-analysis methods. However, a network meta-analysis is a method that enables indirect comparisons of all nonpharmacological interventions with common comparators within a single framework. It allows for a quantitative analysis of the results while simultaneously combining and comparing

all direct and indirect evidence [37]. Therefore, to provide evidence for clinical nursing decisions, we conducted this systematic review and Bayesian network meta-analysis of RCTs to compare and rank the efficacy of various non-pharmacological interventions for managing children's anxiety during anesthesia induction.

Theoretical framework

In his work on attention and effort, Kahneman proposed the theory of “capacity limitations,” which posits that attention is a limited cognitive resource used for recognizing and processing stimuli. When engaging in multiple activities simultaneously, these activities compete for this finite amount of attention [38]. However, activities that engage the senses more, will garner more attention. According to the “multiple source theory” proposed by Wickens, multisensory stimulation, such as those having both visual and auditory inputs, can activate more resources and effectively divert attention, allowing children to focus more on the activity at hand rather than on upcoming stressors, such as an impending anesthesia induction or surgery. Based on the capacity limitation and multiple source theories, nonpharmacological interventions can be classified into either interactive or passive distraction interventions based on whether they involve direct interaction by the child. Interactive distraction interventions directly engage children with toys, technological devices, or people to stimulate multiple senses, such as the auditory, visual, tactile, and kinesthetic systems, thereby diverting attention away from the upcoming anesthesia induction. This approach can involve activities like playing video games or using VR. In contrast, passive distraction interventions involve having children focus on one or two of their senses, such as auditory or visual stimuli, without directly interacting with the stimuli in order to shift their attention. Examples include listening to music or watching cartoons. The interventions in the included studies were categorized into the following groups: the Usual Care group, Parental Presence at Induction of Anesthesia (PPIA) group, Passive Distraction Intervention (PDI) group, Interactive Distraction Intervention (IDI) group, Interactive Distraction Intervention with PPIA (IDI-PPIA) group, Passive Distraction Intervention with PPIA (PDI-PPIA) group, and Intervention for Parents (IPG) group.

Objective

A network meta-analysis assessed the comparative effects of all known nonpharmacological interventions for reducing children's anxiety during anesthesia induction and ranked the most effective interventions.

Methods

We conducted this network meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline extension statement for network meta-analyses [39]. We registered this study in PROSPERO (registration no. CRD42022262874).

Literature search strategy

We searched PubMed, Embase, CINAHL, Cochrane Library, and Web of Science for articles published up to August 2024. The search strategy systematically integrated Medical Subject Headings (MeSH) terms, entry terms, and text-words: child OR children, anxiety (anxiety OR anxious* OR anxiet*), anesthesia induction OR induction of anesthesia OR anaesthesia induction OR induction of anaesthesia, intervention (music OR PPIA OR toy* OR tour* OR internet* OR clown* OR virtual reality* OR game* OR cartoon* OR prepar* OR mask* OR parent*), randomized controlled trial (randomized controlled trial OR trial* OR controlled clinical trial* OR random* OR RCT*). The complete search strategies for all databases are provided in Supplementary Document 2. Additionally, we screened reference lists of relevant primary studies to systematically identify and include eligible studies in the review.

Criteria for inclusion

The inclusion criteria for this study were as follows: (1) study population: children (aged < 18 years) requiring surgery under general anesthesia; (2) intervention: non-pharmacological interventions of unlimited forms; (3) control: the control group received usual care or a different nonpharmacological intervention than the experimental group; (4) outcome: the anxiety levels of children during anesthesia induction (from wearing an anesthetic mask to loss of consciousness or starting intravenous anesthetic agents to loss of consciousness). (5) study design: RCTs.

The exclusion criteria were as follows: (1) repeatedly published or unpublished articles; (2) articles from which the main outcome data could not be obtained; and (3) articles that used two types of distraction interventions simultaneously in the experimental group.

Study selection and quality assessment

First, all search records were imported into EndNote 20, and duplicates were removed. Two independent reviewers, Li and Peng, screened the literature for articles that met the inclusion criteria, with any disagreements resolved through consultation with a third researcher, Liao.

The Cochrane Risk of Bias Tool 2 was used to evaluate the risk of bias of all included articles by two reviewers

separately (Li and Peng). The Cochrane Risk of Bias Tool 2 includes five parts: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result [40]. Each part was determined to have a low risk, some concern, or high risk of bias. A low risk of bias for an article was defined as having a low risk for all the items. A high risk of bias for an article was defined as having a high risk for at least one item. Some concern for an article was defined as having a concern related to at least one part. Disagreements were resolved by a third researcher (Liao).

Data extraction

Two reviewers, Li and Peng, created a comprehensive table summarizing the content of the included studies. This table included article details, such as the author names, countries, publication years, participant demographics, intervention and control methods, duration of interventions, measurement tools for outcomes, sample sizes, and reported outcomes. The data from these studies were collected independently by both reviewers.

Data analysis

A Bayesian network meta-analysis was conducted using Stata 14.0 and OpenBUGS software. A network meta-analysis not only contains the outcomes of direct comparisons, but also combines these results with those of indirect comparisons, which are rarely reported in head-to-head RCTs. The adjusted indirect treatment comparison method is specifically designed to evaluate two treatments when an indirect comparison can be made through a shared comparator [41, 42]. Post-intervention measurements were selected for comparison.

The standardized mean difference (SMD) and 95% percentile intervals are used as summary statistics in network meta-analyses when all studies assess the same outcome; however, they measure the outcomes in different scales. The SMD expresses the size of the intervention effect in each study relative to the between-participant variability in outcome measurements. Thus, studies in which the mean differences are the same proportions of the standard deviation (SD) will have the same SMD, regardless of the actual scales used to make the measurements [43]. In the present study, statistical significance was set at $\alpha = 0.05$ [43] and the SMD was interpreted based on Cohen's criteria; an SMD of 0.2 denoted a small effect size, 0.5 a moderate effect size, and 0.8 a large effect size [44].

$$SMD = \frac{\text{difference in mean outcome between groups}}{\text{standard deviation of outcome among participants}}$$

Global and local inconsistencies were assessed using inconsistency factors and node-splitting analyses, respectively [45, 46]. A p-value of > 0.05 indicated no significant inconsistencies between the direct and indirect comparisons, and, in these cases, the consistency model was adopted. Otherwise, the inconsistency model was used to aggregate effect sizes and their 95% credible intervals (95% CrI) for the various interventions. The network meta-analysis utilized the Bayesian framework and Markov Chain Monte Carlo simulations in OpenBUGS. To mitigate initial value bias, we ran 100,000 iterations on three chains after 50,000 burn-in periods. The model was considered appropriate when the posterior mean residual deviance closely matched the number of unconstrained data points. The intervention hierarchy was assessed using the Surface Under the Cumulative Ranking (SUCRA). A SUCRA value approaching 1 indicated greater efficacy, whereas a value closer to 0 suggested lower efficacy [47].

A subgroup analysis was performed to investigate the effects of six different interventions on anxiety of children across different anesthesia induction methods (e.g., intravenous induction vs. inhalational induction). A funnel plot was used to evaluate the publication bias in included studies. A symmetric funnel plot indicated no publication bias in the network meta-analysis, whereas an asymmetric plot suggested potential bias, leading to the decision to exclude studies with a sample size of < 30 from the sensitivity analysis. Model convergence was assessed using the Potential Scale Reduction Factor (PSRF), with a value close to 1 indicating improved convergence [48].

Results

The search results

Figure 1 shows a flow diagram of the study selection process. A total of 1239 potentially relevant articles were identified through the electronic searches, along with four additional articles from other sources. After removing duplicates, 264 full-text articles were assessed for eligibility, resulting in 34 articles being included in the quantitative synthesis [10, 14, 16–19, 21, 22, 25–34, 49].

Study quality

The quality assessment results for the studies are presented in Fig. 2.

A critical appraisal of the studies indicated that most of the included studies had an acceptably low or moderate risk of bias. The most significant bias was observed in the item, “measurement of the outcome.”

Study characteristics

The main characteristics of the 34 included studies are summarized in Table 1. Of these studies, 11 were

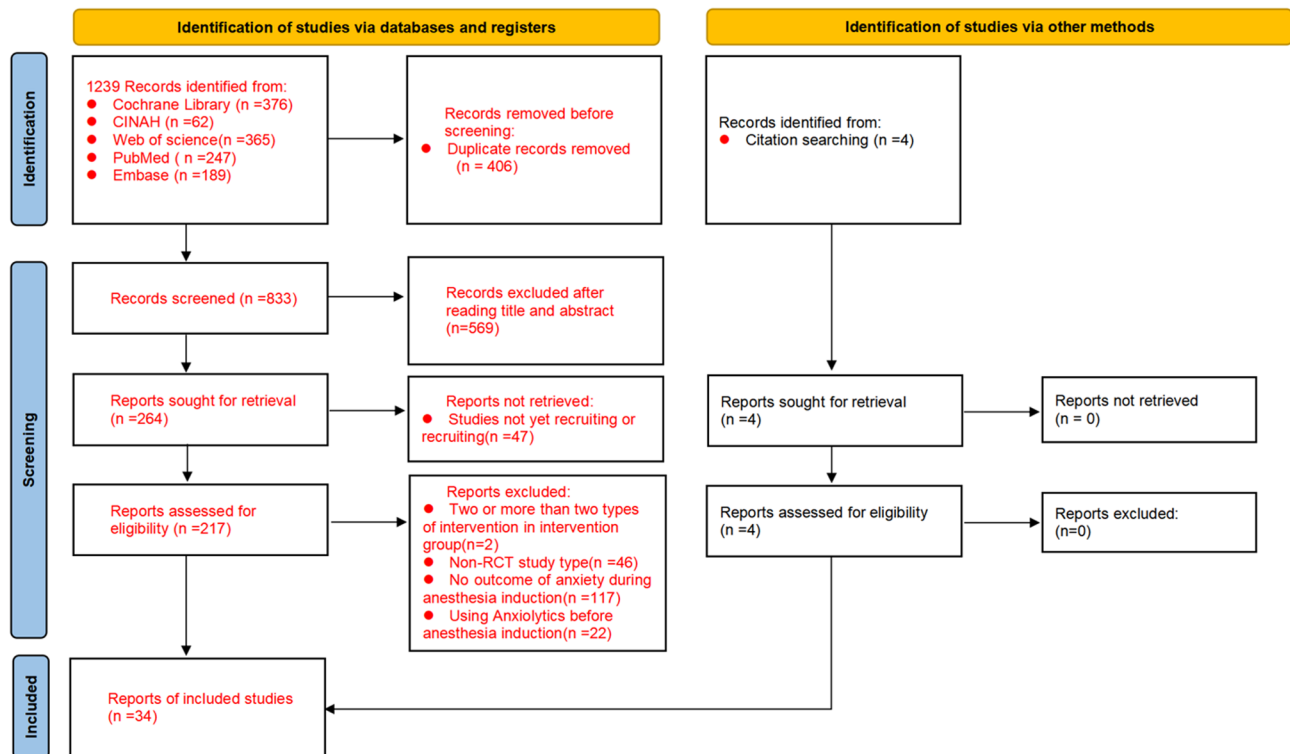


Fig. 1 Study flow diagram

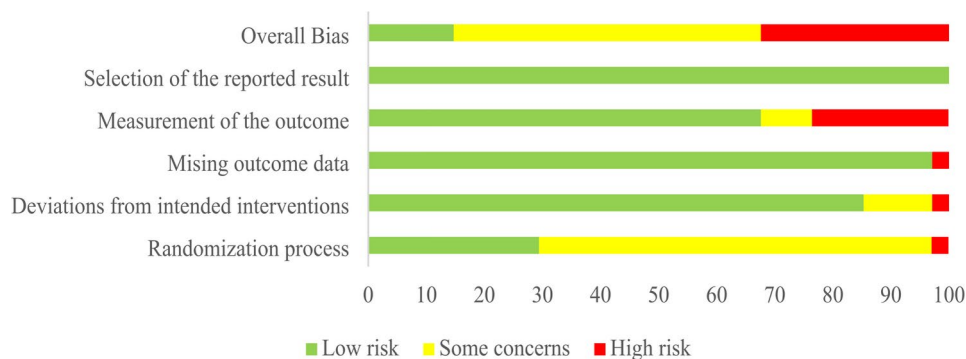


Fig. 2 Risk-of-bias assessment of included randomized controlled trials

conducted in the USA and seven in China. India and Italy each contributed three RCTs, whereas Canada, Turkey, and Korea each contributed two RCTs. Pakistan, Brazil, Denmark, France, the Netherlands, Japan, Sweden, the United Kingdom, and Iran contributed one RCT each. The total number of participants across all the included studies was 3,040, with ages ranging from 1 to 12 years.

In the included studies, 29 RCTs had two arms and five RCTs had three arms. In the included studies, 21 conducted PPIA, nine conducted PDI, seven conducted IDI, four conducted PDI-PPIA, 14 conducted IDI-PPIA, and one conducted IPG. The number of participants per study ranged from 40 to 306. In these studies, IDI encompassed activities like playing on tablets, engaging

in VR games, participating in video games, interacting with clowns or clown doctors, participating in Internet-delivered or preoperative programs, and family-centered preparation [10, 20, 22–24, 54, 55, 58, 62]. PDI included methods such as music therapy, low sensory stimulation, passive video viewing, video clips, introduction or exposure to masks, and streamed videos [26, 27, 32, 55, 60, 63]. IDI-PPIA included parents being present at induction, as well as implementation of interactive distraction techniques for children [14, 18, 19, 21, 25, 28–31, 33, 34, 54, 56, 57, 59, 61]. Similarly, PDI-PPIA involved parental presence during anesthesia induction and passive distraction techniques for children [19, 34, 60]. IPG focused on providing health education to parents [31].

Table 1 Characteristics of studies included in the network meta-analysis

Author and year of publication	Country	Type of anesthesia	Age (years ± SD)	Intervention and control	Inter-vention type	Start time of intervention	End time of intervention	Measure-ment tool of anxiety
Rasti-Emad-Abadi, et al. [22]	Iran	Inhalation	5.11 ± 2.30	Usual care	A	When anesthesia induction starts	Finish anesthesia induction	mYPAS
Lan, et al. 10	China	Inhalation	5.81 ± 2.32	PPiA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			4.8 ± 1.2	Mask preconditioning	C	The day before surgery	Finish anesthesia induction	mYPAS
Kain, et al. [13]	United States	Inhalation	5.0 ± 1.2	Usual care	A			mYPAS
			3.17 (1.83–5.67)	Usual care	A			YPAS
			3.5 (2.58–5.08)	PPiA	B	When anesthesia induction starts	Finish anesthesia induction	YPAS
Hashimoto, et al. [19]	Japan	Inhalation	5 (4.0–6.0)	Video glasses with PPiA	F	In the waiting room	Finish anesthesia induction	mYPAS
			5 (5.0–6.0)	Portable multimedia player with PPiA	E	On the day before surgery	Finish anesthesia induction	mYPAS
Gupta, et al. [32]	India	Inhalation	7.18 ± 2.7	Sequence- flavored mask	C	When anesthesia induction starts	Finish anesthesia induction	mYPAS
Golan, et al. [61] 2009	United States	Inhalation	7 ± 1.97	Usual care	A			mYPAS
			NR	PPiA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
Eijlers, et al. [21]	Netherlands	Inhalation and intravenous	NR	Clowns with PPiA	F	In the waiting room	Finish anesthesia induction	mYPAS
			8.3 (5.7–10.2)	Virtual reality exposure with PPiA	F	In the waiting room	Finish anesthesia induction	mYPAS
Cumino, et al. [31]	Brazil	Inhalation	7.5 (5.6–10.7)	PPiA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			5.29 ± 1.15	Usual care	A			mYPAS
			5.45 ± 1.0	Using smartphone group with PPiA	F	From the waiting room	Finish anesthesia induction	mYPAS
Carlsson, et al. [14]	Sweden	Inhalation and intravenous	5.29 ± 0.96	Informed group(informed parents about anesthesia and surgery)	G	On the day before surgery	NR	mYPAS
			5.6 ± 1.8	Preoperative visit with PPiA	F	One week before surgery	Finish anesthesia induction	mYPAS
Vagnoli, et al. [29]	Italy	Inhalation	5.3 ± 2.2	PPiA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			7.30 ± 2.72	PPiA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			6.85 ± 2.21	Clowns with PPiA	F	Before entering the operation room	Finish anesthesia induction	mYPAS
Gao, et al. [33] 2014	China	Intravenous	4.37 ± 1.09	PPiA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
Chaurasia, et al. [57]	India	Inhalation	4.52 ± 1.21	Play interesting games with PPiA	F	15–20 min before surgery	Finish anesthesia induction	mYPAS
			5.2 ± 1.2	PPiA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS

Table 1 (continued)

Author and year of publication	Country	Type of anesthesia	Age (years \pm SD)	Intervention and control	Inter-vention type	Start time of intervention	End time of intervention	Measure-ment tool of anxiety
Vagnoli, et al. [28] 2010	Italy	Inhalation	5.3 \pm 1.3	Introduce the anesthesia process in a playful way with PPIA	F	NR	NR	mYPAS
			7.36 \pm 2.61	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
Vagnoli, et al. 2019 [30]	Italy	Inhalation	7.04 \pm 2.23	Clowns with PPIA	F	From the waiting room	Finish anesthesia induction	mYPAS
			8.2 \pm 1.3	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			8.5 \pm 1.4	Relaxation-guided imagery with PPIA	F	1 h before surgery	Finish anesthesia induction	mYPAS
Kim, et al. [60]	Korea	Inhalation	5.3 \pm 1.4	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			5.5 \pm 1.0	Video distraction	C	From the waiting room	Finish anesthesia induction	mYPAS
			5.0 \pm 1.3	Video distraction with PPIA	E			mYPAS
Wright, et al. [16] 2010	Canada	Inhalation	NR	Usual care	A			mYPAS-SF
			NR	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS-SF
			6.63 \pm 1.38	Usual care	A			mYPAS-SF
Huang, et al. [26] 2020	China	NR						
Huntington, et al. [58] 2017	United Kingdom	NR	7.53 \pm 1.45	Music therapy	C	From the waiting room	Finish anesthesia induction	mYPAS-SF
			6 \pm 0.83	Usual care	A			mYPAS-SF
Kain, et al. [6] 2004	United States	Inhalation	6 \pm 0.8	Video with information	C	One week before surgery	NR	mYPAS
			5.5 \pm 1.4	Usual care	A			mYPAS
Kain, et al. [63]	United States	Inhalation	5.6 \pm 1.2	Music therapy	C	From the waiting room	Finish anesthesia induction	mYPAS
			5.2 \pm 1.1	Usual care	A			mYPAS
			5.1 \pm 1.4	Low sensory stimulation	C	Enter the operation room	Finish anesthesia induction	mYPAS
Sakizci Uyar, et al. [55]	Turkey	Inhalation	6.6 \pm 1.0	Watching cartoon	C	From the waiting room	Finish anesthesia induction	mYPAS
			6.7 \pm 1.0	Playing tablet	D	From the waiting room	Finish anesthesia induction	mYPAS
Jung, et al. [56]	United States	Inhalation	7.8 \pm 2.3	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			8.2 \pm 2.2	Virtual reality with PPIA	F	From the waiting room	Finish anesthesia induction	mYPAS
Clausen, et al. [18] 2021	Denmark	Inhalation	4.4 \pm 0.2	Usual care	A			mYPAS
			4.4 \pm 0.3	Playing tablet games	D	From the waiting room	Finish anesthesia induction	mYPAS
			7.6 \pm 2.0	Audiovisual or auditory with PPIA	E	One week before surgery		mYPAS
Hatipoglu, et al. [59]	Turkey	Inhalation						
			7.6 \pm 2.3	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			6.6 \pm 0.4	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
Patel, et al. [25]	United States	Inhalation	7.0 \pm 0.4	Playing video game with PPIA	E	20 min before surgery	NR	mYPAS

Table 1 (continued)

Author and year of publication	Country	Type of anesthesia	Age (years ± SD)	Intervention and control	Inter-vention type	Start time of intervention	End time of intervention	Measure-ment tool of anxiety
Wright, et al. [16]	Canada	Inhalation	5.9 ± 2.5	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			5.9 ± 2.2	Internet-delivered preoperative program	D	One week before surgery	NR	mYPAS
			6.3 ± 2.6	Internet-delivered preoperative program with PPIA	F	NR	NR	mYPAS
Kain, et al. [62]	United States	Inhalation	NR	Usual care	A			mYPAS
			NR	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			NR	Family-centered behavioral preparation	D	NR	NR	mYPAS
Kain, et al.[17]	United States	Inhalation	4.5 ± 1.5	Usual care	A			mYPAS
			4.3 ± 1.8	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
			4.8 ± 1.5	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS
Lee, et al. [34] 2012	Korea	Intravenous						
Yao, et al. [52] 2022	China	Inhalation	4.4 ± 1.2	Playing toy with PPIA	E	From the waiting room	Finish anesthesia induction	mYPAS
			4.6 ± 1.3	Watching video with PPIA	F	From the waiting room	Finish anesthesia induction	mYPAS
			4.3 ± 1.1	Usual care	A			mYPAS-SF
Wu, et al. [53]	China	Intravenous	4.6 ± 1.2	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS-SF
			7.58 ± 3.63	Usual care	A			mYPAS-SF
			7.33 ± 2.29	VR	D	On the day before surgery	Finish anesthesia induction	mYPAS-SF
Wang, et al. [49]	China	Inhalation	7.63 ± 2.31	Usual care	A			mYPAS-SF
			7.12 ± 2.12	Watching cartoon or listen to music	C	From the waiting room	Finish anesthesia induction	mYPAS-SF
Akhtar, et al. [51]	Pakistan	Inhalation	3.96 ± 0.63	Incentive-based game	D	From the waiting room	Finish anesthesia induction	mYPAS
			4.01 ± 0.48	Usual care	A	From the waiting room	Finish anesthesia induction	mYPAS
			5.07 ± 3.95	Usual care	A			mYPAS
Li, et al. [50]	China	Inhalation	6.37 ± 3.16	PPIA	B	When anesthesia induction starts	Finish anesthesia induction	mYPAS

SD, standard deviation; PPIA, parental presence at induction of anesthesia; mYPAS, Yale Preoperative Anxiety Scale-Short Form; A, Usual Care group; B, Parental Presence at Anesthesia Induction group; C, Passive Distraction Intervention group; D, Interactive Distraction Intervention group; E, Passive Distraction Intervention with Parental Presence During Anesthesia Induction group; F, Interactive Distraction Intervention with Parental Presence During Anesthesia Induction group; G, Intervention for Parents group

In these studies, the instruments used to measure the children's levels of anxiety during anesthesia induction included the modified Yale Preoperative Anxiety Scale (mYPAS), Yale Preoperative Anxiety Scale (YPAS), and the modified Yale Preoperative Anxiety Scale-Short Form (mYPAS-SF). The mYPAS consists of 22 items categorized into five groups: activity, emotional expressivity, state of arousal, vocalization, and use by parents [65], with a scoring range of 23 to 100. Higher scores indicate higher levels of anxiety. The mYPAS-SF lacks items related to parental dependency, with higher scores indicating higher anxiety levels. The Spielberg State-Trait Anxiety Inventory (STAI) is a self-report tool composed of two distinct scales for assessing the trait and state anxiety levels of parents. Both Likert-type scales range from 20 to 80, with higher scores reflecting greater anxiety. The Induction Compliance Checklist (ICC) is an observational scale that evaluates a child's compliance during anesthesia induction, with higher scores indicating lower behavioral compliance [17].

Kain's articles from 2004, 1998, and 2001 [17, 27, 63] did not report means or standard deviations, instead providing line charts or box plots of mYPAS scores. Therefore, for these articles, data related to means, standard deviations (SD), medians, first quartiles, and third quartiles were extracted using GetData Graph Digitizer (Getdata) [66]. On the other hand, Eijlers's article,

Hashimoto's article, Jung's article, Kain's article, Kerimoglu's article, and Kim's article [19, 21, 24, 56, 60, 64] provided medians, first quartiles, and third quartiles, and we used Wan's method to obtain the means and SDs [67]. The two intervention groups in Hatipoglu's article [59] were combined since both involved passive interventions, in accordance with the Cochrane Handbook for Systematic Reviews of Interventions [68].

Network meta-analysis of the primary outcome of children's anxiety during anesthesia induction

Network map

The network map is shown in Fig. 3. The size of each node represents the number of participants in the included studies. The lines connecting the nodes represent direct comparisons between the studies, with the width of each line indicating the number of articles that compared the same interventions. The network map revealed that the most commonly studied interventions were the IDI-PPIA and PPIA, whereas fewer involved IPG.

Effects of interventions

The global and local inconsistency results showed no statistically significant differences for any interventions in the included studies (all $p > 0.05$). Therefore, a consistency model was used to combine the effect sizes and 95% CrIs in OpenBUGS. The posterior mean residual deviance

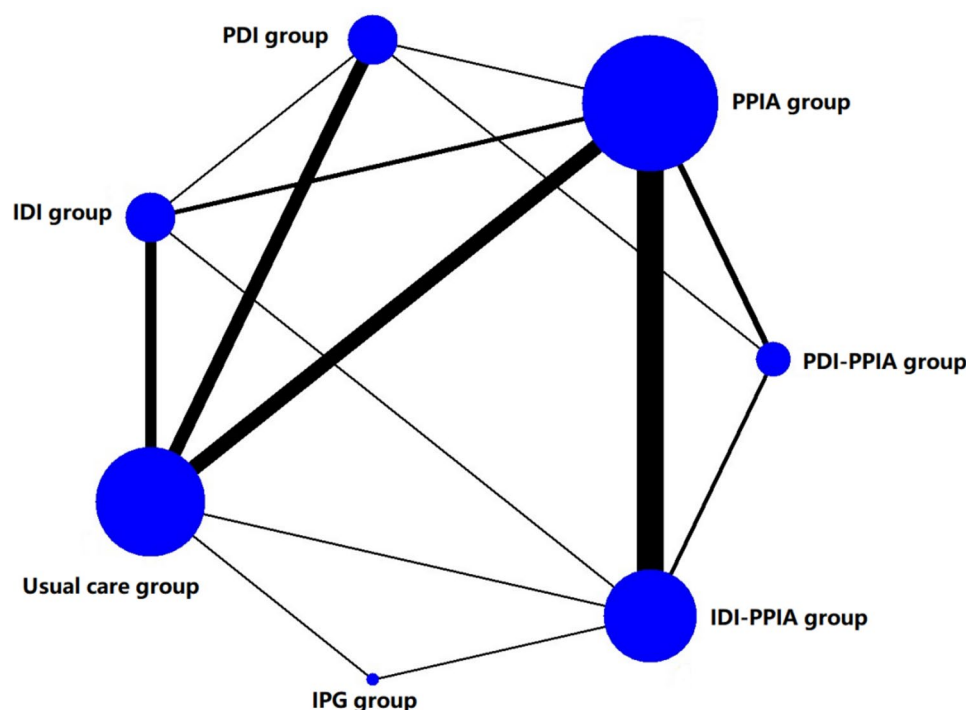


Fig. 3 Network map. PPIA, Parental Presence during Induction of Anesthesia; PDI, Passive Distraction Intervention group; IDI, Interactive Distraction Intervention group; IDI-PPIA, Interactive Distraction Intervention with Parental Presence during Induction of Anesthesia group; PDI-PPIA, Passive Distraction Intervention with Parental Presence during Induction of Anesthesia group; IPG, Intervention for Parents group

Table 2 Network league table showing results of a network meta-analysis using the mean difference and 95% credible intervals for anxiety levels. Note. The treatments should be read from left to right. A mean difference of less than 0 favors the top left treatment

SUCRA=85%							
Passive distraction intervention with PPIA group		SUCRA=83%					
-0.11 (-1.09, 0.87)		Interactive distraction intervention with PPIA group		SUCRA=52%			
-0.70 (-2.68, 1.28)		-0.59 (-2.35, 1.17)		Intervention for parents group		SUCRA=49%	
-0.76 (-1.98, 0.46)		-0.65 (-1.59, 0.29)		-0.06 (-1.96, 1.84)		Interactive distraction intervention group	
-0.79 (-1.97, 0.39)		-0.68 (-1.64, 0.28)		-0.09 (-1.99, 1.81)		-0.03 (-0.97, 0.91)	
-1.03 (-1.97, -0.09)		-0.92 (-1.45, -0.39)		-0.33 (-2.11, 1.45)		-0.27 (-1.13, 0.59)	
-1.94 (-3.02, -0.86)		-1.83 (-2.59, -1.07)		-1.24 (-3.02, 0.54)		-1.18 (-1.92, -0.44)	
						-0.24 (-1.10, 0.62)	
						Passive distraction intervention group	
						SUCRA=32%	
						PPIA group	
						SUCRA=2%	
						Usual care group	

(74.97) was close to the number of unconstrained data points (73) in the model, indicating that the model was consistent and appropriate. Our analysis showed a PSRF close to 1, indicating effective model convergence and increased credibility of the parameter estimates.

The relative effects of the different interventions are presented as a league table in Table 2. According to our findings, PDI-PPIA therapy (SUCRA=85%), IDI-PPIA therapy (SUCRA=83%), IDI therapy (SUCRA=49%), PDI therapy (SUCRA=47%), and PPIA therapy (SUCRA=32%) significantly reduced anxiety levels during anesthesia induction, while IPG did not (SUCRA=52%). The results showed that, compared to usual care, PDI-PPIA therapy (SMD = -1.94, 95% CrI = -3.02, -0.86), IDI-PPIA therapy (SMD = -1.83, 95% CrI = -2.59, -1.07), IDI therapy (SMD = -1.18, 95% CrI = -1.92, -0.44), PDI therapy (SMD = -1.15, 95% CrI = -1.16, -0.44), and PPIA therapy (SMD = -0.91, 95% CrI = -1.54, -0.28) exhibited significant statistical differences. Additionally, compared to PPIA therapy, PDI-PPIA therapy (SMD = -1.03, 95% CrI = -1.97, -0.09) and IDI-PPIA therapy (SMD = -0.92, 95% CrI = -1.45, -0.39) also showed significant statistical differences, while no significant differences were found for the other comparisons.

Sensitivity analysis

Our funnel plot indicated asymmetry and publication bias ($P < 0.05$), as shown in the Supplementary Material. Thus, we excluded studies with sample sizes below 30 for the sensitivity analysis. The global inconsistency and node-splitting analyses showed no significant differences between the interventions (all $P > 0.05$). The posterior mean residual deviance (62.07) aligned with the number

of data points (60), thereby confirming the suitability of the consistency model.

Our sensitivity analysis confirmed the findings across all studies. Compared to the Usual Care group, significant reductions in anxiety during anesthesia induction were observed with PDI-PPIA (SMD = -2.22, 95% CrI = -3.40, -1.04), IDI-PPIA (SMD = -1.94, 95% CrI = -2.82, -1.06), IDI (SMD = -1.29, 95% CrI = -2.09, -0.49), PDI (SMD = -1.19, 95% CrI = -1.90, -0.48), and PPIA (SMD = -0.97, 95% CrI = -1.64, -0.30). Additionally, when compared to PPIA, both PDI-PPIA (SMD = -1.24, 95% CrI = -2.30, -0.18) and IDI-PPIA (SMD = -0.96, 95% CrI = -1.61, -0.31) showed significant reductions in anxiety. However, no significant differences were observed when comparing PDI-PPIA or IDI-PPIA with either IDI or PDI.

Subgroup analysis

Subgroup analyses by induction method were planned but could not be performed for intravenous induction due to network disconnection (only 5 studies), which violated the transitivity assumption required for indirect comparisons. Thus, analyses were limited to inhalation induction studies meeting NMA assumptions.

Twenty-nine articles involving six types of interventions assessed the anxiety levels of 2443 children during inhalation induction. The results showed that, compared with usual care, IDI-PPIA (SMD = -2.21, 95% CrI = -3.03, -1.39), PDI-PPIA (SMD = -1.74, 95% CrI = -2.96, -0.53), IDI (SMD = -1.22, 95% CrI = -2.02, -0.42), PDI (SMD = -1.14, 95% CrI = -1.84, -0.43), and PPIA (SMD = -0.86, 95% CrI = -1.48, -0.23) exhibited significant statistical differences. Additionally, compared with PPIA and PDI, IDI-PPIA showed significant statistical differences (SMD = -1.35, 95% CrI = -1.98, -0.72; SMD = -1.07, 95% CrI

= -2.09, -0.05, respectively). None were found for other comparisons.

Network meta-analysis of the secondary outcome of parental anxiety

This network map is presented in the Supplementary Materials. Ten articles involving five types of interventions assessed the anxiety levels of 853 parents following induction of anesthesia in their children. Of these, eight RCTs included two intervention arms and two included three arms. The network map demonstrated that IDI-PPIA and PPIA were the most frequently studied approaches. The results indicated that, when compared to the Usual Care group, none of the interventions showed statistically significant differences in reducing parental anxiety. Furthermore, no statistically significant differences were observed between any two intervention groups.

Network meta-analysis of the third outcome of induction compliance of children

This network map is included in the Supplementary Materials. Eleven articles explored five types of interventions and evaluated the induction compliance of 1,084 children during anesthesia induction using ICC. Nine studies had two groups and two had three groups. The results showed that PPIA, IDI, and IDI-PPIA were significantly different from those of the Usual Care group, whereas PDI and PDI-PPIA did not show significant differences.

Discussion

To the best of our knowledge, this is the first comprehensive network meta-analysis to consolidate evidence from all eligible studies related to nonpharmacological interventions aimed at reducing anxiety in children during anesthesia induction. We conducted a network meta-analysis of 34 RCTs comparing six different interventions, both directly and indirectly, in 3,040 participants. Compared with the Usual Care group, the PDI-PPIA, IDI-PPIA, IDI, PDI, and PPIA groups experienced significantly reduced anxiety during anesthesia induction.

The network meta-analysis indicated that PDI-PPIA had the highest likelihood (85%) of being the most effective intervention for reducing anxiety during anesthesia induction, followed by IDI-PPIA (83%), IDI (49%), PDI (47%), and PPIA (32%). Our study also indicated that IDI and PDI therapies were effective for anxiolysis when administered independently; this observation aligned with the efficacy demonstrated in earlier research [35, 36]. According to Cohen's criteria [44], an absolute value of $SMD \geq 0.8$ indicates a large effect size. In our

study, SMD values ranged from -1 to -2, far exceeding this threshold and reflecting pronounced anxiety reduction in the intervention groups. To contextualize clinical relevance, we compared these effects to the minimal clinically important difference (MCID) of 0.48 proposed by Jenkins et al. [69] (equivalent to midazolam's anxiolytic efficacy). All non-pharmacological interventions, except interventions for parents, surpassed this benchmark, demonstrating clinically meaningful superiority over midazolam for mitigating pediatric anxiety during anesthesia induction. These findings robustly support the interventions' effectiveness.

There are several potential mechanisms underlying this positive effect. First, because children tend to think in concrete terms rather than abstract concepts [70], distraction techniques work well because they make concepts more concrete and appealing [71]. This redirection helps enhance the child's focus on the intervention and reduces the amount of attention devoted to an upcoming anesthesia induction and surgery. Indeed, our study demonstrated that PPIA is an effective approach for reducing anxiety in children during anesthesia induction, and this finding is consistent with previous systematic reviews [72].

Several underlying mechanisms may have contributed to the positive effects of this particular intervention. First, maternal presence during anesthesia induction and recovery has been shown to reduce salivary cortisol levels and alleviate anxiety in children [73]. Also, unfamiliar operating room environments and instruments can induce panic in children; however, parental accompaniment helps diminish their sense of unfamiliarity, thereby mitigating the adverse stimuli and stress responses associated with the impending procedure [50]. Furthermore, the concurrent application of PDI and PPIA therapies, as well as the combination of IDI and PPIA therapies, has been found to produce a superior therapeutic effect compared with PPIA therapy alone, indicating that these two therapies may enhance the effects of PPIA through a synergistic action. However, it is important to note that there was no significant difference in the effects of PDI-PPIA and IDI-PPIA compared to those of PDI or IDI alone. This finding indicates that, in some cases, employing PDI or IDI individually might be adequate for achieving the therapeutic goal.

Remimazolam, a novel ultra-short-acting benzodiazepine, exhibits superior pharmacokinetic/pharmacodynamic profiles compared with midazolam in pediatric anesthesia and sedation. While effective for anesthesia induction/maintenance and anxiety in children, its pediatric use remains unresolved dosing regimens and limited comparative data. Current evidence is primarily derived from observational studies and case reports, with

few direct comparisons with alternative interventions [74, 75]. Prospective studies using standardized protocols are needed to confirm remimazolam's efficacy in reducing children anxiety during pediatric anesthesia induction. A network meta-analysis should be conducted once sufficient high-quality studies confirm remimazolam's efficacy in reducing children anxiety during anesthesia induction, thereby generating comprehensive evidence to guide the reduction of children anxiety during anesthesia induction.

Current non-pharmacological interventions for anxiety during anesthesia induction in children predominantly utilize passive or active distraction techniques. Studies have demonstrated that anesthesiologist-delivered, patient-centered communication effectively reduces preoperative anxiety in adults [76], though its efficacy in children remains underexplored. Future research should explore its application through: 1) developing personalized, family-integrated intervention protocols guided by preoperative cognitive profiling (e.g., information-seeking or avoidance tendencies); 2) integrating subconscious techniques (e.g., positive suggestion) during anesthesia induction; 3) implementing structured information delivery (e.g., stepwise flowcharts) to reduce cognitive load in children, thereby establishing novel strategies for managing children's anxiety during anesthesia induction.

In our network meta-analysis, the asymmetry of our funnel plot indicated a publication bias in the included studies. Studies with sample sizes of less than 30 in either the intervention or control groups were therefore excluded from the sensitivity analysis. The sensitivity analysis results were consistent with all the research findings, further validating the reliability of our conclusions.

None of the interventions in the studies showed statistically significant differences for reducing parents' anxiety compared to the Usual Care group. This finding suggests that the interventions evaluated in the included studies were ineffective at decreasing parental anxiety, probably because they were primarily aimed at the children. Future studies should focus on designing interventions specifically aimed at decreasing parental anxiety in this context.

Compared with the Usual Care group, the PPIA, IDI, and IDI-PPIA groups exhibited improved compliance during anesthesia induction. Varughese et al. [77] found that higher preoperative m-YPAS scores were associated with poorer compliance. Our research shows that, while PPIA, IDI, and IDI-PPIA reduced anxiety and improved compliance, PDI and PDI-PPIA did not have the same effect on compliance despite lowering the anxiety level, indicating the complex relationship between anxiety and compliance. Future studies should examine other relevant factors to better understand and enhance compliance in children.

Our results indicated that a high risk of bias for studies was primarily concentrated in the "measurement of the outcome" factor. This finding likely results from the visibility of the interventions performed during anesthesia induction by specific personnel or equipment and the fact that anxiety was assessed through direct observation. Therefore, most participants, anesthetists, and observers were not blinded to the interventions being performed.

Strengths and limitations

There were some strengths of our network meta-analysis: (1) We performed an exhaustive comparison of the efficacy of six different nonpharmacological interventions for decreasing children's anxiety during anesthesia induction based on a Bayesian network meta-analysis. The differences between different interventions were distinguished according to the rank probability; (2) Only RCTs were included, which implies that the included studies had rigorous study designs.

Admittedly, this network meta-analysis also had several limitations that should be recognized. (1) Some included studies were deemed to have a high risk of bias regarding quality, particularly due to challenges with blinding the researchers who were measuring outcomes in groups using VR or tablet interventions. This lack of blinding may have inflated estimates of the interventions' effects [78]. (2) Although we carefully searched all available non-pharmaceutical interventions for reducing children's anxiety during anesthesia induction, the number of RCTs is still limited. For IPG, our analyses were based on only one RCT and should, therefore, be interpreted with caution. (3) Our network meta-analysis included studies using different anxiety assessment scales (YPAS, mYPAS, and mYPAS-SF) for pediatric anesthesia induction. While we employed SMDs to harmonize these measurements, the inherent differences between scales may introduce additional heterogeneity that may potentially affect the precision of cross-study effect estimates. Consequently, minor between-intervention differences in relative treatment effects - particularly among adjacently ranked interventions - should be interpreted judiciously, with consideration of this measurement-related variability. (4) While results from the inhalation induction subgroup generally aligned with the overall analysis, the small number of studies investigating intravenous induction ($n=5$) prevented meaningful subgroup comparisons. This limitation is particularly noteworthy, as the procedural stress of intravenous access itself may influence pre-induction anxiety levels, potentially confounding the effects of non-pharmacological interventions. Future studies specifically designed to evaluate anxiolytic effects of non-pharmacological interventions in children undergoing intravenous induction are needed to validate and extend our findings.

Conclusion

We performed a thorough comparison of the effects of six nonpharmacological interventions for reducing children's anxiety during anesthesia induction. Our network meta-analysis demonstrated that PDI-PPIA, IDI-PPIA, IDI, PDI, and PPIA were associated with substantial reductions in anxiety in children during anesthesia induction. Unfortunately, these interventions were not associated with any statistically significant reductions in parental anxiety. PPIA, IDI, and IDI-PPIA also improved compliance during anesthesia induction. Our study provides strong evidence regarding the most effective non-pharmacological methods for reducing anxiety during anesthesia induction in children.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions

LML helped design the study, interpreted data, modified the manuscript and provided critical insights. YYL and SSP were responsible for conceiving the idea, strategy searching, data extraction and analysis, and manuscript writing. (YYL and SSP made same contribution to the work). XQX and LY participated in manuscript writing and reviewing. All authors have read and approved the final version of the manuscript.

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Data availability

The data extracted and analysed in this study are available from the corresponding author on reasonable request.

Declarations

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Competing interests

The authors declare no competing interests.

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