Preventing shivering with adjuvant low dose intrathecal meperidine: A meta-analysis of randomized controlled trials with trial sequential analysis.

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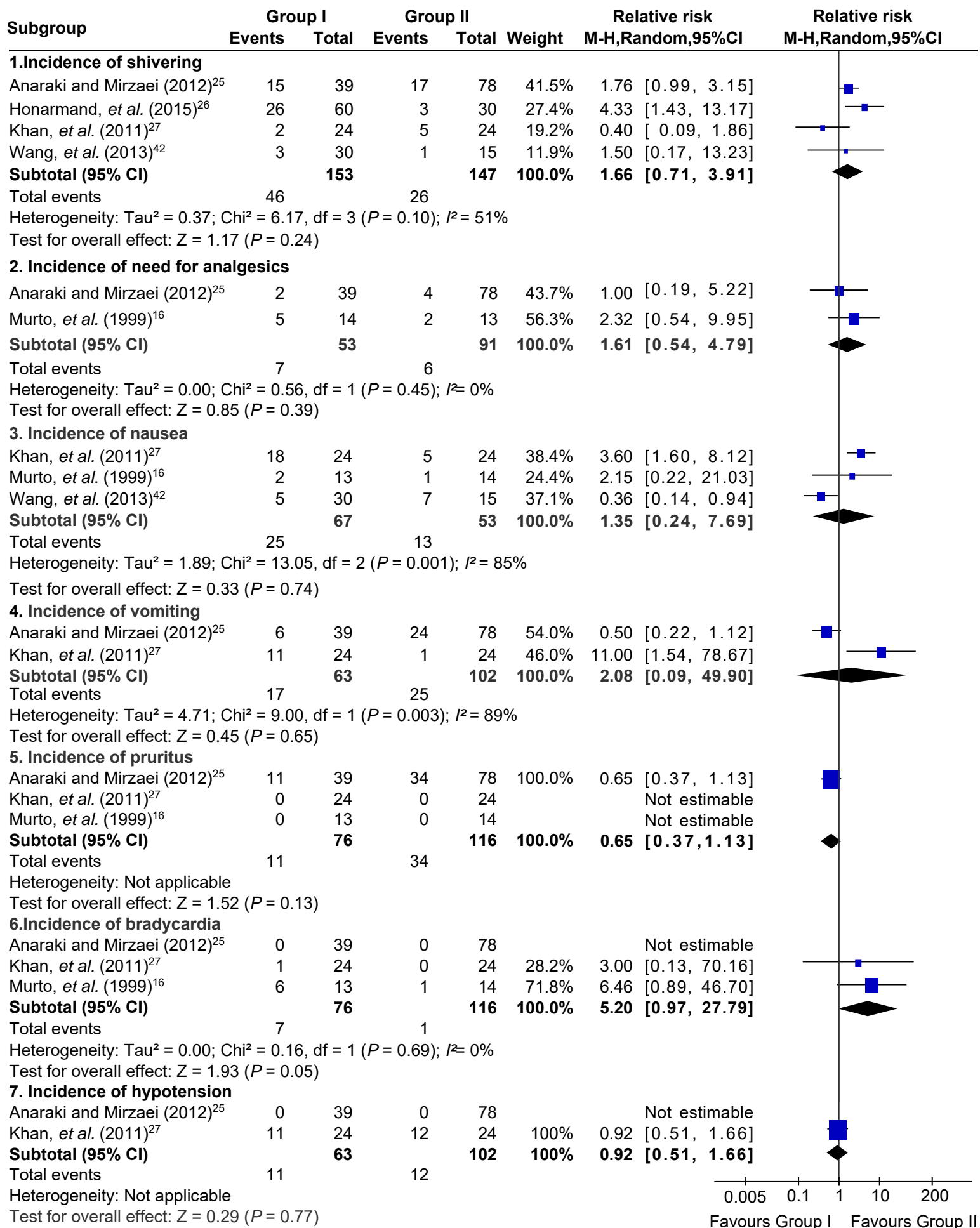Short title: Preventing shivering with adjuvant intrathecal meperidine
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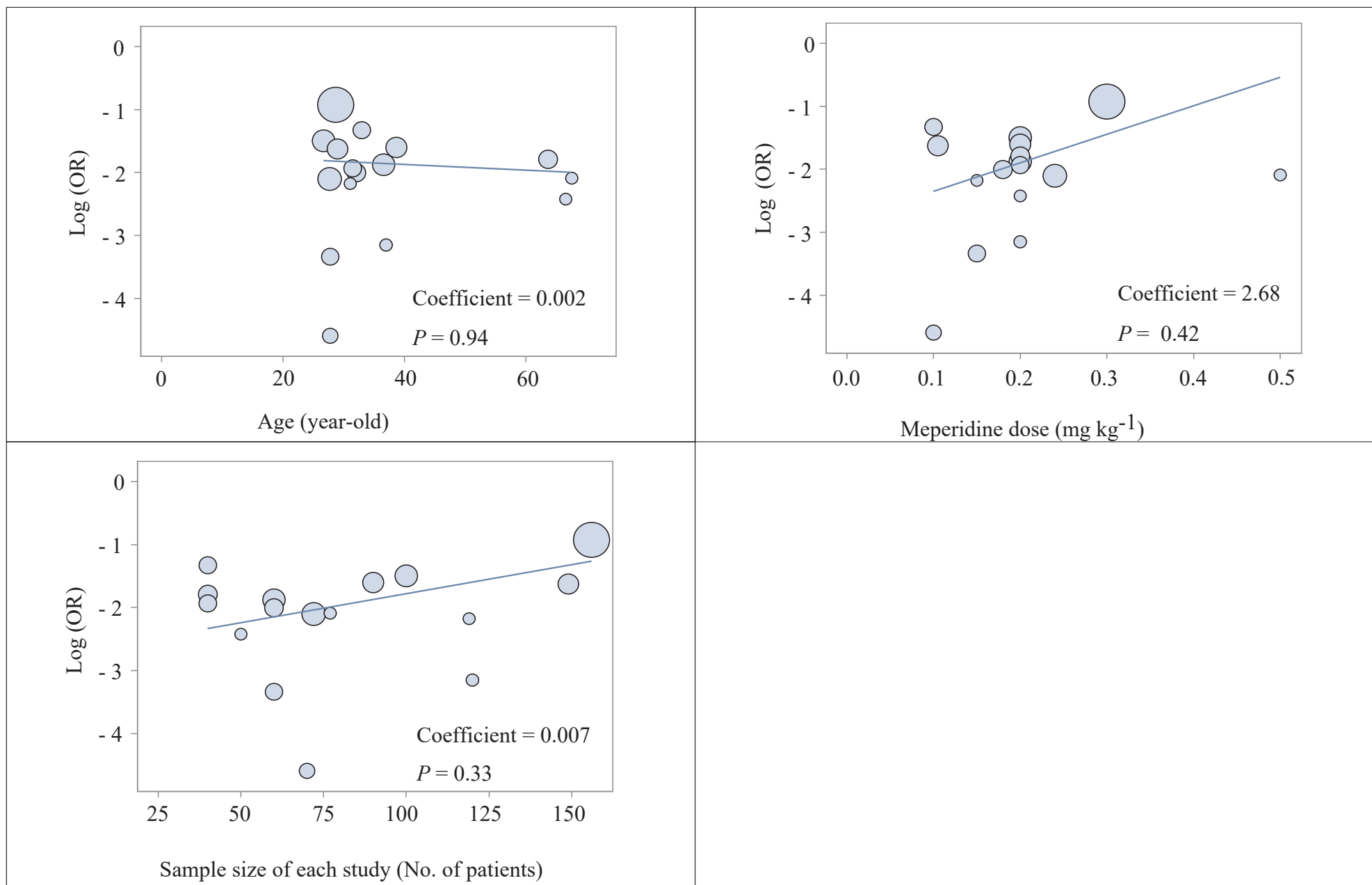Word count for text: 3815 (including Methods)

Supplementary Table 1. Risk of bias of selection randomized controlled trials.

Study (year)	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Anaraki and Mirzaei (2012)[25]	L	U	L	L	L	L	L
Anaraki, *et al.* (2012)[47]	L	L	L	L	L	L	H[a]
Chen, *et al.* (1993)[49]	U	U	L	U	L	L	H[b]
Choi, *et al.* (2000)[53]	U	U	L	U	L	L	L
Chun, *et al.* (2010)[44]	L	U	L	U	L	L	L
Chung, *et al.* (1997)[52]	L	L	L	U	L	L	L
Davoudi, *et al.* (2007)[55]	L	U	L	U	L	L	L
Farzi, *et al.* (2014)[58]	U	U	L	L	L	L	L
Fidan, *et al.* (2008)[45]	U	U	L	L	H	L	L
Fu and Chang (2008)[43]	L	U	L	U	L	L	H[d, g]
Han, *et al.* (2007)[56]	U	U	L	L	L	L	L
Honarmand, *et al.* (2015)[26]	L	L	L	L	L	L	H[c]
Hong and Lee (2005)[28]	L	L	L	L	H	L	H[d, g]
Imarengiaye, *et al.* (2011)[31]	L	L	L	L	L	L	H[e]
Khan, *et al.* (2011)[27]	L	U	L	L	L	L	L
Köroğlu, *et al.* (2003)[50]	U	U	U	U	L	L	L
Murto, *et al.* (1999)[16]	L	U	L	L	L	L	L
Nag and Gode (1984)[54]	U	U	U	U	L	L	L
Rastegarian, *et al.* (2013)[29]	H	L	L	L	L	L	L
Roy, *et al.* (2004)[57]	L	L	L	L	L	L	L
Safavi, *et al.* (2014)[30]	L	L	U	L	L	L	L
Safavi, *et al.* (2014)[46]	L	U	L	L	L	L	U[f]
Shami, *et al.* (2016)[59]	L	L	L	U	L	L	H[a]
Tzeng, *et al.* (1987)[33]	U	U	U	U	L	L	L
Wang, *et al.* (2013)[42]	L	U	L	U	L	L	U[d, g]
Yi, *et al.* (2005)[51]	U	U	U	U	L	L	L
Yu, *et al.* (2002)[32]	L	L	L	U	L	L	L
Zabetian, *et al.* (2013)[48]	L	L	L	L	L	L	L

H, high risk; L, low risk; U, unclear risk; [a] Data error noted in manuscript; [b] Different shivering assessment scale; [c] Data errors noted on table 1; [d] Spinal and epidural anaesthesia combined; [e] Only post-operation shivering assessed; [f] No indication of what kind of shivering assessment scale adopted; [g] Spinal needle size unclear

Subgroup	Group I Events	Total	Group II Events	Total	Weight	Relative risk M-H,Random,95%CI	Relative risk M-H,Random,95%CI
1.Incidence of shivering							
Anaraki and Mirzaei (2012)[25]	15	39	17	78	41.5%	1.76 [0.99, 3.15]	
Honarmand, et al. (2015)[26]	26	60	3	30	27.4%	4.33 [1.43, 13.17]	
Khan, et al. (2011)[27]	2	24	5	24	19.2%	0.40 [0.09, 1.86]	
Wang, et al. (2013)[42]	3	30	1	15	11.9%	1.50 [0.17, 13.23]	
Subtotal (95% CI)		153		147	100.0%	1.66 [0.71, 3.91]	
Total events	46		26				

Heterogeneity: Tau² = 0.37; Chi² = 6.17, df = 3 (P = 0.10); I^2 = 51%
Test for overall effect: Z = 1.17 (P = 0.24)

Subgroup	Group I Events	Total	Group II Events	Total	Weight	Relative risk M-H,Random,95%CI	
2. Incidence of need for analgesics							
Anaraki and Mirzaei (2012)[25]	2	39	4	78	43.7%	1.00 [0.19, 5.22]	
Murto, et al. (1999)[16]	5	14	2	13	56.3%	2.32 [0.54, 9.95]	
Subtotal (95% CI)		53		91	100.0%	1.61 [0.54, 4.79]	
Total events	7		6				

Heterogeneity: Tau² = 0.00; Chi² = 0.56, df = 1 (P = 0.45); I^2 = 0%
Test for overall effect: Z = 0.85 (P = 0.39)

Subgroup	Group I Events	Total	Group II Events	Total	Weight	Relative risk M-H,Random,95%CI	
3. Incidence of nausea							
Khan, et al. (2011)[27]	18	24	5	24	38.4%	3.60 [1.60, 8.12]	
Murto, et al. (1999)[16]	2	13	1	14	24.4%	2.15 [0.22, 21.03]	
Wang, et al. (2013)[42]	5	30	7	15	37.1%	0.36 [0.14, 0.94]	
Subtotal (95% CI)		67		53	100.0%	1.35 [0.24, 7.69]	
Total events	25		13				

Heterogeneity: Tau² = 1.89; Chi² = 13.05, df = 2 (P = 0.001); I^2 = 85%
Test for overall effect: Z = 0.33 (P = 0.74)

Subgroup	Group I Events	Total	Group II Events	Total	Weight	Relative risk M-H,Random,95%CI	
4. Incidence of vomiting							
Anaraki and Mirzaei (2012)[25]	6	39	24	78	54.0%	0.50 [0.22, 1.12]	
Khan, et al. (2011)[27]	11	24	1	24	46.0%	11.00 [1.54, 78.67]	
Subtotal (95% CI)		63		102	100.0%	2.08 [0.09, 49.90]	
Total events	17		25				

Heterogeneity: Tau² = 4.71; Chi² = 9.00, df = 1 (P = 0.003); I^2 = 89%
Test for overall effect: Z = 0.45 (P = 0.65)

Subgroup	Group I Events	Total	Group II Events	Total	Weight	Relative risk M-H,Random,95%CI	
5. Incidence of pruritus							
Anaraki and Mirzaei (2012)[25]	11	39	34	78	100.0%	0.65 [0.37, 1.13]	
Khan, et al. (2011)[27]	0	24	0	24		Not estimable	
Murto, et al. (1999)[16]	0	13	0	14		Not estimable	
Subtotal (95% CI)		76		116	100.0%	0.65 [0.37, 1.13]	
Total events	11		34				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.52 (P = 0.13)

Subgroup	Group I Events	Total	Group II Events	Total	Weight	Relative risk M-H,Random,95%CI	
6.Incidence of bradycardia							
Anaraki and Mirzaei (2012)[25]	0	39	0	78		Not estimable	
Khan, et al. (2011)[27]	1	24	0	24	28.2%	3.00 [0.13, 70.16]	
Murto, et al. (1999)[16]	6	13	1	14	71.8%	6.46 [0.89, 46.70]	
Subtotal (95% CI)		76		116	100.0%	5.20 [0.97, 27.79]	
Total events	7		1				

Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I^2 = 0%
Test for overall effect: Z = 1.93 (P = 0.05)

Subgroup	Group I Events	Total	Group II Events	Total	Weight	Relative risk M-H,Random,95%CI	
7. Incidence of hypotension							
Anaraki and Mirzaei (2012)[25]	0	39	0	78		Not estimable	
Khan, et al. (2011)[27]	11	24	12	24	100%	0.92 [0.51, 1.66]	
Subtotal (95% CI)		63		102	100%	0.92 [0.51, 1.66]	
Total events	11		12				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.29 (P = 0.77)

0.005 0.1 1 10 200
Favours Group I   Favours Group II

Supplementary Figure 1. Comparing dose equal to or less than 0.2 mg kg^{-1} or 12.5 mg (Group I) and dose more than 0.2 mg kg^{-1} or 12.5 mg (Group II) of adjuvant intrathecal meperidine in incidence of shivering and secondary outcomes.

Supplementary Figure 2. Meta-regression of shivering for covariates of age, meperidine dose, and sample size of each study.