小兒外科手術中使用類固醇是否能緩解術後疼痛?

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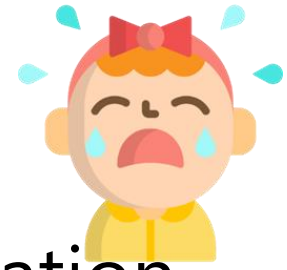
單位：6B兒科病房

前言



- 國際疼痛研究學會 (International Association for the Study of Pain, IASP) 對疼痛的定義：「一種感覺及情緒上的不適經驗，可能與真實或潛在的組織傷害相關之描述。」
- 小兒術後疼痛處置：
  (1) 藥物處置，依醫囑給予相關止痛藥物
  (2) 非藥物處置，家屬安撫、轉移病童注意力 (看電視、玩玩具)、冰敷、改變姿位等
- 病童術後使用Morphine止痛
  - 家長擔憂是否會有藥物成癮、藥物依賴性及副作用問題

評讀文章

Dexamethasone as an Adjuvant for Caudal Blockade in Pediatric Surgical Patients: A Systematic Review and Meta-analysis

Matthew A. Chong,(2018)
Anesthesia & Analgesia, 127(2), 520-528

ANESTHESIA & ANALGESIA
The Official Journal of the STA

Impact Factor of Anesthesia & Analgesia in 2019-2020 : 2.95

步驟 1:系統性文獻回顧探討的問題為何?

Population	pediatric patients (<18 years) receiving a caudal block in anticipation of providing surgical anesthesia or postoperative analgesia for surgery
Intervention	Dexamethasone
Comparison	Placebo
Outcomes	1. Primary duration of analgesia from the caudal block 2. Secondary resting pain scores、opioid and rescue analgesia consumption, parental or patient satisfaction, side effects (eg, postoperative nausea and vomiting)..

步驟 2:系統性文獻回顧的品質如何?(FAITH)

F-研究是否找到 (Find) 所有的相關證據?

良好的文獻搜尋至少應包括二個主要的資料庫(如:Medline, Cochrane 考科藍實證醫學資料庫,EMBASE 等),並且加上文獻引用檢索(參考文獻中相關研究、Web of Science, Scopus 或 Google Scholar)、試驗登錄資料等。文獻搜尋應不只限於英文,並且應同時使用 MeSH 字串及一般檢索詞彙(text words)。

P2

Database and search strategies

- Ovid Medline, Embase, and the Cochrane Library were searched without language restriction from inception to August 18, 2017, for RCTs meeting the listed inclusion criteria.
- Additionally, the first 20 pages of Google Scholar were searched on August 18, 2017, to capture gray literature (eg, nonindexed studies).

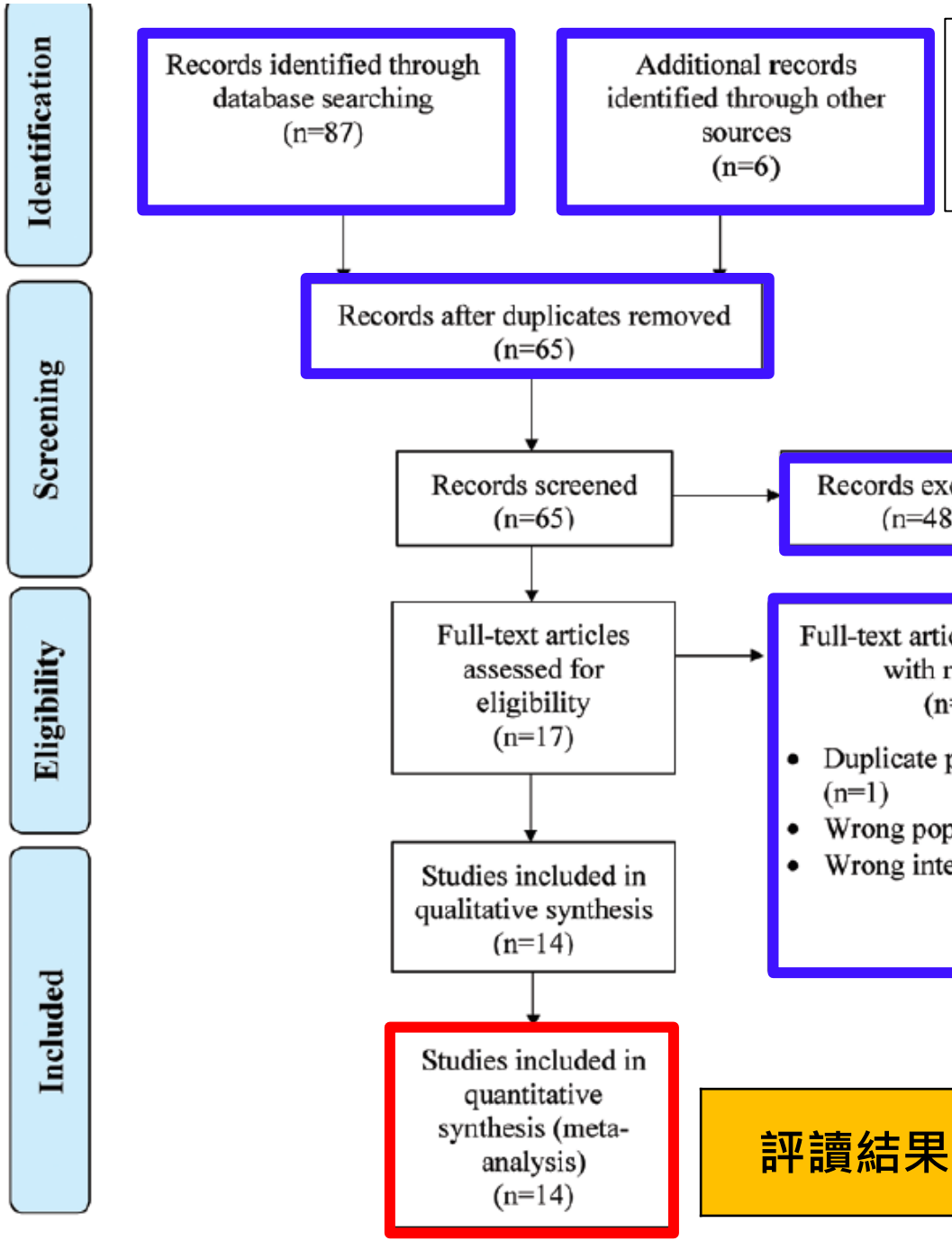


Figure 1. PRISMA flow diagram. The diagram shows the study selection process and provides reasons for exclusion for the records screened. PRISMA indicates Preferred Reporting Items for Systematic Reviews and Meta-analyses.

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評讀結果: □是 □否 ☑不清楚

Digital Content 2 :14篇RCTs的資料分析

Authors (作者)	Year (年份)	Country (國家)	Number of subjects (n) (個案數)	Patient age range (years) (個案年齡層)	Type of Surgery (手術種類)	Caudal local anesthetic dose (局部麻醉劑量)	Caudal dex[a] dose	IV dex[a] dose	Control agent	Rescue Analgesia (加強止痛)	PF[b] dex[a] used? (預防性給予dex)	Pain scale (疼痛評估工具)	Criteria for administration of rescue analgesia (給予加強痛藥之標準)
Abd-Elshafy[9]	2016	Egypt (埃及)	90	2-12	Lower limb orthopedic surgery	0.5mL/kg of bupivacaine 0.25%	0.1mg/kg	0.5mg/kg up to 10mg	Normal saline	Paracetamol	NR[c]	Pediatric objective pain score	Pain score > 4
Abu-Elyazed[10]	2017	Egypt	105	1-6	Inguinal hernia repair	0.75mL/kg of bupivacaine 0.25% up to 20mL or 2mg/kg bupivacaine	0.1mg/kg	N/A[c]	Normal saline	Paracetamol	Yes	Modified objective pain score	Pain score > 4
Almajali[24]	2014	Jordan (約旦)	162	11-14	Urethroplasty	0.5mL/kg of bupivacaine 0.25% up to 2mg/kg	0.1mg/kg	N/A[c]	Normal saline	Paracetamol	NR[c]	4 point numerical rating scale	Pain score >= 4 for two consecutive measurements
Bangash[25]	2014	Pakistan (巴基斯坦)	100	1-5	Orchidopexy	0.5mL/kg of bupivacaine 0.25%	N/A	1.5mg/kg	Normal saline	Acetaminophen	NR[c]	FLACC[f] scale	Pain score = 5
Choudhary[26]	2016	India	128	1-5	Inguinal hernia repair	1mL/kg of ropivacaine 0.2%	0.1mg/kg	N/A[c]	Normal saline	Paracetamol	No	FLACC[f] scale	Pain score >= 4
El-Feky[27]	2015	Egypt	120	3-10	Orchidopexy, inguinal hernia repair, or hypospadias repair	0.5mL/kg of bupivacaine 0.125% with lidocaine 0.5%	0.1mg/kg	N/A[c]	Plain local	Paracetamol	NR[c]	Modified objective pain score	Pain score >= 4
Girgis[28]	2014	Egypt	80	1-6	Inguinal hernia repair	1mL/kg of bupivacaine 0.25%	0.2mg/kg	N/A[c]	Plain local	Paracetamol	NR[c]	Modified objective pain score	Pain score > 4
Hong[29]	2010	South Korea (南韓)	77	1-5	Orchidopexy	1.5mL/kg of ropivacaine 0.15% up to 20mL	N/A[f]	0.5mg/kg up to 10mg	Normal saline	Fentanyl in PACU[d] then acetaminophen	No	FLACC[f] and CHEOPS[g] scale	Pain score >= 5 for two consecutive measurements
Khalil[13]	2013	USA (美國)	29	0.5-6	Urologic surgery	1mL/kg of ropivacaine 0.2%	0.2mg/kg	N/A[c]	Placebo	Morphine in PACU[d]	Yes	Children, Babies, and Infant pain scale	Pain score > 3
Kim[30]	2014	South Korea	80	0.5-5	Orchidopexy	1.5mL/kg of ropivacaine 0.15% up to 20mL	0.1mg/kg	N/A[c]	Plain local	IV Fentanyl in PACU[d] then ibuprofen	No	FLACC[f] and CHEOPS[g] scale	Pain score > 4
Mohamed[31]	2016	Egypt	70	2-5	Hypospadias repair	1mL/kg of bupivacaine 0.25%	0.1mg/kg	N/A[c]	Plain local	PR Paracetamol or IV fentanyl	NR[c]	Children's and Infants' Postoperative Pain Score	Pain score >= 4
Murni-Sari[14]	2015	Malaysia (馬來西亞)	64	3-10	Inguinal hernia repair	0.75mL/kg of levobupivacaine 0.25% up to 20mL	N/A[f]	0.5mg/kg up to 10mg	Normal saline	IV Fentanyl in PACU[d] then paracetamol	NR[c]	Wong-Baker faces scale	Pain score > 4
Srinivasan[32]	2016	India (印度)	105	4-10	Inguinal hernia repair	1.5mL/kg of ropivacaine 0.15%	0.1mg/kg	0.5mg/kg up to 10mg	Normal saline	Paracetamol	NR[c]	Visual analogue scale	NR[c]
Yousef[33]	2014	Egypt	105	1-6	Inguinal hernia repair	1.5mL/kg of ropivacaine 0.15%	0.1mg/kg	N/A[c]	Normal saline	IM Pethidine in PACU[d] then paracetamol	NR[c]	FLACC[f] and CHEOPS[g] scale	Pain score >= 4 for two consecutive measurements

步驟 2:系統性文獻回顧的品質如何?(FAITH)

A-文獻是否經過嚴格評讀 (Appraisal)?

應根據不同臨床問題的文章類型,選擇適合的評讀工具,並說明每篇研究的品質(如針對治療型的臨床問題,選用隨機分配、盲法、及完整追蹤的研究類型)。

Inclusion criteria
Included studies must all be randomized controlled trials (RCTs).

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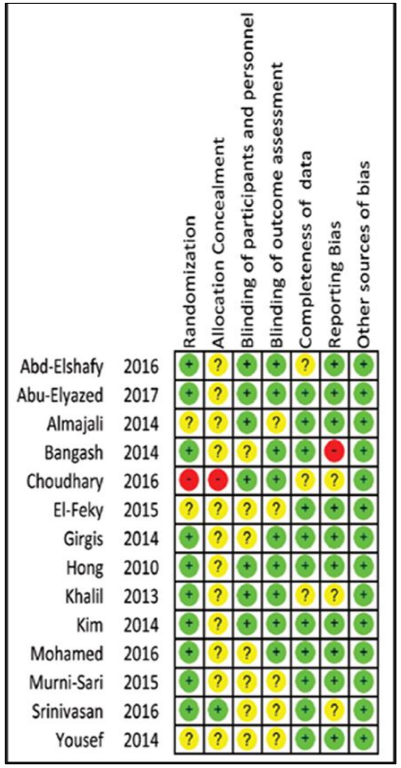
Data extraction and quality assessment
All titles, abstracts, and full texts (where required to assess the study for inclusion) were reviewed in duplicate by 2 of the authors (M.A.C. and C.L.). Any disagreements were resolved by consensus with 1 of the authors. (N.M.B.)
Statistical analysis was Stata (Version 13.1 by StataCorp, College Station, TX), and risk of bias was assessed using the Cochrane tool.

評讀結果: ☑是 □否 □不清楚

步驟 2:系統性文獻回顧的品質如何?(FAITH)

I-是否只納入 (included) 具良好效度的文章?

僅進行文獻判讀是不足夠,系統性文獻回顧需納入至少要有一項研究結果是極小偏誤的試驗。



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每篇文章都至少有一項評估呈現中風險，其中2篇呈現高風險

Figure 2. Cochrane risk of bias scoring for included studies. The green symbol indicates that enough information was reported to judge a low risk of bias. Yellow indicates unclear risk of bias due to insufficient information reported for a definitive judgment. Finally, the red symbol means that sufficient information was reported to judge a high risk of bias.

評讀結果: ☑是 □否 □不清楚

步驟 2:系統性文獻回顧的品質如何?(FAITH)

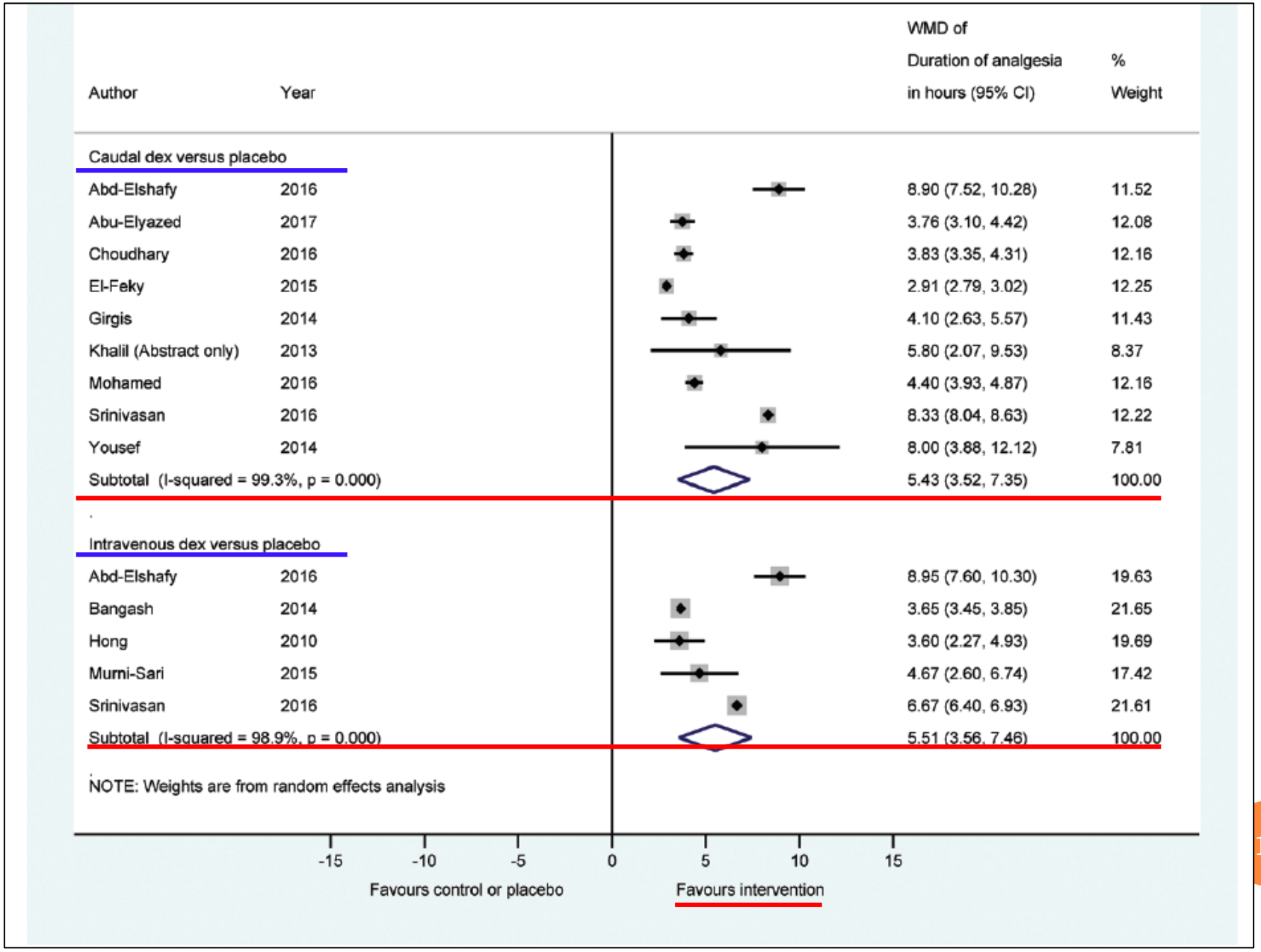
T-作者是否以表格和圖表「總結」 (total up) 試驗結果?

應該用至少 1 個摘要表格呈現所納入的試驗結果。若結果相近,可針對結果進行統合分析(meta-analysis),並以「森林圖」(forest plot)呈現研究結果,最好再加上異質性分析。

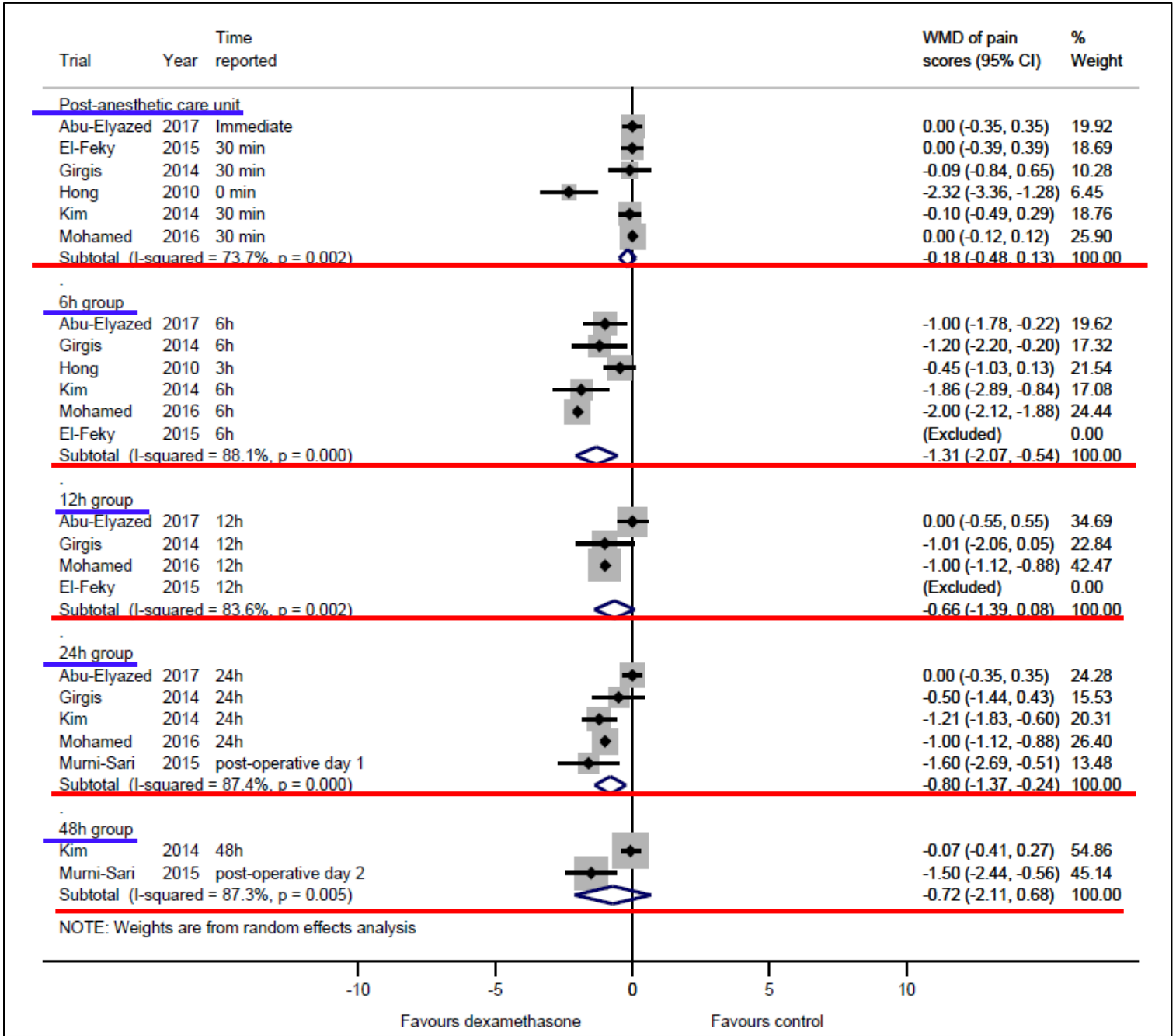
Results

- Details of the 14studies are summarized in **Digital Content 2**.
- **Fig. 3** Forest plot for the primary outcome.
- Subgroup analyses for the primary outcome in **Digital Content 3**.
- Pain scores are shown by time in **Digital Content 4.**
- Funnel plot for the primary outcome in **Digital Content 5.**
- **Table 1.** Summary of Secondary Outcomes.
- **Table 2.** Summary of Findings.

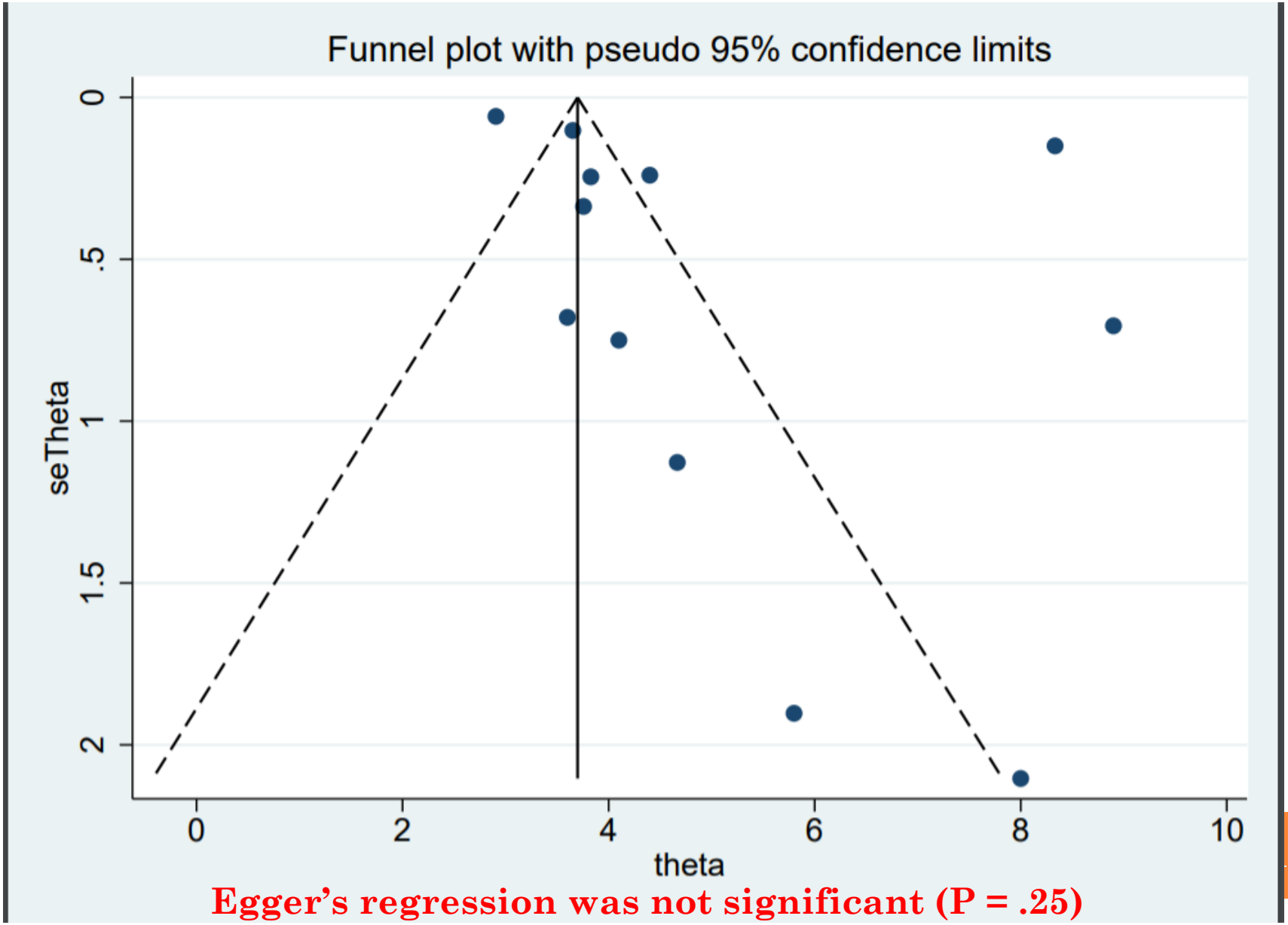
FIG. 3 FOREST PLOT FOR THE PRIMARY OUTCOME:DURATION OF ANALGESIA



Digital Content 4: Pain scores show by time

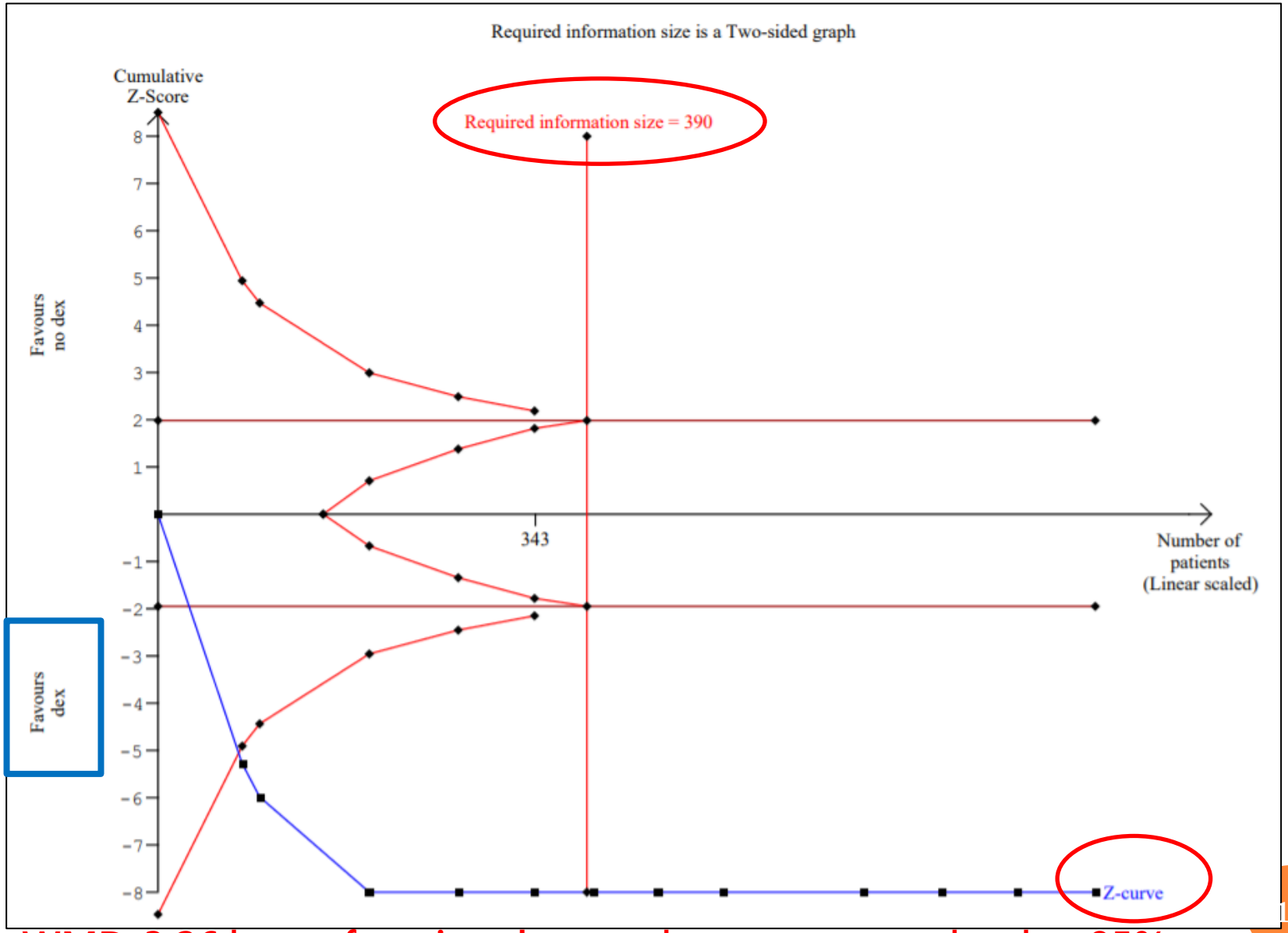


Digital Content 5:Funnel plot for the primary outcome



Egger's regression was not significant (P = .25)

Digital Content 6:Trial Sequential Analysis



WMD, 3.26 hours favoring dexamethasone versus placebo; 95% CI, 1.98–4.54 hours; P < .001

Table 1. Summary of Secondary Outcomes

Secondary Outcome	No. of Patients (No. of Studies)	Relative Risk (95% Confidence Interval)	*P* Value	Number Needed to Treat (95% Confidence Interval)	Heterogeneity (I^2) (%)
Nausea and vomiting	628 (9)	0.47 (0.30–0.73)	.001	11 (8–21)	0.0
Pruritus	206 (3)	1.02 (0.11–9.68)	.98	-	0.0
Bradycardia	206 (3)	1.02 (0.11–9.68)	.98	-	0.0
Residual motor block	155 (2)	0.99 (0.06–15.51)	.99	-	0.0
Respiratory depression	206 (3)	1.02 (0.11–9.68)	.98	-	0.0
Urinary retention	290 (4)	1.45 (0.23–9.04)	.69	-	0.0

Table 2. Summary of Findings

Outcomes	Illustrative Comparative Risks (95% Confidence Interval)		Relative Effect (95% Confidence Interval)	No. of Subjects (No. of Studies)	Quality of the Evidence (GRADE)
	Assumed Risk (Standard Care Group)	Corresponding Risk Reduction in Dexamethasone Group (95% Confidence Interval)			
Duration of analgesia with caudal dexamethasone	The mean duration of analgesia ranged from 3.67 to 7.10 h in the control group	The duration of analgesia was increased by 5.43 h (3.52–7.35) with caudal dexamethasone	WMD 5.43 h (3.52–7.35)	620 (9)	⊕⊕⊕ Moderate[a,b]
Duration of analgesia with intravenous dexamethasone	The mean duration of analgesia ranged from 3.67 to 8.67 h in the control group	The duration of analgesia was increased by 5.51 h (3.56–7.46) with intravenous dexamethasone	WMD 5.51 h (3.56–7.46)	364 (5)	⊕⊕⊕ Moderate[a,b]
Narcotic rescue analgesia requirement in postanesthetic care unit	310 patients requiring narcotic rescue in the control group	217 (153–255) events avoided per 1000 patients administered dexamethasone	RR 0.30 (0.18–0.51)	349 (5)	⊕⊕⊕⊕ High[a]
Rescue analgesia requirement for rest of postoperative period	627 patients requiring postoperative rescue analgesia	338 (51–482) events avoided per 1000 patients administered dexamethasone	RR 0.46 (0.23–0.92)	629 (9)	⊕⊕⊕ Moderate[a,c]
PONV	184 patients experiencing PONV	98 (50–130) events avoided per 1000 patients administered dexamethasone	RR 0.47 (0.30–0.73)	628 (9)	⊕⊕⊕⊕ High[a]

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; PONV, postoperati nausea and vomiting; RR, relative risk; WMD, weighted mean difference.

[a]Minor deficiencies in reporting the method of allocation concealment.

[b]Very high statistical heterogeneity, but all studies favored the intervention.

[c]Very high statistical heterogeneity.

評讀結果:□是 □否 □不清楚

步驟 2:系統性文獻回顧的品質如何?(FAITH)

H-試驗的結果是否相近-異質性 (Heterogeneity)?

在理想情況下,各個試驗的結果應相近或具同質性,若具有異質性,作者應評估差異是否顯著(卡方檢定)。根據每篇個別研究中不同的 PICO 及研究方法,探討造成異質性的原因。

- Dexamethasone prolonged the duration of analgesia by both the caudal route (5.43 hours, 95% confidence interval [CI],3.52–7.35; P < .001; I^2= 99.3%; N = 9; n = 620; GRADE quality = moderate) and
- Intravenous route (5.51 hours; 95% CI, 3.56–7.46; P < .001; I^2= 98.9%; N = 5; n = 364; GRADE quality= moderate) versus control.

評讀結果: □是 ☑否 □不清楚

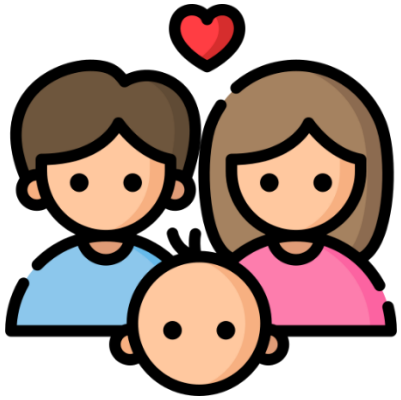
LIMITATIONS

- High statistical heterogeneity for the duration of analgesia analysis.
- Lower statistical heterogeneity among trial conducted in developed countries.
- The minor deficiencies in reporting of allocation concealment.
- Lack of long-term follow-up.

Conclusions

- Total 14 RCTs recruiting 1315 pediatric surgical patients met the inclusion criteria.
- In light of the results and given the off-label status of caudal dexamethasone, suggest that the IV route be utilized.
- IV administration at least, otherdata investigating the usage of perioperative dexamethasone have demonstrated a reasonable safety profile.

DISCUSSION



是否建議小兒外科手術中靜脈給予類固醇來減緩術後疼痛?

(綠牌)同意：18位
(紅牌)不同意：0位
(黃牌)待評估：17位


Thank you!