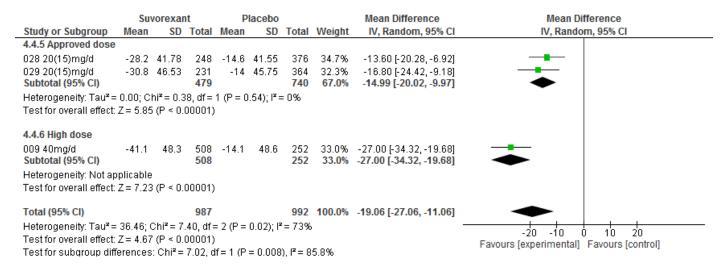
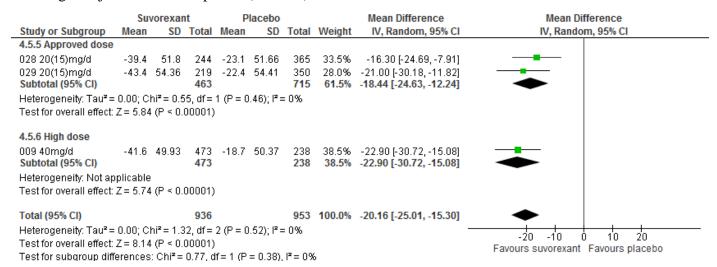
S1 Fig. Forest plots of efficacy secondary outcomes.

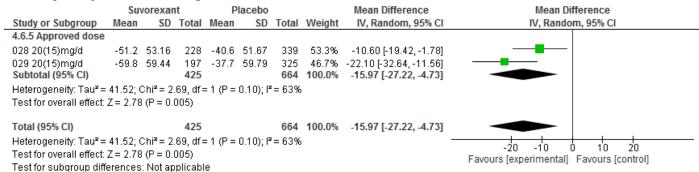
S1-1 Fig. Subjective total sleep time (minutes) at Week 1



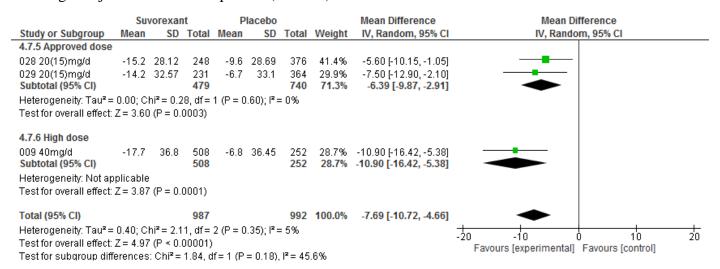
S1-2 Fig. Subjective total sleep time (minutes) at Month 1



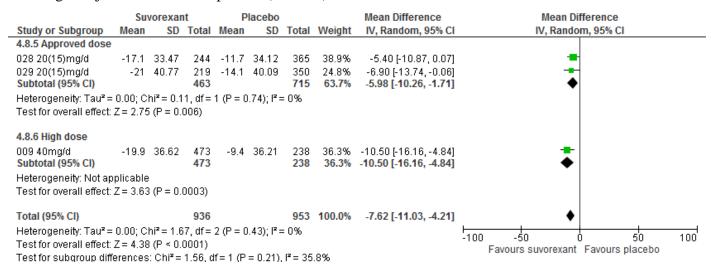
S1-3 Fig. Subjective total sleep time (minutes) at Month 3



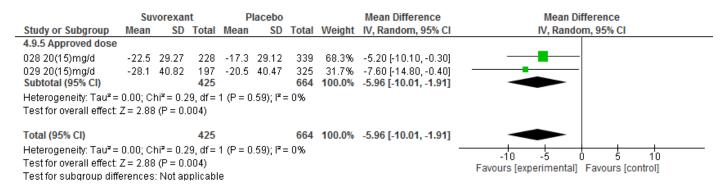
S1-4 Fig. Subjective time to sleep onset (minutes) at Week 1



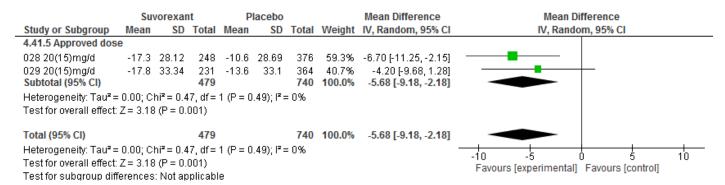
S1-5 Fig. Subjective time to sleep onset (minutes) at Month 1



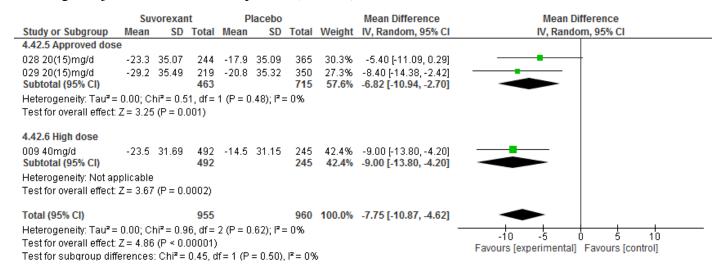
S1-6 Fig. Subjective time to sleep onset (minutes) at Month 3



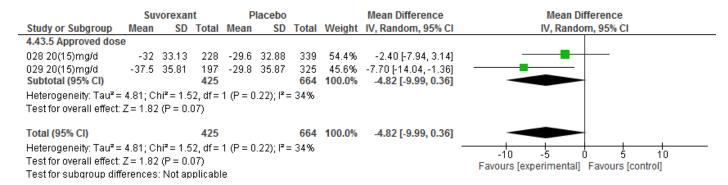
S1-7 Fig. Subjective wake after sleep onset (minutes) at Week 1



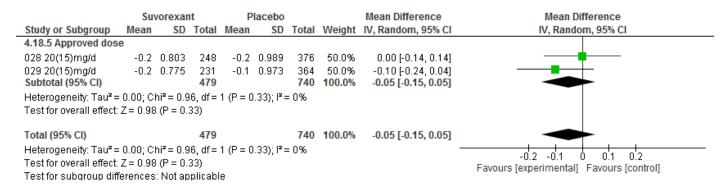
S1-8 Fig. Subjective wake after sleep onset (minutes) at Month 1



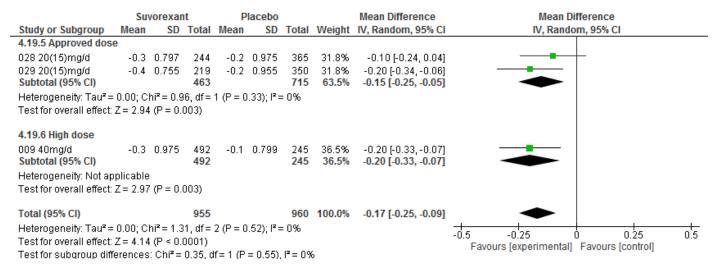
S1-9 Fig. Subjective wake after sleep onset (minutes) at Month 3



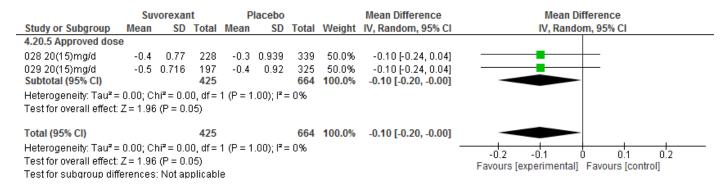
S1-10 Fig. Subjective quality of sleep (1-4 scale) at Week 1



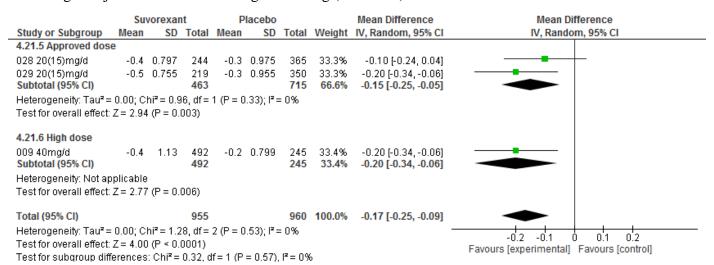
S1-11 Fig. Subjective quality of sleep (1-4 scale) at Month 1



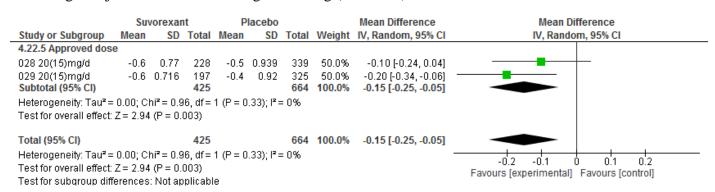
S1-12 Fig. Subjective quality of sleep (1–4 scale) at Month 3



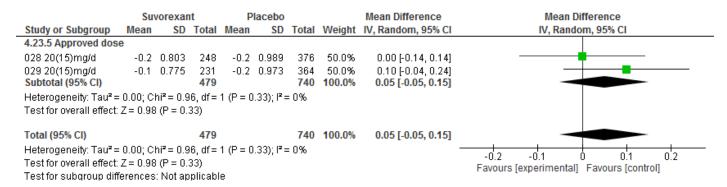
S1-13 Fig. Subjective refreshed feeling on waking (0-4 scale) at Month 1



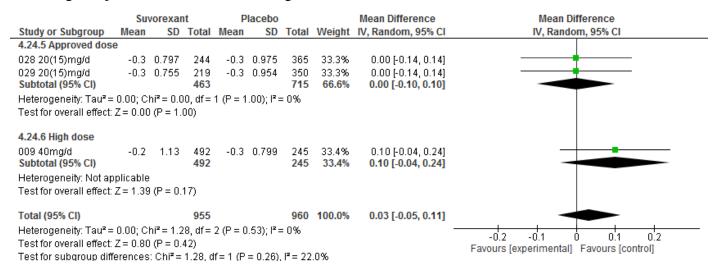
S1-14 Fig. Subjective refreshed feeling on waking (0-4 scale) at Month 3



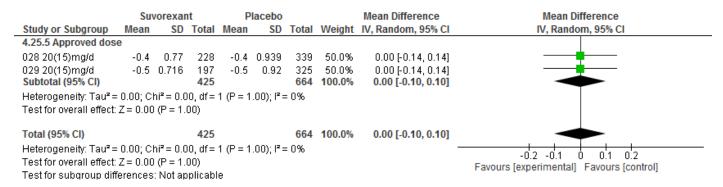
S1-15 Fig. Subjective number of awakenings at Week 1



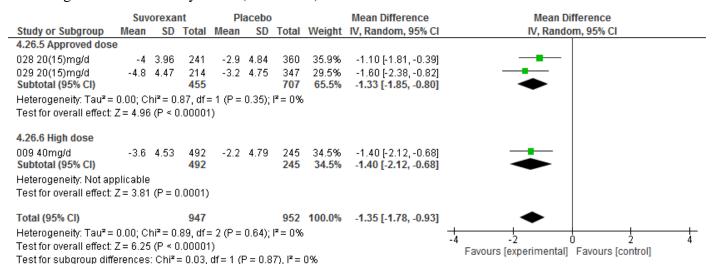
S1-16 Fig. Subjective number of awakenings at Month 1



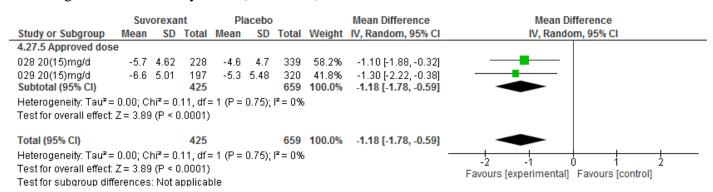
S1-17 Fig. Subjective number of awakenings at Month 3



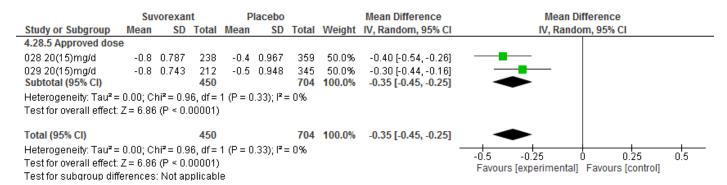
S1-18 Fig. Insomnia Severity Index (0-28 scale) at Month 1



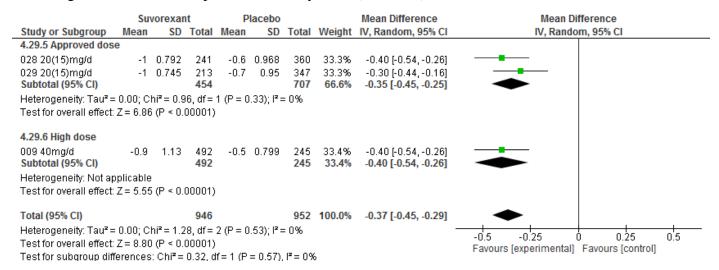
S1-19 Fig. Insomnia Severity Index (0-28 scale) at Month 3



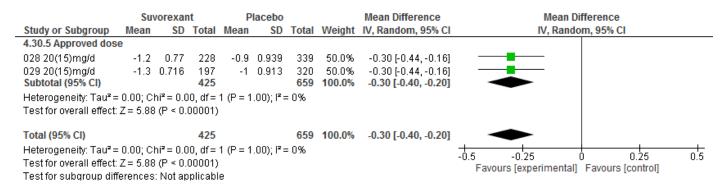
S1-20 Fig. Clinical Global Impression-Severity scale (1–7 scale) at Week 2



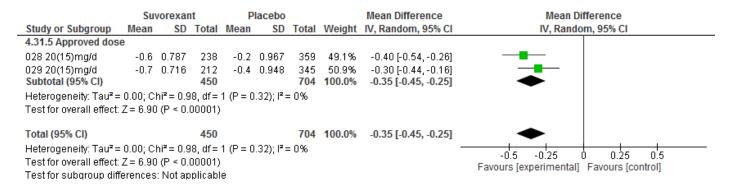
S1-21 Fig. Clinical Global Impression-Severity scale (1–7 scale) at Month 1



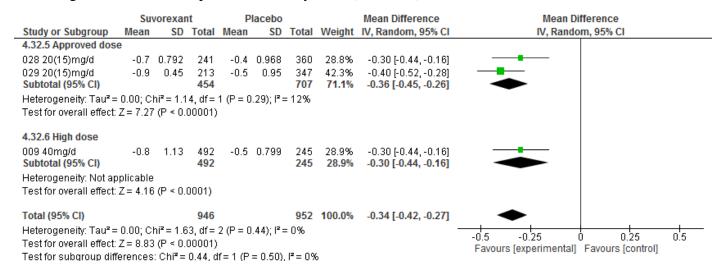
S1-22 Fig. Clinical Global Impression-Severity scale (1–7 scale) at Month 3



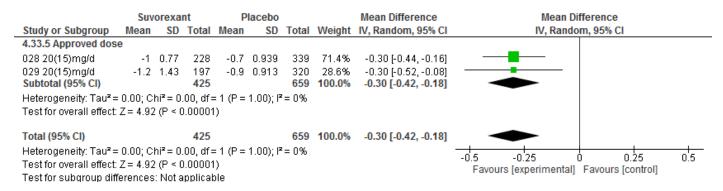
S1-23 Fig. Patient Global Impression-Severity scale (0–5 scale) at Week 2



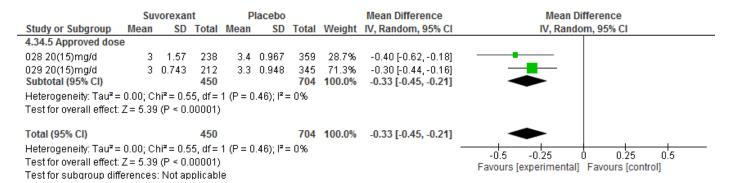
S1-24 Fig. Patient Global Impression-Severity scale (0–5 scale) at Month 1



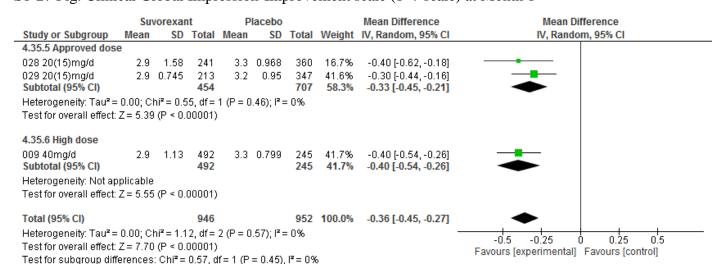
S1-25 Fig. Patient Global Impression-Severity scale (0–5 scale) at Month 3



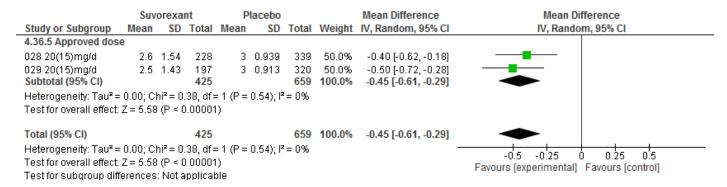
S1-26 Fig. Clinical Global Impression-Improvement scale (1–7 scale) at Week 2



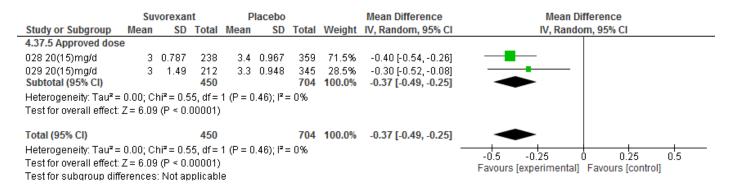
S1-27 Fig. Clinical Global Impression-Improvement scale (1–7 scale) at Month 1



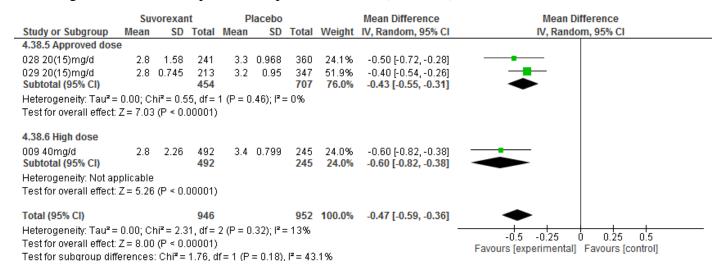
S1-28 Fig. Clinical Global Impression-Improvement scale (1–7 scale) at Month 3



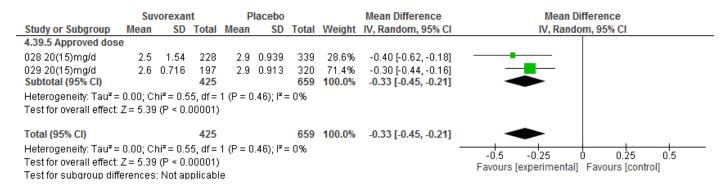
S1-29 Fig. Patient Global Impression-Improvement scale (1–7 scale) at Week 2



S1-30 Fig. Patient Global Impression-Improvement scale (1–7 scale) at Month 1



S1-31 Fig. Patient Global Impression-Improvement scale (1–7 scale) at Month 3



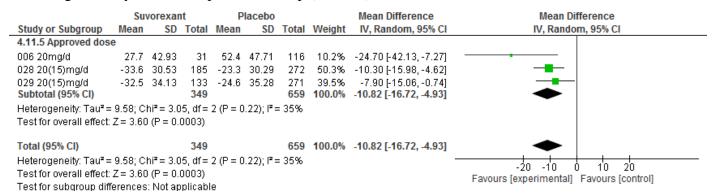
S1-32 Fig. Response rate at Month 3

Suvorex		vorexant Placebo				Risk Ratio	Risk Ratio		
Study or Subgroup	Events Total		Events Total		Weight	M-H, Random, 95% CI	M-H, Random, 95% CI		
5.40.3 ALL									
028 all dose	267	550	199	328	58.2%	0.80 [0.71, 0.90]			
029 all dose	212	517	170	310	41.8%	0.75 [0.65, 0.86]			
Subtotal (95% CI)		1067		638	100.0%	0.78 [0.71, 0.85]	•		
Total events	479		369						
Heterogeneity: Tau ² :	= 0.00; Chi	z = 0.49	i, df = 1 (F	P = 0.48	3); $I^2 = 0\%$	ı			
Test for overall effect	t: Z= 5.27 ((P < 0.0)	0001)						
Total (95% CI)		1067		638	100.0%	0.78 [0.71, 0.85]	•		
Total events	479		369						
Heterogeneity: Tau ²	= 0.00; Chi	z = 0.49	i, df = 1 (F	0.48	3); I² = 0%	-	07 085 1 12 15		
Test for overall effect	t: Z = 5.27 (P < 0.0		0.7 0.85 1 1.2 1.5 Favours suvorexant Favours placebo					
Test for subaroup di							ravouis suvoiexaiit. ravouis piacebo		

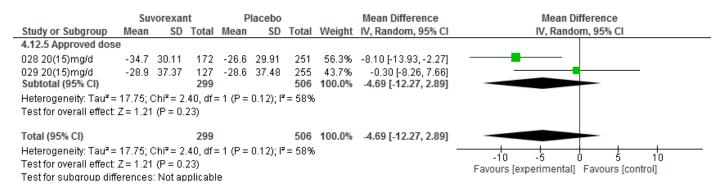
S1-33 Fig. Latency to onset of persistent sleep (minutes) at Day 1

	Suvorexant			Placebo				Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
4.10.5 Approved dos	e									
006 20mg/d	39.6	42.57	33	57	48.35	127	6.6%	-17.40 [-34.18, -0.62]		
028 20(15)mg/d	-29.9	29.06	193	-20.3	28.67	290	67.0%	-9.60 [-14.86, -4.34]		
029 20(15)mg/d	-25.3	41.63	144	-13	42.13	284	26.4%	-12.30 [-20.68, -3.92]		
Subtotal (95% CI)			370			701	100.0%	-10.83 [-15.13, -6.52]	•	
Heterogeneity: Tau² =	= 0.00; C	$hi^2 = 0.9$	12, df=	2(P = 0)	.63); l ^z =	= 0%				
Test for overall effect:	Z = 4.93	(P < 0.	00001)							
Total (95% CI)			370			701	100.0%	-10.83 [-15.13, -6.52]	•	
Heterogeneity: Tau ² =	= 0.00; C	hi = 0.9	2, df=	2 (P = 0	.63); l ^z =	= 0%				
Test for overall effect:	Z = 4.93	(P < 0.	00001)		-20 -10 0 10 20 Favours [experimental] Favours [control]					
Test for subgroup differences: Not applicable									i avours [experimentar] Favours [control]	

S1-34 Fig. Latency to onset of persistent sleep (minutes) at Month 1



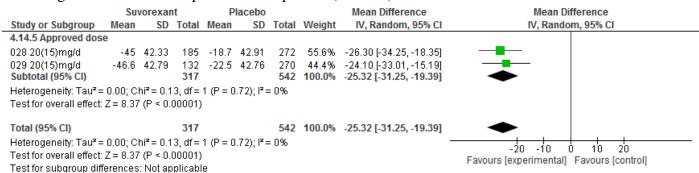
S1-35 Fig. Latency to onset of persistent sleep (minutes) at Month 3



S1-36 Fig. Wakefulness after persistent sleep onset (minutes) at Day 1

	Suvorexant		nt	Placebo				Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
4.13.5 Approved dos	ie										
028 20(15)mg/d	-52.1	37.47	192	-19.6	37.17	287	59.0%	-32.50 [-39.33, -25.67]	-		
029 20(15)mg/d	-58.3	41.02	144	-21.3	40.34	283	41.0%	-37.00 [-45.18, -28.82]			
Subtotal (95% CI)			336			570	100.0%	-34.35 [-39.59, -29.10]	◆		
Heterogeneity: Tau ² =	= 0.00; C	hi² = 0.8	9, df=	1 (P = 0)	.41); l² =	- 0%					
Test for overall effect:	: Z = 12.8	84 (P < 0	0.00001)							
Total (95% CI)			336			570	100.0%	-34.35 [-39.59, -29.10]	•		
Heterogeneity: Tau ² =	= 0.00; C	hi² = 0.8	9, df=	1 (P = 0)	.41); l² =	- 0%			- to 35 to 50		
Test for overall effect:	: Z = 12.8	84 (P < 0		-50 -25 0 25 50 Favours [experimental] Favours [control]							
Test for subgroup dif	ferences	: Not ap	plicabl	e					r avours [experimentar] Favours [control]		

S1-37 Fig. Wakefulness after persistent sleep onset (minutes) at Month 1



S1-38 Fig. Wakefulness after persistent sleep onset (minutes) at Month 3

