# 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 as	sessment			Nº of p	atients	l	Effect		
2 of dies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	300 mg aspirin single dose	600 mg aspirin single dose	Relative (95% Cl)	Absolute (95% Cl)	Certainty (GRADE)	Importance

## Adequate pain relief as reported by the woman

1	randomized very trials seriou	,	not serious	very serious <sup>b,c</sup>	none	8/40 (20.0%)	10/41 (24.4%)	<b>RR 0.82</b> (0.36 to 1.86)	<b>44 fewer per 1000</b> (from 156 fewer to 210 more)	⊕○○○ VERY LOW	IMPORTANT	
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## Need for additional pain relief

1 rai	randomized trials	very serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c</sup>	none	2/40 (5.0%)	3/41 (7.3%)	<b>RR 0.68</b> (0.12 to 3.88)	<b>23 fewer per 1000</b> (from 64 fewer to 211 more)	⊕○○○ VERY LOW	IMPORTANT
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## Maternal adverse effects

1		very not serious	not serious	very serious <sup>d,e</sup>	none	0/40 (0.0%)	0/41 (0.0%)	not estimable	-	⊕⊖⊖⊖ VERY LOW	IMPORTANT
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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 ass	sessment			Nº of p	atients	E	iffect		
l⁰ of udies	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% Cl)	Certainty (GRADE)	Importance

Adequate pain relief as reported by the woman

2	randomized trials	very serious <sup>a</sup>	not serious	serious <sup>b</sup>	very serious <sup>c,d</sup>	none	19/61 (31.1%)	22/60 (36.7%)		<b>55 fewer per 1000</b> (from 176 fewer to	 IMPORTANT
									(,	143 more)	

### Need for additional pain relief

2	randomized trials	very serious <sup>a</sup>	not serious	serious <sup>b</sup>	very serious <sup>c,d,e</sup>	none	4/61 (6.6%)	3/60 (5.0%)	<b>RR 1.32</b> (0.30 to 5.68)	<b>16 more per 1000</b> (from 35 fewer to 234 more)	⊕○○○ VERY LOW	IMPORTANT	
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## Maternal adverse effects

2	randomized trials	very serious <sup>a</sup>	not serious	serious <sup>b</sup>	very serious <sup>c,d,e</sup>	none	1/61 (1.6%)	0/60 (0.0%)	<b>RR 3.00</b> (0.13 to 69.52)	<b>0 fewer per 1000</b> (from 0 fewer to 0 fewer)	⊕○○○ VERY LOW	IMPORTANT
									69.52)	tewer)		

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 asse	essment			Nº of p	atients		Effect		
Nº 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% Cl)	Certainty (GRADE)	Importance
Adequat	e pain relief as	reported by th	e woman									1

104 more)	1	randomized trials	very serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c</sup>	none	8/40 (20.0%)	13/40 (32.5%)	<b>RR 0.62</b> (0.29 to 1.32)	<b>124 fewer per 1000</b> (from 231 fewer to 104 more)	⊕○○○ VERY LOW	IMPORTANT	
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## Need for additional pain relief

1	randomized trials	very serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c</sup>	none	2/40 (5.0%)	1/40 (2.5%)	<b>RR 2.00</b> (0.19 to 21.18)	<b>25 more per 1000</b> (from 20 fewer to 505 more)	⊕○○○ VERY LOW	IMPORTANT	
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## Maternal adverse effects

1	randomized trials	very serious <sup>a</sup>	not serious	not serious	very serious <sup>d</sup>		0/40 (0.0%)	0/40 (0.0%)	not estimable	-	⊕⊖⊖⊖ VERY LOW	IMPORTANT	
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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 as	sessment			Nº of p	atients		Effect		
I	Nº 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% Cl)	Certainty (GRADE)	Importance

## Adequate pain relief (4 hours after administration) – ibuprofen 300–400 mg (A) vs ibuprofen 800 mg (B)

1	randomized	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c</sup>	none	25/80 (31.3%)	25/80 (31.3%)	RR 1.00	0 fewer per 1000	⊕000	CRITICAL
	trials								(0.63 to 1.58)	(from 116 fewer to	VERY LOW	
										181 more)		

### Adequate pain relief (4 hours after administration) - diflunisal 125 mg (A) vs diflunisal 250 mg (B)

1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	12/33 (36.4%)	9/30 (30.0%)	<b>RR 1.21</b> (0.60 to 2.46)	<b>63 more per 1000</b> (from 120 fewer to 438 more)	⊕○○○ VERY LOW	CRITICAL
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## Adequate pain relief (4 hours after administration) - diflunisal 125 mg (A) vs diflunisal 500 mg (B)

1	randomized	serious <sup>a</sup>	not serious	not serious	very serious b,c,d	none	12/33 (36.4%)	14/30 (46.7%)	RR 0.78	103 fewer per 1000	⊕000	CRITICAL
	trials								(0.43 to 1.41)	(from 266 fewer to	VERY LOW	
										191 more)		

## Adequate pain relief (4 hours after administration) - diflunisal 250 mg (A) vs diflunisal 500 mg (B)

1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	9/30 (30.0%)	14/30 (46.7%)	<b>RR 0.64</b> (0.33 to 1.25)	<b>168 fewer per 1000</b> (from 313 fewer to	⊕OOO VERY LOW	CRITICAL
										117 more)		

#### Adequate pain relief (4 hours after administration) - meclofenamate sodium 100 mg (A) vs meclofenamate sodium 200 mg (B)

3 randomized serious <sup>a</sup> no trials	ot serious not serious	not serious	none	110/173 (63.6%)	112/175 (64.0%)	<b>RR 1.00</b> (0.85 to 1.17)	<b>0 fewer per 1000</b> (from 96 fewer to 109 more)	⊕⊕⊕⊖ MODERATE	CRITICAL
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## Adequate pain relief (4 hours after administration) - diclofenac 25 mg (A) vs diclofenac 50 mg (B)

1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	32/52 (61.5%)	34/50 (68.0%)	<b>RR 0.90</b> (0.68 to 1.21)	<b>68 fewer per 1000</b> (from 218 fewer to	⊕OOO VERY LOW	CRITICAL
										143 more)		

			Certainty as	sessment			Nº of p	atients		Effect		
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% Cl)	Absolute (95% Cl)	Certainty (GRADE)	Importance
Adequate	e pain relief (4	hours after ad	lministration) –	diclofenac 25 n	ng (A) vs diclofena	c 100 mg (B)						
1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	32/52 (61.5%)	37/51 (72.5%)	<b>RR 0.85</b> (0.65 to 1.11)	<b>109 fewer per 1000</b> (from 254 fewer to	⊕⊖⊖⊖ VERY LOW	CRITICAL

1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	20/28 (71.4%)	18/26 (69.2%)	<b>RR 1.03</b> (0.73 to 1.46)	<b>21 more per 1000</b> (from 187 fewer to 318 more)	⊕○○○ VERY LOW	CRITICAL
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## Adequate pain relief (4 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 100 mg (B)

1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	12/18 (66.7%)	16/24 (66.7%)	<b>RR 1.00</b> (0.65 to 1.54)	<b>0 fewer per 1000</b> (from 233 fewer to 360 more)	⊕○○○ VERY LOW	CRITICAL
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#### Adequate pain relief (4 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 150 mg (B)

1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	12/18 (66.7%)	17/21 (81.0%)	<b>RR 0.82</b> (0.56 to 1.21)	<b>146 fewer per 1000</b> (from 356 fewer to 170 more)	⊕○○○ VERY LOW	CRITICAL
	triais								(0.50 (0 1.21)	170 more)		

## Adequate pain relief (4 hours after administration) - aceclofenac 100 mg (A) vs aceclofenac 150 mg (B)

138 more)		1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c</sup>	none	16/24 (66.7%)	17/21 (81.0%)	<b>RR 0.82</b> (0.58 to 1.17)	<b>146 fewer per 1000</b> (from 340 fewer to 138 more)	⊕OOO VERY LOW	CRITICAL
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## Adequate pain relief (4 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)

ſ	1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	11/32 (34.4%)	15/29 (51.7%)	<b>RR 0.66</b> (0.37 to 1.20)	<b>176 fewer per 1000</b> (from 326 fewer to	⊕OOO VERY LOW	CRITICAL
											103 more)		

## Adequate pain relief (4 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)

1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	11/32 (34.4%)	15/31 (48.4%)	<b>RR 0.71</b> (0.39 to 1.30)		⊕⊖⊖⊖ VERY LOW	CRITICAL
										145 more)		

			Certainty as	sessment			Nº of p	atients		Effect		
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% Cl)	Absolute (95% Cl)	Certainty (GRADE)	Importance
Adequat	e pain relief (4	after administ	tration) – flurbip	orofen 50 mg (A	A) vs flurbiprofen 1	00 mg (B)						
1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	15/29 (51.7%)	15/31 (48.4%)	<b>RR 1.07</b> (0.64 to 1.77)	<b>34 more per 1000</b> (from 174 fewer to 373 more)	⊕○○○ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	lministration) –	ibuprofen 300-	-400 mg (A) vs ibuj	orofen 900 mg (B)						
1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	17/20 (85.0%)	17/20 (85.0%)	<b>RR 1.00</b> (0.77 to 1.30)	<b>0 fewer per 1000</b> (from 195 fewer to 255 more)	⊕○○○ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	ministration) –	diflunisal 125 r	ng (A) vs diflunisal	250 mg (B)				-		
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	13/33 (39.4%)	10/30 (33.3%)	<b>RR 1.18</b> (0.61 to 2.29)	<b>60 more per 1000</b> (from 130 fewer to 430 more)	⊕OOO VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	  ministration) –	diflunisal 125 r	ng (A) vs diflunisal	500 mg (B)	ł		ļ	<u> </u>		
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	13/33 (39.4%)	16/30 (53.3%)	<b>RR 0.74</b> (0.43 to 1.27)	<b>139 fewer per 1000</b> (from 304 fewer to 144 more)	⊕○○○ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	lministration) –	diflunisal 250 r	ng (A) vs diflunisal	500 mg (B)	I	I	1	I		
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	10/30 (33.3%)	16/30 (53.3%)	<b>RR 0.63</b> (0.34 to 1.15)	<b>197 fewer per 1000</b> (from 352 fewer to 80 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	ministration) –	meclofenamat	e sodium 100 mg (	A) vs meclofenama	te sodium 200 m	g (B)		•		
3	randomized trials	serious <sup>a</sup>	not serious	not serious	not serious	none	103/173 (59.5%)	105/175 (60.0%)	<b>RR 1.00</b> (0.84 to 1.18)	<b>0 fewer per 1000</b> (from 96 fewer to 108 more)	⊕⊕⊕⊖ MODERATE	CRITICAL
Adequat	e pain relief (6	hours after ad	  ministration) –	ketoprofen 25	mg (A) vs ketoprof	en 50 mg (B)	ł	I	<u>I</u>	1		
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1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	18/28 (64.3%)	17/26 (65.4%)	<b>RR 0.98</b> (0.66 to 1.46)	<b>13 fewer per 1000</b> (from 222 fewer to 301 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL

			Certainty as	sessment			Nº of p	atients		Effect	l	
№ of udies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% CI)	Absolute (95% Cl)	Certainty (GRADE)	Importance

Adequate pain relief (6 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 100 mg (B)

1	randomized	serious <sup>a</sup>	not serious	not serious	very serious b,c	none	14/18 (77.8%)	20/24 (83.3%)	RR 0.93	58 fewer per 1000	⊕000	CRITICAL
	trials								(0.69 to 1.27)	(from 258 fewer to	VERY LOW	
										225 more)		

#### Adequate pain relief (6 hours after administration) – aceclofenac 50 mg (A) vs aceclofenac 150 mg (B)

1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c</sup>	none	14/18 (77.8%)	19/21 (90.5%)	<b>RR 0.86</b> (0.65 to 1.14)	<b>127 fewer per 1000</b> (from 317 fewer to 127 more)	⊕○○○ VERY LOW	CRITICAL	
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## Adequate pain relief (6 hours after administration) - aceclofenac 100 mg (A) vs aceclofenac 150 mg (B)

1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c</sup>	none	20/24 (83.3%)	19/21 (90.5%)	<b>RR 0.92</b> (0.73 to 1.16)	<b>72 fewer per 1000</b> (from 244 fewer to 145 more)	⊕○○○ VERY LOW	CRITICAL
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#### Adequate pain relief (6 hours after administration) - etodolac 25 mg (A) vs etodolac 100 mg (B)

1 ra	randomized	serious <sup>a</sup>	not serious	serious <sup>e</sup>	very serious b,c,d	none	11/40 (27.5%)	15/40 (37.5%)	RR 0.73	101 fewer per 1000	$\oplus O O O$	CRITICAL
	trials								(0.39 to 1.39)	(from 229 fewer to	VERY LOW	
										146 more)		

## Adequate pain relief (6 hours after administration) - flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)

1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	13/32 (40.6%)	18/29 (62.1%)	<b>RR 0.65</b> (0.39 to 1.09)	<b>217 fewer per 1000</b> (from 379 fewer to	⊕OOO VERY LOW	CRITICAL
										56 more)		

#### Adequate pain relief (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)

1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	13/32 (40.6%)	19/31 (61.3%)	<b>RR 0.66</b> (0.40 to 1.10)	<b>208 fewer per 1000</b> (from 368 fewer to	CRITICAL
									(0.10 10 1120)	61 more)	

## Adequate pain relief (6 hours after administration) – flurbiprofen 50 mg (A) vs flurbiprofen 100 mg (B)

trials	.3%) <b>RR 1.01</b> 6 more per 1000     ⊕○○○     CRITICA       (0.68 to 1.51)     (from 196 fewer to 313 more)     VERY LOW     CRITICA	۹L

			Certainty as	sessment			Nº of p	atients		Effect		
Nº 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% Cl)	Certainty (GRADE)	Importance
Adequat	e pain relief (6	hours after ad	ministration) –	fenoprofen 50	mg (A) vs fenopro	fen 100 mg (B)						
2	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	28/50 (56.0%)	33/50 (66.0%)	<b>RR 0.85</b> (0.62 to 1.16)	<b>99 fewer per 1000</b> (from 251 fewer to 106 more)	⊕○○○ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	ministration) –	fenoprofen 50	mg (A) vs fenopro	fen 200 mg (B)						
2	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	28/50 (56.0%)	32/49 (65.3%)	<b>RR 0.86</b> (0.62 to 1.17)	<b>91 fewer per 1000</b> (from 248 fewer to 111 more)	⊕○○○ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	ministration) –	fenoprofen 50	mg (A) vs fenopro	fen 300 mg (B)	·	·				•
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	17/27 (63.0%)	19/27 (70.4%)	<b>RR 0.89</b> (0.61 to 1.31)	<b>77 fewer per 1000</b> (from 274 fewer to 218 more)	⊕○○○ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	ministration) –	fenoprofen 100	) mg (A) vs fenopro	ofen 200 mg (B)	ł		ļ			ł
2	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	33/50 (66.0%)	32/49 (65.3%)	<b>RR 1.01</b> (0.76 to 1.34)	<b>7 more per 1000</b> (from 157 fewer to 222 more)	⊕○○○ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	ministration) –	fenoprofen 100	) mg (A) vs fenopr	ofen 300 mg (B)						1
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	19/26 (73.1%)	19/27 (70.4%)	<b>RR 1.04</b> (0.74 to 1.46)	<b>28 more per 1000</b> (from 183 fewer to 324 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL
Adequat	e pain relief (6	hours after ad	ministration) –	fenoprofen 200	) mg (A) vs fenopr	ofen 300 mg (B)	•	•				
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c</sup>	none	19/26 (73.1%)	19/27 (70.4%)	<b>RR 1.04</b> (0.74 to 1.46)	<b>28 more per 1000</b> (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	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	10/24 (41.7%)	11/23 (47.8%)	<b>RR 0.87</b> (0.46 to 1.65)	<b>62 fewer per 1000</b> (from 258 fewer to 311 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL	
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			Certainty as	sessment			Nº of p	atients		Effect		
Nº 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% Cl)	Certainty (GRADE)	Importance
Adequate	e pain relief (6	hours after ad	ministration) –	fenoprofen 12	.5 mg (A) vs fenopr	ofen 50 mg (B)						
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	10/24 (41.7%)	11/23 (47.8%)	<b>RR 0.87</b> (0.46 to 1.65)	<b>62 fewer per 1000</b> (from 258 fewer to 311 more)	⊕○○○ VERY LOW	CRITICAL
Adequate	e pain relief (6	hours after ad	ministration) –	fenoprofen 12	.5 mg (A) vs fenopr	ofen 100 mg (B)						
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	10/24 (41.7%)	15/23 (65.2%)	<b>RR 0.64</b> (0.37 to 1.12)	<b>235 fewer per 1000</b> (from 411 fewer to 78 more)	⊕○○○ VERY LOW	CRITICAL
Adequate	e pain relief (6	hours after ad	ministration) –	fenoprofen 12	.5 mg (A) vs fenopr	ofen 200 mg (B)	1					•
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	10/24 (41.7%)	13/23 (56.5%)	<b>RR 0.74</b> (0.41 to 1.33)	<b>147 fewer per 1000</b> (from 333 fewer to 187 more)	⊕OOO VERY LOW	CRITICAL
Adequate	e pain relief (6	hours after ad	ministration) –	fenoprofen 25	mg (A) vs fenoprof	ien 50 mg (B)		I	I			
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	11/23 (47.8%)	11/23 (47.8%)	<b>RR 1.00</b> (0.55 to 1.83)	<b>0 fewer per 1000</b> (from 215 fewer to 397 more)	⊕OOO VERY LOW	CRITICAL
Adequate	e pain relief (6	hours after ad	ministration) –	fenoprofen 25	mg (A) vs fenoprol	ien 100 mg (B)	1					
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	11/23 (47.8%)	15/23 (65.2%)	<b>RR 0.73</b> (0.44 to 1.23)	<b>176 fewer per 1000</b> (from 365 fewer to 150 more)	⊕OOO VERY LOW	CRITICAL
Adequate	e pain relief (6	hours after ad	ministration) –	fenoprofen 25	mg (A) vs fenoprol	en 200 mg (B)	!	<u>,</u>	<u>,</u>		<u></u>	
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	11/23 (47.8%)	13/23 (56.5%)	<b>RR 0.85</b> (0.48 to 1.48)	<b>85 fewer per 1000</b> (from 294 fewer to 271 more)	⊕OOO VERY LOW	CRITICAL
Need for	additional ana	algesia (4 hours	s after administ	ration) – ibupr	ofen 300–400 mg (/	A) vs ibuprofen 800	) mg (B)	1	1			
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	4/80 (5.0%)	7/80 (8.8%)	<b>RR 0.57</b> (0.17 to 1.88)	<b>38 fewer per 1000</b> (from 73 fewer to 77 more)	⊕○○○ VERY LOW	CRITICAL

We of studies     Study disign     Risk of blas     Inconsistency     Indirectness     Imprecision     Other considerations     NSAID     Higher single same MSAID     Relative (95% C1)     Absolute (95% C1)     Certaintry (GRADE)       1     randomized trials     not serious     not serious     serious**     very serious***     none     1/20 (5.0%)     0/20 (0.0%)     RR 3.00 (0.31 to 69.52)     of new per 1000 (from of new per 1000 (from of new per 1000 (from 14 fewer to 326 more)     VERY LOW       2     randomized trials     and serious     not serious     very serious***     none     2/2/9 (22.9%)     24/95 (25.3%)     RR 9.91 (0.55 to 1.50)     23 fewer per 1000 (from 14 fewer to 326 more)     0/000 (from 14 fewer to 326 more)       1     randomized trials     not serious     not serious **     very serious***     none     1/32 (3.1%)     0/29 (0.0%)     RR 2.73 (0.12 to 61.21 to 62				Certainty as	sessment			Nº of p	atients		Effect		
1   randomized trials   not serious   not serious   serious*   very serious %c/c   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 (from 0 fewer to 0 (from 0 fewer to 0 (from 114 fewer to 126 more)   0     2   randomized trials   serious *   not serious   not serious very serious %c/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)   0     1   randomized trials   not serious   not serious serious %c/c   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 trials   0     1   randomized trials   not serious   serious *   very serious %c/c   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 trew rD   0     1   randomized trials   not serious   serious *   very serious %c/c   none   1/32 (3.1%)   0/31 (0.0%)   RR 2.91 (0.12 to fewer 10   0   0     1   randomized trials   not serious   serious *   very serious %c/c   none   0/31 (0.0%)   Not setino (from 0 fewer to 0 trew rD   0		-	Risk of bias	Inconsistency	Indirectness	Imprecision		NSAID	dose of the				Importance
trials   trials   (from 0 fewer to 0 fewer)   VERY LOW     Need for additional analgesia (6 hours after administration) - metolenamate sodium 100 mg (A) vs metolenamate sodium 200 mg (B)   2     2   randomized trials   serious <sup>2</sup> not serious   not serious   very serious <sup>3,c.</sup> 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)   \$\PS(VOW)     Need for additional analgesia (6 hours after administration) - flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)   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)   \$\PS(VOW)     Need for additional analgesia (6 hours after administration) - flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)   1/32 (3.1%)   0/31 (0.0%)   RR 2.73 (0.12 to 64.42)   0 fewer per 1000 (from 0 fewer to 0 fewer)   \$\PS(VOW)     1   randomized trials   not serious   serious <sup>2</sup> very serious <sup>14.4</sup> 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)   \$\PS(VOW)     Need for additional analgesia (6 hours after administration) - flurbiprofen 50 mg (A) vs flurbiprofen 100 mg (B)   1/32 (3.1%)   0/31 (0.0%)   0/31 (0.0%)   not serious   \$\PS(VOW)     1   randomized trials	Need for	additional and	algesia (6 hour	s after administ	ration) – ibupro	ofen 300–400 mg (/	A) vs ibuprofen 900	) mg (B)					
2   randomized trials   serious*   not serious   very serious <sup>b.c.</sup> none   22/96 (22.9%)   24/95 (25.3%)   (0.55 to 1.50)   23 fewer per 1000   (#CVP LOW     Need for additional analgesia (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 50 mg (B)   1   randomized   not serious   very serious <sup>b.c.d</sup> none   1/32 (3.1%)   0/29 (0.0%)   (Bt 2.73)   0 fewer per 1000   (#OCOO)   VERY LOW     Need for additional analgesia (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)   1   1/32 (3.1%)   0/29 (0.0%)   (Bt 2.73)   0 fewer per 1000   (#OCOO)   VERY LOW     Need for additional analgesia (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)   0/31 (0.0%)   (Bt 2.91)   0 fewer per 1000   (#OCOO)   VERY LOW     1   randomized   not serious   not serious <sup>c</sup> very serious <sup>b.c.d</sup> none   1/32 (3.1%)   0/31 (0.0%)   (Bt 2.91)   (from 0 fewer to 0)   VERY LOW     1   randomized   not serious   not serious <sup>c</sup> very serious <sup>b.c.d</sup> none   0/32 (0.0%)   0/31 (0.0%)   not serious   WERY LOW     1   randomized   fnot serious   <	1		not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	1/20 (5.0%)	0/20 (0.0%)	(0.13 to	(from 0 fewer to 0		CRITICAL
trials	Need for	additional ana	algesia (6 hour	s after administ	ration) – meclo	fenamate sodium	100 mg (A) vs mecl	ofenamate sodiu	ım 200 mg (B)				
1   randomized trials   not serious   not serious   serious <sup>a</sup> very serious <sup>b.c.d</sup> 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 64.42)     Need for additional analgesia (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)   Image: comparison of the serious in the seriou	2		serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c</sup>	none	22/96 (22.9%)	24/95 (25.3%)		(from 114 fewer to		CRITICAL
trials   Image: serious and serious after administration) – flurbibrofen 25 mg (A) vs flurbibrofen 100 mg (B)     Need for additional analgesia (6 hours after administration) – flurbibrofen 25 mg (A) vs flurbibrofen 100 mg (B)   RR 2.91   O fewer per 1000   CPC (G) (D) (From 0 fewer) 0   CPC (From	Need for	additional and	algesia (6 hour	s after administ	ration) – flurbij	profen 25 mg (A) v	s flurbiprofen 50 m	g (B)		•			•
1   randomized trials   not serious   not serious   serious °   very serious %.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     Need for additional analgesia (6 hours after administration) – flurbiprofen 50 mg (A) vs flurbiprofen 100 mg (B)     1   randomized trials   not serious   not serious °   very serious c#   none   0/29 (0.0%)   0/31 (0.0%)   not estimable   -   ♥○○○     1   randomized trials   not serious   serious °   very serious c#   none   0/29 (0.0%)   0/31 (0.0%)   not estimable   -   ♥○○○   VERY LOW     Maternal drug adverse effects (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 250 mg (B)     1   randomized trials   not serious   not serious c#   none   0/33 (0.0%)   0/30 (0.0%)   not estimable   -   ♥○○○   VERY LOW     Maternal drug adverse effects (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 500 mg (B)   0/30 (0.0%)   not estimable   -   ♥○○○   VERY LOW     Maternal drug adverse effects (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 500 mg (B)   0/30 (0.0%)   not estim	1		not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	1/32 (3.1%)	0/29 (0.0%)	(0.12 to	(from 0 fewer to 0		CRITICAL
trialstria	Need for	additional ana	algesia (6 hour	s after administ	ration) – flurbij	profen 25 mg (A) v	s flurbiprofen 100 r	ng (B)		J		1	<u>I</u>
1   randomized trials   not serious   not serious c.e.   very serious c.e.   none   0/29 (0.0%)   0/31 (0.0%)   not estimable   -	1		not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	1/32 (3.1%)	0/31 (0.0%)	(0.12 to	(from 0 fewer to 0		CRITICAL
trialstrialsImage: serious and	Need for	additional ana	algesia (6 hour	s after administ	ration) – flurbij	profen 50 mg (A) v	s flurbiprofen 100 r	ng (B)					I
1   randomized trials   serious <sup>a</sup> not serious   not serious <sup>c,g</sup> none   0/33 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○ VERY LOW     Maternal drug adverse effects (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 500 mg (B)     1   randomized trials   serious <sup>a</sup> not serious   very serious <sup>c,g</sup> none   0/33 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○ VERY LOW     1   randomized trials   serious <sup>a</sup> not serious   very serious <sup>c,g</sup> none   0/33 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○ VERY LOW     1   randomized trials   serious <sup>a</sup> not serious   very serious <sup>c,g</sup> none   0/30 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○ VERY LOW     1   randomized serious <sup>a</sup> not serious   not serious <sup>c,g</sup> none   0/30 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○ VERY LOW	1		not serious	not serious	serious <sup>e</sup>	very serious <sup>c,g</sup>	none	0/29 (0.0%)	0/31 (0.0%)	not estimable	-		CRITICAL
trials   trials   VERY LOW     Maternal drug adverse effects (4 hours after administration) – diflunisal 125 mg (A) vs diflunisal 500 mg (B)   Very LOW     1   randomized trials   serious <sup>a</sup> not serious   very serious <sup>c,g</sup> none   0/33 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○ VERY LOW     Maternal drug adverse effects (4 hours after administration) – diflunisal 250 mg (A) vs diflunisal 500 mg (B)   0/30 (0.0%)   not estimable   -   ⊕○○○ VERY LOW     1   randomized   serious <sup>a</sup> not serious   not serious <sup>c,g</sup> none   0/30 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○     1   randomized   serious <sup>a</sup> not serious   very serious <sup>c,g</sup> none   0/30 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○	Materna	drug adverse	effects (4 hou	rs after administ	ration) – diflur	nisal 125 mg (A) vs	diflunisal 250 mg (	в)		<u>,</u>			<u> </u>
1   randomized trials   serious <sup>a</sup> not serious   not serious   very serious <sup>c,g</sup> none   0/33 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○ VERY LOW     Maternal drug adverse effects (4 hours after administration) – diflunisal 250 mg (A) vs diflunisal 500 mg (B)   none   0/30 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○     1   randomized   serious <sup>a</sup> not serious   very serious <sup>c,g</sup> none   0/30 (0.0%)   0/30 (0.0%)   not estimable   -   ⊕○○○	1		serious <sup>a</sup>	not serious	not serious	very serious <sup>c,g</sup>	none	0/33 (0.0%)	0/30 (0.0%)	not estimable	-		CRITICAL
trials   very LOW     Maternal drug adverse effects (4 hours after administration) – diflunisal 250 mg (A) vs diflunisal 500 mg (B)     1   randomized   serious a not serious   not serious c.g   none   0/30 (0.0%)   0/30 (0.0%)   not estimable   - $\oplus \bigcirc \bigcirc \bigcirc$	Materna	drug adverse	effects (4 hou	rs after administ	ration) – diflur	nisal 125 mg (A) vs	diflunisal 500 mg (	В)					
1 randomized serious <sup>a</sup> not serious not serious very serious <sup>c,g</sup> none 0/30 (0.0%) 0/30 (0.0%) not estimable - ⊕○○○	1		serious <sup>a</sup>	not serious	not serious	very serious <sup>c,g</sup>	none	0/33 (0.0%)	0/30 (0.0%)	not estimable	-		CRITICAL
	Materna	drug adverse	effects (4 hou	rs after administ	ration) – diflur	nisal 250 mg (A) vs	diflunisal 500 mg (	В)					
	1		serious <sup>a</sup>	not serious	not serious	very serious <sup>c,g</sup>	none	0/30 (0.0%)	0/30 (0.0%)	not estimable	-		CRITICAL

			Certainty as	sessment			Nº of p	atients		Effect		
Nº 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% Cl)	Certainty (GRADE)	Importance
Materna	l drug adverse	effects (4 hou	rs after administ	tration) – ibupr	ofen 300–400 mg	(A) vs ibuprofen 80	0 mg (B)					
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>c,g</sup>	none	0/80 (0.0%)	0/80 (0.0%)	not estimable	-	⊕○○○ VERY LOW	CRITICAL
Materna	l drug adverse	effects (6 hou	rs after administ	tration) – ibupr	ofen 300 mg (A) ve	ibuprofen 900 mg	(B)		•			
1	randomized trials	not serious	not serious	serious <sup>e</sup>	very serious <sup>b,c,d</sup>	none	3/20 (15.0%)	3/20 (15.0%)	<b>RR 1.00</b> (0.23 to 4.37)	<b>0 fewer per 1000</b> (from 115 fewer to 505 more)	⊕○○○ VERY LOW	-
Materna	l drug adverse	effects (6 hou	rs after administ	tration) – diflui	nisal 125 mg (A) vs	diflunisal 250 mg (I	3)					-
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>c,g</sup>	none	0/33 (0.0%)	0/30 (0.0%)	not estimable	-	⊕○○○ VERY LOW	CRITICAL
Materna	l drug adverse	effects (6 hou	rs after administ	tration) – diflur	nisal 125 mg (A) vs	diflunisal 500 mg (l	3)	•	•			
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>c,g</sup>	none	0/33 (0.0%)	0/30 (0.0%)	not estimable	-	⊕○○○ VERY LOW	CRITICAL
Materna	l drug adverse	effects (6 hou	rs after administ	tration) – diflui	nisal 250 mg (A) vs	diflunisal 500 mg (l	3)	ł				4
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>c,g</sup>	none	0/30 (0.0%)	0/30 (0.0%)	not estimable	-	⊕○○○ VERY LOW	CRITICAL
Materna	l drug adverse	effects (6 hou	rs after administ	tration) – ketop	orofen 25 mg (A) v	s ketoprofen 50 mg	(B)	ļ				<b>.</b>
1	randomized trials	very serious	not serious	serious <sup>e</sup>	very serious <sup>c,g</sup>	none	0/28 (0.0%)	0/26 (0.0%)	not estimable	-	⊕○○○ VERY LOW	CRITICAL
Materna	l drug adverse	effects (6 hou	rs after administ	tration) – acecl	ofenac 50 mg (A) v	s aceclofenac 100 r	ng (B)	Į	II			I
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	1/18 (5.6%)	0/24 (0.0%)	<b>RR 3.95</b> (0.17 to 91.61)	<b>0 fewer per 1000</b> (from 0 fewer to 0 fewer)	⊕○○○ VERY LOW	CRITICAL
Materna	l drug adverse	effects (6 hou	rs after administ	tration) – acecl	ofenac 50 mg (A) v	s aceclofenac 150 r	ng (B)					
1	randomized trials	serious <sup>a</sup>	not serious	not serious	very serious <sup>b,c,d</sup>	none	1/18 (5.6%)	0/21 (0.0%)	<b>RR 3.47</b> (0.15 to 80.35)	<b>0 fewer per 1000</b> (from 0 fewer to 0 fewer)	⊕○○○ VERY LOW	CRITICAL

		Certainty as	sessment			Nº of p	atients		Effect		
Nº c studi	 Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Higher single dose of the same NSAID	Relative (95% Cl)	Absolute (95% Cl)	Certainty (GRADE)	Importance

Maternal drug adverse effects (6 hours after administration) – aceclofenac 100 mg (A) vs aceclofenac 150 mg (B)

1	randomized	serious <sup>a</sup>	not serious	not serious	very serious <sup>c,g</sup>	none	0/24 (0.0%)	0/21 (0.0%)	not estimable	-	⊕000	CRITICAL
	trials										VERY LOW	

Maternal drug adverse effects (6 hours after administration) – flurbiprofen 25 mg (A) vs flurbiprofen 100 mg (B)

1	randomized	not serious	not serious	serious <sup>e</sup>	very serious <sup>c,g</sup>	none	0/32 (0.0%)	0/29 (0.0%)	not estimable	-	⊕000	CRITICAL
	trials										VERY LOW	

## 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 <sup>e</sup>	very serious <sup>c,g</sup>	none	0/32 (0.0%)	0/31 (0.0%)	not estimable	-	⊕○○○ VERY LOW	CRITICAL
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## Maternal drug adverse effects (6 hours after administration) – flurbiprofen 50 mg (A) vs flurbiprofen 100 mg (B)

1	randomized not se trials	rious not serious	serious <sup>e</sup>	very serious <sup>c,g</sup>	none	0/29 (0.0%)	0/31 (0.0%)	not estimable	-	⊕○○○ VERY LOW	CRITICAL	
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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.