Supplementary Appendix

SUPPLEMENTARY APPENDIX

This supplementary appendix has been provided by the authors to give readers more information about their work.

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Supplementary Appendix

Trial Organization

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Inclusion and Exclusion Criteria

Inclusion criteria:

(1) Age ≥ 18 years.
(2) Using opioids for >3 months for chronic, non-cancer pain with a stable daily dose for at least 4 weeks.

Exclusion criteria:

(1) Patients with chronic pain secondary to a neoplasm or metastasis as goals of care are different in this patient population.
(2) Patients requiring urgent sleep physician referral (within four weeks) due to serious medical conditions or safety critical-occupations according to the 2011 Canadian Thoracic Society (CTS) guidelines (e.g. unstable ischaemic heart disease, recent cerebrovascular disease, congestive heart failure, refractory systemic hypertension, pulmonary hypertension, hypercapnic respiratory failure or pregnancy).[1]
(3) Conditions potentially interfering with comprehension and delivery of informed consent or the educational intervention, such as neurological or psychiatric disorders.
(4) Patients with a prior diagnosis of sleep-related breathing disorder within the last 3 years with treatment. Patients who may have had sleep studies 3 or more years earlier may be included, if they have been lost to follow-up by a sleep physician, are not on treatment or are non-compliant to treatment (mean CPAP nightly use <4 hours, or median nightly CPAP use <50% of total sleep time.

Supplementary Appendix

Measures in Study

The eligible participants underwent different measures including the STOP-Bang questionnaire, the Epworth Sleepiness Scale, Mallampati score, Friedman staging, and thyromental distance. This was followed by an in-laboratory overnight polysomnogram and oximeter at home. This section describes some of the measures.

a) STOP-Bang Questionnaire [2]

Snoring?
Do you **Snore Loudly** (loud enough to be heard through closed doors or your bed-partner elbows you for snoring at night)?

Tired?
Do you often feel **Tired, Fatigued, or Sleepy** during the daytime (such as falling asleep during driving)?

Observed?
Has anyone **Observed** you **Stop Breathing** or **Choking/Gasping** during your sleep?

Pressure?
Do you have or are being treated for **High Blood Pressure**?

Body Mass Index more than 35 kg/m^2?

Age older than 50 year old?

Neck size large? (Measured around Adams apple)
For male, is your shirt collar 17 inches or larger?
For female, is your shirt collar 16 inches or larger?

Gender = Male?

Scoring Criteria:
Low risk of OSA: Yes to 0-2 questions
High risk of OSA: Yes to 3-4 questions
Very high risk of OSA: Yes to 5-8 questions

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b) Epworth Sleepiness Scale [3]

Name: _____Today's date: _____

Your age (Yrs.): _____ Your sex (Male = M, Female = F): _____

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired?

This refer to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the **most appropriate number** for each situation:

0 = would **never** doze
1 = **slight chance** of dozing
2 = **moderate chance** of dozing
3 = **high chance** of dozing

It is important that you answer each question as best you can.

Situation	**Chance of Dozing (0-3)**
Sitting and reading _____	_____
Watching TV _____	_____
Sitting, inactive in a public place (e.g. a theater or a meeting) _____	_____
As a passenger in a car for an hour without a break _____	_____
Lying down to rest in the afternoon when circumstance permit _____	_____
Sitting and talking to someone _____	_____
Sitting quietly after a lunch without alcohol _____	_____
Ina car, while stopped for a few minutes in the traffic _____	

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c) Friedman Staging, Mallampati score and Thyromental Distance

All three measures, Freidman staging, Mallampati score, and thyromental distance (distance from the thyroid notch to tip of jaw) predict ease of intubation.[4] A Pearson correlation showed that there was a moderate association between Friedman and Mallampati classification, r= 0.5, P<0.0001. Therefore, in the study, only Mallampati classification was presented and used in the models.

d) Polysomnography

In-laboratory polysomnography was used to determine sleep-disordered breathing. Apnoea was defined as ≥90% drop in air flow from baseline for ≥ 10 sec. Apnoeas were further classified as obstructive, central or mixed in nature. The apnoea was defined as obstructive or central due to the presence or absence of respiratory effort, respectively. A mixed apnoea was scored if there was absent inspiratory effort in the initial portion of the event, followed by resumption of inspiratory effort in the second portion of the event. Hypopnoea was defined as ≥ 30% reduction in airflow for ≥ 10 seconds and a ≥ 3% decrease in the SpO_2 or associated with an arousal. Hypopnoeas were not further classified in this study due to the difficulty in accurately differentiating central from obstructive. Sleep related hypoxemia was defined as greater than 30% of total sleep time at a SpO_2 of less than 90%.[5]

Patients were classified as having obstructive sleep apnoea if the obstructive apnoea-hypopnoea index and mixed index was ≥ 5 events per hour and ≥ 50% were scored as obstructive in origin. Patients were classified as having central sleep apnoea when the central apnoea index were ≥ 5 events per hour and > 50% were scored as central in origin. Sleep apnoea was deemed indeterminate when the total apnoea-hypopnoea index was ≥ 5 events per hour and the obstructive or central apnoea-hypopnoea indices were < 5 events per hour.

e) Oximetry

The wristwatch pulse oximeter (PULSOX-300, Konica Minolta) was worn by patients during the same night as they underwent polysomnography. The oximetry data was extracted from the overnight recording with a commercially available software program and the oximetry data will be analysed in a subsequent manuscript.

f) Patient Opioid Education Measure (POEM)

Patients were assessed on their opioid-related knowledge via the Patient Opioid Education Measure (POEM) at the first visit.[6] They were educated on opioids via an education sheet, relevant pamphlet and video from Institute for Safe Medication Practices (ISMP) Canada. The Patient Opioid Education Measure was repeated around 6-8 weeks during subsequent pain clinic visit. If patients were not scheduled for pain clinic visit within 6-8 weeks' period by the pain physician, the study personnel called the patients to collect answers on the POEM questionnaire and treatment therapy.

Supplementary Appendix

Additional Results

Patient Opioid Education Measure (POEM)

To measure the patient's opioid-related knowledge, POEM was completed at three different times, pre-training, post-training, and at a follow-up visit. In the unadjusted model, the mean score at the pre-training period was 65.16; 95% CI 63.82- 66.49. At post-training it decreased significantly by an average of 4.50 (2.81- 6.18) and at the follow-up visit, it did not increase significantly by 1.86 (-0.18,3.90), compared to pre-training (baseline). Adjustment of age, gender and BMI in the model did not change the results in any meaningful way (analysis not shown). We were unable to demonstrate any improvement in knowledge on opioids via an education sheet, relevant pamphlet and video from Institute for Safe Medication Practices (ISMP) Canada.

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Supplementary Appendix

Supplementary Tables

e-Table 1 Number of Patients Using Opioid Medications and Doses.*

Opioid Medication[7]	Number	Dose [a]	Morphine Milligram Equivalents per day [a]
Morphine [b]	34	91.6 (5-950)	91.6 (5-950)
Hydromorphone [c]	41	23.8 (0.3-124)	120.6 (1.5-620)
Oxycodone [d]	82	46.4 (5-260)	69.0 (7.5-390)
Tramadol [e]	33	194.7 (37-550)	22.9 (3.7-60)
Codeine [f]	25	141.6 (30-600)	18.7 (4.5-60)
Methadone	14	34.4 (4-140)	318.3 (16-1680)
Buprenorphine[g]	9	9.5 (5-20)	112.2 (20-200)
Fentanyl[h]	21	61.9 (12.5-200)	552.6 (90-1440)
Meperidine	1	30.0 (30)	3.0 (3)
Tapentadol	5	220.0 (100-400)	88.0 (40-160)

*Daily opioids doses were converted to approximate MME using the approach set forth by the US Centers for Disease Control and Prevention.[7]
[a] Doses are presented as mean (range) per day in milligram
[b] Morphine and Hydrocodone
[c] Hydromorphone, Dilaudid, Hydromorph Contin
[d] Oxycodone, Oxycontin, Oxycocet, Percocet
[e] Tramadol, Tramacet
[f] Codeine, Tylenol # 1, Tylenol # 2, Tylenol # 3, Tylenol # 4
[g] Buprenorphine: patch, tablet
[h] Fentanyl: patch

Supplementary Appendix

e-Table 2. Demographic Data of Subjects Grouped by Polysomnography Completion.

Variables*	Participants did not complete PSG	Participants completed PSG
N=332	128	204
Body mass index, mean (SD), kg/m²	29.3±7.5	28.6±6.3
Age, mean (SD), year	52.4±13.1	52±13.1
Neck circumference, mean (SD), cm	38.2±4.8	38.8±5
Male, no. (%)	46(35.9)	84(41.2)
STOP-Bang score, mean (SD)	3.4±1.6	3.6±1.7
Epworth Sleepiness Scale, mean (SD), score	7±5.4	8.5±5.4†
Daytime SpO_2, mean (SD), %	95.5±1.7	95.1±2.3
Thyromental distance, mean (SD), cm	8.3±1.9	8.6±1.9
Morphine Milligram Equivalents per day (MME) median (IQR), mg/24h	53.3(20-162.5)	70(30-165)
Medical History, no. (%)		
Active smoker	31(24.2)	47(23)
Asthma/COPD	17(13.2)	27(13.2)

PSG = Polysomnography; IQR = interquartile range; Daytime SpO_2 = oxyhaemoglobin saturation; COPD = chronic obstructive pulmonary disease.
*Plus-minus values are means ± SD. Numbers and percentages are for categorical variables. T-test or Wilcoxon rank-sum test and chi-square analysis were conducted to examine differences in the characteristic for participants who completed PSG and did not.
†P <0.05.

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e-Table 3. Demographic Data of Patients Grouped by Severity of Sleep Apnoea.

			Sleep Apnoea Severity			
CHARACTERISTICS*	**N**	**All patients**	**No Sleep Apnoea (AHI<5)**	**Mild Sleep Apnoea (AHI 5 - <15)**	**Moderate Sleep Apnoea (AHI 15 - <30)**	**Severe Sleep Apnoea (AHI ≥30)**
No of patients	204	204	84	55	28	37
Body Mass Index, mean (SD), kg/m^2	204	28.6±6.4	27.3±6.2	28.6±4.9	29.8±7.5	30.5±7.3†
Age, mean (SD), year	204	52±13.1	46.9±13.4	55.1±10.7	54.3±14.1	57.4±10.9‡
Neck circumference, mean (SD), cm	202	38.8±5	37.5±4.9	38.5±4.4	40.7±5.6	40.7±4.7†
Male, no. (%)	204	84(41.2)	26(31)	22(40)	14(50)	22(59.5)†
STOP-Bang score, mean (SD)	202	3.6±1.7	2.9±1.6	3.4±1.4	4.5±1.8	4.5±1.3‡
Epworth Sleepiness Scale score, mean (SD)	201	8.5±5.4	7.5±5.3	8.3±5.4	8.3±5.4	10.9±4.8†
Daytime SpO_2, mean (SD), %	194	95.1±2.3	95.9±1.9	95.2±1.8	94.1±2.5	93.9±2.8‡
Morphine Milligram equivalents per day (MME), median (IQR), mg/24h	203	70 (30-165)	60 (24.5-120)	60 (22.5-180)	80 (30-180)	95 (30-193)
Thyromental distance, mean (SD), cm	202	8.6±1.9	8.7±1.8	8.4±1.9	8.4±1.8	9±2
Mallampati score, no						
<3 & ≥3	204	99 & 105	47 & 37	27 & 28	11 & 17	14 & 23
SLEEP PARAMETERS						
Apnoea-hypopnoea index, median (IQR), events/hour	204	6.4 (2.3-19.1)	1.5 (0.8-3)	8 (5.9-11.4)	19.1 (17.3-24.9)	49.8 (39.8-70.8)‡
Obstructive apnoea index, median (IQR), events/hour	204	4.6 (1.5-13.5)	1.3(0.5-2.5)	5.6 (4.6-9.4)	16.3 (12.8-19.6)	32.7 (20.4-43.2)‡
Central apnoea index, median (IQR), events/hour	204	0.4(0-1.9)	0.05(0-0.45)	0.8(0.2-1.8)	2.3(0.2-6.3)	4.5(0.4-38.3)‡
Mixed apnoea index, median (IQR), events/hour	204	0(0-0)	0.0(0-0)	0(0-0)	0(0-0)	0.2(0-1.5)‡
Hypopnoea index, median (IQR), events/hour	203	4.09 (1.3-10.6)	1.3 (0.5-2.5)	5.6 (4.2-8.6)	13.4 (6.4-18)	21.3 (8.8-35.5)‡
Mean SpO_2, mean (SD), %	204	94.2±4.9	95±2.1	93.9±2.4	93.7±1.9	93.3±2.1‡
Min SpO_2, mean (SD), %	204	86.2±6.4	90.1±3.5	86.5±4.6	81.8±7.5	80.5±6.5‡
CT 90, median (IQR), %	203	0.2 (0-4.7)	0 (0-0.1)	0.3 (0-3.7)	1.9 (0.7-7.7)	4.8 (1.1-16.3)‡
Oxygen Desaturation, median (IQR), Index (≥3%)	196	9.1 (2.5-26.4)	1.8 (1-4)	9.5 (5.8-14.4)	22.5 (15.2-34.6)	49.1 (33.9-69.4)‡

IQR = interquartile range; AHI = apnoea-hypopnoea index; Daytime SpO_2 = oxyhaemoglobin saturation; CT90 = Cumulative time SpO_2 <90%;
* Plus-minus values are means ± SD. Numbers and percentages are for categorical variables. One-way analysis of variance or Kruskal-Wallis test and chi-square analysis were conducted, as appropriate to examine differences in the characteristics for severity of sleep apnoea.
† P <0.05.
‡ P <0.001.

Supplementary Appendix

e-Table 4. The percentage of patients with CAI ≥5 in the different types of opioids.

	CAI <5	CAI ≥5
Opioids	**n (%)**	**n (%)**
N	**171**	**32**
Morphine	27(15.8)	7(21.9)
Hydromorphone	35(20.5)	6(18.8)
Oxycodone	65(38)	16(50)
Tramadol	32(18.7)	1(3.1) †
Codeine	23(13.4)	2(6.3)
Methadone	10(5.8)	4(12.5)
Buprenorphine	9(5.3)	0(0)
Fentanyl Patch	14(8.2)	7(21.9) †

CAI = central apnoea index.
†P<0.05.

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e-Table 5. Internal validation of models.

Model	Statistic	Original	Corrected	Optimism
AHI ≥ 15	Somers D	0.5724	0.5155	0.0569
	Brier's	0.1694	0.1847	-0.0153
AHI ≥ 5	Somers D	0.5007	0.4366	0.0641
	Brier's	0.1981	0.2133	-0.0153
CAI ≥ 5	Somers D	0.5936	0.5637	0.0298
	Brier's	0.1049	0.1129	-0.0081
Central Sleep	Somers D	0.6946	0.6885	0.0061
Apnoea	Brier's	0.0703	0.0753	-0.0050

AHI = apnoea-hypopnoea index; CAI = central apnoea index.

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