Comparison 2: Single-dose oral analgesic compared with a higher single dose of the same analgesic

Comparison 2a(i): Single-dose aspirin compared with a higher single dose of aspirin (300 mg versus 600 mg)

Source: Shepherd E, Grivell RM. Aspirin (single dose) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2020;(7):CD012129.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	300 mg aspirin single dose	600 mg aspirin single dose	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief as reported by the woman												
1	randomized trials	very serious [a]	not serious	not serious	very serious [b,c]	none	8/40 (20.0%)	10/41 (24.4%)	**RR 0.82** (0.36 to 1.86)	**44 fewer per 1000** (from 156 fewer to 210 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Need for additional pain relief												
1	randomized trials	very serious [a]	not serious	not serious	very serious [b,c]	none	2/40 (5.0%)	3/41 (7.3%)	**RR 0.68** (0.12 to 3.88)	**23 fewer per 1000** (from 64 fewer to 211 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Maternal adverse effects												
1	randomized trials	very serious [a]	not serious	not serious	very serious [d,e]	none	0/40 (0.0%)	0/41 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	IMPORTANT

CI: confidence interval; RR: risk ratio.
a. All of the pooled effect provided by study "C".
b. Wide confidence interval crossing the line of no effect.
c. Less than 300 women and less than 30 events.
d. No events.
e. Less than 300 women.

Comparison 2a(ii): Single-dose aspirin compared with a higher single dose of aspirin (600 mg versus 1200 mg)

Source: Shepherd E, Grivell RM. Aspirin (single dose) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2020;(7):CD012129.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	600 mg aspirin single dose	1200 mg aspirin single dose	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief as reported by the woman												
2	randomized trials	very serious [a]	not serious	serious [b]	very serious [c,d]	none	19/61 (31.1%)	22/60 (36.7%)	**RR 0.85** (0.52 to 1.39)	**55 fewer per 1000** (from 176 fewer to 143 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Need for additional pain relief												
2	randomized trials	very serious [a]	not serious	serious [b]	very serious [c,d,e]	none	4/61 (6.6%)	3/60 (5.0%)	**RR 1.32** (0.30 to 5.68)	**16 more per 1000** (from 35 fewer to 234 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Maternal adverse effects												
2	randomized trials	very serious [a]	not serious	serious [b]	very serious [c,d,e]	none	1/61 (1.6%)	0/60 (0.0%)	**RR 3.00** (0.13 to 69.52)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: confidence interval; RR: risk ratio.
a. All of the pooled effect provided by studies "C".
b. One of the studies reporting this outcome excluded breastfeeding women – thus the data cannot be extrapolated to all women during postnatal period.
c. Wide confidence interval crossing the line of no effect.
d. Less than 300 women.
e. Few events.

Comparison 2a(iii): Single-dose aspirin compared with a higher single dose of aspirin (300 mg versus 1200 mg)

Source: Shepherd E, Grivell RM. Aspirin (single dose) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2020;(7):CD012129.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	300 mg aspirin single dose	1200 mg aspirin single dose	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief as reported by the woman												
1	randomized trials	very serious [a]	not serious	not serious	very serious [b,c]	none	8/40 (20.0%)	13/40 (32.5%)	**RR 0.62** (0.29 to 1.32)	**124 fewer per 1000** (from 231 fewer to 104 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Need for additional pain relief												
1	randomized trials	very serious [a]	not serious	not serious	very serious [b,c]	none	2/40 (5.0%)	1/40 (2.5%)	**RR 2.00** (0.19 to 21.18)	**25 more per 1000** (from 20 fewer to 505 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Maternal adverse effects												
1	randomized trials	very serious [a]	not serious	not serious	very serious [d]		0/40 (0.0%)	0/40 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	IMPORTANT

CI: confidence interval; RR: risk ratio.
a. All of the pooled effect provided by study "C".
b. Wide confidence interval crossing the line of no effect.
c. Less than 300 women and few events.
d. No events.

Comparison 2b: Single-dose NSAID compared with a higher single dose of the same NSAID

Source: Wuytack F, Smith V, Cleary BJ. Oral non-steroidal anti-inflammatory drugs (single-dose) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2021;(1):CD011352.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 hours after administration) – ibuprofen 300–400 mg (A) vs ibuprofen 800 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	25/80 (31.3%)	25/80 (31.3%)	**RR 1.00** (0.63 to 1.58)	**0 fewer per 1000** (from 116 fewer to 181 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 250 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	12/33 (36.4%)	9/30 (30.0%)	**RR 1.21** (0.60 to 2.46)	**63 more per 1000** (from 120 fewer to 438 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	12/33 (36.4%)	14/30 (46.7%)	**RR 0.78** (0.43 to 1.41)	**103 fewer per 1000** (from 266 fewer to 191 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diflunisal 250 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	9/30 (30.0%)	14/30 (46.7%)	**RR 0.64** (0.33 to 1.25)	**168 fewer per 1000** (from 313 fewer to 117 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – meclofenamate sodium 100 mg (A) vs meclofenamate sodium 200 mg (B)												
3	randomized trials	serious [a]	not serious	not serious	not serious	none	110/173 (63.6%)	112/175 (64.0%)	**RR 1.00** (0.85 to 1.17)	**0 fewer per 1000** (from 96 fewer to 109 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Adequate pain relief (4 hours after administration) – diclofenac 25 mg (A) vs diclofenac 50 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c]	none	32/52 (61.5%)	34/50 (68.0%)	**RR 0.90** (0.68 to 1.21)	**68 fewer per 1000** (from 218 fewer to 143 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 hours after administration) – diclofenac 25 mg (A) vs diclofenac 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c]	none	32/52 (61.5%)	37/51 (72.5%)	**RR 0.85** (0.65 to 1.11)	**109 fewer per 1000** (from 254 fewer to 80 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – ketoprofen 25 mg (A) vs ketoprofen 50 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c]	none	20/28 (71.4%)	18/26 (69.2%)	**RR 1.03** (0.73 to 1.46)	**21 more per 1000** (from 187 fewer to 318 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 100 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	12/18 (66.7%)	16/24 (66.7%)	**RR 1.00** (0.65 to 1.54)	**0 fewer per 1000** (from 233 fewer to 360 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 150 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	12/18 (66.7%)	17/21 (81.0%)	**RR 0.82** (0.56 to 1.21)	**146 fewer per 1000** (from 356 fewer to 170 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aceclofenac 100 mg (A) vs aceclofenac 150 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	16/24 (66.7%)	17/21 (81.0%)	**RR 0.82** (0.58 to 1.17)	**146 fewer per 1000** (from 340 fewer to 138 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c,d]	none	11/32 (34.4%)	15/29 (51.7%)	**RR 0.66** (0.37 to 1.20)	**176 fewer per 1000** (from 326 fewer to 103 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c,d]	none	11/32 (34.4%)	15/31 (48.4%)	**RR 0.71** (0.39 to 1.30)	**140 fewer per 1000** (from 295 fewer to 145 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 after administration) – flurbiprofen 50 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c]	none	15/29 (51.7%)	15/31 (48.4%)	**RR 1.07** (0.64 to 1.77)	**34 more per 1000** (from 174 fewer to 373 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – ibuprofen 300–400 mg (A) vs ibuprofen 900 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c]	none	17/20 (85.0%)	17/20 (85.0%)	**RR 1.00** (0.77 to 1.30)	**0 fewer per 1000** (from 195 fewer to 255 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – diflunisal 125 mg (A) vs diflunisal 250 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	13/33 (39.4%)	10/30 (33.3%)	**RR 1.18** (0.61 to 2.29)	**60 more per 1000** (from 130 fewer to 430 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – diflunisal 125 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	13/33 (39.4%)	16/30 (53.3%)	**RR 0.74** (0.43 to 1.27)	**139 fewer per 1000** (from 304 fewer to 144 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – diflunisal 250 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	10/30 (33.3%)	16/30 (53.3%)	**RR 0.63** (0.34 to 1.15)	**197 fewer per 1000** (from 352 fewer to 80 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – meclofenamate sodium 100 mg (A) vs meclofenamate sodium 200 mg (B)												
3	randomized trials	serious [a]	not serious	not serious	not serious	none	103/173 (59.5%)	105/175 (60.0%)	**RR 1.00** (0.84 to 1.18)	**0 fewer per 1000** (from 96 fewer to 108 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Adequate pain relief (6 hours after administration) – ketoprofen 25 mg (A) vs ketoprofen 50 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c]	none	18/28 (64.3%)	17/26 (65.4%)	**RR 0.98** (0.66 to 1.46)	**13 fewer per 1000** (from 222 fewer to 301 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 100 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	14/18 (77.8%)	20/24 (83.3%)	**RR 0.93** (0.69 to 1.27)	**58 fewer per 1000** (from 258 fewer to 225 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 150 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	14/18 (77.8%)	19/21 (90.5%)	**RR 0.86** (0.65 to 1.14)	**127 fewer per 1000** (from 317 fewer to 127 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aceclofenac 100 mg (A) vs aceclofenac 150 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	20/24 (83.3%)	19/21 (90.5%)	**RR 0.92** (0.73 to 1.16)	**72 fewer per 1000** (from 244 fewer to 145 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – etodolac 25 mg (A) vs etodolac 100 mg (B)												
1	randomized trials	serious [a]	not serious	serious [e]	very serious [b,c,d]	none	11/40 (27.5%)	15/40 (37.5%)	**RR 0.73** (0.39 to 1.39)	**101 fewer per 1000** (from 229 fewer to 146 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c]	none	13/32 (40.6%)	18/29 (62.1%)	**RR 0.65** (0.39 to 1.09)	**217 fewer per 1000** (from 379 fewer to 56 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c]	none	13/32 (40.6%)	19/31 (61.3%)	**RR 0.66** (0.40 to 1.10)	**208 fewer per 1000** (from 368 fewer to 61 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – flurbiprofen 50 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c]	none	18/29 (62.1%)	19/31 (61.3%)	**RR 1.01** (0.68 to 1.51)	**6 more per 1000** (from 196 fewer to 313 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – fenoprofen 50 mg (A) vs fenoprofen 100 mg (B)												
2	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c]	none	28/50 (56.0%)	33/50 (66.0%)	**RR 0.85** (0.62 to 1.16)	**99 fewer per 1000** (from 251 fewer to 106 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 50 mg (A) vs fenoprofen 200 mg (B)												
2	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c]	none	28/50 (56.0%)	32/49 (65.3%)	**RR 0.86** (0.62 to 1.17)	**91 fewer per 1000** (from 248 fewer to 111 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 50 mg (A) vs fenoprofen 300 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c]	none	17/27 (63.0%)	19/27 (70.4%)	**RR 0.89** (0.61 to 1.31)	**77 fewer per 1000** (from 274 fewer to 218 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 100 mg (A) vs fenoprofen 200 mg (B)												
2	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c]	none	33/50 (66.0%)	32/49 (65.3%)	**RR 1.01** (0.76 to 1.34)	**7 more per 1000** (from 157 fewer to 222 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 100 mg (A) vs fenoprofen 300 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c]	none	19/26 (73.1%)	19/27 (70.4%)	**RR 1.04** (0.74 to 1.46)	**28 more per 1000** (from 183 fewer to 324 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 200 mg (A) vs fenoprofen 300 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c]	none	19/26 (73.1%)	19/27 (70.4%)	**RR 1.04** (0.74 to 1.46)	**28 more per 1000** (from 183 fewer to 324 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 12.5 mg (A) vs fenoprofen 25 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c,d]	none	10/24 (41.7%)	11/23 (47.8%)	**RR 0.87** (0.46 to 1.65)	**62 fewer per 1000** (from 258 fewer to 311 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – fenoprofen 12.5 mg (A) vs fenoprofen 50 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c,d]	none	10/24 (41.7%)	11/23 (47.8%)	**RR 0.87** (0.46 to 1.65)	**62 fewer per 1000** (from 258 fewer to 311 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 12.5 mg (A) vs fenoprofen 100 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c,d]	none	10/24 (41.7%)	15/23 (65.2%)	**RR 0.64** (0.37 to 1.12)	**235 fewer per 1000** (from 411 fewer to 78 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 12.5 mg (A) vs fenoprofen 200 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c,d]	none	10/24 (41.7%)	13/23 (56.5%)	**RR 0.74** (0.41 to 1.33)	**147 fewer per 1000** (from 333 fewer to 187 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 25 mg (A) vs fenoprofen 50 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c,d]	none	11/23 (47.8%)	11/23 (47.8%)	**RR 1.00** (0.55 to 1.83)	**0 fewer per 1000** (from 215 fewer to 397 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 25 mg (A) vs fenoprofen 100 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c,d]	none	11/23 (47.8%)	15/23 (65.2%)	**RR 0.73** (0.44 to 1.23)	**176 fewer per 1000** (from 365 fewer to 150 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 25 mg (A) vs fenoprofen 200 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [b,c,d]	none	11/23 (47.8%)	13/23 (56.5%)	**RR 0.85** (0.48 to 1.48)	**85 fewer per 1000** (from 294 fewer to 271 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (4 hours after administration) – ibuprofen 300–400 mg (A) vs ibuprofen 800 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	4/80 (5.0%)	7/80 (8.8%)	**RR 0.57** (0.17 to 1.88)	**38 fewer per 1000** (from 73 fewer to 77 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Need for additional analgesia (6 hours after administration) – ibuprofen 300–400 mg (A) vs ibuprofen 900 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c,d]	none	1/20 (5.0%)	0/20 (0.0%)	**RR 3.00** (0.13 to 69.52)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – meclofenamate sodium 100 mg (A) vs meclofenamate sodium 200 mg (B)												
2	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	22/96 (22.9%)	24/95 (25.3%)	**RR 0.91** (0.55 to 1.50)	**23 fewer per 1000** (from 114 fewer to 126 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c,d]	none	1/32 (3.1%)	0/29 (0.0%)	**RR 2.73** (0.12 to 64.42)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c,d]	none	1/32 (3.1%)	0/31 (0.0%)	**RR 2.91** (0.12 to 68.81)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – flurbiprofen 50 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [c,g]	none	0/29 (0.0%)	0/31 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 250 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,g]	none	0/33 (0.0%)	0/30 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,g]	none	0/33 (0.0%)	0/30 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – diflunisal 250 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,g]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Maternal drug adverse effects (4 hours after administration) – ibuprofen 300–400 mg (A) vs ibuprofen 800 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,g]	none	0/80 (0.0%)	0/80 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – ibuprofen 300 mg (A) vs ibuprofen 900 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [b,c,d]	none	3/20 (15.0%)	3/20 (15.0%)	**RR 1.00** (0.23 to 4.37)	**0 fewer per 1000** (from 115 fewer to 505 more)	⨁◯◯◯ VERY LOW	-
Maternal drug adverse effects (6 hours after administration) – diflunisal 125 mg (A) vs diflunisal 250 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,g]	none	0/33 (0.0%)	0/30 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – diflunisal 125 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,g]	none	0/33 (0.0%)	0/30 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – diflunisal 250 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,g]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – ketoprofen 25 mg (A) vs ketoprofen 50 mg (B)												
1	randomized trials	very serious [f]	not serious	serious [e]	very serious [c,g]	none	0/28 (0.0%)	0/26 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 100 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	1/18 (5.6%)	0/24 (0.0%)	**RR 3.95** (0.17 to 91.61)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 150 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c,d]	none	1/18 (5.6%)	0/21 (0.0%)	**RR 3.47** (0.15 to 80.35)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% CI)		
Maternal drug adverse effects (6 hours after administration) – aceclofenac 100 mg (A) vs aceclofenac 150 mg (B)												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,g]	none	0/24 (0.0%)	0/21 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [c,g]	none	0/32 (0.0%)	0/29 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [c,g]	none	0/32 (0.0%)	0/31 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – flurbiprofen 50 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [e]	very serious [c,g]	none	0/29 (0.0%)	0/31 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio.
a. Most of the pooled effect provided by studies “B” or “C” but without a substantial proportion (i.e. < 50%) from studies “C”.
b. Wide confidence interval crossing the line of no effect.
c. Less than 300 participants.
d. Few events.
e. Some studies included in this outcome excluded breastfeeding women – the evidence cannot be extrapolated to all women during the postpartum period.
f. Most of the pooled effect provided by studies “B” or “C” but with a substantial proportion (i.e. > 50%) from studies “C”.
g. No events.