

**Sublingual Dexmedetomidine for Agitation Associated with Schizophrenia or Bipolar Disorder: A Post Hoc Analysis of Number Needed to Treat, Number Needed to Harm, and Likelihood to Be Helped or Harmed**

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Table S1. Response rate, absolute risk reduction, and number needed to treat at time points from 10 minutes to 24 hours postdose in the pooled population of adults with schizophrenia or bipolar disorder

Time postdose	PEC Response <sup>a</sup>				Absolute Risk Reduction <sup>b</sup>			Number Needed to Treat		
	n (%)				% (95% CI)			(95% CI)		
	Sublingual dexmedetomidine				Sublingual dexmedetomidine			Sublingual dexmedetomidine		
	180 ug n=251	120 ug n=255	120 or 180 ug n=506	Placebo n=252	180 ug n=251	120 ug n=255	120 or 180 ug n=506	180 ug n=251	120 ug n=255	120 or 180 ug n=506
10 minutes	30 (12.0)*	22 (8.6)	52 (10.3)*	14 (5.6)	6.4 (1.5, 11.3)	3.1 (-1.4, 7.5)	4.7 (.8, 8.6)	16 (9, 68)	33 (ns) <sup>c</sup>	22 (12, 118)
20 minutes*	72 (28.7)	53 (20.8)	125 (24.7)	33 (13.1)	15.6 (8.6, 22.6)	7.7 (1.2, 14.2)	11.6 (6.0, 17.2)	7 (5, 12)	14 (8, 84)	9 (6, 17)
30 minutes*	106 (42.2)	94 (36.9)	200 (39.5)	64 (25.4)	16.8 (8.7, 25.0)	11.5 (3.5, 19.5)	14.1 (7.3, 21.0)	6 (5, 12)	9 (6, 29)	8 (5, 14)
45 minutes*	152 (60.6)	131 (51.4)	283 (55.9)	83 (32.9)	27.6 (19.2, 36.0)	18.4 (10.0, 26.9)	23.0 (15.8, 30.2)	4 (3, 6)	6 (4, 11)	5 (4, 7)
1 hour*	186 (74.1)	170 (66.7)	356 (70.4)	95 (37.7)	36.4 (28.3, 44.5)	29.0 (20.6, 37.3)	32.7 (25.5, 39.8)	3 (3, 4)	4 (3, 5)	4 (3, 4)
1.5 hours*	217 (86.5)	187 (73.3)	404 (79.8)	99 (39.3)	47.2 (39.8, 54.5)	34.0 (25.9, 42.2)	40.6 (33.6, 47.5)	3 (2, 3)	3 (3, 4)	3 (3, 3)
2 hours*	225 (89.6)	199 (78.0)	424 (83.8)	109 (43.3)	46.4 (39.2, 53.6)	34.8 (26.8, 42.7)	40.5 (33.6, 47.4)	3 (2, 3)	3 (3, 4)	3 (3, 3)
4 hours*	219 (87.3)	178 (69.8)	397 (78.5)	100 (39.7)	47.6 (40.3, 54.9)	30.1 (21.9, 38.4)	38.8 (31.8, 45.8)	3 (2, 3)	4 (3, 5)	3 (3, 4)
6 hours*	221 (88.0)	187 (73.3)	408 (80.6)	112 (44.4)	43.6 (36.3, 50.9)	28.9 (20.7, 37.1)	36.2 (29.2, 43.2)	3 (2, 3)	4 (3, 5)	3 (3, 4)
8 hours*	223 (88.8)	185 (72.5)	408 (80.6)	131 (52.0)	36.9 (29.6, 44.2)	20.6 (12.3, 28.8)	28.6 (21.6, 35.7)	3 (3, 4)	5 (4, 9)	4 (3, 5)
24 hours*	147 (58.6)	135 (52.9)	282 (55.7)	86 (34.1)	24.4 (16.0, 32.9)	18.8 (10.3, 27.3)	21.6 (14.3, 28.9)	5 (4, 7)	6 (4, 10)	5 (4, 7)

\*Nominal  $P < .05$  in the main studies, indicating treatment response rates significantly different from placebo, based on Fisher's exact test.

<sup>a</sup>Defined as a  $\geq 40\%$  reduction from baseline as measured by the 5-item Positive and Negative Syndrome Scale-Excited Component.

<sup>b</sup>Sublingual dexmedetomidine vs placebo.

<sup>c</sup>Not statistically significant; the 95% CI contains "infinity".

Abbreviations: CI, confidence interval; ns, not statistically significant; PEC, Positive and Negative Syndrome Scale-Excited Component.

Table S2. Incidence of somnolence events by time of onset and association with mean ACES score for adults with schizophrenia and bipolar disorder.

	Somnolence, hours postdose	Sublingual dexmedetomidine						Placebo			All sublingual dexmedetomidine		
		180 ug			120 ug			Events, n	ACES score, mean	ACES score, SD	Events, n	ACES score, mean	ACES score, SD
<b>Schizophrenia</b>													
Any Severity <sup>a</sup>	0 to 2 h	25	2.4	0.58	26	2.5	1.03	9	2.3	0.50	51	2.4	0.83
	>2 to 4 h	2	4.0	1.41	1	5.0		1	2.0		3	4.3	1.15
	>4 to 8 h	1	2.0		.	.		.	.		1	2.0	
	Any hour (0 - 8)	28	2.5	0.75	27	2.6	1.12	10	2.3	0.48	55	2.5	0.94
Mild	0 to 2 h	21	2.5	0.60	23	2.5	1.08	9	2.3	0.50	44	2.5	0.88
	>2 to 4 h	2	4.0	1.41	1	5.0		1	2.0		3	4.3	1.15
	>4 to 8 h	1	2.0		.	.		.	.		1	2.0	
	Any hour (0 - 8)	24	2.6	0.78	24	2.6	1.18	10	2.3	0.48	48	2.6	0.99
Moderate	0 to 2 h	4	2.0	0.00	3	2.3	0.58	.	.		7	2.1	0.38
	Any hour (0 - 2)	4	2.0	0.00	3	2.3	0.58	.	.		7	2.1	0.38
<b>Bipolar Disorder</b>													
Any Severity	0 to 2 h	26	2.2	0.40	25	2.2	0.66	5	2.6	0.55	51	2.2	0.54
	>2 to 4 h	1	7.0		1	2.0		1	5.0		2	4.5	3.54
	Any hour (0 - 4)	27	2.4	1.01	26	2.2	0.65	6	3.0	1.10	53	2.3	0.85
Mild	0 to 2 h	15	2.3	0.46	18	2.3	0.77	5	2.6	0.55	33	2.3	0.64
	>2 to 4 h	1	7.0		1	2.0		1	5.0		2	4.5	3.54
	Any hour (0 - 4)	16	2.6	1.26	19	2.3	0.75	6	3.0	1.10	35	2.4	1.01
Moderate	0 to 2 h	11	2.1	0.30	7	2.0	0.00	.	.		18	2.1	0.24
	Any hour (0 - 2)	11	2.1	0.30	7	2.0	0.00	.	.		18	2.1	0.24

<sup>a</sup> Excludes one subject who received sublingual dexmedetomidine 180 ug and experienced moderate somnolence on Day 3 and reported an ACES score of 7 at Day 1, hour 8. Excludes one subject who received sublingual dexmedetomidine 120 ug and experienced mild somnolence on Day 6 and reported an ACES score of 6 at Day 1, hour 8.

ACES rates overall agitation and sedation, where 1 indicates marked agitation; 2 - moderate agitation; 3 - mild agitation; 4 - normal behavior; 5 - mild calmness; 6 - moderate calmness; 7 - marked calmness; 8 - deep sleep; and 9 - unarousable.

Severity of somnolence was assessed by the investigator(s) and rated as mild, moderate, or severe, as defined in the study protocol: Mild: Is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual activities of daily living. Moderate: Is usually alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the subject.

Severe: Interrupts usual activities of daily living, significantly affects clinical status, or may require intensive therapeutic intervention.

Abbreviations: ACES, Agitation-Calmness Evaluation Scale; SD, standard deviation

Table S3. Incidence of delayed<sup>a</sup> adverse events with sublingual dexmedetomidine or placebo, number needed to harm, and likelihood to be helped or harmed in adults with schizophrenia

	Incidence n (%)			Number Needed to Harm <sup>b</sup> (95% CI)		Likelihood to be Helped or Harmed (NNH/NNT <sup>c</sup> )	
	Sublingual dexmedetomidine			Sublingual dexmedetomidine		Sublingual dexmedetomidine	
	180 ug n=126	120 ug n=129	Placebo n=126	180 ug n=126	120 ug n=129	180 ug n=126	120 ug n=129
<b>Adverse event of special interest</b>							
Cardiac/vascular disorder	6 (4.8)	8 (6.2)	3 (2.4)	42 (ns) <sup>e</sup>	27 (ns) <sup>e</sup>	21.0	6.8
Hypotension/bradycardia(s)	0	4 (3.1)	0	(nd)	33 (17, 914)	NA	8.3
Hypotension	0	4 (3.1)	0	(nd)	33 (17, 914)	NA	8.3
<b>Adverse event<sup>d</sup></b>							
Orthostatic hypotension	6 (4.8)	2 (1.6)	0	21 (12, 96)	65 (ns) <sup>e</sup>	10.5	16.3
Headache	3 (2.4)	5 (3.9)	3 (2.4)	(nd)	67 (ns) <sup>e</sup>	NA	16.8
Somnolence	4 (3.2)	2 (1.6)	1 (0.8)	42 (ns) <sup>e</sup>	133 (ns) <sup>e</sup>	21.0	33.3
Dizziness	2 (1.6)	1 (0.8)	0	63 (ns) <sup>e</sup>	129 (ns) <sup>e</sup>	31.5	32.3
Dry mouth	0	1 (0.8)	1 (0.8)	-126 (ns) <sup>e</sup>	-5418 (ns) <sup>e</sup>	NA	NA

<sup>a</sup> Occurring after the first 2 hours postdose

<sup>b</sup> A negative NNH denotes an advantage for sublingual dexmedetomidine relative to placebo and is not interpretable as a harm.

<sup>c</sup> Using NNT for response at 2 hours postdose (refer to Table 1).

<sup>d</sup> Reported by at least 2% of subjects in the safety population (all subjects who received a dose of study drug).

<sup>e</sup> Not statistically significant; the 95% CI contains "infinity".

Abbreviations: CI, confidence interval; NA, not applicable; NNT, number needed to treat; NNH, number needed to harm; nd, no difference; ns, not statistically significant.

Table S4. Incidence of delayed<sup>a</sup> adverse events with sublingual dexmedetomidine or placebo, number needed to harm, and likelihood to be helped or harmed in adults with bipolar disorder

	Incidence n (%)			Number Needed to Harm <sup>b</sup> (95% CI)		Likelihood to be Helped or Harmed (NNH/NNT <sup>c</sup> )	
	Sublingual dexmedetomidine			Sublingual dexmedetomidine		Sublingual dexmedetomidine	
	180 ug n=126	120 ug n=126	Placebo n=126	180 ug n=126	120 ug n=126	180 ug n=126	120 ug n=126
<b>Adverse event of special interest</b>							
Cardiac/vascular disorder	9 (7.1)	7 (5.6)	2 (1.6)	18 (10, 180)	26 (ns) <sup>e</sup>	6.0	6.5
Hypotension/bradycardia(s)	3 (2.4)	3 (2.4)	0	42 (ns) <sup>e</sup>	42 (ns) <sup>e</sup>	14.0	10.5
Bradycardia(s)	3 (2.4)	2 (1.6)	0	42 (ns) <sup>e</sup>	63 (ns) <sup>e</sup>	14.0	15.8
Hypotension	3 (2.4)	3 (2.4)	0	42 (ns) <sup>e</sup>	42 (ns) <sup>e</sup>	14.0	10.5
<b>Adverse event<sup>d</sup></b>							
Orthostatic hypotension	5 (4.0)	4 (3.2)	1 (0.8)	32 (ns) <sup>e</sup>	42 (ns) <sup>e</sup>	10.7	10.5
Dizziness	3 (2.4)	3 (2.4)	0	42 (ns) <sup>e</sup>	42 (ns) <sup>e</sup>	14.0	10.5
Nausea	3 (2.4)	2 (1.6)	0	42 (ns) <sup>e</sup>	63 (ns) <sup>e</sup>	14.0	15.8
Dry mouth	2 (1.6)	1 (0.8)	0	63 (ns) <sup>e</sup>	126 (ns) <sup>e</sup>	21.0	31.5
Headache	1 (0.8)	2 (1.6)	3 (2.4)	-63 (ns) <sup>e</sup>	-126 (ns) <sup>e</sup>	NA	NA

<sup>a</sup>Occurring after the first 2 hours postdose

<sup>b</sup>A negative NNH denotes an advantage for sublingual dexmedetomidine relative to placebo and is not interpretable as a harm.

<sup>c</sup>Using NNT for response at 2 hours postdose (refer to Table 1).

<sup>d</sup>Reported by at least 2% of subjects in the safety population (all subjects who received a dose of study drug).

<sup>e</sup>Not statistically significant; the 95% CI contains “infinity”.

Abbreviations: CI, confidence interval; NA, not applicable; NNT, number needed to treat; NNH, number needed to harm; ns, not statistically significant.

Table S5. Response rate (based on CGI-I), absolute risk reduction, and number needed to treat at time points from 10 minutes to 24 after a dose of sublingual dexmedetomidine in patients with schizophrenia or bipolar disorder

Time postdose	CGI-I Response <sup>a</sup>				Absolute Risk Reduction <sup>b</sup>			Number Needed to Treat		
	n (%)				% (95% CI)			(95% CI)		
	Sublingual dexmedetomidine				Sublingual dexmedetomidine			Sublingual dexmedetomidine		
	180 ug	120 ug	120 ug or 180 ug	Placebo	180 ug (95% CI)	120 ug (95% CI)	120 ug or 180 ug (95% CI)	180 ug	120 ug	120 ug or 180 ug
Schizophrenia	n=125	n=129	n=254	n=126	n=125	n=129	n=254	n=125	n=129	n=254
30 minutes*	49 (39.2)	39 (30.2)	88 (34.6)	20 (15.9)	23.3 (12.7, 34.0)	14.4 (4.2, 24.5)	18.8 (10.1, 27.4)	5 (3, 8)	7 (5, 24)	6 (4, 10)
1 hour*	86 (68.8)	66 (51.2)	152 (59.8)	34 (27.0)	41.8 (30.6, 53.0)	24.2 (12.6, 35.8)	32.9 (23.0, 42.7)	3 (2, 4)	5 (3, 8)	4 (3, 5)
2 hours*	108 (86.4)	84 (65.1)	192 (75.6)	45 (35.7)	50.7 (40.4, 61.0)	29.4 (17.7, 41.1)	39.9 (30.0, 49.8)	2 (2, 3)	4 (3, 6)	3 (3, 4)
4 hours*	106 (84.8)	80 (62.0)	186 (73.2)	41 (32.5)	52.3 (41.9, 62.6)	29.5 (17.8, 41.2)	40.7 (30.9, 50.5)	2 (2, 3)	4 (3, 6)	3 (2, 4)
Bipolar Disorder	n=126	n=126	n=252	n=126	n=126	n=126	n=252	n=126	n=126	n=252
30 minutes	37 (29.4)	38 (30.2)	75 (29.8)*	24 (19.0)	10.3 (-0.2, 20.8)	11.1 (0.6, 21.7)	10.7 (1.8, 19.6)	10 (ns) <sup>c</sup>	9 (5, 178)	10 (6, 55)
1 hour*	89 (70.6)	75 (59.5)	164 (65.1)	37 (29.4)	41.3 (30.0, 52.5)	30.2 (18.5, 41.9)	35.7 (25.8, 45.6)	3 (2, 4)	4 (3, 6)	3 (3, 4)
2 hours*	109 (86.5)	88 (69.8)	197 (78.2)	48 (38.1)	48.4 (38.0, 58.8)	31.7 (20.1, 43.4)	40.1 (30.2, 50.0)	3 (2, 3)	4 (3, 5)	3 (3, 4)
4 hours*	103 (81.7)	82 (65.1)	185 (73.4)	43 (34.1)	47.6 (36.9, 58.3)	31.0 (19.2, 42.7)	39.3 (29.4, 49.2)	3 (2, 3)	4 (3, 6)	3 (3, 4)
Pooled	n=251	n=255	n=506	n=252	n=251	n=255	n=506	n=251	n=255	n=506
30 minutes*	86 (34.3)	77 (30.2)	163 (32.2)	44 (17.5)	16.8 (9.3, 24.3)	12.7 (5.4, 20.1)	14.8 (8.5, 21.0)	6 (5, 11)	8 (5, 19)	7 (5, 12)
1 hour*	175 (69.7)	141 (55.3)	316 (62.5)	71 (28.2)	41.5 (33.6, 49.5)	27.1 (18.9, 35.4)	34.3 (27.3, 41.3)	3 (3, 3)	4 (3, 6)	3 (3, 4)
2 hours*	217 (86.5)	172 (67.5)	389 (76.9)	93 (36.9)	49.5 (42.2, 56.9)	30.5 (22.3, 38.8)	40.0 (33.0, 47.0)	3 (2, 3)	4 (3, 5)	3 (3, 4)
4 hours*	209 (83.3)	162 (63.5)	371 (73.3)	84 (33.3)	49.9 (42.5, 57.4)	30.2 (21.9, 38.5)	40.0 (33.0, 47.0)	3 (2, 3)	4 (3, 5)	3 (3, 4)

\*Nominal  $P < .05$ , indicating treatment response rates significantly different from placebo, based on Fisher's exact test.

<sup>a</sup>Responder defined as achieving a score of 1 ("very much improved" or 2 "much improved") on the CGI-I scale.

<sup>b</sup>Sublingual dexmedetomidine vs placebo.

<sup>c</sup>Not statistically significant; the 95% CI contains "infinity".

Abbreviations: CGI-I, Clinical Global Impressions-Improvement; CI, confidence interval; ns, not statistically significant.

Table S6. PEC change scores and effect size difference from placebo as measured by Cohen’s d from baseline from 10 minutes to 24 after a dose of sublingual dexmedetomidine in subjects with schizophrenia, bipolar disorder, and pooled

Time postdose	Placebo			Sublingual dexmedetomidine 120 ug			Sublingual dexmedetomidine 180 ug			Sublingual dexmedetomidine Pooled		
	n	Mean (SD) change from baseline		n	Mean (SD) change from baseline	Cohen’s d (95% CI)	n	Mean (SD) change from baseline	Cohen’s d (95% CI)	n	Mean (SD) change from baseline	Cohen’s d (95% CI)
<b>Schizophrenia</b>												
Predose	126			129			125			254		
10 minutes	126	-1.3 (2.17)		129	-1.3 (2.50)	.15 (-.10, .40)	125	-2.0 (3.19)	.13 (-.12, .38)	254	-1.7 (2.88)	.13 (-.07, .33)
20 minutes	126	-2.5 (3.20)		129	-2.8 (4.03)	.23 (-.02, .48)	125	-3.9 (4.54)	.21 (-.04, .46)	254	-3.4 (4.31)	.21 (.01, .41)
30 minutes	126	-3.1 (3.56)		129	-4.4 (4.90)	.44 (.19, .69)	125	-5.7 (5.27)	.42 (.17, .67)	254	-5.0 (5.11)	.41 (.20, .61)
45 minutes	126	-3.6 (3.78)		129	-5.7 (5.18)	.67 (.41, .92)	125	-7.6 (5.32)	.66 (.40, .91)	254	-6.6 (5.33)	.62 (.41, .83)
1 hour	126	-4.1 (4.16)		129	-6.9 (5.06)	.81 (.55, 1.06)	125	-8.8 (4.96)	.82 (.56, 1.08)	254	-7.8 (5.09)	.78 (.57, .99)
1.5 hours	126	-4.6 (4.38)		129	-8.0 (5.00)	.92 (.66, 1.18)	125	-9.8 (4.60)	.97 (.70, 1.23)	254	-8.9 (4.88)	.92 (.71, 1.13)
2 hours	126	-4.7 (4.69)		129	-8.4 (4.83)	.98 (.72, 1.24)	125	-10.4 (4.34)	1.03 (.76, 1.29)	254	-9.4 (4.69)	.99 (.78, 1.21)
4 hours	82	-6.4 (4.24)		105	-9.1 (4.58)	.76 (.46, 1.06)	122	-10.3 (4.26)	.80 (.51, 1.08)	227	-9.8 (4.44)	.77 (.54, 1.00)
6 hours	107	-5.4 (4.28)		116	-8.0 (4.25)	.79 (.52, 1.07)	124	-9.4 (3.99)	.82 (.55, 1.09)	240	-8.8 (4.17)	.80 (.58, 1.02)
8 hours	118	-5.7 (4.04)		119	-8.0 (3.92)	.76 (.50, 1.03)	125	-9.5 (3.94)	.76 (.50, 1.02)	244	-8.7 (3.99)	.76 (.54, .97)
24 hours	126	-4.4 (3.66)		126	-5.4 (4.03)	.45 (.20, .70)	124	-6.8 (4.41)	.43 (.18, .68)	250	-6.1 (4.27)	.42 (.22, .63)
<b>Bipolar Disorder</b>												
Predose	126			126			126			252		
10 minutes	126	-1.0 (1.85)		126	-1.6 (2.65)	.26 (.01, .50)	126	-1.6 (3.06)	.23 (-.02, .48)	252	-1.6 (2.85)	.23 (.02, .43)
20 minutes	126	-1.9 (3.00)		126	-2.9 (3.83)	.33 (.08, .58)	126	-3.1 (4.45)	.30 (.05, .55)	252	-3.0 (4.14)	.30 (.09, .50)
30 minutes	126	-2.8 (3.85)		126	-4.3 (4.86)	.39 (.14, .64)	126	-4.6 (5.08)	.38 (.13, .63)	252	-4.5 (4.96)	.37 (.16, .57)
45 minutes	126	-3.6 (4.14)		126	-6.3 (5.30)	.60 (.35, .86)	126	-6.7 (5.12)	.62 (.36, .87)	252	-6.5 (5.20)	.59 (.38, .80)
1 hour	126	-4.4 (4.53)		126	-7.5 (5.19)	.73 (.48, .99)	126	-8.4 (5.17)	.74 (.48, .99)	252	-7.9 (5.19)	.72 (.51, .93)
1.5 hours	126	-4.7 (4.52)		126	-8.6 (5.28)	.91 (.65, 1.17)	126	-9.7 (4.90)	.95 (.69, 1.21)	252	-9.2 (5.12)	.91 (.70, 1.12)
2 hours	126	-4.9 (4.67)		126	-9.0 (5.26)	.97 (.71, 1.23)	126	-10.4 (4.45)	1.06 (.79, 1.32)	252	-9.7 (4.91)	1.00 (.78, 1.21)
4 hours	76	-7.1 (4.47)		108	-9.5 (4.24)	.69 (.39, .99)	115	-10.6 (3.57)	.76 (.46, 1.05)	223	-10.1 (3.94)	.74 (.50, .97)
6 hours	99	-6.6 (4.84)		113	-9.2 (4.35)	.66 (.38, .93)	119	-9.9 (3.68)	.71 (.43, .98)	232	-9.6 (4.02)	.70 (.48, .93)
8 hours	118	-6.2 (4.61)		116	-8.5 (4.18)	.59 (.33, .86)	123	-9.1 (3.63)	.63 (.37, .89)	239	-8.8 (3.91)	.63 (.42, .84)
24 hours	125	-4.1 (4.04)		125	-5.6 (4.16)	.41 (.16, .66)	124	-5.9 (4.38)	.40 (.15, .65)	249	-5.8 (4.27)	.40 (.20, .61)

Time postdose	Placebo			Sublingual dexmedetomidine 120 ug			Sublingual dexmedetomidine 180 ug			Sublingual dexmedetomidine Pooled		
	n	Mean (SD) change from baseline	n	Mean (SD) change from baseline	Cohen's d (95% CI)	n	Mean (SD) change from baseline	Cohen's d (95% CI)	n	Mean (SD) change from baseline	Cohen's d (95% CI)	
Pooled												
Predose	252		255			251			506			
10 minutes	252	-1.2 (2.02)	255	-1.4 (2.57)	.20 (.03, .38)	251	-1.8 (3.13)	.18 (.00, .35)	506	-1.6 (2.86)	.18 (.04, .32)	
20 minutes	252	-2.2 (3.11)	255	-2.9 (3.92)	.28 (.10, .45)	251	-3.5 (4.50)	.25 (.08, .43)	506	-3.2 (4.23)	.25 (.11, .40)	
30 minutes	252	-3.0 (3.70)	255	-4.4 (4.87)	.41 (.24, .59)	251	-5.2 (5.19)	.40 (.22, .57)	506	-4.8 (5.04)	.39 (.24, .53)	
45 minutes	252	-3.6 (3.96)	255	-6.0 (5.24)	.63 (.46, .81)	251	-7.2 (5.23)	.64 (.46, .82)	506	-6.6 (5.26)	.61 (.46, .75)	
1 hour	252	-4.2 (4.34)	255	-7.2 (5.13)	.77 (.59, .95)	251	-8.6 (5.06)	.78 (.59, .96)	506	-7.9 (5.14)	.75 (.60, .90)	
1.5 hours	252	-4.6 (4.44)	255	-8.3 (5.14)	.92 (.73, 1.10)	251	-9.8 (4.75)	.96 (.77, 1.14)	506	-9.0 (5.00)	.92 (.77, 1.07)	
2 hours	252	-4.8 (4.67)	255	-8.7 (5.05)	.97 (.79, 1.16)	251	-10.4 (4.39)	1.05 (.86, 1.23)	506	-9.6 (4.80)	1.00 (.84, 1.15)	
4 hours	158	-6.7 (4.35)	213	-9.3 (4.41)	.73 (.52, .94)	237	-10.5 (3.94)	.78 (.58, .99)	450	-9.9 (4.20)	.76 (.59, .92)	
6 hours	206	-5.9 (4.59)	229	-8.6 (4.33)	.72 (.53, .92)	243	-9.7 (3.84)	.76 (.57, .96)	472	-9.2 (4.11)	.75 (.60, .91)	
8 hours	236	-5.9 (4.34)	235	-8.2 (4.05)	.67 (.49, .86)	248	-9.3 (3.79)	.69 (.51, .88)	483	-8.8 (3.95)	.69 (.54, .84)	
24 hours	251	-4.2 (3.85)	251	-5.5 (4.09)	.43 (.25, .61)	248	-6.4 (4.41)	.41 (.23, .59)	499	-5.9 (4.27)	.41 (.27, .56)	

Abbreviations: CI, confidence interval; SD, standard deviation.