5 APPENDIX E: Forest plots

5.1 MIDAZOLAM

PLACEBO COMPARISONS

Oral Midazolam vs. placebo/no drug treatment

	Oral Midaz	Place	bo		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
2.1.1 painful procedures							
Mortazavi 2009 (dental) Subtotal (95% CI)	20	20 20	9	20 20	100.0% 100.0 %	2.16 [1.34, 3.47] 2.16 [1.34, 3.47]	
Total events Heterogeneity: Not applic Test for overall effect: Z=		02)	9				
Total (95% CI) Total events	20	20	9	20	100.0%	2.16 [1.34, 3.47]	•
Heterogeneity: Not applic Test for overall effect: Z=		02)					0.1 0.2 0.5 1 2 5 10 Placebo Oral Midazolam

Figure 1 Mortazavi 2009: Completion of procedure [low quality evidence]

	Oral N	/lid	Placebo/No tre	atment		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Events Total		M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.1.1 painful procedures							
Liacouras 1998 (IV place)	59	62	47	61	100.0%	1.24 [1.07, 1.43]	
Subtotal (95% CI)		62		61	100.0%	1.24 [1.07, 1.43]	•
Total events	59		47				
Heterogeneity: Not applicab	ole						
Test for overall effect: $Z = 2$.	80 (P = 0.1	005)					
Total (95% CI)		62		61	100.0%	1.24 [1.07, 1.43]	•
Total events	59		47				
Heterogeneity: Not applicab	ole					1.	02 05 1 2 5 10
Test for overall effect: $Z = 2$.	80 (P = 0.1	005)				0.1	0.2 0.5 1 2 5 10 po/No treatment Oral Midazolam
Test for subgroup differenc	es: Not ap	plicabl	е			Flacek	JO/NO (Jeal(Hellt Oral Wildazolai))

Figure 2 Liacouras 1998: Completion of procedure [moderate quality evidence]

Oral Midazolam + analgesia vs. placebo + analgesia

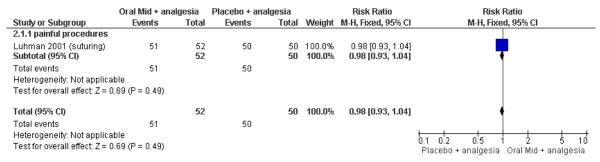


Figure 3 Luhman 2001: Completion of procedure [moderate quality evidence]

	Oral Mid + ana	algesia	Placebo + ana	algesia		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
2.2.1 painful procedures							
Fatovich 1995 a(suturing)	19	32	16	23	54.8%	0.85 [0.58, 1.27]	
Fatovich 1995 b(suturing) Subtotal (95% CI)	14	25 57	16	27 50	45.2% 100.0 %	0.94 [0.59, 1.51] 0.89 [0.66, 1.21]	•
Total events Heterogeneity: Chi ² = 0.11, Test for overall effect: Z = 0.		²= 0%	32				
Total (95% CI)		57		50	100.0%	0.89 [0.66, 1.21]	•
Total events Heterogeneity: Chi ^z = 0.11, Test for overall effect: Z = 0.		l² = 0%	32				0.1 0.2 0.5 1 2 5 10 Oral Mid + analgesia Placebo + analgesia

Figure 4 <u>Fatovich 1995</u>: Anxiety (no. of patients) assessed by observers using the Venham scale [moderate quality evidence]

	Oral Mid +	- analg	esia	Placebo	+ analg	esia		Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	
2.3.1 painful procedures										
Fatovich 1995 a+b(suture) Subtotal (95% CI)	3.2	2.9	57 57	4.8	3.4	50 50	100.0% 100.0 %	-1.60 [-2.81, -0.39] - 1.60 [-2.81, -0.39]		
Heterogeneity: Not applicable Test for overall effect: Z = 2.60)								
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 2.60 Test for subgroup differences:	(P = 0.009)		57			50	100.0%	-1.60 [-2.81, -0.39]	-10 -5 0 5 10 Oral Mid + analgesia Placebo + analgesia	

Figure 5 <u>Fatovich 1995</u>: Distress assessed by parents using the VAS scale [moderate quality evidence]

Oral Midazolam + non-pharmacological vs. placebo + non-pharmacological

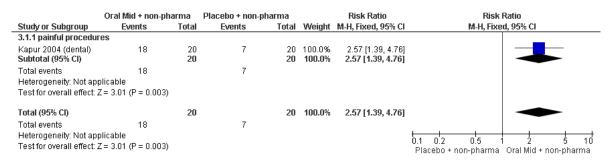


Figure 6 Kapur 2004: Completion of procedure [low quality evidence]

	Oral Mid +	non-pha	гта	Placebo	Placebo+ non-pharma Mean Difference				Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI		
3.2.1 painful procedu	res										
Kapur 2004 (dental) Subtotal (95% CI)	25.88	7.5	20 20	35.71	15.11	20 20	100.0% 100.0 %	-9.83 [-17.22, -2.44] - 9.83 [-17.22, -2.44]			
Heterogeneity: Not ap Test for overall effect:	•	0.009)									
Total (95% CI) Heterogeneity: Not ap Test for overall effect:	•	0.009)	20			20	100.0%	-9.83 [-17.22, -2.44]	-20 -10 0 10 20 Oral Mid + non-pharma Placebo+ non-pharma		
Test for subgroup diffe	erences: Not	applicab	le						Oral wild + Horr-phannal Flacebo+ Horr-phanna		

Figure 7 Kapur 2004: Duration of procedure [low quality evidence]

Intranasal midazolam vs. placebo

ı	ntranasal Mida	zolam	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% (Cl M-H, Fixed, 95% Cl
4.1.1 painful procedures							
Fishbein 1997 b (Venipuncture) Subtotal (95% Cl)	15	19 19	16	19 19	100.0% 100.0 %	0.94 [0.69, 1.27 0.94 [0.69, 1.2 7	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.42 (P = 0	15		16				
Total (95% CI) Total events Heterogeneity: Not applicable	15	19	16	19	100.0%	0.94 [0.69, 1.27	0.1 0.2 0.5 1 2 5 10
Test for overall effect: $Z = 0.42$ (P = 0	1.68)					li li	ntranasal Midazolam Placebo

Figure 8 <u>Fishbein 1997</u>: Distress assessed by an observer using the OBRS scale [low quality evidence]

Intranasal midazolam + analgesia vs. placebo + analgesia

	Intranasal Mid + an	sia Placebo + analgesia			Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
5.1.1 painful procedures							
Theorux 1992 (suturing) Subtotal (95% CI)	15	22 22	9	27 27	100.0% 100.0 %	2.05 [1.12, 3.75] 2.05 [1.12, 3.75]	
Total events Heterogeneity: Not applicat Test for overall effect: Z = 2.			9				
Total (95% CI)		22		27	100.0%	2.05 [1.12, 3.75]	-
Total events Heterogeneity: Not applicat Test for overall effect: Z = 2.			9				0.1 0.2 0.5 1 2 5 10 Placebo + analgesia Intranasal Mid + analgesia

Figure 9 <u>Theroux 1992</u>: Parents' satisfaction (no. of patients) [low quality evidence]

Int	tranasal Mid + an	algesia	Placebo + ana	Ilgesia		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
5.2.1 painful procedures							
Ljungman 2000 xo (needle) Subtotal (95% Cl)	3	15 15	0	10 10	100.0% 100.0 %	4.81 [0.28, 84.20] 4.81 [0.28, 84.20]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.08 (P :	3 = 0.28)		0				
Total (95% CI)		15		10	100.0%	4.81 [0.28, 84.20]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.08 (P	3 = 0.28)		0				0.01 0.1 10 11 Placebo + analgesia Intranasal Mid + analg

Figure 10 <u>Ljungman 2000</u>: Patients' preference (no. of patients) [very low quality evidence]

In	tranasal Mid + ar	Placebo + ana	algesia		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
5.3.1 painful procedures							
Ljungman 2000 xo (needle) Subtotal (95% CI)	13	27 27	0	22 22		22.18 [1.39, 353.32] 22.18 [1.39, 353.32]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 2.19 (P	13 = 0.03)		0				
Total (95% CI)		27		22	100.0%	22.18 [1.39, 353.32]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 2.19 (P)	13 = 0.03)		0				0.01 0.1 10 10 Placeho + analogo ia Intranacal Mid + analogo

Figure 11 <u>Ljungman 2000</u>: Parents' preference (no. of patients) [low quality evidence]

HEAD to HEAD COMPARISONS

Oral midazolam vs. oral triclofos sodium

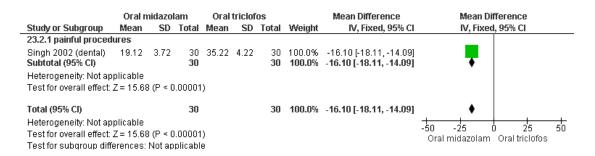


Figure 12 Singh 2002: Length of induction [low quality evidence]

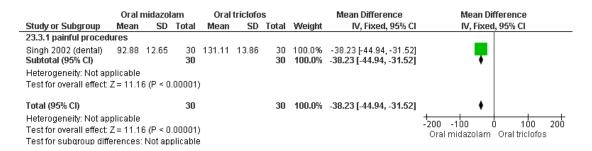


Figure 13 Singh 2002: Recovery tine [low quality evidence]

Sublingual midazolam vs. oral chloral hydrate

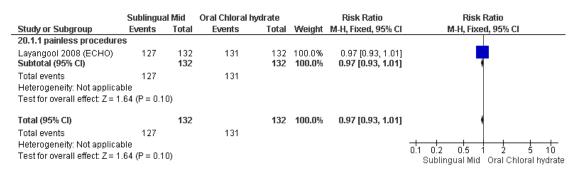


Figure 14 Layagool 2008: Completion of procedure [very low quality]

	Sublir	ngual I	Mid	Oral Ch	loral hyd	Irate		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
20.2.1 painless procedur	es								
Layangool 2008 (ECHO) Subtotal (95% CI)	11.3	8.6	131 131	25.1	20.2	131 131	100.0% 100.0 %	-13.80 [-17.56, -10.04] - 13.80 [-17.56, -10.04]	
Heterogeneity: Not applica Test for overall effect: Z = 3		0.0000	01)						
Total (95% CI)			131			131	100.0%	-13.80 [-17.56, -10.04]	•
Heterogeneity: Not applica	able								-20 -10 0 10 20
Test for overall effect: $Z = 3$	7.19 (P < I	0.0000	01)						Sublingual Mid Oral Chloral hydrate
Test for subgroup differen	ices: Not a	applica	able						Subilingual Miu Oral Chioral hydrate

Figure 15 Layagool 2008: Induction time [low quality]

	Sublin	igual l	Mid	d Oral Chloral hydrate				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
20.3.1 painless procedure	es								
Layangool 2008 (ECHO) Subtotal (95% CI)	10.2	4.8	131 131	10.6	5	131 131	100.0% 100.0 %	-0.40 [-1.59, 0.79] - 0.40 [-1.59, 0.79]	
Heterogeneity: Not applica Test for overall effect: Z = 0		0.51)							
Total (95% CI)			131			131	100.0%	-0.40 [-1.59, 0.79]	•
Heterogeneity: Not applica	able								-20 -10 0 10 20
Test for overall effect: Z = 0	0.66 (P = 0)	0.51)							Sublingual Mid Oral Chloral hydra
Test for subgroup different	ces: Not a	pplica	able						Oubinigual Miu Olai Ciliolai liyula

Figure 16 Layagool 2008: Duration of procedure [low quality]

Sublingual Mid		Mid	Oral Ch	loral hyd	Irate		Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	
20.4.1 painless procedure	es									
Layangool 2008 (ECHO) Subtotal (95% CI)	78.9	29.3	131 131	40.1	14.8	131 131	100.0% 100.0 %	38.80 [33.18, 44.42] 38.80 [33.18, 44.42]		
Heterogeneity: Not applica Test for overall effect: Z = 1		< 0.000	001)							
Total (95% CI)			131			131	100.0%	38.80 [33.18, 44.42]	•	
Heterogeneity: Not applica									-50 -25 0 25 50	
Test for overall effect: Z = 1 Test for subgroup differen	,		,						Sublingual Mid Oral Chloral hydra	

Figure 17 Layagool 2008: Total time [low quality]

	Sublingua	al Mid	Oral Chloral h	nydrate		Risk Ratio	Risk I	Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixe	d, 95% CI
20.1.1 painless procedure	es						_	
Layangool 2008 (ECHO) Subtotal (95% CI)	1	132 132	14	132 132	100.0% 100.0 %	0.07 [0.01, 0.54] 0.07 [0.01, 0.54]		
Total events Heterogeneity: Not applica Test for overall effect: Z = 2		1)	14					
Total (95% CI)		132		132	100.0%	0.07 [0.01, 0.54]		
Total events Heterogeneity: Not applica Test for overall effect: Z = 2		1)	14				0.1 0.2 0.5 1 Sublingual Mid	2 5 10 Oral Chloral hydrate

Figure 18 Layangool 2008: Vomiting [low quality evidence]

Rectal midazolam + placebo (for nitrous oxide) + topical anaesthesia + non-pharmacological intervention (distraction) vs. nitrous oxide (70%) + placebo (for midazolam) + topical anaesthesia + non-pharmacological intervention (distraction)



Figure 19 Zier 2008: Vomiting during drug nitrous oxide administration [moderate quality evidence]

COMBINATION COMPARISONS

Oral midazolam + topical anaesthesia + local anaesthesia vs. oral midazolam + nitrous oxide/oxygen + topical anaesthesia + local anaesthesia

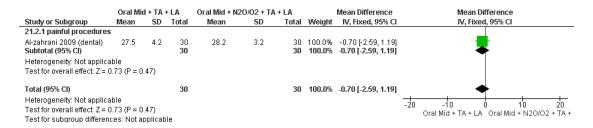


Figure 20 Al-zahrani 2009: Induction time [low quality evidence]

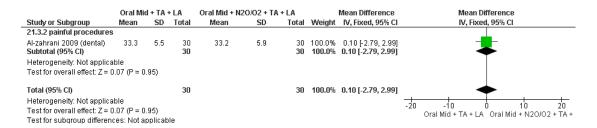


Figure 21 Al-zahrani 2009: Duration of procedure [low quality evidence]

Oral midazolam + nitrous oxide + analgesia vs. nitrous oxide + placebo + analgesia

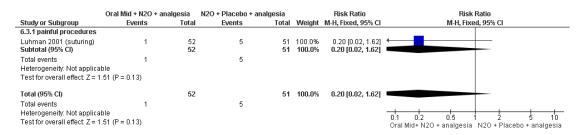


Figure 22 Luhman 2001: Vomiting [low quality evidence]

Oral midazolam + intravenous propofol + lidocaine vs. intravenous propofol + lidocaine

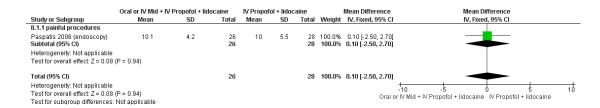


Figure 23 Paspatis 2006: Duration of procedure [low quality evidence]

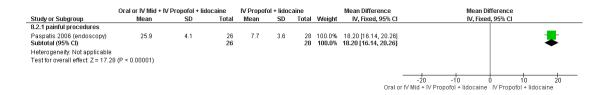


Figure 24 Paspatis 2006: Recovery time [moderate quality evidence]

Intravenous midazolam + intravenous meperidine vs. placebo + intravenous meperidine

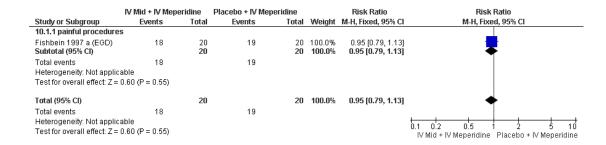


Figure 25 <u>Fishbein 1997</u>: Distress assessed by observer using OBRS [moderate quality evidence]

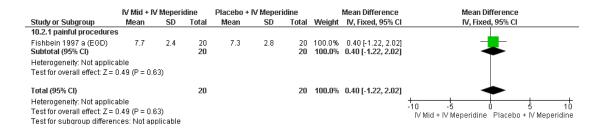


Figure 26 Fishbein 1997: Duration of procedure [low quality evidence]

Intravenous midazolam + intravenous propofol + lidocaine vs. intravenous propofol + lidocaine

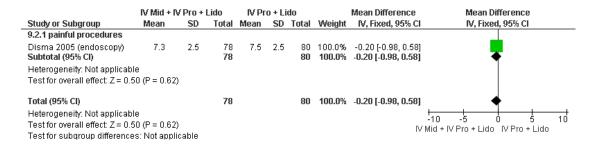


Figure 27 <u>Disma 2005</u>: Duration of procedure [moderate quality evidence]

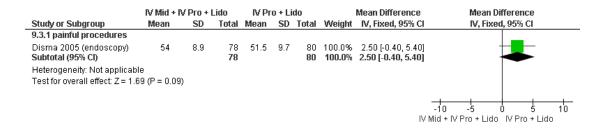


Figure 28 Disma 2005: Recovery time [low quality evidence]

Oral or R	Mid + IV Propofol	+ lidocaine	IV Propofol + lic	docaine		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
5.1.1 painful procedures							
Disma 2005 (endoscopy)	0	78	5	80	100.0%	0.09 [0.01, 1.66]	
Subtotal (95% CI)		78		80	100.0%	0.09 [0.01, 1.66]	
Total events	0		5				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.62 (P = 0.1	1)						
Total (95% CI)		78		80	100.0%	0.09 [0.01, 1.66]	
Total events	0		5				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.62 (P = 0.1)	1)					01-	0.1 0.2 0.5 1 2 5 10 or IV Mid + IV Propofol + lidocaine IV Propofol + lidocaine

Figure 29 <u>Disma 2005</u>: Assisted ventilation (bag-valve mask) [low quality evidence]

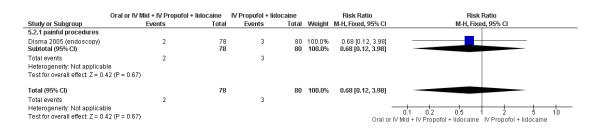


Figure 30 Disma 2005: Oxygen desaturation <90% [low quality evidence]

Intravenous midazolam + intravenous morphine + intravenous bolusinfusions placebo vs. Intravenous bolus infusion propofol + intravenous morphine + intravenous placebo + lidocaine

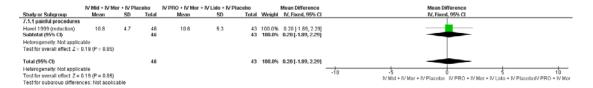


Figure 31 Havel 1999: Induction time [low quality evidence]

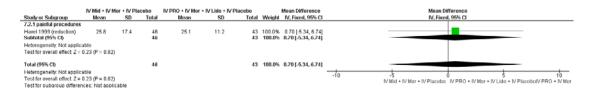


Figure 32 Havel 1999: Duration of procedure [low quality evidence]

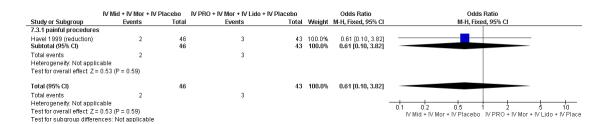


Figure 33 Havel 1999: Pain (no. of patients) [very low quality evidence]

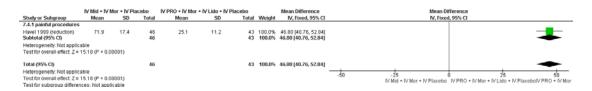


Figure 34 Havel 1999: Recovery time [low quality evidence]



Figure 35 Havel 1999: Total time [low quality evidence]

Intravenous midazolam + intravenous fentanyl (analgesic) vs. intravenous fentanyl (analgesic)

	IV Mid +	IV Fent	anyl	IV Fo	entan	yl		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C	CI IV, Fixed, 95% CI
11.2.1 painful procedures									
Antment 2005 (bonemarrow) Subtotal (95% CI)	5.3	1.41	20 20	5.45	1.5	20 20		-0.15 [-1.05, 0.75 - 0.15 [-1.05, 0.75	
Heterogeneity: Not applicable Test for overall effect: Z = 0.33 (f	P = 0.74)								
Total (95% CI)			20			20	100.0%	-0.15 [-1.05, 0.75	5]
Heterogeneity: Not applicable Test for overall effect: Z = 0.33 (I		hla							-20 -10 0 10 20 IV Mid + IV Fentanyl IV Fentanyl

Test for subgroup differences: Not applicable

Figure 36 Antment 2005: Pain assessed by the anaesthetist using CHEOPS scale [very low quality evidence]

	IV Mid +	IV Alfent	tanyl	IV A	fentar	nyl .		Mean Difference	e Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95%	CI IV, Fixed, 95% CI
11.3.1 painful procedures									
Antment 2005 (bonemarrow) Subtotal (95% CI)	3.5	2.89	20 20	3.8	1.82	20 20	100.0% 100.0 %	-0.30 [-1.80, 1.2 - 0.30 [-1.80, 1.2 0	
Heterogeneity: Not applicable Test for overall effect: Z = 0.39 (P = 0.69)								
Total (95% CI) Heterogeneity: Not applicable			20			20	100.0%	-0.30 [-1.80, 1.20	· +
Test for overall effect: Z = 0.39 (blo							-10 -5 0 5 10 IV Mid + IV Alfentanyl IV Alfentanyl

Figure 37 Antment 2005: Pain assessed by the anaesthetist using the VAS scale [very low quality evidence]

Intravenous midazolam + intravenous remifentanil (analgesic) vs. intravenous remifentanil (analgesic)

	IV Mid + IV	Remifen	rtanil	IV Rei	mifent	anil		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% (CI IV, Fixed, 95% CI
12.2.1 painful procedures									
Antment 2005 (bonemarrow)	4.7	0.92	20	4.75	1.11	20	100.0%	-0.05 [-0.68, 0.58	8]
Subtotal (95% CI)			20			20	100.0%	-0.05 [-0.68, 0.58	3j ₹
Heterogeneity: Not applicable									
Test for overall effect: $Z = 0.16$ (P = 0.88)								
Total (95% CI)			20			20	100.0%	-0.05 [-0.68, 0.58	3]
Heterogeneity: Not applicable									-20 -10 0 10 20
Test for overall effect: Z = 0.16 (-20 -10 0 10 20 IV Mid + IV Remifentanil IV Remifentanil

Figure 38 <u>Antment 2005</u>: Pain assessed by the anaesthetist using the CHEOPS scale [very low quality evidence]

	IV Mid + IV	Remifen	tanil	IV Rei	mifent	anil		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C	CI IV, Fixed, 95% CI
12.3.1 painful procedures									
Antment 2005 (bonemarrow)	1.75	1.37	20	1.8	1.23	20	100.0%	-0.05 [-0.86, 0.78	6]
Subtotal (95% CI)			20			20	100.0%	-0.05 [-0.86, 0.76	ij ▼
Heterogeneity: Not applicable									
Test for overall effect: $Z = 0.12$ (P = 0.90)								
Total (95% CI)			20			20	100.0%	-0.05 [-0.86, 0.76	6]
Heterogeneity: Not applicable									-10 -5 0 5
Test for overall effect: Z = 0.12 (_							-10 -5 0 5 IV Mid + IV Remifentanil IV Remifentanil

Figure 39 Antment 2005: Pain assessed by the anaesthetist using the VAS scale [very low quality evidence]

Intravenous midazolam + intravenous ketamine vs. intavenous ketamine + placebo

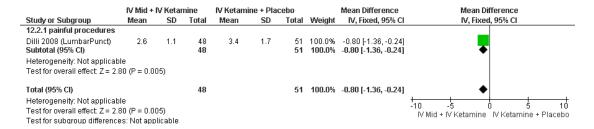


Figure 40 Dilli 2008: Induction time [very low quality evidence]

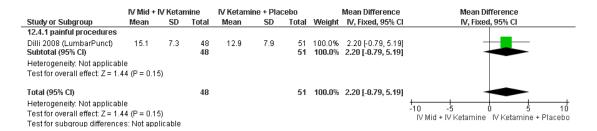


Figure 41 Dilli 2008: Recovery time [very low quality evidence]

Ir	ntravenous Mid + IV K	etamine	IV Ketamine + F	Placebo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
12.3.1 painful procedures	;						
Wathen 2000 (mixed) Subtotal (95% CI)	112	137 137	115	129 129	100.0% 100.0 %	0.92 [0.83, 1.01] 0.92 [0.83, 1.01]	•
Total events Heterogeneity: Not applica Test for overall effect: Z = 1			115				
Total (95% CI)		137		129	100.0%	0.92 [0.83, 1.01]	•
Total events Heterogeneity: Not applica Test for overall effect: Z = 1			115				0.1 0.2 0.5 1 2 5 10 IV Ketamine + Placebo Intravenous Mid + IV Ketamin

Figure 42 Wathen 2000: Parents' satisfaction [moderate quality evidence]

	IV Mid + IV Keta	mine	IV Ketamine + Pla	cebo		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	
7.5.1 painful procedures								
Sherwin 2000 (catheter)	1	53	6	51	19.2%	0.16 [0.02, 1.29]	-	
Wathen 2000 (mixed) Subtotal (95% CI)	13	137 190	25	129 180	80.8% 100.0 %	0.49 [0.26, 0.92] 0.43 [0.24, 0.77]		
Total events	14		31					
Heterogeneity: Chi ² = 1.04	df = 1 (P = 0.31)	$I^2 = 3\%$						
Test for overall effect: Z = 2	2.81 (P = 0.005)							
Total (95% CI)		190		180	100.0%	0.43 [0.24, 0.77]	•	
Total events	14		31					
Heterogeneity: Chi ² = 1.04	, df = 1 (P = 0.31)	I ² = 3%					0.1 0.2 0.5 1 2	
Test for overall effect: Z = 2	2.81 (P = 0.005)						0.1 0.2 0.0 1 2	nine + Placebo

Figure 43 Sherwin 2000; Wathen 2000: Vomiting (during visit and at home 12 hrs after discharge and well into recovery) [low quality evidence]

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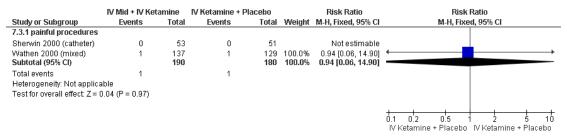


Figure 44 Sherwin 2000; Wathen 2000: Assisted ventilation (bag mask) [low quality evidence]

	IV Mid + IV Ket	tamine	IV Ketamine + P	Placebo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
7.4.1 painful procedures							
Dilli 2008 (LumbarPunct)	3	48	0	51	13.6%	7.43 [0.39, 140.15]	-
Sherwin 2000 (catheter)	1	53	1	51	28.6%	0.96 [0.06, 14.98]	
Wathen 2000 (mixed) Subtotal (95% CI)	10	137 238	2	129 231	57.8% 100.0 %		
Total events Heterogeneity: Chi ² = 1.25, Test for overall effect: Z = 2		; I² = 0%	3				
Total (95% CI)		238		231	100.0%	4.01 [1.27, 12.68]	
Total events Heterogeneity: Chi ² = 1.25 Test for overall effect: Z = 2		; I² = 0%	3				0.1 0.2 0.5 1 2 5 10 Favours IV Mid + IV Ket Favours IV Ket + Placeb

Figure 45 Sherwin 2000; Wathen 2000; Dilli 2008: Oxygen desaturation <90% [low quality evidence]

ROUTE OF ADMINISTRATION

Oral midazolam vs. intranasal midazolam

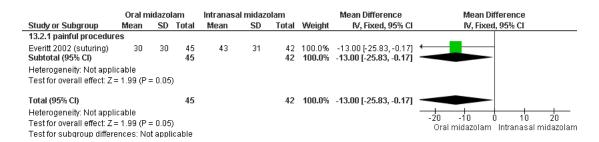


Figure 46 Everitt 2002: Distress assessed by observer using the VAS scale [very low quality evidence]

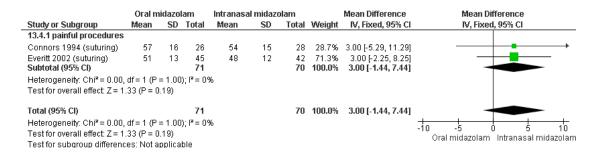


Figure 47 Connors 1994; Evertitt 2002: Total time [very low quality evidence]

Oral midazolam + nitrous oxide (40/45%) + lidocaine vs. intranasal midazolam + nitrous oxide (40/45%) + lidocaine

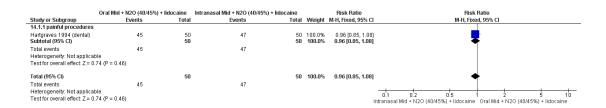


Figure 48 Hartgraves 1994: Completion of procedure [low quality evidence]

	Oral Mid + N2O (4	40/45%) + lidor	caine	Intranasal Mid + N	20 (40/45%) + lic	docaine		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total W		IV, Fixed, 95% CI	IV, Fixed, 95% CI
14.2.1 painful procedures									
Lee-Kim 2004 (dental) Subtotal (95% CI)	15.5	5	20 20	5.55	2.2			9.95 [7.56, 12.34] 9.95 [7.56, 12.34]	-
Heterogeneity: Not applicab Test for overall effect; Z = 8.									
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 8. Test for subgroup difference	15 (P < 0.00001)		20			20 10	00.0%	9.95 [7.56, 12.34]	-20 -10 0 10 20 Oral Mid + N2O (40/45%) + lidocaine Intranasal Mid + N2O (40/45%) + lidocai

Figure 49 Lee-Kim 2004: Induction time [moderate quality evidence]

	Oral Mid + N2O (4	40/45%) + lido	caine	Intranasal Mid + N	2O (40/45%) + lic	locaine		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
14.3.1 painful									_
Lee-Kim 2004 (dental) Subtotal (95% CI)	38.1	7.58	20 20	29.3	11.6	20 20		8.80 [2.73, 14.87] 8.80 [2.73, 14.87]	
Heterogeneity: Not applical Test for overall effect: Z = 2									
Total (95% CI) Heterogeneity: Not applical Test for overall effect: Z = 2 Test for subgroup difference	.84 (P = 0.005)	е	20			20	100.0%	8.80 [2.73, 14.87]	-10 -10 0 10 20 Oral Mid + N2O (40/45%) + lidocaine Intranasal Mid + N2O (40/45%) + lidocaine

Figure 50 Lee-Kim 2004: Total time [low quality evidence]

Oral Midazolam + nitrous oxide (40/45%) + lidocaine vs. Intranasal Midazolam + nitrous oxide (40/45%) + lidocaine

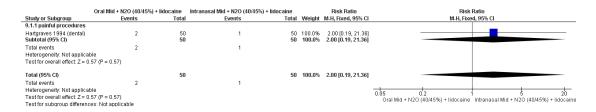


Figure 51 <u>Hartgraves 1994</u>: Oxygen desaturation < 90% [very low quality evidence]

Intranasal midazolam + analgesia vs. intramuscular midazolam+ analgesia

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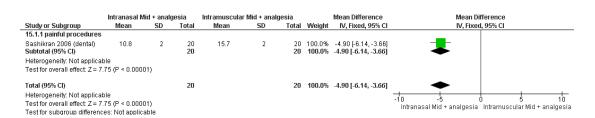


Figure 52 Sashikran 2006: Induction time [moderate quality evidence]

	Intranasal N	/lid + anal	gesia	Intramuscula	r Mid + ana	lgesia		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
15.2.1 painful procedures	;								
Sashikran 2006 (dental) Subtotal (95% CI)	38	3.6	20 20	62.4	3.1	20 20		-24.40 [-26.48, -22.32] -24.40 [-26.48, -22.32]	‡
Heterogeneity: Not applica Test for overall effect: Z = 2		001)							
Total (95% CI)			20			20	100.0%	-24.40 [-26.48, -22.32]	◆
Heterogeneity: Not applica Test for overall effect: Z = 2 Test for subgroup different	22.97 (P < 0.00								-20 -10 0 10 20 Intranasal Mid + analgesia Intramuscular Mid + analgesi

Figure 53 Sashikran 2006: Recovery time [moderate quality evidence]

DOSE COMPARISONS

Intranasal midazolam 0.3mg/kg + nitrous oxide vs. intranasal midazolam 0.2 mg/kg + nitrous oxide

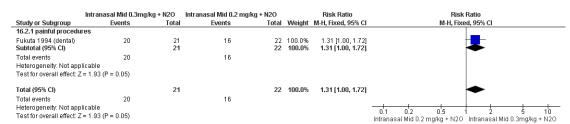


Figure 54 Fukuta 1994: Completion of procedure [low quality evidence]

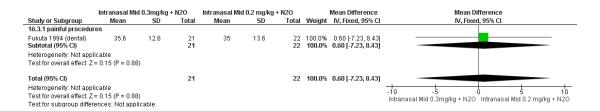


Figure 55 Fukuta 1994: Duration of procedure [low quality evidence]

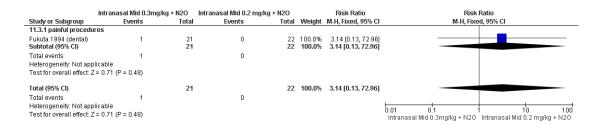


Figure 56 Fukuta 1994: Oxygen desaturation <90% [very low quality evidence]

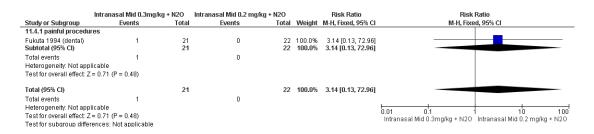


Figure 57 Fukuta 1994: Vomiting [very low quality evidence]

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Rectal midazolam 2mg/kg + lidocaine vs. rectal midazolam 1mg/kg + lidocaine

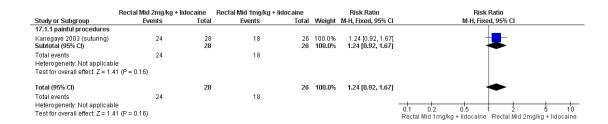


Figure 58 Kanegaye 2003: Parents' satisfaction [low quality evidence]

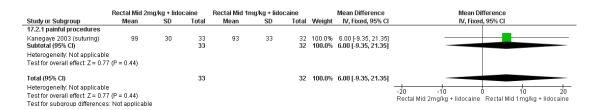


Figure 59 Kanegaye 2003: Total time [low quality evidence]

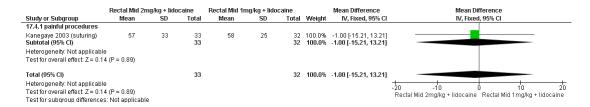


Figure 60 Kanegaye 2003: Recovery time [low quality evidence]

5.2 TRICLOFOS SODIUM

HEAD to HEAD COMPARISON

Oral triclofos sodium vs. oral midazolam

	ОгаІ	Triclo	fos	Oral N	Aidazol	am		Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI			
2.2.1 painful procedu	res											
Singh 2002 (dental) Subtotal (95% CI)	35.22	4.22	30 30	19.12	3.72	30 30	100.0% 100.0 %	16.10 [14.09, 18.11] 16.10 [14.09, 18.11]	-			
Heterogeneity: Not ap	plicable											
Test for overall effect:	Z=15.6	8 (P <	0.0000	1)								
Total (95% CI)			30			30	100.0%	16.10 [14.09, 18.11]	•			
Heterogeneity: Not ap	plicable								-50 -25 0 25 50			
Test for overall effect:	Z = 15.6	8 (P <	0.0000	1)					-50 -25 0 25 50 Oral Triclofos Oral Midazolam			
Test for subgroup diff	erences:	Not a	pplicab	le					Oral Titologo Oral Milidazolatii			

Figure 61 Singh 2002: Induction time [low quality evidence]

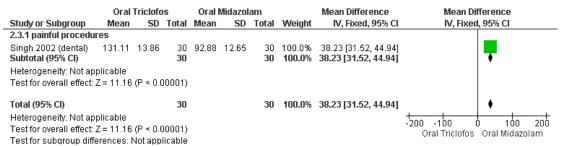


Figure 62 Singh 2002: Recovery time [low quality evidence]

5.3 NITROUS OXIDE

Nitrous oxide vs. behavioural management

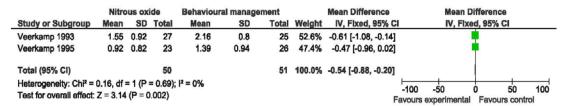


Figure 63 <u>Veerkamp 1993</u>; <u>Veerkamp 1995</u>: Anxiety assessed using the Venham scale [very low quality evidence]

Nitrous oxide vs. oral midazolam

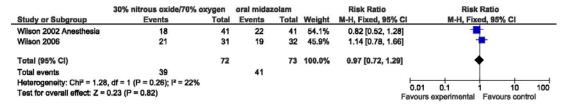


Figure 64 Wilson 2002; Wilson 2006: Patients' preference [moderate quality evidence]

5.4 SEVOFLURANE

COMBINATION COMPARISONS

Sevoflurane + nitrous oxide + intravenous midazolam vs. medical air + intravenous midazolam

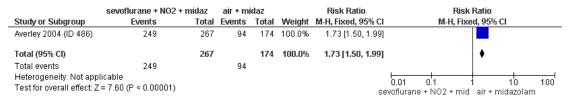


Figure 65 Averley 2004: Completion of procedure [High quality evidence]

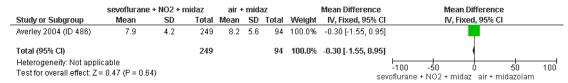


Figure 66 Averley 2004: Recovery time [moderate quality evidence]

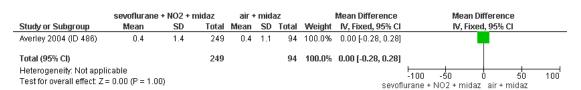


Figure 67 Averley 2004: Pain assessed by children using VAS [moderate quality evidence]

	sevoflurane	+ NO2 + n	nidaz	air +	mida	iz		Mean Difference		Mear	Diffe	егепсе	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fi	xed, 9	95% CI	
Averley 2004 (ID 486)	0.8	1.3	249	0.8	1.3	94	100.0%	0.00 [-0.31, 0.31]					
Total (95% CI)			249			94	100.0%	0.00 [-0.31, 0.31]					
Heterogeneity: Not app Test for overall effect: Z		0)						sevnfl	-100 urane	-50 + NO2 + mic	0 laz a	50 9ir + midaz	100

Figure 68 Averley 2004: Anxiety assessed by children using VAS [moderate quality evidence]

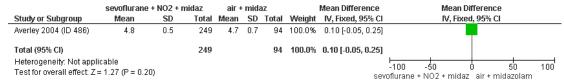


Figure 69 Averley 2004: Parents' satisfaction [moderate quality evidence]

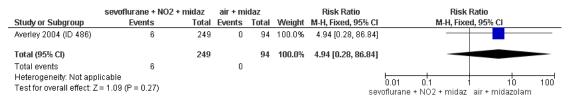


Figure 70 Averley 2004: Vomiting [very low quality evidence]

Sevoflurane + nitrous oxide + intravenous midazolam vs. nitrous oxide + intravenous midazolam

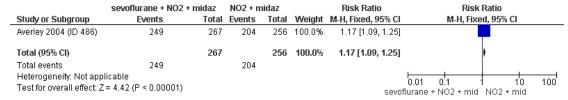


Figure 71 Averley 2004: Completion of procedure [High quality evidence]

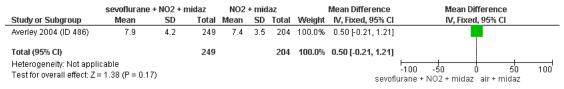


Figure 72 Averley 2004: Recovery time [moderate quality evidence]

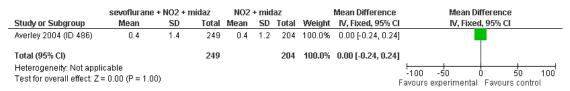


Figure 73 Averley 2004: Pain assessed by children using VAS [moderate quality evidence]

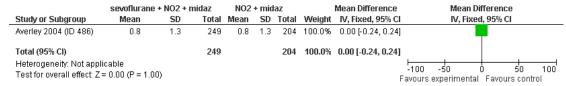


Figure 74 Averley 2004: Anxiety assessed by children using VAS [moderate quality evidence]

sevoflura		+ NO2 + r	nidaz	NO2 + midaz				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C	I IV, Fixed, 95% CI
Averley 2004 (ID 486)	4.8	0.5	249	4.8	0.6	204	100.0%	0.00 [-0.10, 0.10	1
Total (95% CI)			249			204	100.0%	0.00 [-0.10, 0.10	1
Heterogeneity: Not app Test for overall effect: Z))							-100 -50 0 50 100 Favours experimental Favours control

Figure 75 Averley 2004: Parents' satisfaction [moderate quality evidence]

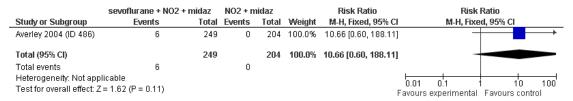


Figure 76 Averley 2004: Vomiting [very low quality evidence]

Sevoflurane + nitrous oxide vs. nitrous oxide

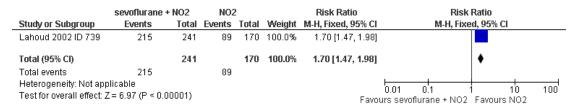


Figure 77 Lahoud 2002: Completion of procedure [moderate quality evidence]

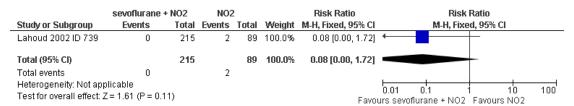


Figure 78 <u>Lahoud 2002</u>: Anxiety (no. of patients) assessed using the Venham scale [very low quality evidence]

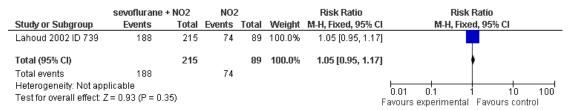


Figure 79 Lahoud 2002: Patients' satisfaction (no. of patients) [low quality evidence]

5.5 PROPOFOL

COMBINATION COMPARISONS

Intravenous propofol + propofol maintenance + local anaesthesia vs. intravenous midazolam + intravenous ketamine + intravenous fentanyl

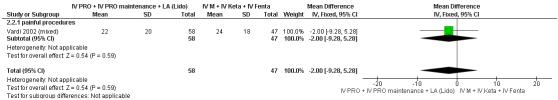


Figure 80 Vardi 2002: Duration of procedure [low quality evidence]

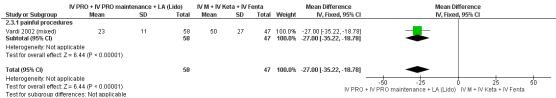


Figure 81 Vardi 2002: Recovery time [low quality evidence]

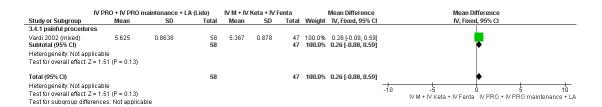


Figure 82 <u>Vardi 2002</u>: Satisfaction at induction period assessed by four observers using the Ramsay scale [very low quality evidence]

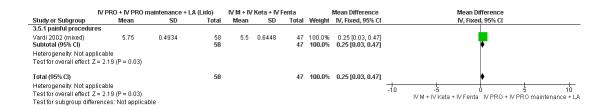


Figure 83 <u>Vardi 2002</u>: Satisfaction scores at sedation period assessed by four observers using the Ramsay scale [very low quality evidence]

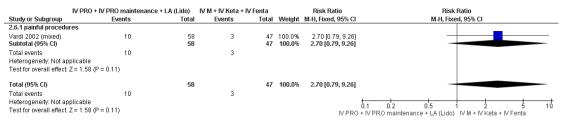


Figure 84 <u>Vardi 2002</u>: Assisted ventilation (bag mask) [very low quality evidence]

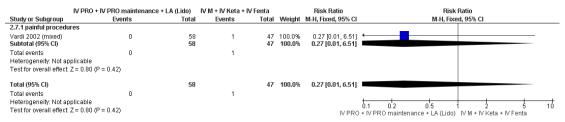


Figure 85 Vardi 2002: Endotracheal intubation [very low quality evidence]

5.6 OPIOIDS

COMBINATION COMPARISONS

Intravenous fentanyl + intravenous propofol versus intravenous propofol + placebo

	IV Fenta + N	/ PRO + 0 ₂	+ TA	Placebo + P	V PRO + 0, +	- TA		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD ²	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
1.4.1 painful procedures									
Cechvala 2008 (lumbarpun) Subtotal (95% CI)	26.36	16.4	22 22	38.86	17.1			-12.50 [-22.40, -2.60] - 12.50 [-22.40, -2.60]	
Heterogeneity: Not applicable Test for overall effect: Z = 2.47	(P = 0.01)								
									-10 -5 0 5 10

Figure 86 <u>Cechvala 2008</u>; <u>Hollman 2008</u>: Recovery time [moderate quality evidence]

	enta + IV PRO +	_	Placebo + IV PRO + (~		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.3.1 painful procedures							
Cechvala 2008 (lumbarpun)	16	21	5	21	100.0%	3.20 [1.44, 7.13]	-
Subtotal (95% CI)		21		21	100.0%	3.20 [1.44, 7.13]	•
Total events	16		5				
Heterogeneity: Not applicable							
Test for overall effect: $Z = 2.84$ (P = 0	1.004)						
Total (95% CI)		21		21	100.0%	3.20 [1.44, 7.13]	-
Total events	16		5				
Heterogeneity: Not applicable							11 12 15 1 2 5
Test for overall effect: Z = 2.84 (P = 0	1.004)						0.1 0.2 0.5 1 2 5 IV PRO + Placebo IV Fenta + IV PR

Figure 87 <u>Cechvala 2008</u>; <u>Hollman 2008</u>: Parents' preference [moderate quality evidence]

P	V Fenta + IV PRO + 0) ₂ + TA	Placebo + IV PRO + 0	D ₂ + TA		Risk Ratio	Risk Ratio
Study or Subgroup	Events	_ Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.5.1 painful procedures							
Cechvala 2008 (lumbarpun)	1	22	1	22	100.0%	1.00 [0.07, 15.00]	· · ·
Subtotal (95% CI)		22		22	100.0%	1.00 [0.07, 15.00]	
Total events	1		1				
Heterogeneity: Not applicable							
Test for overall effect: $Z = 0.00$ (P	= 1.00)						
Total (95% CI)		22		22	100.0%	1.00 [0.07, 15.00]	
Total events	1		1				
Heterogeneity: Not applicable							01 02 05 1 2 5 10
Test for overall effect: $Z = 0.00$ (P	= 1.00)						IVPRO + Placebo IV Fenta + IV PRO

Figure 88 <u>Cechvala 2008</u>; <u>Hollman 2008</u>: Assisted ventilation (assisted ventilation by flow inflating anaesthesia bag) [low quality evidence]

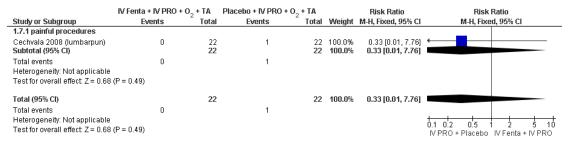


Figure 89 <u>Cechvala 2008</u>; <u>Hollman 2008</u>: Oxygen desaturation [low quality evidence]

	Fenta + IV PRO +	4	Placebo + IV PRO + 0	4		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
1.8.1 painful procedures							
Cechvala 2008 (lumbarpun)	0	22	1	22	100.0%	0.33 [0.01, 7.76]	←
Subtotal (95% CI)		22		22	100.0%	0.33 [0.01, 7.76]	
Total events	0		1				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.68 (P =	0.49)						
Total (95% CI)		22		22	100.0%	0.33 [0.01, 7.76]	
Total events	0		1				
Heterogeneity: Not applicable							1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1
Test for overall effect: Z = 0.68 (P =	= 0.49)						0.1 0.2 0.5 1 2 5

Figure 90 Cechvala 2008; Hollman 2008: Vomiting [low quality evidence]

Intravenous fentanyl + intravenous propofol + topical anaesthesia versus intravenous propofol + topical anaesthesia

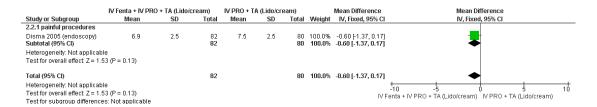


Figure 91 Disma 2005: Duration of procedure [low quality evidence]

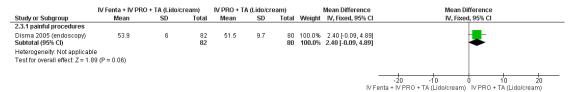


Figure 92 Disma 2005: Recovery time (Aldrete score \geq 8) [low quality evidence]

IV	Fenta + IV PRO + TA (Lid	lo/cream)	IV PRO + TA (Lido/	сгеат)		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
2.5.1 painful procedures							
Disma 2005 (endoscopy) Subtotal (95% CI)	0	82 82	5	80 80	100.0% 100.0 %	0.09 [0.00, 1.58] 0.09 [0.00, 1.58]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.65 (I	0 P = 0.10)		5				
Total (95% CI)		82		80	100.0%	0.09 [0.00, 1.58]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.65 (I	0 P = 0.10)		5			IV F	0.1 0.2 0.5 1 2 5 1

Figure 93 <u>Disma 2005</u>: Assisted ventilation (bag mask) [low quality evidence]

IV	Fenta + IV PRO + TA (Lid	o/cream)	IV PRO + TA (Lido	cream)		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
2.4.1 painful procedures							
Disma 2005 (endoscopy) Subtotal (95% CI)	2	82 82	3	80 80	100.0% 100.0 %	0.65 [0.11, 3.79] 0.65 [0.11, 3.79]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.48 (I	2 P = 0.63)		3				
Total (95% CI)		82		80	100.0%	0.65 [0.11, 3.79]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.48 (I	2 P = 0.63)		3			IV F	0.1 0.2 0.5 1 2 5 10 enta + IV PRO + TA (Lido/cream)

Figure 94 Disma 2005: Oxygen desaturation <90% [low quality evidence]

Intravenous fentanyl + intravenous propofol + topical anaesthesia versus intravenous midazolam + intravenous propofol + topical anaesthesia

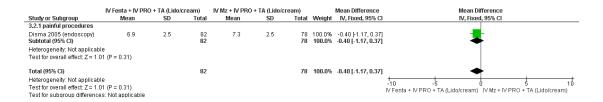


Figure 95 Disma 2005: Duration of procedure [moderate quality evidence]

	IV Fenta + IV PRO	+ TA (Lido/c	ream)	IV Mz + IV PRO	+ TA (Lido/crea	am)		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
3.3.1 painful procedures									
Disma 2005 (endoscopy) Subtotal (95% CI)	53.9	6	82 82	54	8.9			-0.10 [-2.46, 2.26] - 0.10 [-2.46, 2.26]	
Heterogeneity: Not applicab Test for overall effect: Z = 0.0									
									-20 -10 0 10 20 IV Fenta + IV PRO + TA (Lido/cream) IV Mz + IV PRO + TA (Lido/cream)

Figure 96 Disma 2005: Recovery time (Aldrete score \geq 8) [moderate quality evidence]

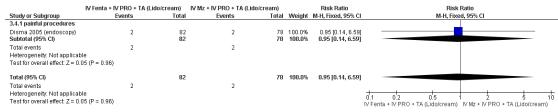


Figure 97 Disma 2005: Oxygen desaturation <90% [very low quality evidence]

Intravenous fentanyl + intravenous midazolam vs. intravenous midazolam + intravenous ketamine

	IV Mid + IV Fe	ntanyl	IV Mid + IV Ke	tamine		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
6.1.1 painful procedures							
Kennedy 1998(orthopaedic)	127	130	129	130	100.0%	0.98 [0.95, 1.01]	
LucasDaSilva 2007(cathet) Subtotal (95% CI)	28	28 158	29	29 159	100.0%	Not estimable 0.98 [0.95, 1.01]	7
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.01			158				
Total (95% CI)		158		159	100.0%	0.98 [0.95, 1.01]	•
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.01			158				0.1 0.2 0.5 1 2 5 10 IV Mid + IV Ketamine IV Mid + IV Fentanyl

Figure 98 <u>LucasDaSilva 2007</u>; <u>Kennedy 199</u>8: Completion of procedure [low quality evidence]

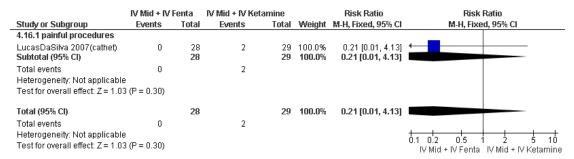


Figure 99 <u>LucasDaSilva 2007</u>: Oxygen desaturation <90% [low quality evidence]

	IV Mid +	IV Fent	anyl	IV Mid +	IV Ketar	nine		Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	
6.5.1 painful procedures										
Kennedy 1998(orthopaedic) Subtotal (95% Cl)	13.4	9.1	130 130	13.1	13.5	130 130	100.0% 100.0 %	0.30 [-2.50, 3.10] 0.30 [-2.50, 3.10]	-	
Heterogeneity: Not applicable Test for overall effect: Z = 0.21 (P = 0.83)									
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.21 (Test for subgroup differences: I		able	130			130	100.0%	0.30 [-2.50, 3.10]	-100 -50 0 IV Mid + IV Fentanyl IV Mid +	50 100 IV Ketamine

Figure 100 Kennedy 1998: Induction time [low quality evidence]

	IV Mid +	· IV Fent	anyl	IV Mid +	IV Keta	mine		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
6.6.1 painful procedures									
Kennedy 1998(orthopaedic) Subtotal (95% CI)	2.7	2.16	130 130	1.08	1.12	130 130	100.0% 100.0 %	1.62 [1.20, 2.04] 1.62 [1.20, 2.04]	, and the second
Heterogeneity: Not applicable Test for overall effect: $Z = 7.59$		001)							
Total (95% CI)			130			130	100.0%	1.62 [1.20, 2.04]	◆
Heterogeneity: Not applicable Test for overall effect: Z = 7.59	(P < 0.000	,							-10 -5 0 5 10 IV Mid + IV Fentanyl IV Mid + IV Ketamine
Test for subgroup differences:	: Not appli	cable							,

Figure 101 Kennedy 1998: Distress assessed by observer using the OBSDR scale [low quality evidence]

	IV Mid +	IV Fent	anyl	IV Mid +	IV Ketai	mine		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
6.7.1 painful procedures									
Kennedy 1998(orthopaedic)	5.49	3.26	130	4.48	3.26	130	100.0%	1.01 [0.22, 1.80]	
Subtotal (95% CI)			130			130	100.0%	1.01 [0.22, 1.80]	•
Heterogeneity: Not applicable									
Test for overall effect: $Z = 2.50$	(P = 0.01)								
Total (95% CI)			130			130	100.0%	1.01 [0.22, 1.80]	*
Heterogeneity: Not applicable									1. 1. 1.
Test for overall effect: Z = 2.50	(P = 0.01)								-10 -5 0 5 10 IV Mid + IV Fentanyl IV Mid + IV Ketamin
Test for subaroup differences:	: Not applic	able							IV MIG * IV FEILLAITH IV MIG * IV KELAITIII

Figure 102 <u>Kennedy 1998</u>: Anxiety assessed by parent using the VAS scale [low quality evidence]

	IV Mid +	V Fent	anyl	IV Mid +	IV Ketar	mine		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
6.8.1 painful procedures									
Kennedy 1998(orthopaedic) Subtotal (95% CI)	5.55	3.33	130 130	4.21	3.3	130 130	100.0% 100.0 %	1.34 [0.53, 2.15] 1.34 [0.53, 2.15]	
Heterogeneity: Not applicable Test for overall effect: Z = 3.26)							
Total (95% CI) Heterogeneity: Not applicable			130			130	100.0%	1.34 [0.53, 2.15]	•
Test for overall effect: Z = 3.26	(P = 0.001								-10 -5 Ö 5 10 IV Mid + IV Fentanyl IV Mid + IV Ketamin

Figure 103 <u>Kennedy 1998</u>: Pain during procedure assessed by parent using the VAS scale [low quality evidence]

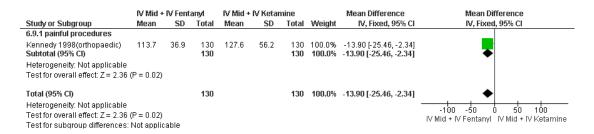


Figure 104 Kennedy 1998: Total time [low quality evidence]

	IV Mid + IV Fe	ntanyl	IV Mid + IV Ket	amine		Risk Ratio	Risk Rat	tio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 9	95% CI
6.15.1 painful procedures								
Kennedy 1998(orthopaedic) Subtotal (95% CI)	31	130 130	8	130 130	100.0% 100.0 %	3.88 [1.85, 8.11] 3.88 [1.85, 8.11]		
Total events Heterogeneity: Not applicable Test for overall effect: Z = 3.60	31 (P = 0.0003)		8					
Total (95% CI)		130		130	100.0%	3.88 [1.85, 8.11]		
Total events Heterogeneity: Not applicable Test for overall effect: Z = 3.60	31 (P = 0.0003)		8				0.1 0.2 0.5 1 IV Mid + IV Fenta IV	2 5 10 Mid + IV Ketamine

Figure 105 Kennedy 1998: Oxygen desaturation <90% [low quality evidence]

	IV Mid + IV Fe	ntanyl	IV Mid + IV Ket	tamine		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
6.11.1 painful procedures							
Kennedy 1998(orthopaedic) Subtotal (95% CI)	0	130 130	2	130 130	100.0% 100.0 %	0.20 [0.01, 4.13] 0.20 [0.01, 4.13]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.04 (0 (P = 0.30)		2				
Total (95% CI)		130		130	100.0%	0.20 [0.01, 4.13]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.04 (0 (P = 0.30)		2				0.1 0.2 0.5 1 2 5 10 IV Mid + IV Fenta IV Mid + IV Ketamir

Figure 106 <u>Kennedy 1998</u>: Assisted ventilation (bag mask) [low quality evidence]

	IV Mid + IV Fer	ntanyl	IV Mid + IV Ket	amine		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
6.13.1 painful procedures							
Kennedy 1998(orthopaedic) Subtotal (95% CI)	0	130 130	1	130 130	100.0% 100.0 %	0.33 [0.01, 8.11] 0.33 [0.01, 8.11]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.67	0 (P = 0.50)		1				
Total (95% CI)		130		130	100.0%	0.33 [0.01, 8.11]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.67	0 (P = 0.50)		1				0.1 0.2 0.5 1 2 5 10 IV Mid + IV Fenta IV Mid + IV Ketamine

Figure 107 Kennedy 1998: Vomiting during procedure [low quality evidence]

I.	/ Mid + IV Fe	ntanyl	IV Mid + IV Ke	tamine		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
6.14.1 painful procedures							
Kennedy 1998(orthopaedic) Subtotal (95% CI)	3	130 130	11	130 130	100.0% 100.0 %	0.27 [0.08, 0.96] 0.27 [0.08, 0.96]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 2.03 (P	3 = 0.04)		11				
Total (95% CI)		130		130	100.0%	0.27 [0.08, 0.96]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 2.03 (P	3 = 0.04)		11				0.1 0.2 0.5 1 2 5 10

Figure 108 Kennedy 1998: Vomiting during recovery [low quality evidence]

Intravenous fentanyl + intravenous propofol + topical anaesthesia versus intravenous propofol + intravenous ketamine + topical anaesthesia

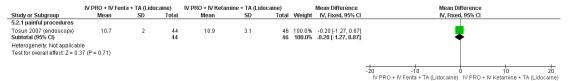


Figure 109 Tosun 2007: Duration of procedure [moderate quality evidence]

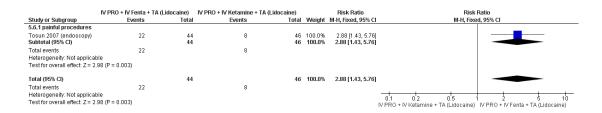


Figure 110 Tosun 2007: Pain (no. of patients) during induction [low quality evidence]

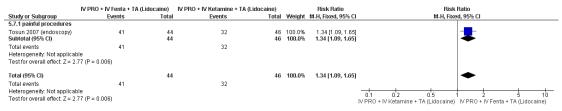


Figure 111 Tosun 2007: Pain (no. of patients) during procedure [low quality evidence]

	IV PRO + IV Fen	ta + TA (Lido	ocaine)	IV PRO + IV Ketai	nine + TA (Lid	locaine)		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
5.3.1 painful procedures									
Tosun 2007 (endoscopy) Subtotal (95% CI)	116.3	28.1	44 44	115.5	29.8	46 46		0.80 [-11.16, 12.76] 0.80 [-11.16, 12.76]	
Heterogeneity: Not applica Test for overall effect: $Z = 0$									
									-20 -10 0 10 20
									IV PRO + IV Fenta + TA (Lidocaine) IV PRO + IV Ketamine + TA (Lidocain

Figure 112 Tosun 2007: Recovery time [low quality evidence]

	IV PRO + IV Fenta + TA (Li	docaine) N	V PRO + IV Ketamine + TA (L	idocaine)		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
5.4.1 painful procedures							_
Tosun 2007 (endoscopy) Subtotal (95% Cl)	4	44 44	3	46 46	100.0% 100.0 %	1.39 [0.33, 5.88] 1.39 [0.33, 5.88]	
Total events Heterogeneity: Not applicabl Test for overall effect: Z = 0.4			3				
Total (95% CI) Total events Heterogeneity: Not applicabl Test for overall effect Z = 0.4		44	3	46	100.0%	1.39 [0.33, 5.88]	01 0.2 0.5 2 5 10 IVPRO+IVFenta+TA (Lidocaine) IVPRO+IV Ketamine + TA (Lidocaine)

Figure 113 Tosun 2007: Oxygen desaturation <90% [low quality evidence]



Figure 114 Tosun 2007: Vomiting [low quality evidence]