Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Any TEAE mild	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg BID for 6 weeks	49/136	51/133	0.94 (0.69; 1.28)	-0.02 (-0.14; 0.09)		
Any TEAE mild	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	49/136	65/127	0.70 (0.53; 0.93)	-0.15 (-0.27; -0.03)	-7 (-30; -4)	-152 (-270; -33)
At least one	Norton, 2002 ³⁵⁵	20mg/day vs.	62/138	68/137	0.91	-0.05		
adverse event	275	40mg/d			(0.70; 1.16)	(-0.16; 0.07)		
At least one	Norton, 2002 ³⁵⁵	20mg/day vs.	62/138	73/140	0.86	-0.07		
adverse event	278	80mg/d			(0.68; 1.10)	(-0.19; 0.05)		
At least one	Norton, 2002 ³⁵⁵	40mg/day vs.	68/137	73/140	0.95	-0.03		
adverse event	277	80mg/d	4/400	4/407	(0.76; 1.20)	(-0.14; 0.09)		
Constipation	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	4/138	4/137	0.99 (0.25; 3.89)	0.00 (-0.04; 0.04)		
Constipation	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	4/138	6/140	0.68 (0.20; 2.34)	-0.01 (-0.06; 0.03)		
Constipation	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	4/137	6/140	0.68 (0.20; 2.36)	-0.01 (-0.06; 0.03)		
Constipation	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg BID for 6 weeks	16/136	18/133	0.87 (0.46; 1.63)	-0.02 (-0.10; 0.06)		
Constipation	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	16/136	6/127	2.49 (1.01; 6.17)	0.07 (0.00; 0.14)	14 (7; 205)	70 (5; 136)

Appendix Table F42. Outcomes after different doses of duloxetine

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Constipation	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	6/127	18/133	0.35 (0.14; 0.85)	-0.09 (-0.16; -0.02)	-11 (-52; -6)	-88 (-157; -19)
Constipation	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	48/826	1149/14352	0.73 (0.55; 0.96)	-0.02 (-0.04; -0.01)	-46 (-186; -26)	-21 (-39; -5)
Diarrhea	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	5/138	4/137	1.24 (0.34; 4.52)	0.01 (-0.03; 0.05)		
Diarrhea	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	5/138	4/140	1.27 (0.35; 4.62)	0.01 (-0.03; 0.05)		
Diarrhea	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	4/137	4/140	1.02 (0.26; 4.00)	0.00 (-0.04; 0.04)		
Diarrhea	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	1/136	0/133	2.93 (0.12; 71.39)	0.01 (-0.01; 0.03)		
Diarrhea	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	1/136	4/127	0.23 (0.03; 2.06)	-0.02 (-0.06; 0.01)		
Diarrhea	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	4/127	0/133	9.42 (0.51; 173.25)	0.03 (0.00; 0.07)		
Diarrhea	Gahimer, 2007 ²⁹¹ 15178	20-60mg/day vs. 20-120mg once/twice a day	11/826	502/14352	0.38 (0.21; 0.69)	-0.02 (-0.03; -0.01)	-46 (-75; -33)	-22 (-30; -13)
Dizziness	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	2/138	6/137	0.33 (0.07; 1.61)	-0.03 (-0.07; 0.01)		
Dizziness	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	2/138	7/140	0.29 (0.06; 1.37)	-0.04 (-0.08; 0.01)		
Dizziness	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	6/137	7/140	0.88 (0.30; 2.54)	-0.01 (-0.06; 0.04)		

Appendix Table F42. Outcomes after different doses of duloxetine (continued)

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% CI)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Dizziness	Castro-Diaz, 2007 ²⁵⁴ 2 69	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	14/136	4/133	3.42 (1.16; 10.13)	0.07 (0.01; 0.13)	14 (8; 71)	73 (14; 132)
Dizziness	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg BID for 6 weeks	14/136	10/127	1.31 (0.60; 2.84)	0.02 (-0.05; 0.09)		
Dizziness	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	10/127	4/133	2.62 (0.84; 8.14)	0.05 (-0.01; 0.10)		
Dizziness	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	31/826	852/14,352	0.63 (0.44; 0.90)	-0.02 (-0.04; -0.01)	-46 (-120; -28)	-22 (-35; -8)
Dry mouth	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	4/138	5/137	0.79 (0.22; 2.89)	-0.01 (-0.05; 0.03)		
Dry mouth	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	4/138	7/140	0.58 (0.17; 1.94)	-0.02 (-0.07; 0.02)		
Dry mouth	Norton, 2002 ³⁵⁵ 277	40mg/day vs.80mg/d	5/137	7/140	0.73 (0.24; 2.24)	-0.01 (-0.06; 0.03)		
Dry mouth	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	22/136	19/133	1.13 (0.64; 1.99)	0.02 (-0.07; 0.10)		
Dry mouth	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	22/136	15/127	1.37 (0.74; 2.52)	0.04 (-0.04; 0.13)		

Appendix Table F42. Outcomes after different doses of duloxetine (continued)

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Dry mouth	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	15/127	19/133	0.83 (0.44; 1.56)	-0.02 (-0.11; 0.06)		
Dry mouth	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	63/826	1559/14,352	0.70 (0.55; 0.89)	-0.03 (-0.05; -0.01)	-31 (-74; -20)	-32 (-51; -14)
Fatigue	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	1/138	8/137	0.12 (0.02; 0.98)	-0.05 (-0.09; -0.01)	-20 (-106; -11)	-51 (-93; -9)
Fatigue	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	1/138	10/140	0.10 (0.01; 0.78)	-0.06 (-0.11; -0.02)	-16 (-52; -9)	-64 (-109; -19)
Fatigue	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	8/137	10/140	0.82 (0.33; 2.01)	-0.01 (-0.07; 0.04)		
Fatigue	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	12/136	8/133	1.47 (0.62; 3.47)	0.03 (-0.03; 0.09)		
Fatigue	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg BID for 6 weeks	12/136	6/127	1.87 (0.72; 4.83)	0.04 (-0.02; 0.10)		
Fatigue	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg BID for 2 weeks escalating to 40mg b.i.d. for 6 weeks	6/127	8/133	0.79 (0.28; 2.20)	-0.01 (-0.07; 0.04)		
Fatigue	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	41/826	1102/14,352	0.65 (0.48; 0.88)	-0.03 (-0.04; -0.01)	-37 (-85; -24)	-27 (-43; -12)
Headache	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	7/138	10/137	0.69 (0.27; 1.77)	-0.02 (-0.08; 0.03)		
Headache	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	7/138	8/140	0.89 (0.33; 2.38)	-0.01 (-0.06; 0.05)		
Headache	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	10/137	8/140	1.28 (0.52; 3.14)	0.02 (-0.04; 0.07)		

Appendix Table F42. Outcomes after different doses of duloxetine (continued)

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Headache	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	11/136	9/133	1.20 (0.51; 2.79)	0.01 (-0.05; 0.08)		
Headache	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	11/136	11/127	0.93 (0.42; 2.08)	-0.01 (-0.07; 0.06)		
Headache	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	11/127	9/133	1.28 (0.55; 2.98)	0.02 (-0.05; 0.08)		
Headache	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	68/826	1029/14352	1.15 (0.91; 1.45)	0.01 (-0.01; 0.03)		
Hyperhidrosis	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	54/826	549/14352	1.71 (1.30; 2.24)	0.03 (0.01; 0.04)	37 (23; 100)	27 (10; 44)
Insomnia	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	2/138	7/137	0.28 (0.06; 1.34)	-0.04 (-0.08; 0.01)		
Insomnia	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	2/138	7/140	0.29 (0.06; 1.37)	-0.04 (-0.08; 0.01)		
Insomnia	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	7/137	7/140	1.02 (0.37; 2.84)	0.00 (-0.05; 0.05)		
Insomnia	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	14/136	8/133	1.71 (0.74; 3.94)	0.04 (-0.02; 0.11)		
Insomnia	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg BID for 6 weeks	14/136	6/127	2.18 (0.86; 5.50)	0.06 (-0.01; 0.12)		

Appendix Table F42. Outcomes after different doses of duloxetine (continued)

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Insomnia	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	6/127	8/133	0.79 (0.28; 2.20)	-0.01 (-0.07; 0.04)		
Insomnia	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	59/826	1179/14352	0.87 (0.68; 1.12)	-0.01 (-0.03; 0.01)		
Nasopharyngitis	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	8/138	4/137	1.99 (0.61; 6.44)	0.03 (-0.02; 0.08)		
Nasopharyngitis	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	8/138	6/140	1.35 (0.48; 3.80)	0.02 (-0.04; 0.07)		
Nasopharyngitis	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	4/137	6/140	0.68 (0.20; 2.36)	-0.01 (-0.06; 0.03)		
Nausea	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	9/138	9/137	0.99 (0.41; 2.43)	0.00 (-0.06; 0.06)		
Nausea	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	9/138	13/140	0.70 (0.31; 1.59)	-0.03 (-0.09; 0.04)		
Nausea	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	9/137	13/140	0.71 (0.31; 1.60)	-0.03 (-0.09; 0.04)		
Nausea	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	40/136	22/133	1.78 (1.12; 2.82)	0.13 (0.03; 0.23)	8 (4; 34)	129 (30; 228)
Nausea	Castro- Diaz,2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	40/136	32/127	1.17 (0.78; 1.74)	0.04 (-0.07; 0.15)		
Nausea	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	32/127	22/133	1.52 (0.94; 2.47)	0.09 (-0.01; 0.18)		
Nausea	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	19/826	2204/14352	0.15 (0.10; 0.23)	-0.13 (-0.14; -0.12)	-8 (-8; -7)	-131 (-142; -119)

Appendix Table F42. Outcomes after different doses of duloxetine (continued)

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% CI)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Nausea mild	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	56/136	78/133	0.70 (0.55; 0.90)	-0.17 (-0.29; -0.06)	-6 (-18; -3)	-175 (-292; -57)
Nausea mild	Castro-Diaz, 2007 ²⁵⁴ 264	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	56/136	64/127	0.82 (0.63; 1.07)	-0.09 (-0.21; 0.03)		
Nausea moderate	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	48/127	43/133	1.17 (0.84; 1.63)	0.05 (-0.06; 0.17)		
Nausea severe	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	14/136	12/133	1.14 (0.55; 2.37)	0.01 (-0.06; 0.08)		
Nausea severe	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	14/136	15/127	0.87 (0.44; 1.73)	-0.02 (-0.09; 0.06)		
Nausea severe	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	15/127	12/133	1.31 (0.64; 2.69)	0.03 (-0.05; 0.10)		
Sinusitis	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	4/138	4/137	0.99 (0.25; 3.89)	0.00 (-0.04; 0.04)		
Sinusitis	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	4/138	4/140	1.01 (0.26; 3.98)	0.00 (-0.04; 0.04)		
Sinusitis	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	4/137	4/140	1.02 (0.26; 4.00)	0.00 (-0.04; 0.04)		

Appendix Table F42. Outcomes after different doses of duloxetine (continued)

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% CI)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Somnolence	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	15/136	11/133	1.33 (0.64; 2.80)	0.03 (-0.04; 0.10)		
Somnolence	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	15/136	6/127	2.33 (0.93; 5.83)	0.06 (0.00; 0.13)		
Somnolence	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	6/127	11/133	0.57 (0.22; 1.50)	-0.04 (-0.10; 0.02)		
Somnolence	Gahimer, 2007 ²⁹¹ 15,178	20-60mg/day vs. 20-120mg once/twice a day	60/826	990/14352	1.05 (0.82; 1.35)	0.00 (-0.01; 0.02)		
TEAE moderate	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	65/136	64/133	0.99 (0.77; 1.27)	0.00 (-0.12; 0.12)		
TEAE moderate	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	42/127	64/133	0.69 (0.51; 0.93)	-0.15 (-0.27; -0.03)	-7 (-31; -4)	-151 (-268; -33)
TEAE severe	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	20/136	19/133	1.03 (0.58; 1.84)	0.00 (-0.08; 0.09)		
TEAE severe	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	20/136	20/127	0.93 (0.53; 1.65)	-0.01 (-0.10; 0.08)		

Appendix Table F42. Outcomes after different doses of duloxetine (continued)

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% CI)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
TEAE severe	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. D for 2 weeks escalating to 40mg b.i.d. for 6 weeks	20/127	19/133	1.10 (0.62; 1.97)	0.01 (-0.07; 0.10)		
Upper respiratory tract infection	Norton, 2002 ³⁵⁵ 275	20mg/day vs.40mg/d	2/138	2/137	0.99 (0.14; 6.95)	0.00 (-0.03; 0.03)		
Upper respiratory tract infection	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	2/138	1/140	2.03 (0.19; 22.12)	0.01 (-0.02; 0.03)		
Upper respiratory tract infection	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	2/137	1/140	2.04 (0.19; 22.28)	0.01 (-0.02; 0.03)		
Adverse effects leading to discontinuation	Duckett, 2007 ²⁸⁵ 215	60mg/day vs. 40mg twice daily	21/67	74/148	0.63 (0.42; 0.93)	-0.19 (-0.32; -0.05)	-5 (-20; -3)	-187 (-324; -49)
Discontinuation due to any adverse event	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	22/136	10/133	2.15 (1.06; 4.37)	0.09 (0.01; 0.16)	12 (6; 98)	87 (10; 163)
Discontinuation due to any adverse event	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	22/136	15/127	1.37 (0.74; 2.52)	0.04 (-0.04; 0.13)		
Discontinuation due to any adverse event	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	15/127	10/133	1.57 (0.73; 3.37)	0.04 (-0.03; 0.11)		
Discontinuation due to asthenia	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	2/136	1/133	1.96 (0.18; 21.31)	0.01 (-0.02; 0.03)		

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Discontinuation due to asthenia	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	2/136	0/127	4.67 (0.23; 96.38)	0.01 (-0.01; 0.04)		
Discontinuation due to asthenia	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	0/127	1/133	0.35 (0.01; 8.49)	-0.01 (-0.03; 0.01)		
Discontinuation	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	13/138	17/137	0.76 (0.38; 1.50)	-0.03 (-0.10; 0.04)		
Discontinuation	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	13/138	21/140	0.63 (0.33; 1.20)	-0.06 (-0.13; 0.02)		
Discontinuation	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	17/137	21/140	0.83 (0.46; 1.50)	-0.03 (-0.11; 0.05)		
Discontinuation due to dizziness	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	0/138	2/137	0.20 (0.01; 4.10)	-0.01 (-0.04; 0.01)		
Discontinuation due to dizziness	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	0/138	1/140	0.34 (0.01; 8.23)	-0.01 (-0.03; 0.01)		
Discontinuation due to dizziness	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	2/137	1/140	2.04 (0.19; 22.28)	0.01 (-0.02; 0.03)		
Discontinuation due to dizziness	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	2/136	0/133	4.89 (0.24; 100.92)	0.01 (-0.01; 0.04)		
Discontinuation due to dizziness	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	2/136	2/127	0.93 (0.13; 6.53)	0.00 (-0.03; 0.03)		
Discontinuation due to dizziness	Castro-Diaz, 2007 ²⁵⁴	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	2/127	0/133	5.23 (0.25; 107.98)	0.02 (-0.01; 0.04)		

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Discontinuation due to fatigue	Castro-Diaz, 2007 ²⁵⁴	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	0/136	0/133	0.00 (0.00; 0.00)	0.00 (-0.01; 0.01)		
Discontinuation due to fatigue	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. D for 6 weeks	0/136	1/127	0.31 (0.01; 7.58)	-0.01 (-0.03; 0.01)		
Discontinuation due to fatigue	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	1/127	0/133	3.14 (0.13; 76.39)	0.01 (-0.01; 0.03)		
Discontinuation due to headache	Castro-Diaz, 2007 ²⁵⁴ 275	20mg/day vs. 40mg/d	1/138	1/137	0.99 (0.06; 15.71)	0.00 (-0.02; 0.02)		
Discontinuation due to headache	Castro-Diaz, 2007 ²⁵⁴ 278	20mg/day vs. 80mg/d	1/138	2/140	0.51 (0.05; 5.53)	-0.01 (-0.03; 0.02)		
Discontinuation due to headache	Castro-Diaz, 2007 ²⁵⁴ 277	40mg/day vs. 80mg/d	1/137	2/140	0.51 (0.05; 5.57)	-0.01 (-0.03; 0.02)		
Discontinuation due to headache	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	3/136	0/133	6.85 (0.36; 131.29)	0.02 (-0.01; 0.05)		
Discontinuation due to headache	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	3/136	1/127	2.80 (0.30; 26.59)	0.01 (-0.01; 0.04)		

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% Cl)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Discontinuation due to headache	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. D for 6 weeks	1/127	0/133	3.14 (0.13; 76.39)	0.01 (-0.01; 0.03)		
Discontinuation due to insomnia	Castro-Diaz, 2007 ²⁵⁴ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. for 6 weeks	2/136	1/133	1.96 (0.18; 21.31)	0.01 (-0.02; 0.03)		
Discontinuation due to insomnia	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	2/136	1/127	1.87 (0.17; 20.35)	0.01 (-0.02; 0.03)		
Discontinuation due to insomnia	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. D for 6 weeks	1/127	1/133	1.05 (0.07; 16.56)	0.00 (-0.02; 0.02)		
Discontinuation due to menorhagia	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	2/138	0/137	4.96 (0.24; 102.46)	0.01 (-0.01; 0.04)		
Discontinuation due to menorhagia	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	2/138	0/140	5.07 (0.25; 104.69)	0.01 (-0.01; 0.04)		
Discontinuation due to menorhagia	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	0/137	0/140		0.00 (-0.01; 0.01)		
Discontinuation due to nausea	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	2/138	5/137	0.40 (0.08; 2.01)	-0.02 (-0.06; 0.02)		
Discontinuation due to nausea	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	2/138	6/140	0.34 (0.07; 1.65)	-0.03 (-0.07; 0.01)		
Discontinuation due to nausea	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	5/137	6/140	0.85 (0.27; 2.73)	-0.01 (-0.05; 0.04)		

Outcome	Reference sample size	Daily dose mg/day	Active events/ randomized	Control events/ randomized	Relative risk (95% Cl)	Absolute risk difference (95% CI)	Number needed to treat (95% CI)	Attributable events/1000 treated (95% CI)
Discontinuation due to nausea	Norton, 2002 ³⁵⁵ 269	80mg/day vs. 20mg b.i.d. for 2 weeks escalating to 40mg b.i.d. D for 6 weeks	4/136	3/133	1.30 (0.30; 5.72)	0.01 (-0.03; 0.04)		
Discontinuation due to nausea	Castro-Diaz, 2007 ²⁵⁴ 263	80mg/day vs. 40mg QD for 2 weeks escalating to 40mg b.i.d. for 6 weeks	4/136	2/127	1.87 (0.35; 10.02)	0.01 (-0.02; 0.05)		
Discontinuation due to nausea	Castro-Diaz, 2007 ²⁵⁴ 260	100mg/day vs. 20mg b.i.d. D for 2 weeks escalating to 40mg b.i.d. for 6 weeks	2/127	3/133	0.70 (0.12; 4.11)	-0.01 (-0.04; 0.03)		
Discontinuation due to somnolence	Norton, 2002 ³⁵⁵ 275	20mg/day vs. 40mg/d	1/138	0/137	2.98 (0.12; 72.48)	0.01 (-0.01; 0.03)		
Discontinuation due to somnolence	Norton, 2002 ³⁵⁵ 278	20mg/day vs. 80mg/d	1/138	2/140	0.51 (0.05; 5.53)	-0.01 (-0.03; 0.02)		
Discontinuation due to somnolence	Norton, 2002 ³⁵⁵ 277	40mg/day vs. 80mg/d	0/137	2/140	0.20 (0.01; 4.22)	-0.01 (-0.04; 0.01)		
Discontinuation due to lack of efficacy leading to discontinuation	Duckett, 2007 ²⁸⁵ 215	60mg/day vs. 40mg twice daily	14/67	37/148	0.84 (0.49; 1.44)	-0.04 (-0.16; 0.08)		