UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

Maryland Sleep Society Annual Conference

Oct 28th 2023

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[Sleep Original Research]

CHEST

Factors Associated With Residual Apnea-Hypopnea Index Variability During CPAP Treatment

Check for updates

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Chest. 2023 May 1;163(5):1258-65.
https://doi.org/10.1016/j.chest.2022.12.048

Introduction

- One billion people across the world have moderate to severe OSA
- PAP therapy is the most commonly used treatment modality
- Uniqueness of OSA follow up visit - tele monitoring
- Telemonitoring - Day to day information on adherence and efficacy by measuring residual AHI

Residual AHI

- 2006 study showed 17% of patients with OSA treated with CPAP had a residual AHI > 10
- Two recent studies examined efficacy of APAP in alleviating OSA showed 26% of patients with rAHI >5 and 18% had rAHI >10
- Mean rAHI gives poor information of day to day AHI variability
- Higher variability can cause OSA symptoms and partial PAP failure.
- CPAP factors- type of mask, fit and high pressure settings
- Clinical factors - variation in cardiac function, stroke etc

Research Question

What are the clinical factors associated with a high residual apnea-hypopnea index (rAHI) level and variability?

Methods

- Retrospective analysis of two merged French telemonitoring databases
- 1126 patients in total
- APAP or CPAP > 90 days between Jan 2018 to May 2021
- Hidden Markov model was applied to analyze the day-to-day residual AHI variability

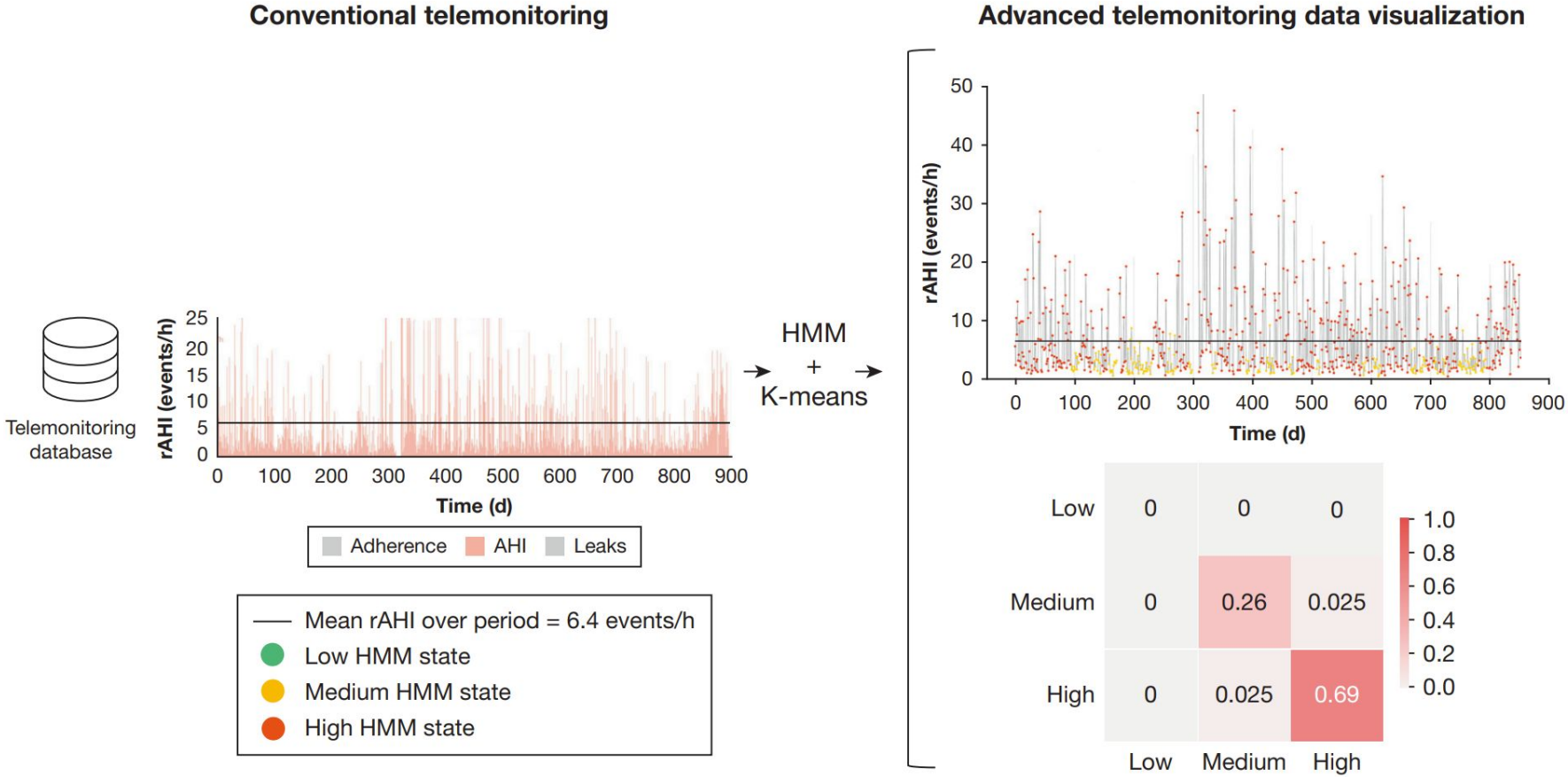
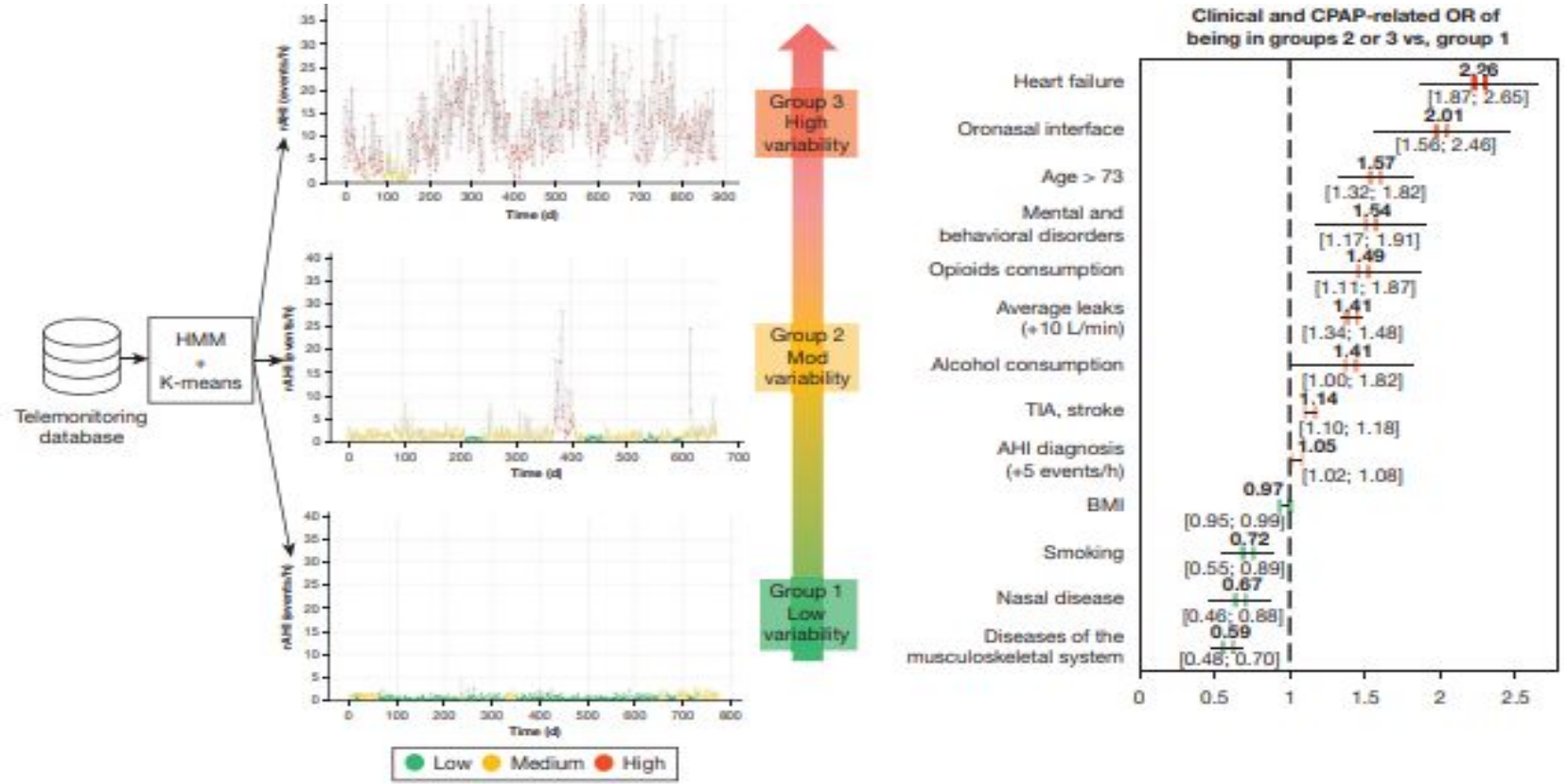

Conventional telemonitoring
Advanced telemonitoring data visualization
Telemonitoring database
rAHI (events/h)
Time (d)
Adherence
AHI
Leaks
HMM
+
K-means
Mean rAHI over period = 6.4 events/h
Low HMM state
Medium HMM state
High HMM state
Low
Medium
High
0
0.26
0.025
0.69
1.0
0.8
0.6
0.4
0.2
0.0

TABLE 1] Anthropometric Characteristics, Main Comorbidities, and CPAP Metrics According to Groups of Residual AHI

Variable	Low-Variability Group (n = 393)	Moderate-Variability Group (n = 420)	High-Variability Group (n = 313)	All Patients (n = 1,126)
Age, y	63.0 (55.0-71.0)	66.0 (56.0-72.0)	70.0 (61.0-77.0)	66.0 (57.0-73.0)
Sex, male	246 (62.6)	302 (71.9)	243 (77.6)	791 (70.2)
BMI, kg/m^2	31.8 (27.8-37.2)	30.4 (26.8-34.9)	29.3 (26.1-32.8)	30.6 (26.8-35.2)
Current smoker	57 (14.5)	59 (14.0)	34 (10.9)	150 (13.3)
Alcohol, higher than maximum recommended daily consumption	46 (11.7)	53 (12.6)	70 (22.4)	169 (15.0)
Opioids consumption	12 (3.1)	18 (4.3)	16 (5.1)	46 (4.1)
Hypertension	232 (59.0)	248 (59.0)	211 (67.4)	691 (61.4)
Diabetes	87 (22.1)	106 (25.2)	64 (20.4)	257 (22.8)
Heart failure	6 (1.5)	20 (4.8)	28 (8.9)	54 (4.8)
History of cardiac arrhythmias	36 (9.2)	38 (9.0)	57 (18.2)	131 (11.6)
OSA and CPAP metrics				
AHI, events/h	36.0 (30.0-48.0)	37.0 (30.0-48.0)	38.0 (30.0-50.0)	37.0 (30.0-49.0)
CPAP total use, d	972.0 (581.0-1,187.0)	986.5 (623.8-1,188.3)	987.0 (525.0-1,227.0)	985.5 (575.8-1,201.5)
Leaks, L/min	3.4 (1.1-10.4)	5.6 (1.5-27.5)	12.5 (2.7-35.6)	5.5 (1.5-27.3)

Group Characteristics

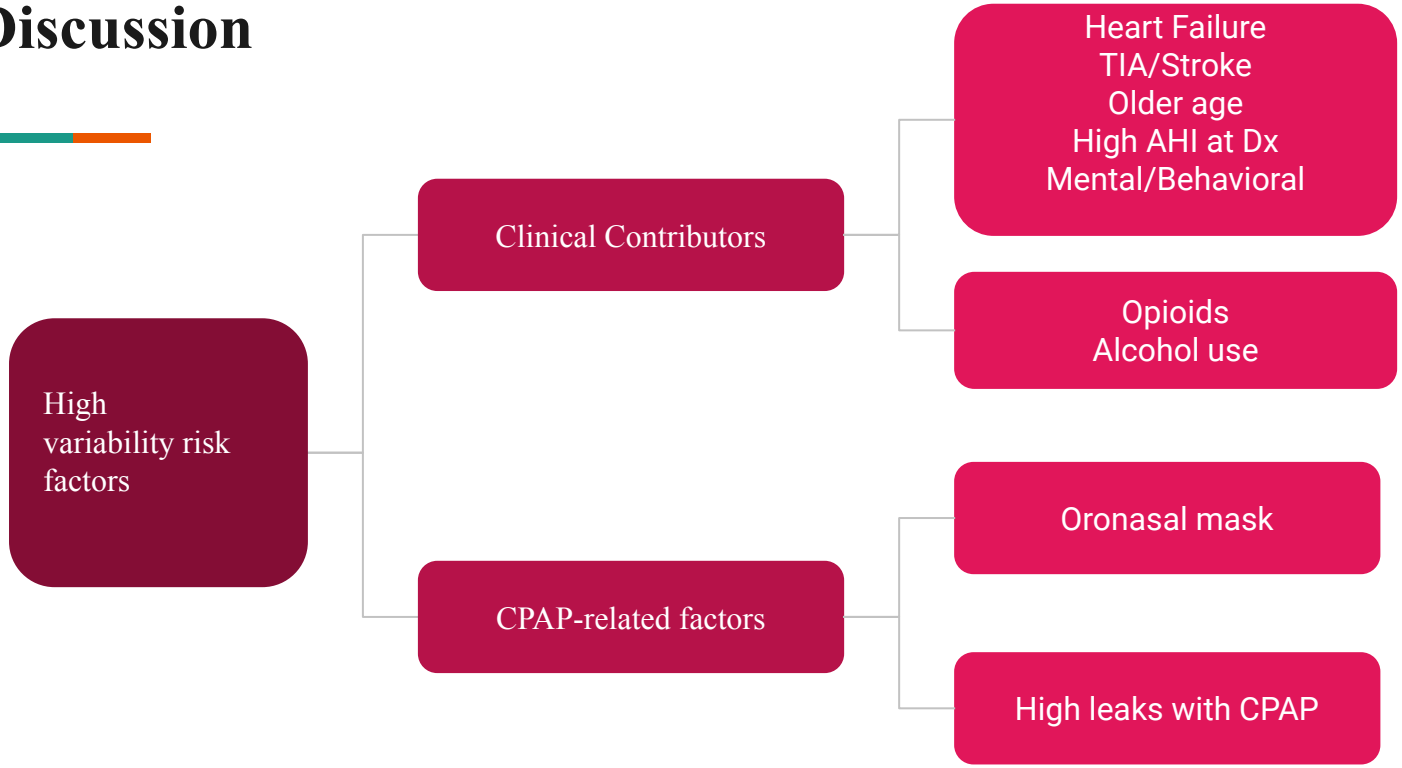


Groups of rAHI with variability

Variable	Coefficient	OR	95% CI
Heart failure	0.81[a]	2.26	1.87-2.65
Oronasal mask	0.70[a]	2.01	1.56-2.46
Age, ≥ 73 y	0.45[a]	1.57	1.32-1.82
Mental and behavioral disorders	0.43[b]	1.54	1.17-1.91
Opioids consumption	0.40[a]	1.49	1.11-1.87
Average leaks, 5 L/min	0.35[a]	1.41	1.34-1.48
Alcohol consumption	0.34	1.41	1.00-1.82
Transient ischemic attack or stroke	0.13[a]	1.14	1.10-1.18
AHI diagnosis, 5 events/h	0.05[b]	1.05	1.02-1.08
BMI	−0.03[a]	0.97	0.95-0.99
Smoking	−0.33[c]	0.72	0.55-0.89
Nasal disease	−0.39[c]	0.67	0.46-0.88
Diseases of the musculoskeletal system	−0.53[a]	0.59	0.48-0.70

Factors Associated with rAHI instability in moderate and high variability groups

Discussion



- First study to identify factors associated with trajectories of rAHI variability

Limitations

- Unselected patient group of routine follow-ups
- Lifestyle related confounders reported as mean values (eg. variability in daily alcohol use, weight, physical activity)
- Telemonitoring of some CPAP brands do not distinguish between central and obstructive events
- Did not consider insomnia

Found association between clinical factors, CPAP-related factors and rAHI variability but *causal association cannot be confirmed*

Future implications

- Automated identification of trajectories of rAHI variability in CPAP telemonitoring-> Early identification of Treatment Emergent CSA-> prevent discontinuation of CPAP or switch to suitable ventilatory support
- Potential warning signal for deterioration of cardiac function
- Patients with high rAHI variability with oronasal mask-> consider nasal mask (while monitoring evolution of rAHI variability)

SLEEPJ, 2020, 1–11

doi: 10.1093/sleep/zsz220
Advance Access Publication Date: 6 November 2019
Original Article

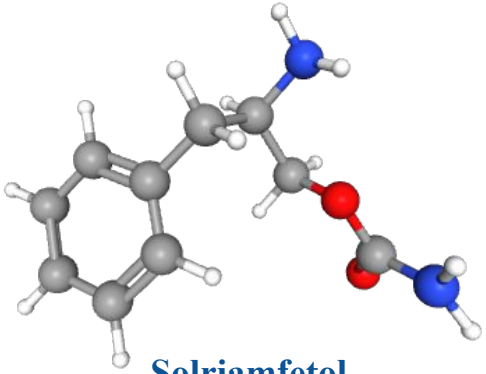
ORIGINAL ARTICLE

Long-term study of the safety and maintenance of efficacy of solriamfetol (JZP-110) in the treatment of excessive sleepiness in participants with narcolepsy or obstructive sleep apnea

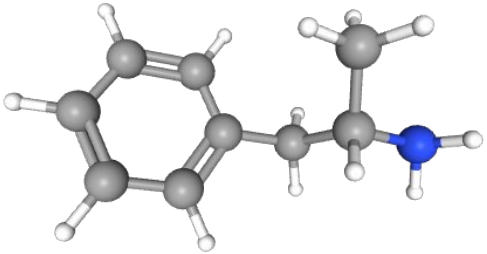
Atul Malhotra[1,*] Colin Shapiro[2], Jean-Louis Pepin[3,4], Jan Hedner[5], Mansoor Ahmed[6], Nancy Foldvary-Schaefer[7], Patrick J. Strollo Jr[8], Geert Mayer[9,10], Kathleen Sarmiento[11], Michelle Baladi[12], Patricia Chandler[12], Lawrence Lee[12] and Richard Schwab[13]

Introduction

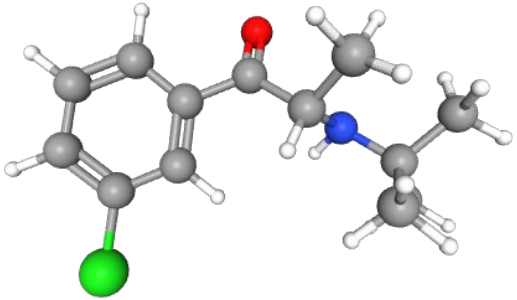
- Excessive daytime sleepiness (EDS) is a prominent symptom in OSA and narcolepsy; associated with poor health related quality of life.
- OSA is highly prevalent and EDS can be seen upto 33 % of patients despite PAP treatment.
- Stimulants like amphetamines are commonly used but there are no long term Safety and efficacy data in patients with narcolepsy.
- Modafinil and armodafinil have clear efficacy data but not helpful in some patients.
- Goal of this study is to demonstrate long term efficacy of Solriamfetol in patients who already completed phase 3 clinical trial.



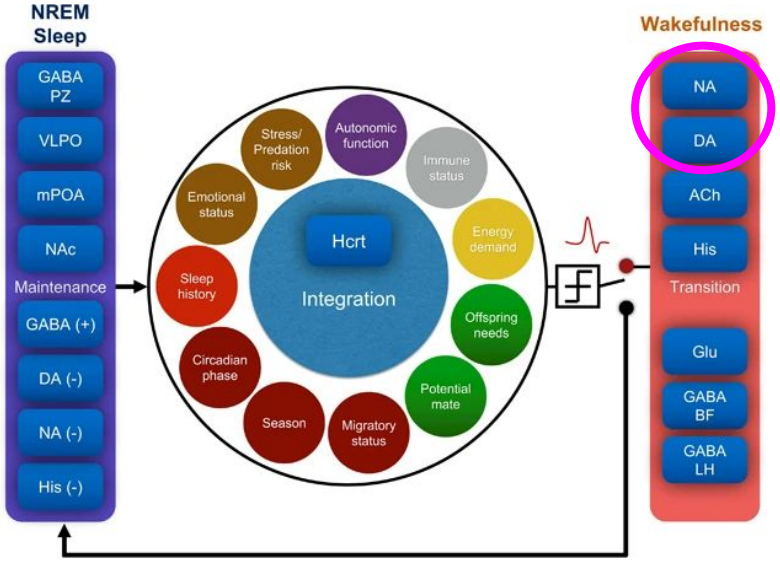
Solriamfetol

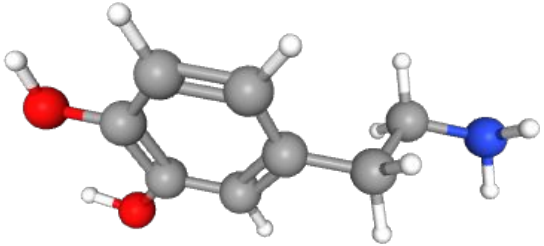


Amphetamine skeleton

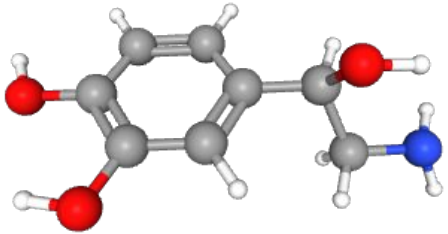


Bupropion





Dopamine



Norepinephrine

Patient Enrollment

Subjects with **Narcolepsy** or **OSA** who had previously completed a phase 2 or phase 3 trial of Solriamfetol.

2 groups defined based on subject's timing relative from previous study:

Group A

Completed Phase 3, 12-week study

Either **Narcolepsy** or **OSA**

Enrolled immediately into this study for 40 weeks

Group B

Completed Phase 2 study or 6-week Phase 3 study

Either **Narcolepsy** or **OSA**

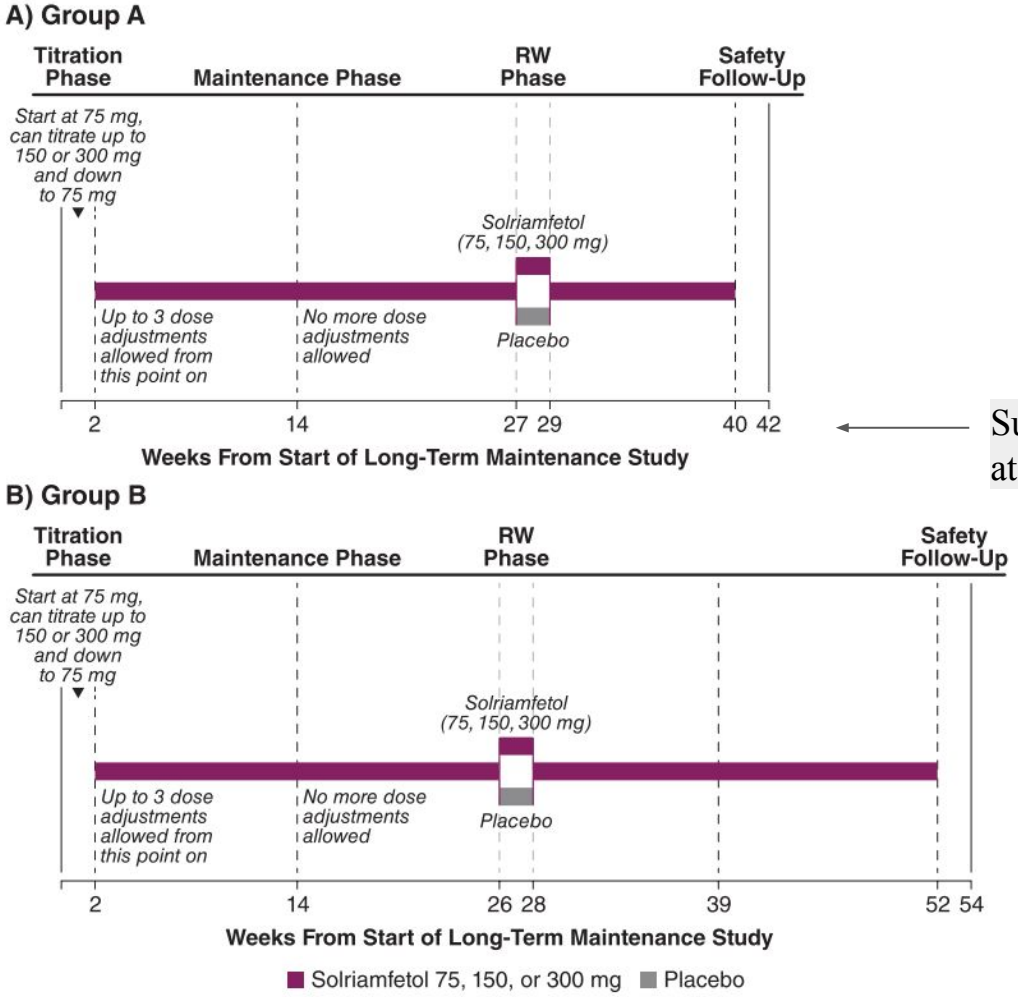
Enrolled some time later into this study for 52 weeks.

Study design

Group A
n = 519

Groups A+B
n = 643

Group B
n = 124



Subject assessments taken at these visits

RW phase, n = 282:
Narcolepsy, n = 79
OSA, n = 203

Subject assessment tools

Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in contrast to just feeling tired?
This refers to your usual way of life in recent times.
Even if you haven't done some of these activities 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	**2**	moderate chance of dozing
1	slight chance of dozing	**3**	high chance of dozing

It is important that you put a number (0-3) in each of the brackets

SITUATION	CHANCE of DOZING
Sitting and reading	( )
Watching TV	( )
Sitting inactive in a public place (eg theatre or a meeting)	( )
As a passenger in a car for an hour without a break	( )
Lying down to rest in the afternoon when circumstances permit	( )
Sitting and talking to someone	( )
Sitting quietly after lunch without alcohol	( )
In a car, while stopped for a few minutes in traffic	( )
	/24 TOTAL

PGI-C and CGI-C

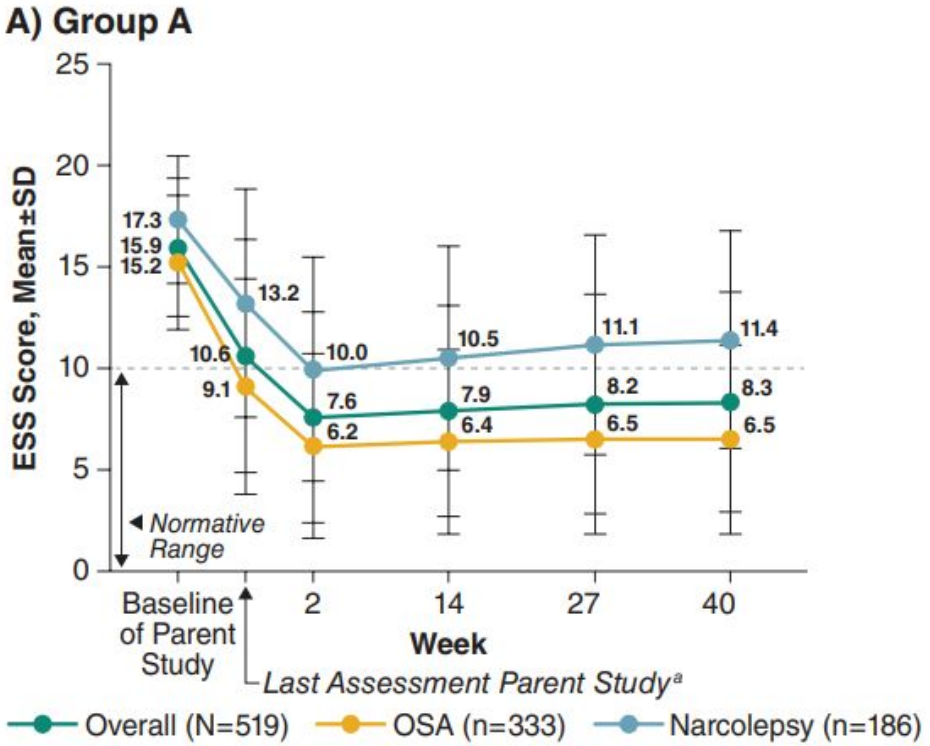
Since the start of the study, my overall status is:

1 ☐ Very Much Improved
2 ☐ Much Improved
3 ☐ Minimally Improved
4 ☐ No Change
5 ☐ Minimally Worse
6 ☐ Much Worse
7 ☐ Very Much Worse

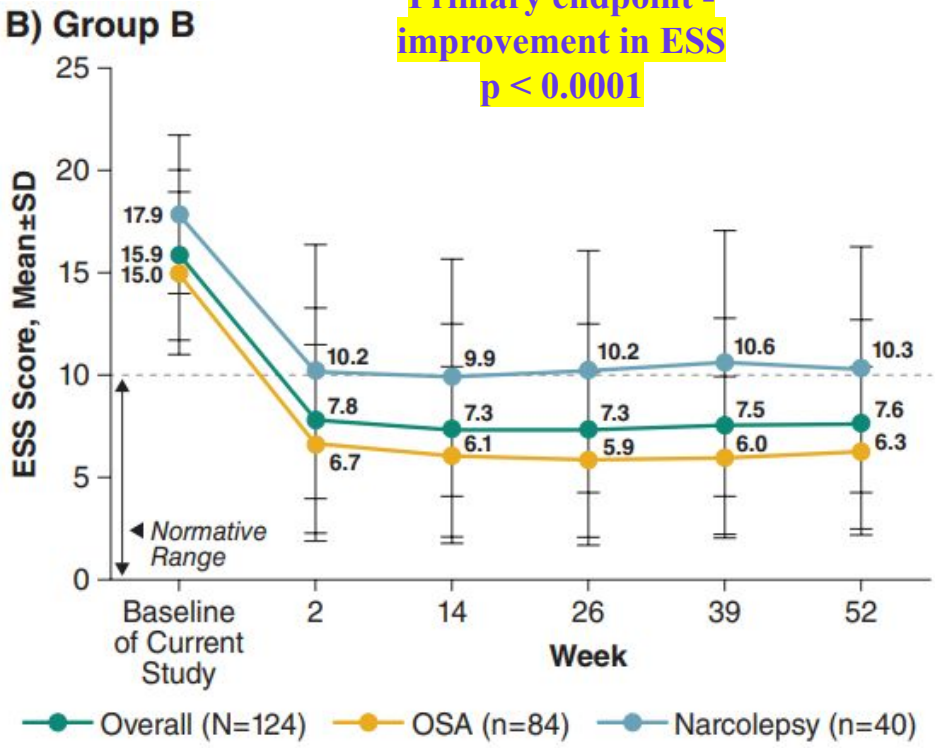
Primary endpoint: a change in the ESS from the start to the end of the RW phase

Secondary endpoints: percentage of subjects with any worsening on PGI-C or CGI-C at the end of the RW phase.

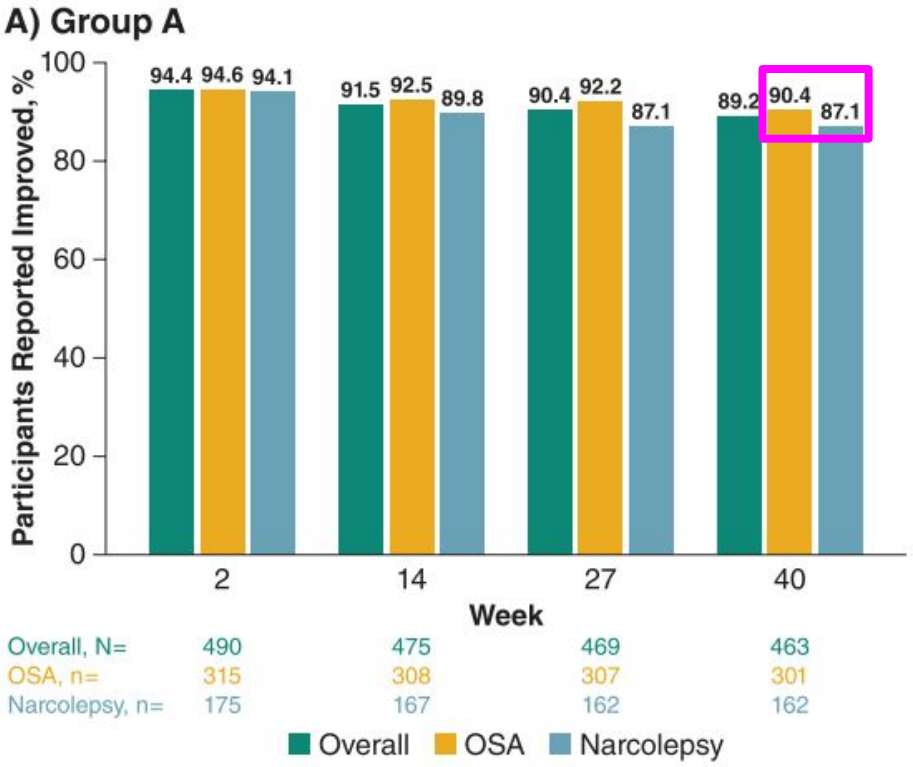
Drop in ESS seen as early as 2 weeks, and sustained

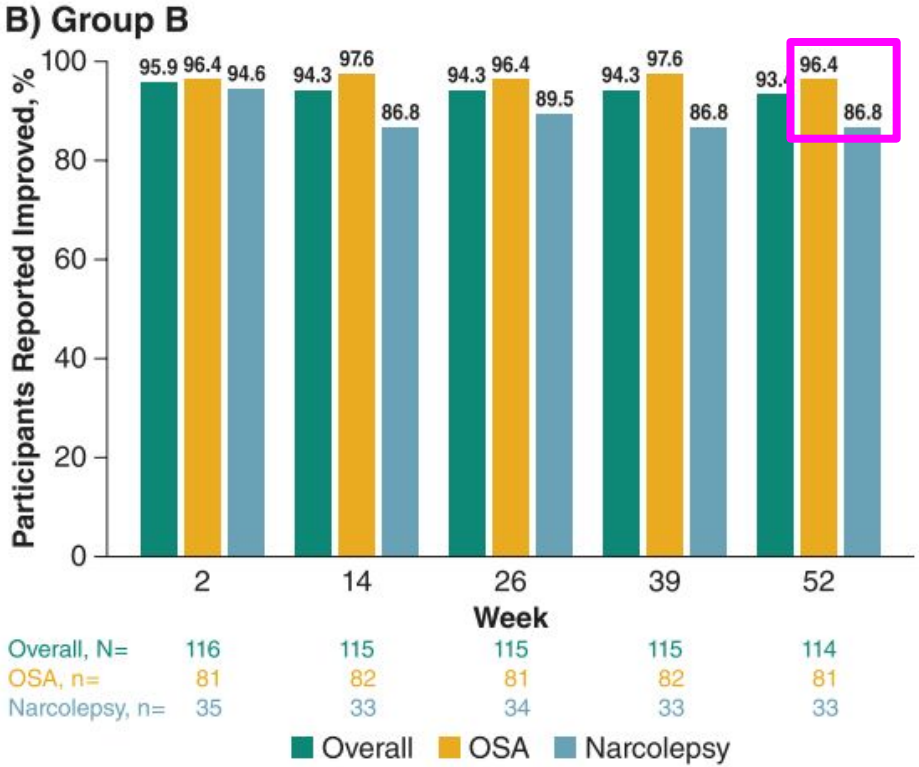


Primary endpoint - improvement in ESS $p < 0.0001$

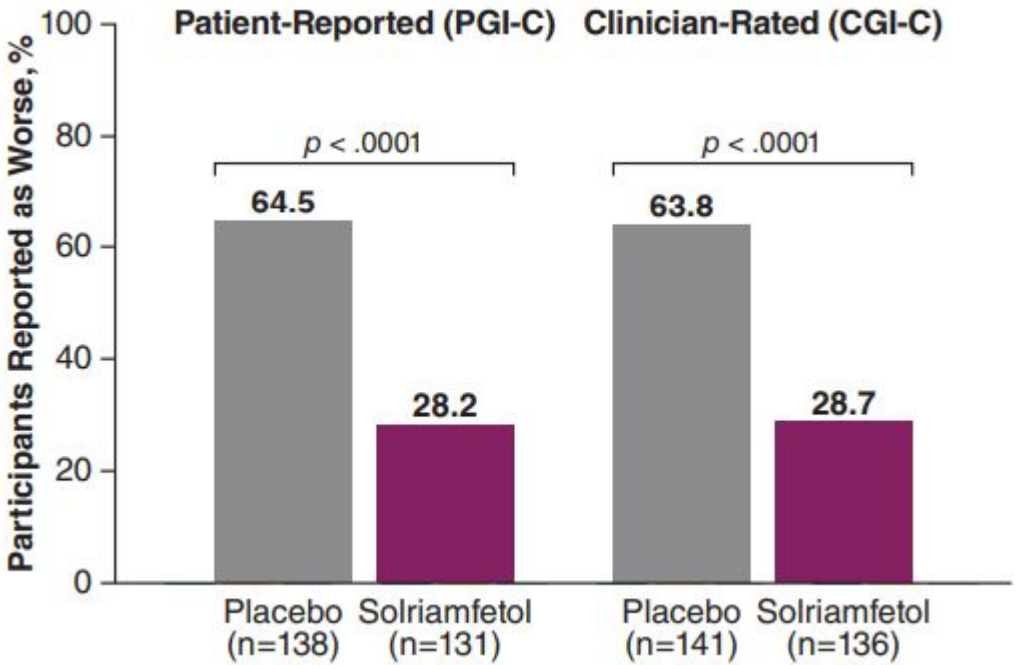


Improvement in PGI-C mirrors drop in ESS

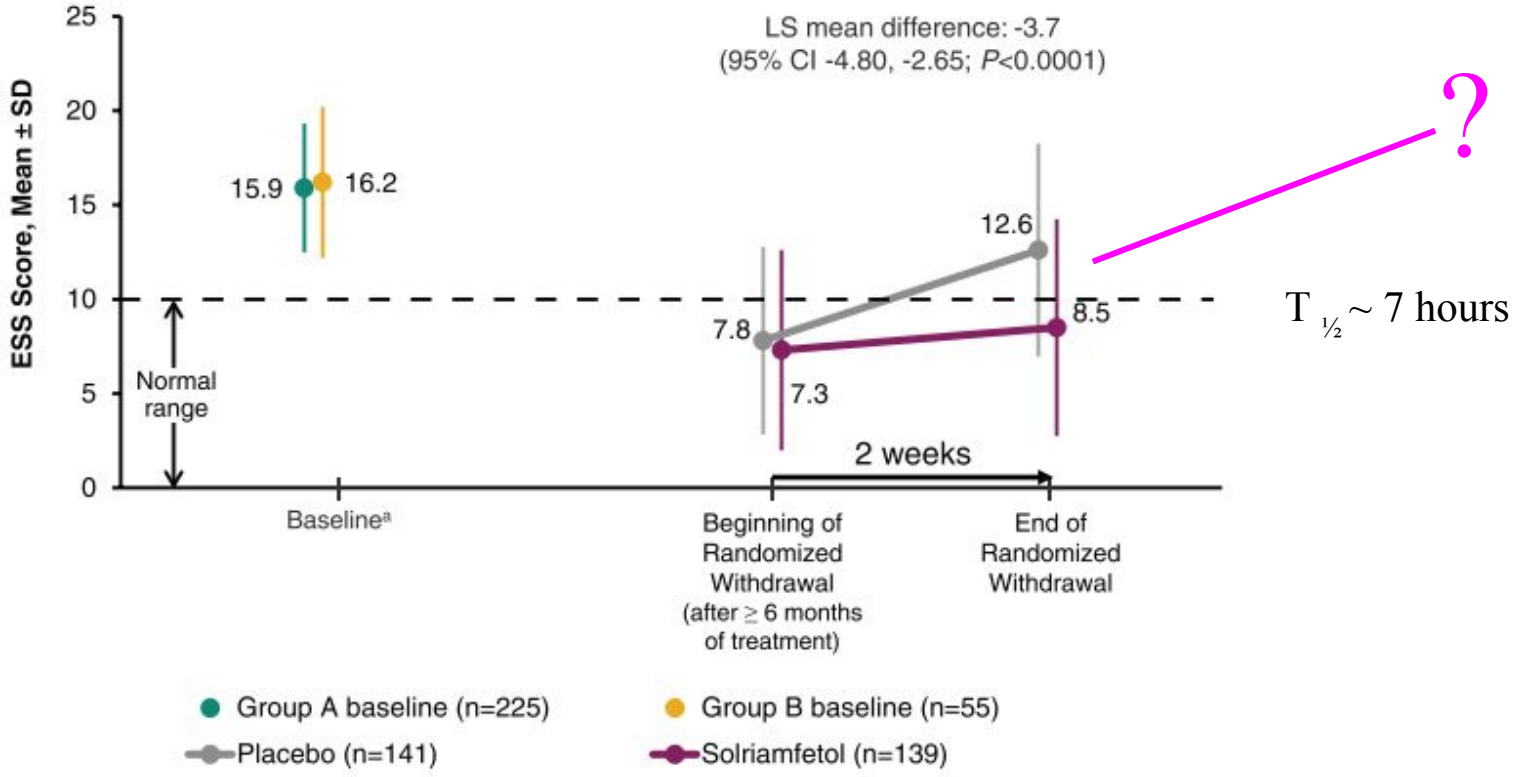




Participants who reported as worse



No rebound hypersomnia upon sudden withdrawal



Adverse effects of Solriamfetol

482 (75%) subjects had at least 1 TEAE,
Narcolepsy (74.8%), OSA (75.1%)

Table 2. TEAEs across the study (safety population, groups A and B combined)

	Number (%) of participants in combined solriamfetol groups		
TEAE	Overall (*N* = 643)	OSA (*n* = 417)	Narcolepsy (*n* = 226)
At least 1 TEAE	482 (75.0)	313 (75.1)	169 (74.8)
Severity of TEAEs			
Mild	188 (29.2)	128 (30.7)	60 (26.5)
Moderate	246 (38.3)	157 (37.6)	89 (39.4)
Severe	48 (7.5)	28 (6.7)	20 (8.8)
Serious TEAEs	27 (4.2)	21 (5.0)	6 (2.7)
TEAEs leading to discontinuation	59 (9.2)	36 (8.6)	23 (10.2)
Death	1 (0.2)*	1 (0.2)	0
Most common TEAEs†			
Headache	71 (11.0)	40 (9.6)	31 (13.7)
Nausea	57 (8.9)	31 (7.4)	26 (11.5)
Nasopharyngitis	54 (8.4)	35 (8.4)	19 (8.4)
Insomnia	51 (7.9)	35 (8.4)	16 (7.1)
Dry mouth	47 (7.3)	33 (7.9)	14 (6.2)
Anxiety	46 (7.2)	25 (6.0)	21 (9.3)
Decreased appetite	32 (5.0)	14 (3.4)	18 (8.0)
Upper respiratory tract infection	32 (5.0)	22 (5.3)	10 (4.4)

*Due to sepsis.
†≥5% in combined solriamfetol groups for any indication.

Highlights

- Safety profile similar to previous 12 week studies
- Similar reduction in ESS in both groups although narcolepsy subjects had higher baseline ESS
- **Narcolepsy** subjects more likely to withdraw due to lack of efficacy
- No rebound hypersomnia upon withdrawal or evidence of developing tolerance.
- 43% with narcolepsy, 85% with OSA reported normal ESS at the end of study period


THANK YOU
Any Questions?