CENTRAL SLEEP APNEA AND CHRONIC OPIOD USE

Kathleen Sarmiento, MD
UC San Francisco
Associate Professor of Medicine

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Kathleen (Katie) Sarmiento, MD, is an Associate Professor of Medicine at UC San Francisco, the Director of Sleep Medicine at the San Francisco VA Health Care System, and the National Lead for VA TeleSleep, an enterprise-wide initiative to build a high-performing sleep telemedicine network. She has been instrumental in building infrastructure for and leading VA Sleep operations. She has an active clinical practice in Pulmonary, Critical Care and Sleep Medicine. Her research interests are focused on health services research, including strategies to improve access to sleep care in rural areas, reduce wait times, lower cost, and de-implement low-value steps in obtaining care.

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Katie Sarmiento, MD
UCSF/SFVAHCS
Kathleen.Sarmiento@va.gov
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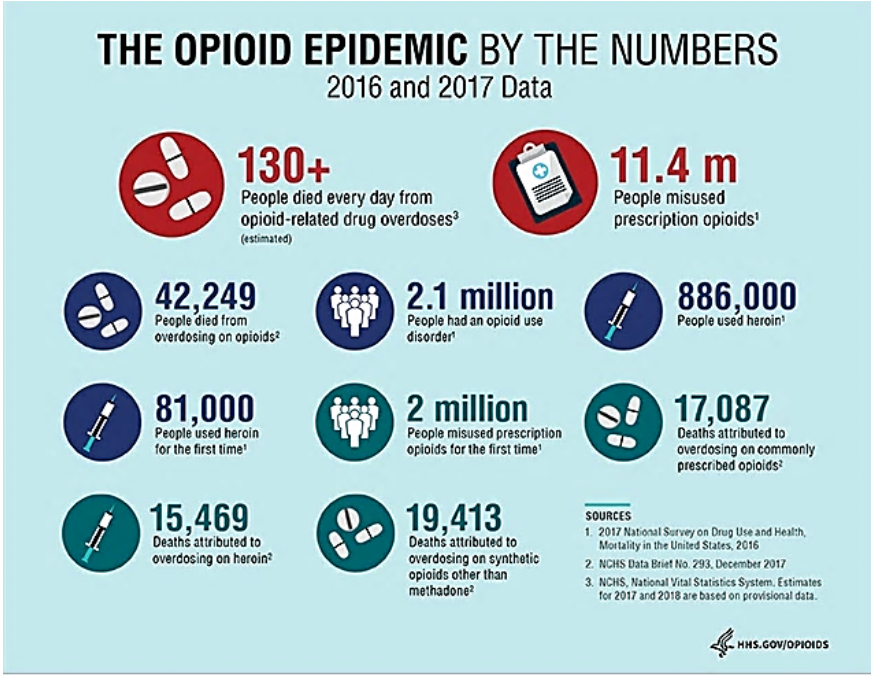
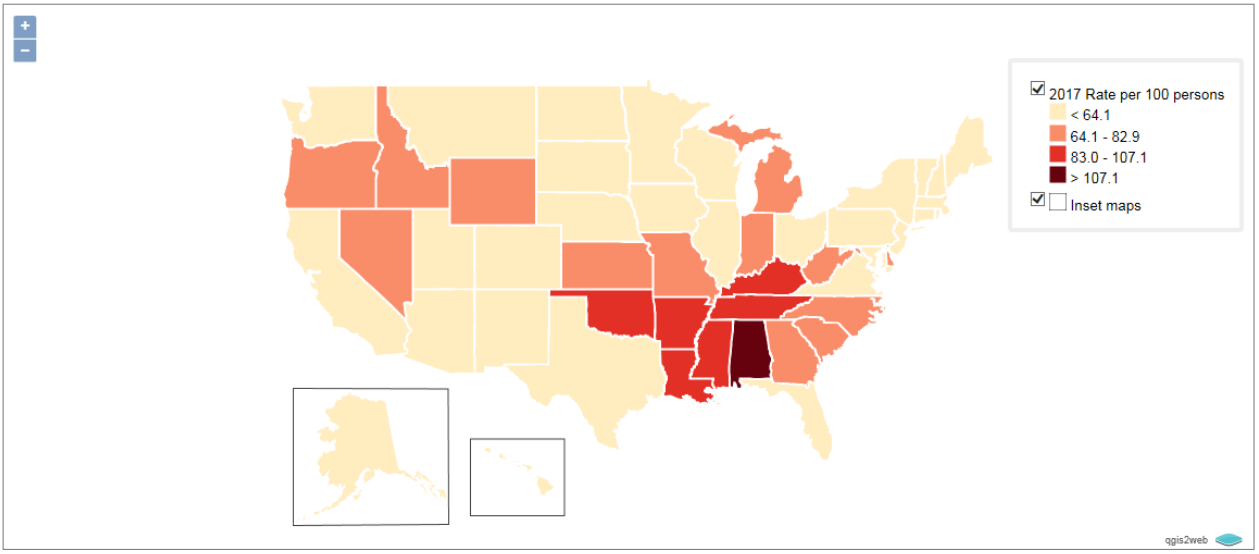


National Prescribing Rates of Opioids



Effects of Opioids

- Central depression of the respiratory rate
- Depression of reflex ventilatory responses to hypoxia and hypercapnia
- Reduced arousability (decreased cortical input)
- Increased upper airway collapsibility

Sleep Disordered Breathing

http://dx.doi.org/10.5664/jcsm.3950

Sleep Disordered Breathing and Chronic Respiratory Failure in Patients with Chronic Pain on Long Term Opioid Therapy

Anand R. Rose, M.D.[1,2]; Peter G. Catcheside, Ph.D.[1,2]; R. Doug McEvoy, M.D.[1,2]; Denzil Paul, MBiotech[1,2]; Dilip Kapur, M.B.Ch.B.[3]; Emily Peak, B.Behav.Sc.[1,2]; Andrew Vakulin, Ph.D.[1,2,4]; Nicholas A. Antic, M.B.B.S., Ph.D.[1,2]

- Aims
  - Assess prevalence of SDB In chronic opioid pain clinic population
  - Type of SDB
  - Impact on daytime awake ABG
  - PVT
- N=24 with matched sleep clinic comparison group and unmatched healthy controls
- Home PSG, awake ABG, Spirometry, PVT
- Mean MEQ 140, median 120 mg/24h

J Clin Sleep Med 2014;10(8):847-852

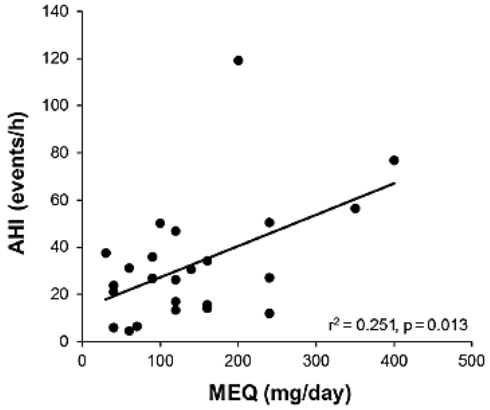
Awake Hypercapnia and SDB

Table 2—Arterial blood gas and pulmonary function results in opioid-treated chronic pain patients

	Mean ± SD	Median [IQR]
$PaCO_2$ (mm Hg)*	44.8 ± 4.1	44.9 [42.7–47.2]
PaO_2 (mm Hg)	81.4 ± 9.9	78.3 [74.0–86.5]
pH	7.39 ± 0.02	7.39 [7.38–7.41]
HCO_3^- (mmol/L)	26.9 ± 2.2	26.7 [25.4–28.0]
FEV_1 (L)	2.8 ± 0.9	2.7 [2.2–3.4]
FEV_1 (% predicted)	82.7 ± 16.8	81.0 [73.3–99.0]
FER (FEV_1/FVC %)	77.8 ± 5.9	76.4 [74.4–79.9]
FER (% predicted)	98.8 ± 8.0	96.5 [93.8–101.3]

N = 20. *Normal $PaCO_2$ range = 35–45 mm Hg. IQR, interquartile range.

Figure 1—Relationship between morphine equivalent dose (MEQ) and apnea hypopnea index (AHI), N = 24.



J Clin Sleep Med 2014;10(8):847-852

Table 1—Anthropometric, polysomnography, and psychomotor vigilance test data

	Opioid-Treated Patients	Healthy Controls	Sleep Clinic Controls
N (N Males)	24 (12)	20 (15)	20 (11)
Age (years)	52.4 ± 9.4	50.6 ± 10.1	52.9 ± 9.8
BMI (kg/m²)	34.9 ± 9.4*	24.5 ± 2.6	34.9 ± 8.4*
ESS	12.3 ± 5.4*	5.0 ± 3.0	10.0 ± 5.6*
Polysomnography study			
Total Sleep Time (min)	393.6 ± 94.2*	323.3 ± 81.1	336.2 ± 64.0
%NREM	86.6 ± 8.4*	80.0 ± 6.4	83.6 ± 6.2
%REM	13.2 ± 8.4*	20.0 ± 6.4	16.4 ± 6.2
%SWS	18.7 ± 13.1	19.5 ± 9.8	22.0 ± 10.6
Central Apnea Index (/h)§	3.9 ± 8.3*,†	0.3 ± 0.6	0.3 ± 0.5
Mixed Apnea Index (/h)§	0.1 ± 0.2	0.0 ± 0.0	0.1 ± 0.1
Obstructive Apnea Index (/h)§	3.0 ± 6.0	1.0 ± 1.1	5.4 ± 11.3
Hypopnea Index (/h)	26.0 ± 20.5*	7.1 ± 3.5	23.1 ± 17.1*
AHI (/h)	32.7 ± 25.6*	8.3 ± 4.0	28.9 ± 24.6*
NREM AHI (/h)§	31.4 ± 26.8*	5.7 ± 3.8	26.2 ± 25.7*
REM AHI (/h)	37.1 ± 28.1*	18.3 ± 8.9	40.8 ± 23.7*
Arousal index (/h)	8.0 ± 4.1*,†	14.9 ± 6.9	20.1 ± 13.8
Awake SpO_2 (%)	94.3 ± 1.6*	96.5 ± 1.3	94.3 ± 1.6*
%Sleep Time SpO_2 < 90%§	10.4 ± 17.6*	0.1 ± 0.3	6.0 ± 14.5*
Average SpO_2 desaturation (%)§	4.0 ± 1.4*	2.4 ± 0.8	3.8 ± 1.8*
Psychomotor vigilance test			
Reaction Time (sec)§	0.43 ± 0.27*	0.28 ± 0.03	
1/Reaction Time (sec^{-1})	2.82 ± 0.82*	3.70 ± 0.38	
Lapses > 500 msec§,‡	12.6 ± 21.5*	1.5 ± 1.2	

Values are mean ± SD. * Indicates $p < 0.05$ vs healthy controls; † $p < 0.05$ vs sleep lab controls. § Indicates non-normally distributed variables for which nonparametric tests were applied. ‡ Due to a device download problem PVT lapse data were restricted to 22 opioid patients versus 10 healthy controls.

J Clin Sleep Med 2014;10(8):847-852

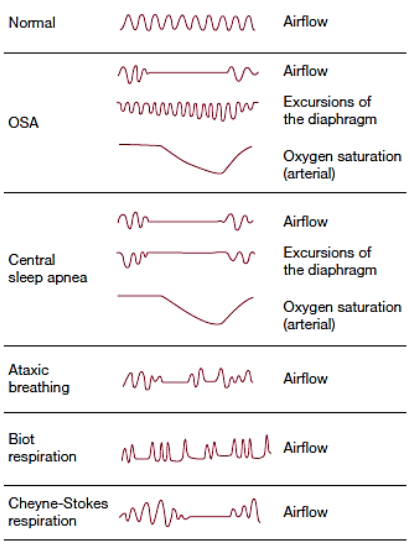
Mechanisms of SDB

- All narcotics partially or completely inhibit μ-opioid receptors on central and peripheral respiratory neurons
- Areas affected by opioids:
  - Pre-Bötzinger complex: generates respiratory rhythm, central chemoreception of CO2
  - Carotid body Glomus cells: peripheral→central feedback of CO2, O2, H+, K+
  - Bulbospinal inspiratory and expiratory premotor neurons (innervating intercostals, diaphragm, abdomen)
  - Hypoglossal motor nucleus: upper airway patency during sleep

Mechanisms of SDB

- Reduced efferent output to spinal motor neurons (intercostals and diaphragm)→alveolar hypoventilation
- Reduced efferent output to cranial motor neurons that maintain upper airway patency → UA collapsibility
- OSA
  - Reduction in upper airway muscle tone > NIP lower respiratory muscles
  - Presence of traditional RF
- CSA
  - Depression of hypoxic and hypercapnic ventilatory drives
  - Recovery of hypoxic ventilatory drive but continued suppression of hypercapnic drive
  - Upper airway may still be collapsed, but masked by no effort to breath

SDB Manifestations of Opioid Use



+ Hypoxemia

CHEST 2016; 150(4):934-944

Prevalence and Type of SDB

- Prevalence of SDB 42-85%
- CSA vs. OSA?
- Severity of SBD unrelated to sleep complaints

Table 2. Opioid Medications and Respiratory Parameters

			Overall SDB		Obstructive SDB		Central SDB			
Author, Year	Opioid	MEDD	AHI	SDB%	OAI	OSA%	CAI	CSA%	Hypoxemia	Ataxia
Teichtahl et al., 2001[1]	M	187.5-450	20.4 ± 20.7	70	0.7 ± 2.1	10	12.4 ± 15.5	60	Lower baseline Spo_2	NR
Wang et al., 2005[2]	M	NR	17.5 ± 17.3	NR	10.8[a] ± 10.3	NR	6.7 ± 14.2	30	Lower baseline Spo_2	NR
Walker et al., 2007[3]	M, A	7.5–750 (143.9)	43.5 ± 35.2	NR	16.8 ± 24.0	NR	12.8 ± 22.4	NR	Lower baseline Spo_2	70%
Webster et al., 2008[4]	M, A	15-5,985 (266)[a]	NR	75	NR	39	NR	24	NR	NR
Mogri et al., 2009[5]	NR	7.5-935 (180)	NR	85	NR	36	NR	24	Lower baseline Spo_2	NR
Sharkey et al., 2010[6]	M	93.8-1162 (406)	NR	42	NR	39[b]	NR	14	NR	NR
Jungquist et al., 2012[7]	M, A	5-960	22.7 ± 25	77	4.4 ± 9	NR	5.0 ± 13	18	NR	NR
Farney et al., 2013[8]	B	NR	20.4 ± 32	63	2.3 ± 3.9	8[c]	11.4 ± 28.1	30[c]	Lower baseline Spo_2	73%
Prevalence of sleep-disordered breathing				70%		Prevalence of CSA		24%		

Opioid class: M = methadone; A = any other full μ-agonists (oxycodone, morphine, fentanyl, hydrocodone, hydromorphone, propoxyphene); B = buprenorphine (partial μ-agonist). Spo_2 = oxygen saturation; MEDD = morphine equivalent daily dose. Range (mean) mg/d. See Appendix 1 for calculation; SDB = sleep-disordered breathing; No = no correlation was found; Yes = positive correlation was found; AHI = Apnea/Hypopnea Index (total apneas and hypopneas/hours of sleep); OAI = Obstructive Apnea Index (total obstructive apneas/hours of sleep); CAI = Central Apnea Index (total central apneas/hours of sleep); SDB% = prevalence of sleep-disordered breathing (AHI ≥ 5/h); OSA% = prevalence of obstructive sleep apnea (OAI ≥ 5/h); CSA% = prevalence of central sleep apnea (CAI ≥ 5/h); hypoxemia = statement or statistic showing significant reduction of Spo_2 baseline or increase % time below 90% compared with controls; ataxia = statement or statistic reporting the presence of ataxic, irregular breathing (e.g., Biot's respiration) in opioid cases. NR = not reported or insufficient information from the study to report or calculate.

[a]Median value reported.

[b]OAI includes hypopneas (i.e., obstructive apneas plus hypopneas/h sleep).

[c]Unpublished data.

Anesth Analg 2015;120:1273–85

Chronic Opioids and Sleep Architecture/Symptoms

- Induction phase
  - Reduced SWS, REM, TST, SE
  - Increased awakenings, prolonged REM latency
- Maintenance phase
  - SWS, REM, awakenings, REM latency normalize
  - Daytime sleepiness
- Withdrawal phase
  - Insomnia, frequent awakenings, Reduced REM
- Abstinence phase
  - Increased TST
  - SWS & REM rebound (13-22wks)

Sleep Med Rev 2007;11:35-46

Architecture, Symptoms & Outcomes

- Does abnormal architecture, CSA severity, blood methadone concentration impact daytime function and excessive sleepiness in MMT?
- N=50 MMT, 20 controls

Table 3—Subjective Daytime Sleepiness, Psychological Function, and Daytime Function in Patients on MMT

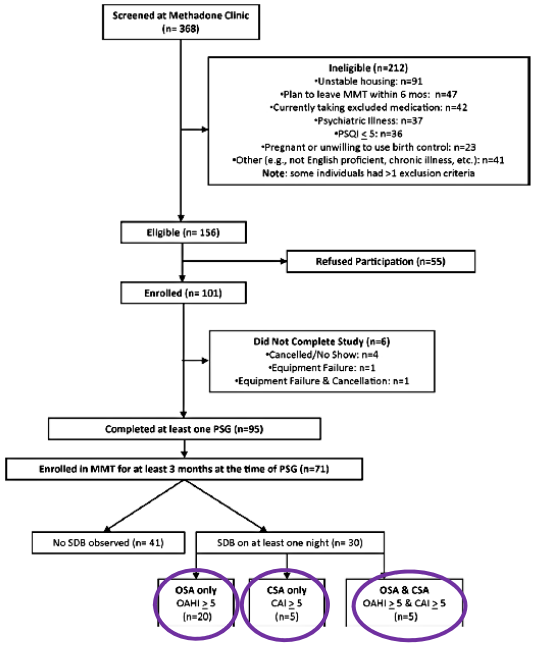
	Central apnea index		P value	Methadone blood level		P value
	< 5 (n = 35)	> 5 (n = 35)		Low (n = 25)	High (n = 25)	
ESS	6.63 ± 5.02	8.20 ± 4.90	0.31	6.16 ± 4.59	8.04 ± 5.29	0.26
FOSQ						
Overall	15.81 ± 3.10	14.67 ± 3.37	0.19	15.58 ± 2.86	15.37 ± 3.55	0.92
GP	3.25 ± 0.63	3.07 ± 0.63	0.30	3.20 ± 0.59	3.19 ± 0.68	0.79
SO	3.35 ± 0.74	3.13 ± 0.74	0.58	3.32 ± 0.72	3.24 ± 0.78	0.44
AL	2.95 ± 0.74	2.82 ± 0.76	0.58	2.88 ± 0.70	2.95 ± 0.79	0.56
V	3.13 ± 0.78	2.87 ± 0.87	0.37	3.06 ± 0.77	3.04 ± 0.85	0.86
IR	3.21 ± 1.01	2.82 ± 1.08	0.17	3.14 ± 1.11	3.05 ± 0.97	0.36
MMSE	28.71 ± 1.64	28.53 ± 2.75	0.74	28.80 ± 1.68	28.52 ± 2.31	0.82
BDI	14.80 ± 10.25	14.27 ± 11.69	0.70	12.92 ± 10.35	16.36 ± 10.74	0.26

Notes: Comparisons were made between patients with and without central sleep apnea and having lower and higher methadone blood concentrations. Mann-Whitney rank sum tests were tested. No significance reached the < 0.05 level. The 5 subscales of the Functional Outcome of Sleep Questionnaire (FOSQ) are general productivity (GP), social outcome (SO), activity level (AL), vigilance (V) and intimate relationship and sexual activity (IR). MMSE refers with the Mini-mental State Examination; BDI, Beck Depression Inventory; ESS, Epworth Sleepiness Scale.

Table 1—Sleep Architecture and Sleep-Disordered Breathing Data Comparison Between Patients on MMT and Control Subjects

Parameter	Patients n = 50	Controls n = 20	p Value
TST, min	380 ± 55.8	382 ± 55.5	0.87
Sleep efficiency, %	88.2 ± 9.8	85.7 ± 8.54	0.14
Sleep latency, min	9.72 ± 9.1	13.9 ± 17.4	0.45
REM latency, min	105 ± 57	92.3 ± 46.7	0.48
Arousal index	13.2 ± 5.02	13.2 ± 4.98	0.99
Sleep stage, min			
1	26.8 ± 17.3	37.7 ± 16.1	0.006[a]
2	243 ± 63.3	209 ± 33.9	0.03[a]
SWS	55.2 ± 40.4	64.7 ± 37.8	0.26
REM	55.2 ± 28.8	70.9 ± 23.0	0.03[a]
OSAHI, /h	10.8 ± 10.3	9.4 ± 9.1	0.59
CAI, /h	6.7 ± 14.2	0.25 ± 0.33	< 0.001[a]

J Clin Sleep Med 2008;4(6):557-562



- OSA>CSA
- CSA not associated with methadone dose or other drug use
- Sleep disturbance not associated with OSA or CSA (PSQI)

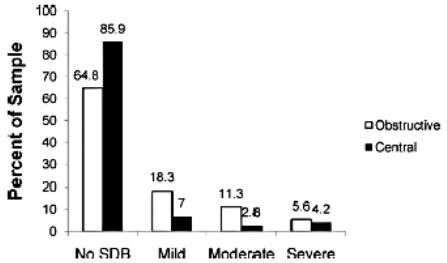


Fig. 2. Distribution of apnea by severity, percentage of MMT patients with n sleep-disordered breathing (SDB; OAHI < 5 and CAI < 5) or mild (5 ≤ OAHI < 15 a 5 ≤ CAI < 15), moderate (15 ≤ OAHI < 30 or 15 ≤ CAI < 30), or severe (OAHI ≥ 30 a CAI ≥ 30) sleep apnea. *N* = 71.

Drug and Alcohol Dependence 108 (2010) 77–83

Buprenorphine + Naloxone

- Partial μ-opioid agonist
- N=70, admitted for buprenorphine/naloxone treatment

TABLE 1 Demographics and possible risk factors for sleep disordered breathing

	Males	Females	All
Subjects	28	42	70
Age years	28.5±9.3 (18–53)	34.1±13.6 (19–73)	31.8±12.3 (18–73)
BMI kg·m^{-2}	24.4±4.7 (15.3–37.9)	25.1±6.6 (16.2–41.0)	24.9±5.9 (15.3–41.0)
Mallampati score 1–4	2.9±0.7 (2.0–4.0)	2.6±0.8 (1.0–4.0)	2.7±0.7 (1.0–4.0)
STOP-Bang score 0–8	3.2±1.1 (1.0–6.0)	2.3±1.2 (0.0–6.0)	2.7±1.2 (0.0–6.0)
Buprenorphine			
Total dose mg	21.5±17.5 (2.0–76.0)	16.5±10.7 (2.0–48.0)	18.5±13.0 (2.0–76.0)
Dosage mg·h^{-1}	0.4±0.2 (0.1–1.1)	0.4±0.2 (0.1–1.1)	0.4±0.2 (0.1–1.1)

Data are presented as n or mean±SD (range). BMI: body mass index; STOP-Bang: snore, tiredness, obstruction (witnessed apnoea), pressure (hypertension), BMI (>35 kg·m^{-2}), age (>50) neck circumference >15.75 inches, gender (male).

TABLE 3 Respiratory measurements

	Males	Females	All
Subjects	28	42	70
AHI	15.2±26.3 (0.0–106.2)	23.9±35.6 (0.0–180.0)	20.4±32.3 (0.0–180.0)
CAI	6.3±19.0 (0.0–176.4)	14.9±32.6 (0.0–97.6)	11.4±28.1 (0.0–176.4)
OAI	2.0±2.3 (0.0–8.6)	2.5±4.7 (0.0–26.5)	2.3±3.9 (0.0–26.5)
HI	6.9±4.8 (0.0–71.8)	6.5±9.6 (0.0–42.6)	6.6±11.8 (0.0–71.8)
Baseline Sp_{O_2} %	92.7±3.0 (86.0–98.0)	91.0±3.5 (83.0–98.0)	91.7±3.4 (83.0–98.0)
% of TST where Sp_{O_2} <90%	13.4±22.4 (0.0–76.2)	29.8±36.6 (0.0–100.0)	23.2±32.5 (0.0–100.0)

Data are presented as n or mean±SD (range). AHI: apnoea/hypopnoea index; CAI: central apnoea index; OAI: obstructive apnoea index; HI: hypopnoea index; Sp_{O_2}: arterial oxygen saturation measured by pulse oximetry; TST: total sleep time.

Timing of Opioid Dosing?

- Very small study, n=15
- Aim: evaluate effect of IR and ER hydromorphone dosing (AM vs. PM) on AHI, pain scores, adverse events/safety

Table 1 Study protocol

Study Phase	Screening	Baseline	Open-Label IR Hydromorphone		
Activity	Visit 1	Visit 2: sleep study 1	Titration	Stabilization	Visit 3: sleep study 2
# Days/hours	Up to 30 days before baseline visit	24 hours	Up to 14 days	At least 7 days	24 hours

Study Phase	Double-Blind ER Hydromorphone					Follow-up
Treatment period	Period 1 (QAM or QPM dosing regimen)			Period 2 (alternate dosing regimen)		
Activity	Titration	Stabilization	Visit 4: sleep study 3	Stabilization	Visit 5: sleep study 4	Visit 6
# Days/hours	Up to 32 days	14–21 days	24 hours	14–21 days	24 hours	5–9 days after visit 5

ER = extended release; IR = immediate release; QAM = morning hydromorphone dosing time; QPM = evening hydromorphone dosing time.

Pain Medicine 2015; 16: 460–471

Table 3 Polysomnography-derived endpoints

	No Treatment (N = 15)	IR Hydromorphone (N = 15)	ER Hydromorphone QAM (N = 14)	ER Hydromorphone QPM (N = 15)
Respiratory events				
Number of apneas	37.1 (37.6)	76.5 (107.2)	52.9 (62.1)	62.3 (59.5)[a]
Apnea–hypopnea index (per hour)	12.0 (10.2)	18.0 (18.6)	12.9 (12.8)	17.1 (15.6)[a]
Central apnea index (per hour)	0.9 (0.9)	5.5 (12.2)	2.2 (2.6)	1.8 (1.6)[a]
Obstructive apnea index (per hour)	5.6 (6.0)	7.9 (10.9)	6.9 (10.3)	7.9 (8.8)
Sleep stage summary				
Sleep onset latency (minutes)	49.2 (61.6)	48.1 (45.2)	55.4 (44.2)	35.8 (32.9)
Sleep efficiency (%)	76.4 (12.5)	81.6 (10.9)	81.0 (12.0)	83.6 (10.0)[a]
Minutes of wake time after sleep onset	53.3 (36.4)	25.7 (18.7)[a]	31.2 (29.0)[a]	34.1 (31.2)[a]
Minutes of rapid eye movement stage	63.3 (28.0)	71.9 (22.0)	67.0 (21.4)	88.1 (42.6)
Pulse oximetry data				
Average saturation (%)	92.8 (2.3)	91.7 (2.2)[a]	92.5 (2.2)	92.0 (3.0)[a]
Lowest saturation (%)	86.0 (6.3)	84.1 (5.5)[a]	86.0 (4.1)	84.6 (7.3)
Total desaturations: all sleep stages	46.6 (40.4)	62.1 (69.6)	33.8 (34.7)	71.6 (85.0)
Time below 90% (minutes)	47.7 (76.1)	71.9 (103.4)	64.3 (114.2)	78.3 (131.4)
Time below 88% (minutes)	11.9 (30.6)	23.9 (51.2)	17.7 (39.2)	40.8 (91.3)
Heart rate data				
Mean heart rate (bpm)	69.1 (10.0)	69.5 (10.1)	67.1 (7.7)	65.6 (9.0)
High heart rate (bpm)	100.3 (12.3)	97.4 (10.4)	96.3 (11.2)	99.6 (12.7)
Low heart rate (bpm)	50.5 (13.2)	55.5 (6.9)	50.8 (12.0)	52.1 (8.6)
Arousal summary				
Number of arousals	130.5 (56.6)	117.1 (77.0)	120.3 (101.9)	142.1 (26.7)
Periodic limb movement				
Number of leg movements	79.9 (98.3)	17.9 (26.7)[a]	37.0 (53.3)[a]	11.4 (26.7)[a,b]
Number of body position changes	15.4 (8.4)	10.5 (6.2)[a]	11.8 (9.0)[a]	14.1 (12.6)[a]

[a] $P \leq 0.05$ vs no treatment, paired *t*-test.
[b] $P \leq 0.05$ for comparison of ER hydromorphone QAM vs QPM dosing based on LS means (i.e., adjusted means, not shown) using linear mixed model with fixed effects for sequence, period, and treatment, and a random effect for subject nested in sequence.
All values reported as mean (SD).
ER = extended release; IR = immediate release; QAM = morning hydromorphone dosing time; QPM = evening hydromorphone dosing time; SD = standard deviation.

Pain Medicine 2015; 16: 460–471

Table 4 Pain questionnaire and MOS sleep scale

	No Treatment (N = 15)	IR Hydromorphone (N = 15)	ER Hydromorphone QAM (N = 14)	ER Hydromorphone QPM (N = 15)
Short-Form McGill Pain Questionnaire	N = 15	N = 15	N = 12	N = 14
VAS score (mm)	55.5 (23.1)	47.2 (23.8)	46.0 (26.2)	38.3 (22.4)[a,b]
Total pain score	19.0 (9.2)	14.8 (8.8)[a]	12.3 (8.1)[a]	11.2 (7.9)[a,b]
Present Pain Index, N (%)[c]	N = 15	N = 15	N = 11	N = 15
No pain	0 (0%)	0 (0%)	0 (0%)	1 (7)
Mild	1 (7%)	6 (40%)	4 (36%)	5 (33%)
Discomforting	7 (47%)	6 (40%)	5 (46%)	8 (53%)
Distressing	3 (20%)	1 (7%)	1 (9%)	0 (0%)
Horrible	4 (27%)	1 (7%)	1 (9%)	0 (0%)
Excruciating	0 (0%)	1 (7%)	0 (0%)	1 (7%)
MOS sleep scale	N = 15	N = 15	N = 12	N = 15
Sleep disturbance domain	54.2 (26.8)	30.8 (20.5)[a]	26.3 (20.5)[a]	26.2 (19.3)[a]
Snoring domain	37.3 (28.2)	21.3 (22.0)[a]	18.3 (18.0)	25.3 (27.7)[a]
Awakening short of breath or headache domain	36.0 (34.0)	14.7 (16.0)[a]	23.3 (25.4)[a]	10.7 (14.9)[a]
Sleep quantity domain	6.3 (1.0)	6.7 (1.5)	7.2 (1.5)[a]	6.9 (1.4)
Daytime somnolence domain	35.6 (15.3)	33.8 (16.4)	41.1 (16.5)	34.2 (20.6)
Sleep problem index	51.2 (20.6)	38.0 (14.8)[a]	36.1 (17.9)[a]	32.8 (15.0)[a]

[a] $P \leq 0.05$ vs no treatment, paired *t*-test.
[b] $P \leq 0.05$ vs IR hydromorphone, paired *t*-test.
[c] $P \leq 0.05$ for paired comparisons of ER hydromorphone QAM, ER hydromorphone QPM, or IR hydromorphone dosing with no treatment; P = NS for paired comparisons of ER hydromorphone QAM or QPM vs IR hydromorphone, or for ER hydromorphone QAM vs QPM dosing. All used Wilcoxon signed rank test.
All values reported as mean (SD) except Present Pain Index. ER = extended release; IR = immediate release; MOS = Medical Outcomes Study; QAM = morning hydromorphone dosing time; QPM = evening hydromorphone dosing time; SD = standard deviation.

Pain Medicine 2015; 16: 460–471

Screening for SDB

- 2 accepted RF for CSA:
  - Dose of Opioid (morphine equivalent daily dose; MEDD): MEDD>200mg/d
  - Low/normal BMI
- Patients with suggested awake daytime hypercapnia
  - ABG, HCO3>27
- Symptoms of sleep disruption

Potential Treatments for Opioid-Related SDB

- PAP Therapy
- Withdrawal/reduction of opioid dose
- Oxygen
- Medications (acetazolamide, theophylline)
- Other accepted treatments for OSA if predominant

Discontinuation of Opioids: Effect on SDB

Table 1—Polysomnography results

	Initial PSG	Subsequent PSG following detoxification
Total sleep time (min)	367.5	231.5
Sleep efficiency (%)	90.3	55
Slow wave sleep (% total)	1.4	6.4
REM sleep (% total)	1.1	16.6
Obstructive apnea/hypopneas (#)	37	5
Central apneas (#)	260	3
RDI	50.3	2.9
Minimum oxygen saturation (%)	43	88
T < 90% (min)	15.0	1.4
Arousal index	28.1	5.2

Data from initial and subsequent polysomnograms. PSG, polysomnography; RDI, respiratory disturbance index (apneas plus hypopneas plus respiratory event related arousals per hour of sleep).

J Clin Sleep Med 2012;8(5):579-580

Table 1—Polysomnographic data on and off opioids, and off and on continuous positive air pressure therapy.

	On Opioids—Type of Study				Off Opioids—Type of Study		
	PSG	CPAP/Bilevel Titration	Bilevel Titration	ASV Titration	PSG	PSG	CPAP Titration
Date, mo/d/y	5/9/06	5/23/06	2/3/07	3/6/07	3/5/08	9/28/10	10/12/10
Total recording time, min	424	404	494	472	414	439	393
Total sleep time, min	301	261	263	360	374	408	347
Sleep efficiency, %	71	65	53	76	90	93	88
Stage N1 sleep, %	11	11	19	11	7	6	4
Stage N2 sleep, %	74	84	69	76	81	72	87
Stage N3 sleep, %	0.2	4	0	4	0	0	0
REM sleep, %	15	0.6	12	9	12	22	9
Arousal index, events/h	43	37	24	21	11	15	7
Apnea-hypopnea index, events/h	64	42	63	17	4.7	9.6	2.6
Hypopnea index, events/h	33.8	7	10	15	3.5	9.4	2.4
Obstructive apnea index, events/h	0.2	0	1	1	0.2	0.1	0
CAI, total, events/h	30	35	52	1	1	0.1	0.2
CAI, NREM sleep, events/h	32	35	58	1	1		
CAI, REM sleep, events/h	11	0	13	0	4		
CAI, supine position, events/h	14	67	66	0			
CAI, non-supine position, events/h	0	0	0	0			
Baseline SaO_2, %	97	98	97	96	95	97	97
Minimum SaO_2, %	86	90	92	91	88	89	93
< 90% SaO_2, % TST	7	0	0	0	0	0	0
DArI, events/h	39	21	18	15	3	10	3
Periodic limb movement index, events/h	0	0	0	0	3	0	1

ASV = adaptive servoventilation, Baseline SaO_2 = saturation while in bed before sleep onset, CAI = central apnea index, CPAP = continuous positive airway pressure, DArI = arousal index due to disordered breathing, NREM = non-rapid eye movement, PSG = polysomnography, REM = rapid eye movement, SaO_2 = arterial oxyhemoglobin saturation measured by pulse oximetry, TST = total sleep time.

Sleep Med. 2017;13(6):829–833

CPAP, ASV

- Prospective multisite interventional trial
- Aim: to determine the efficacy of autoASV after 3mo of home use.
- Chronic opioids >4mo, MEQ>100mg/d
- Intervention
  - Baseline PSG
  - Titration with CPAP, ASV +/- mandatory PS
  - Home ASV x 3mo

Table 3 Participants' flow throughout the study

	Males	Females	Total
Completed study part I: diagnostic PSG screening	31	43	74
Met the criterion AHI of at least 20 and a CAI of ≥10	10	12	22
Met the criterion of at least 25 % of TST below 90 % SaO_2 and AHI ≥10	3	5	8
Met both criteria	2	3	5
Failed both criteria	16	23	39
Randomized for the study (fulfilled inclusion/exclusion criteria)	*15*	*19*	*34*
Completed study part 2: titration with CPAP, ASV manual (PSmin 6), and ASV auto	13	18	31
Completed study part 3: 3-month at-home treatment with ASV (auto or manual)	8	11	19[a]

[a] From the 25 who started the at-home treatment phase of the study with ASV auto or ASV manual (PSmin 6), there were 19 completers

Sleep Breath (2015) 19:1285–1292

Table 5 Comparison of respiratory variables across diagnostic PSG and titration studies (CPAP, ASV, and ASV manual (PSmin 6))

	Diagnostic PSG (*N*=31)	CPAP (*N*=31)	ASV (*N*=31)	ASV manual (PSmin 6) (*N*=31)	*p* values for pairwise comparisons			
					Overall *p* value (Friedman test)	CPAP vs. ASV	CPAP vs. ASV manual (PSmin 6)	ASV vs. ASV manual (PSmin 6)
AHI	32.5 (38.8±31.1)	10.1 (17.4±20.1)	1.4 (4.5±7.3)	2.1 (7.6±16.7)	*<0.001*	*<0.001*	*0.009*	>0.99
CAI	6.4 (16.1±18.8)	2.4 (8.4±12.4)	0.0 (0.2±0.8)	0.0 (0.2±0.9)	*<0.001*	*<0.001*	*<0.001*	>0.99
OAI	1.9 (9.7±15.2)	2.8 (4.5±6.3)	0.0 (0.3±0.5)	0.0 (0.5±1.1)	*<0.001*	*<0.001*	*<0.001*	>0.99
HI	10.2 (14.8±12.6)	2.8 (4.5±5.1)	1.4 (4.6±7.4)	3.2 (7.9±16.2)	0.441	–	–	–
ODI[a]	24.2 (32.8±29.2)	6.0 (15.1±20.2)	1.9 (5.9±8.6)	2.6 (9.5±19.2)	0.161	–	–	–
Av. O_2 saturation	93.4 (92.9±3.4)	94.9 (94.6±2.3)	94.6 (94.6±2.6)	94.6 (94.5±3.2)	0.627	–	–	–
Min. O_2 saturation	80.5 (79.9±7.8)	85.0 (85.5±6.0)	85.0 (82.9±16.2)	86.6 (79.7±22.8)	0.991	–	–	–

Data are expressed as median (mean±standard deviation). The above *p* values for the pairwise comparisons, using the Wilcoxon signed-rank test, have undergone Bonferroni adjustment

HI hypopnea index, *ODI* oxygen saturation index

[a] Defined as the number of times per hour that the oxygen saturation dropped below 4 % of baseline

Sleep Breath (2015) 19:1285–1292

Table 6 Comparison of PSG sleep architectural variables across diagnostic PSG and titration study (CPAP, ASV, and ASV manual (PSmin 6)) nights

	Diagnostic PSG (*N*=31)	CPAP (*N*=31)	ASV (*N*=31)	ASV manual (PSmin 6) (*N*=31)	Overall *p* value (Friedman test)
Arousal index	20.3 (22.9±13.8)	11.8 (14.9±8.0)	16.6 (17.7±9.4)	16.1 (19.2±11.7)	*0.028*[a]
Total sleep time (TST) (min)	407.0 (409±57.8)	387.0 (386.8±60.2)	376.5 (377.6±85.0)	385.0 (380.4±67.2)	0.798
Sleep efficiency (%)	89.1 (87.9±8.3)	90.0 (86.8±9.7)	87.7 (83.3±13.9)	86.7 (84.9±10.2)	0.419
Wake after sleep onset (min)	39.6 (47.4±33.5)	37.1 (50.6±40.6)	45.8 (62.3±50.9)	51.2 (59.0±42.1)	0.313
Stage 1 (% TST)	7.8 (11.0±10.2)	5.6 (8.4±6.9)	6.8 (9.2±8.5)	7.3 (9.4±7.0)	0.201
Stage 2 (% TST)	70.9 (73.3±13.0)	78.3 (76.2±12.2)	74.3 (73.2±11.1)	78.1 (77.0±11.2)	0.206
Stage 3/4 (% TST)	0.2 (4.3±7.1)	0.8 (3.6±5.8)	0.6 (5.3±9.5)	0.3 (3.3±5.8)	0.296
REM (% TST)	11.2 (11.4±8.3)	9.3 (11.8±9.1)	10.3 (12.3±9.4)	8.3 (10.3±8.0)	0.407
Sleep onset latency (min)	4.0 (9.0±12.1)	4.6 (8.8±10.5)	4.3 (12.9±28.4)	4.0 (9.0±13.6)	0.575

Data are expressed as median (mean±standard deviation)

[a] Pairwise comparisons, using the Wilcoxon signed-rank test and undergoing Bonferroni adjustment, indicated that the arousal index was significantly (p=0.021) greater during ASV manual (PSmin 6) titration compared to CPAP. No significant differences were noted for CPAP versus ASV manual (PSmin 6) (p=0.288) or ASV versus ASV manual (PSmin 6) (p>0.99)

Sleep Breath (2015) 19:1285–1292

Table 7 Comparison of respiratory disturbance indices between CPAP titration and at-home use

	3-month follow-up					
	AHI (*N*=24)	CAI (*N*=24)	OAI (*N*=24)	HI (*N*=24)	Adherence	
					All days	Days used
CPAP titration	11.3 (20.3±21.8)	2.6 (10.3±13.5)	3.0 (5.2±6.7)	3.5 (5.3±5.5)	2.4±2.3 (*N*=5)	3.7±1.6 (*N*=5)
ASV home use[a]	5.8 (8.6±7.9)	0.8 (1.5±2.0)	0.7 (1.4±1.7)	3.8 (5.7±5.3)	2.4±2.3 (*N*=25)	3.6±2.1 (*N*=24)[b]
p value[c]	*0.021*	*0.006*	*0.002*	0.648		

Data are expressed as median (mean±standard deviation)

[a] The ASVauto and ASV manual (PSmin 6) data combined as the respiratory variables from patients using these devices were not significantly different (see Table 5)

[b] One patient did not use the autoSV machine

[c] Wilcoxon signed-rank test

Sleep Breath (2015) 19:1285–1292

CPAP vs. ASV

- Retrospective review
- N=20 (4 OSA, 16 CSA)
- Aim: evaluate efficacy of ASV on eliminating SDB secondary to opioid use compared to CPAP.
- Baseline AHI 61/h, CAI 32/h

Table 4—Polysomnographic findings at baseline, CPAP 1, CPAP 2, and ASV (n = 9)

Variables	Baseline	CPAP 1	CPAP 2	ASV	p value
Total recording time, h	7 ± 1	6.9 ± 1	7 ± 1	7 ± 1	0.978
Total sleep time, h	5.5 ± 1	5.6 ± 1	5.4 ± 1	5.2 ± 1	0.905
Sleep efficiency, %	80 ± 19	82 ± 10	77 ± 14	74 ± 10	0.647
N1, % TST	28 ± 20	14 ± 12	25 ± 26	18 ± 12	0.191
N2, % TST	61 ± 16	81 ± 11	68 ± 26	72 ± 12	0.222
N3, % TST	0 ± 0	0 ± 1	0 ± 0	1 ± 3	0.439
REM, % TST	11 ± 9	5 ± 4	7 ± 5	8 ± 6	0.058
ArI, n/h	25 ± 16	24 ± 19	23 ± 13	17 ± 8	0.321
AHI, n/h	45 ± 22	34 ± 19	33 ± 18	21 ± 14	0.016
AHI final PAP level, n/h	n/a	42 ± 24	32 ± 20	12 ± 14*	0.006
CAI, n/h	20 ± 21	20 ± 14	19 ± 17	0 ± 0*	0.006
NREM CAI, n/h	23 ± 27	20 ± 15	21 ± 20	0 ± 0*	0.014
REM CAI, n/h	4 ± 7	6 ± 8	3 ± 3	0 ± 0*	0.211
OAI, n/h	4 ± 4	1 ± 2¶	1 ± 1	0 ± 0	0.002
ArI-DB, n/h	20 ± 14	17 ± 18	17 ± 13	14 ± 8	0.533
Baseline SpO_2	95 ± 2	95 ± 2	95 ± 2	94 ± 2	0.421
Minimum SpO_2	83 ± 10	87 ± 4	85 ± 5	86 ± 6	0.417
Oxygen desaturation index	30 ± 24	16 ± 16¶	15 ± 11	9 ± 15	0.0002
PLMSI, n/h	0 ± 1	0 ± 0	0 ± 1	1 ± 1	0.24
Expiratory pressure, cm H_2O	n/a	10 ± 4	11 ± 4	10 ± 3	0.031

Values reported are mean ± SD. ASV, adaptive servoventilation; Baseline SpO_2, saturation in supine position during relaxed wakefulness; PLMSI, periodic leg movements index during sleep; TST, total sleep time; AHI, apnea hypopnea index; REM, rapid eye movement; OAI, obstructive apnea index; CAI, central apnea index; ArI-DB, arousal index associated with disordered breathing. Analysis of variance with repeated measures and Bonferroni correction factor were used for comparisons of Baseline vs. CPAP 1, CPAP 1 vs. CPAP 2, and CPAP 2 vs. ASV. ¶Significant when comparing CPAP 1 to baseline. *Significant when comparing ASV to CPAP 2.

J Clin Sleep Med 2014;10(6):637-643

ASV vs. Bilevel ST (and patient outcomes!)

- Prospective, blinded randomized cross-over
- N=18
- Chronic opioids x 6mo
- PSG with SDB and CAI >5/h
- All on bilevel-ST at baseline for >4wks
- Intervention
  - PSG with ASVAuto
  - PSG with Bilevel-ST

Journal of Clinical Sleep Medicine, Vol. 10, No. 8, 2014

Table 3—PSG results

Polysomnographic Results	ASVAuto (N = 18) Mean ± SD	ASVAuto (N = 18) Median	Bilevel-ST (N = 18) Mean ± SD	Bilevel-ST (N = 18) Median	p-value (Paired t-test)
Total sleep time	356.3 ± 82.9	360.5	388.3 ± 75.2	413.5	0.0291*
Sleep efficiency (%)	82.8 ± 15.3	84.4	87.1 ± 8.8	89.2	0.5509
Slow wave sleep (%)	17.0 ± 15.6	11.8	22.9 ± 21.9	16.8	0.1633
REM sleep (%)	11.5 ± 7.0	10.3	10.7 ± 6.1	9.4	0.6637
AHI, Total	2.5 ± 3.5	0.3	16.3 ± 20.9	6.6	0.0005*
AHI, REM	1.0 ± 2.1	0.0	5.0 ± 8.5	0.0	0.0117*
AHI, NREM	2.6 ± 3.8	0.4	17.3 ± 21.7	7.1	0.0005*
AI, Total	0.4 ± 0.8	0.0	11.0 ± 19.6	1.8	< 0.0001*
AI, REM	0.1 ± 0.5	0.0	3.5 ± 7.6	0.0	0.0625
AI, NREM	0.5 ± 0.9	0.0	11.6 ± 20.4	2.0	< 0.0001*
HI, Total	2.0 ± 3.3	0.3	5.3 ± 6.5	3.5	0.0518
HI, REM	0.9 ± 1.8	0.0	1.5 ± 2.3	0.0	0.4805
HI, NREM	2.1 ± 3.5	0.4	5.7 ± 7.0	3.5	0.0417*
CAI, Total	0.4 ± 0.8	0.0	9.4 ± 18.8	1.5	0.0002*
CAI, REM	0.0 ± 0.0	0.0	2.4 ± 6.1	0.0	0.2500
CAI, NREM	0.5 ± 0.9	0.0	10.0 ± 19.5	1.6	< 0.0001*
Average O_2 saturation (%)	95.7 ± 1.4	96.0	96.1 ± 1.7	96.0	0.1215
Lowest O_2 saturation (%)	90.4 ± 3.7	91.0	88.9 ± 4.9	91.0	0.1304
Total arousal index	24.4 ± 14.9	21.3	30.7 ± 18.0	26.7	0.0304*
Respiratory-arousal Index	1.1 ± 1.7	0.3	4.8 ± 4.8	3.3	0.0055*

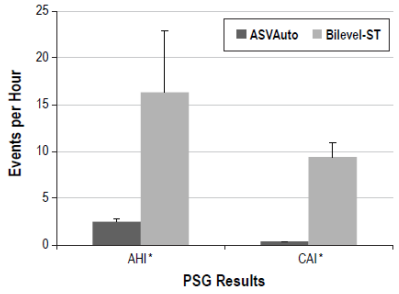
Treatment Order: 9 Participants ASVAuto/bilevel-ST, 9 Participants bilevel-ST/ASVAuto. All treatment order effects for the following results were not statistically significant. * $p < 0.05$. REM, rapid eye movement; AHI, apnea hypopnea index; NREM, non rapid eye movement; AI, apnea index; HI, hypopnea index; CAI, central apnea index.

Journal of Clinical Sleep Medicine, Vol. 10, No. 8, 2014

Table 5—Morning After Questionnaire

	ASVAuto (N = 18)	Bilevel-ST (N = 17)	p-value (Paired t-test*)
How do you feel right now?			
Alert and Awake	33.3% (6)	5.9% (1)	
Rested	50.0% (9)	52.9% (9)	0.0337*
Barely awake	11.1% (2)	11.8% (2)	
Tired and Sleepy	5.6% (1)	29.4% (5)	
Quality of Sleep			
Restful	70.6% (12)	47.1% (8)	0.4805
In-between	11.8% (2)	35.3% (6)	
Restless	17.7% (3)	17.7% (3)	

Values are presented as % (N). * Signed rank test based on scored data.



There was a significant reduction in total number of abnormal breathing events during sleep (AHI and CAI) with ASVAuto compared to bilevel with back-up respiratory rate. PSG, polysomnography; AHI, apnea hypopnea index; CAI, central apnea index. * $p < 0.001$.

Table 6—PAP Comfort Questionnaire

	ASVAuto (N = 18) Mean ± SD	Bilevel-ST (N = 17) Mean ± SD	p-value (Paired t-test)
Satisfaction with PAP 0 = Very Dissatisfied, 100 = Very Satisfied	76.0 ± 27.2	67.8 ± 28.0	0.4450
Refreshed after waking in the morning 0 = Exhausted, 100 = Very Refreshed	71.4 ± 22.6	60.5 ± 25.6	0.1324
Discomfort from Pressure 0 = No Discomfort, 100 = Severe Discomfort	14.8 ± 24.1	31.4 ± 33.2	0.1249

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ASV and (more) Patient Outcomes

- Case Series, n=6
- Chronic opioids >6mo
- CSA: CAI >5/h with >50% central events

Table 2 Baseline polysomnography of six patients with opioid-induced CSA

	S1 (%)	S2 (%)	SWS (%)	REM (%)	AHI (per hr)	H + O (total #)	MA (total #)	CA (total #)	CA (% total)	T90 (hours)
Patient 1	4.9	73	0.1	9.7	39.5	41	77	124	51	0
Patient 2	2.3	78	0	6.7	44.9	15	21	192	84	4.5
Patient 3	2.2	84.9	1.4	1.1	50.3	37	11	260	84	0.25
Patient 4	7.3	69.7	6.3	11.2	106	300	31	331	50	6.4
Patient 5	1.9	59.6	11.3	3.4	39.6	58	1	171	74	5.7
Patient 6	3.4	31.6	41.1	10.4	28.4	38	0	140	79	0.03

S1 Stage 1, *S2* stage 2, *SWS* slow wave sleep, *REM* rapid eye movement, *AHI* apnea–hypopnea index, *per hr* per hour, *H + O* hypopnea and apnea combined, *MA* mixed apnea, *CA* central apnea, *T90* hours of total sleep time with SaO_2 less than 90%

Sleep Breath (2009) 13:201–206

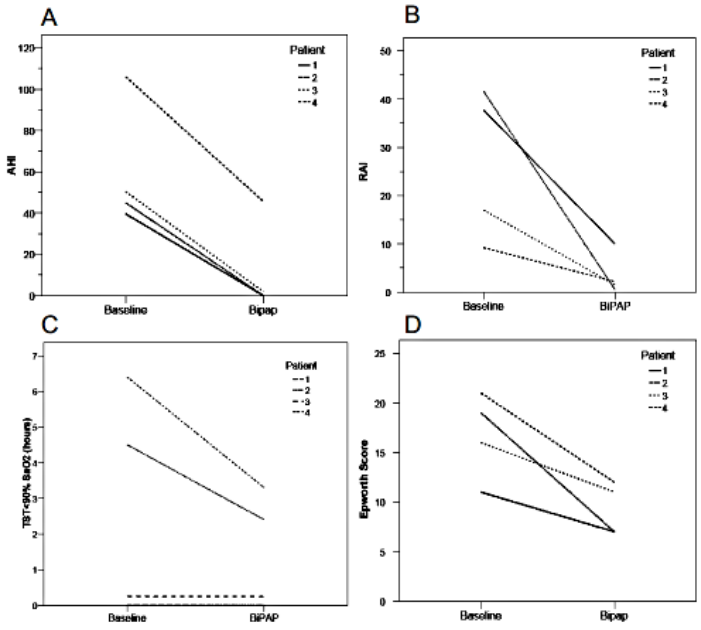


Fig. 2 a–c: In the four patients undergoing BLV titration, comparisons from baseline to values recorded during optimal BLV. **a** Change in AHI, **b** changes in RAI, **c** changes in T90, **d** changes in Epworth Score from first clinic evaluation to final follow-up after using BLV settings achieved changes in AHI, RAI, and total time <90% seen in **a**, **b**, and **c**

Sleep Breath (2009) 13:201–206

CPAP for Opioid-related CSA

Table 3 Comparison of sleep parameters of subjects on successful therapy

	CPAP		BiPAP		ASV	
	O-CSA (n=8)	I-CSA (n=23)	O-CSA (n=6)	I-CSA (n=13)	O-CSA (n=12)	I-CSA (n=19)
Diagnostic AHI, h^{-1}	34.2±13.6	30.1±17.4	51.6±36.3	42.5±24.0	39.4±31.9	46.1±22.3
Residual AHI, h^{-1}	5.6±2.9	5.2±3.7	4.4±2.9	3.2±2.1	5.2±2.4	5.4±4.1
N1 NREM (%)	11.3±9.6	13.1±21.7*	9.9±8.9	12.6±22.3*	11.7±11.8	18.7±19.2
N2 NREM (%)	74.4±13.7	66.1±20.2	76.3±11.5	68.9±21.4	75.7±13.1	71.8±21.6
N3 NREM (%)	2.7±4.2	2.3±4.9	2.4±3.7	2.1±4.4	1.9±6.7	2.3±5.7
REM (%)	11.7±11.3	15.5±10.6	14.1±11.1	16.7±15.0	7.9±12.3	15.2±14.8
%ST-SpO_2<90 %	5.3±5.7*	2.4±3.7*	3.2±4.1*	2.9±4.1*	8.3±4.6*	2.7±4.2*
SpO_2 nadir, %	88.1±3.2	88.0±3.4	87.0±4.1	92.7±2.6	88.6±3.1	90.0±3.3
Arousal index, h^{-1}	24.5±11.8	20.1±7.9	21.6±9.2	17.3±9.3	15.7±8.2	16.8±7.5

%ST-SpO_2<90 % percentage sleep time with SpO_2<90 %

*p<0.05, compared to baseline

Sleep Breath (2014) 18:367–373

Ampakines

- Class of synthetic compounds that enhance glutamatergic neurotransmission
  - Interact with AMPA receptor as a positive allosteric modulator
- Crosses BBB, minimal side effects at therapeutic doses
- Prevents opioid-induced respiratory depression

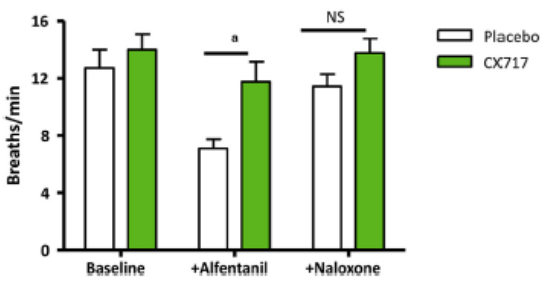


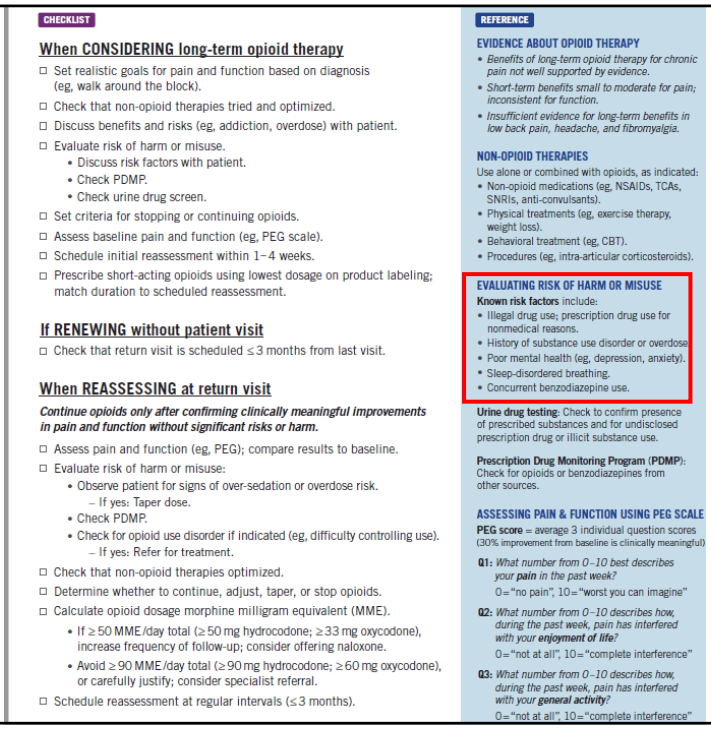
Fig. 6. Preadministration of the ampakine CX717 (1500 mg, oral) countered the decrease in respiratory frequency induced by alfentanil in human subjects (n = 15). [a] P<.01. NS, not significant. (*Adapted from* Oertel BG, Felden L, Tran PV, et al. Selective antagonism of opioid-induced respiratory depression by an AMPAKINE molecule in humans without loss of opioid analgesia. Clin Pharmacol Ther 2010;87:204–11; with permission.)

Sleep Med Clin 2016;11:227-39

CDC Recommendations for Opiate Rx

- 12 recommendations
- E-resources
  - Patients
  - Providers

JAMA. 2016;315(15):1624-1645



CHECKLIST

When CONSIDERING long-term opioid therapy

- ☐ Set realistic goals for pain and function based on diagnosis (eg, walk around the block).
- ☐ Check that non-opioid therapies tried and optimized.
- ☐ Discuss benefits and risks (eg, addiction, overdose) with patient.
- ☐ Evaluate risk of harm or misuse.
  - Discuss risk factors with patient.
  - Check PDMP.
  - Check urine drug screen.
- ☐ Set criteria for stopping or continuing opioids.
- ☐ Assess baseline pain and function (eg, PEG scale).
- ☐ Schedule initial reassessment within 1–4 weeks.
- ☐ Prescribe short-acting opioids using lowest dosage on product labeling; match duration to scheduled reassessment.

If RENEWING without patient visit

- ☐ Check that return visit is scheduled ≤3 months from last visit.

When REASSESSING at return visit

Continue opioids only after confirming clinically meaningful improvements in pain and function without significant risks or harm.

- ☐ Assess pain and function (eg, PEG); compare results to baseline.
- ☐ Evaluate risk of harm or misuse:
  - Observe patient for signs of over-sedation or overdose risk.
    - If yes: Taper dose.
  - Check PDMP.
  - Check for opioid use disorder if indicated (eg, difficulty controlling use).
    - If yes: Refer for treatment.
- ☐ Check that non-opioid therapies optimized.
- ☐ Determine whether to continue, adjust, taper, or stop opioids.
- ☐ Calculate opioid dosage morphine milligram equivalent (MME).
  - If ≥50 MME/day total (≥50 mg hydrocodone; ≥33 mg oxycodone), increase frequency of follow-up; consider offering naloxone.
  - Avoid ≥90 MME/day total (≥90 mg hydrocodone; ≥60 mg oxycodone), or carefully justify; consider specialist referral.
- ☐ Schedule reassessment at regular intervals (≤3 months).

REFERENCE

EVIDENCE ABOUT OPIOID THERAPY

- *Benefits of long-term opioid therapy for chronic pain not well supported by evidence.*
- *Short-term benefits small to moderate for pain; inconsistent for function.*
- *Insufficient evidence for long-term benefits in low back pain, headache, and fibromyalgia.*

NON-OPIOID THERAPIES

Use alone or combined with opioids, as indicated:

- Non-opioid medications (eg, NSAIDs, TCAs, SNRIs, anti-convulsants).
- Physical treatments (eg, exercise therapy, weight loss).
- Behavioral treatment (eg, CBT).
- Procedures (eg, intra-articular corticosteroids).

EVALUATING RISK OF HARM OR MISUSE

Known risk factors include:

- Illegal drug use; prescription drug use for nonmedical reasons.
- History of substance use disorder or overdose
- Poor mental health (eg, depression, anxiety).
- Sleep-disordered breathing.
- Concurrent benzodiazepine use.

Urine drug testing: Check to confirm presence of prescribed substances and for undisclosed prescription drug or illicit substance use.

Prescription Drug Monitoring Program (PDMP): Check for opioids or benzodiazepines from other sources.

ASSESSING PAIN & FUNCTION USING PEG SCALE

PEG score = average 3 individual question scores (30% improvement from baseline is clinically meaningful)

Q1: *What number from 0–10 best describes your **pain** in the past week?*
0="no pain", 10="worst you can imagine"

Q2: *What number from 0–10 describes how, during the past week, pain has interfered with your **enjoyment of life**?*
0="not at all", 10="complete interference"

Q3: *What number from 0–10 describes how, during the past week, pain has interfered with your **general activity**?*
0="not at all", 10="complete interference"

Summary

- SDB with chronic opioid use can look like anything
- Judicious use of opioids when necessary: IR>ER
- Concomitant centrally acting meds (benzos, hypnotics, antidepressants): caution due to impact on metabolism of opioid
- Decrease/taper opioids when possible
- Consider undocumented opioid use when unexplained hypoxemia or CSA/ataxic respiratory patterns are observed, +/- evidence of chronic compensated respiratory acidosis.
- Consider sleep testing in patients with symptoms or risk factors (or just test them all, given the high reported prevalence)
- Treatment with ASV for opioid-related CSA is effective

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Questions

- Does screening for SDB reduce morbidity/mortality in patients on chronic opiates?
- Should patients on chronic opioids undergo sleep testing?
- Does use of PAP/NIV reduce morbidity/mortality?
- Can Sleep testing be suggestive of chronic opioid use?

Thank you!