UT Southwestern Medical Center

UPDATES IN INTERNAL MEDICINE 2021:

Updates in Sleep Medicine

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DISCLOSURES

- NONE

OBJECTIVES

- Discuss the effects on sleep during the COVID-19 pandemic
- Discuss the impact on sleep medicine since the COVID-19 pandemic
- Review testing modalities for sleep-related breathing disorders
- Discuss new medications for the treatment of hypersomnia and insomnia

HOW WELL DO WE SLEEP?

- Sleep is a vital aspect to life
- Sleep disturbances prevalent in the US 15-25%
  - Declared a public health epidemic!

Grandner et al., *Sleep*, Volume 35, Issue 3, 1 March 2012

Figure 2. Prevalence of Short Sleep Duration (<7 hours) for Adults Aged ≥ 18 Years, by County, United States, 2014

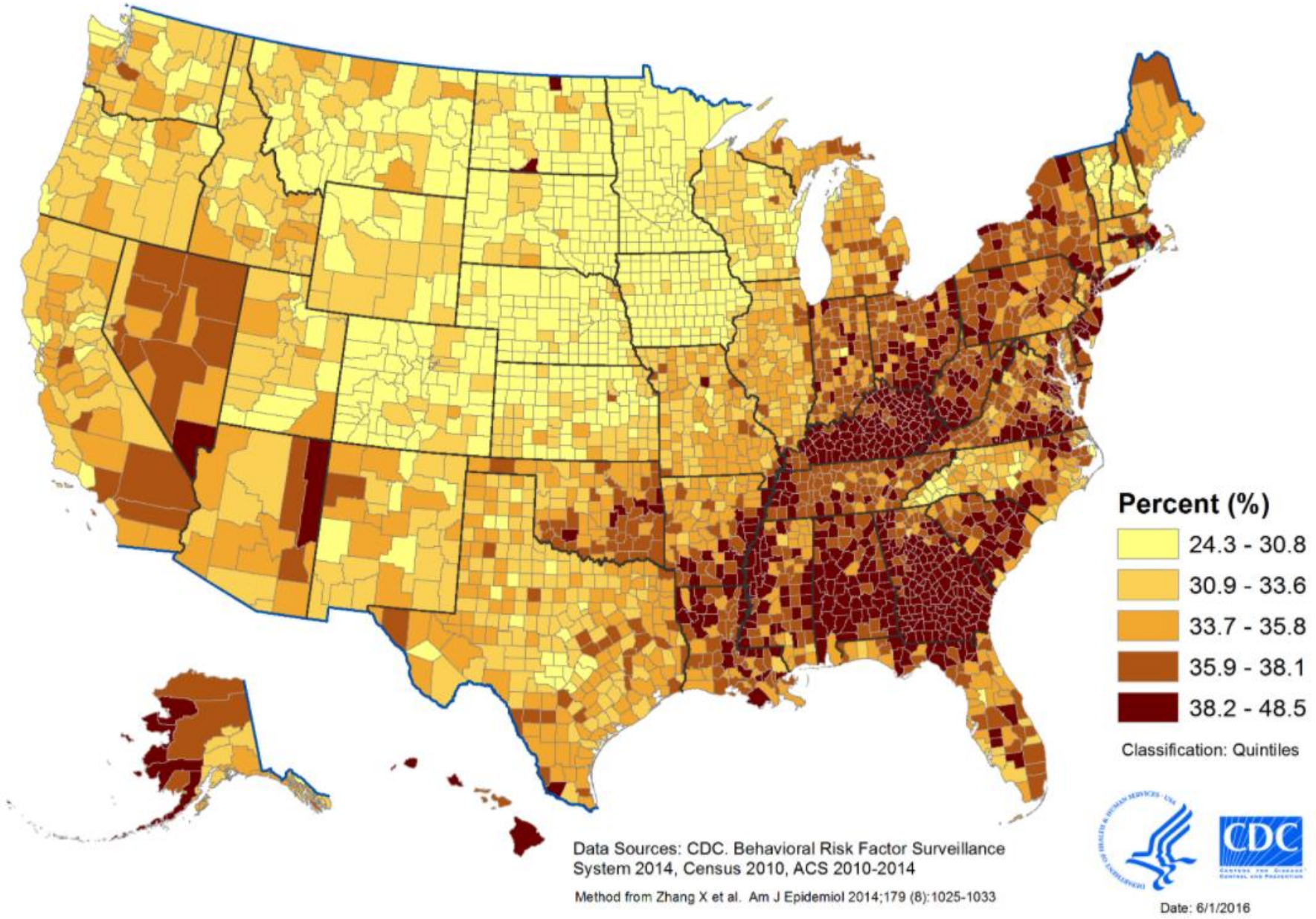
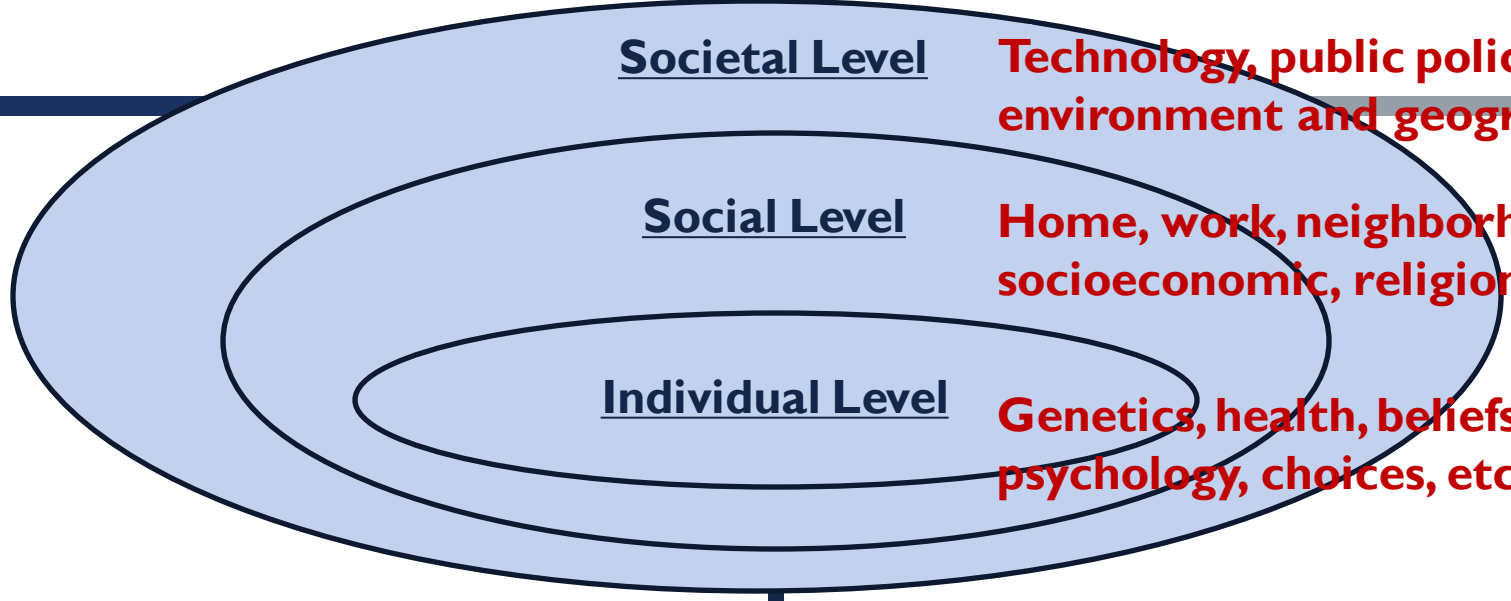


Table 3. Age-Adjusted[a] Percentage Reporting Chronic Health Conditions by Sleep Duration—Behavioral Risk Factor Surveillance System, United States, 2014

	Short sleep (<7 hours)		Sufficient sleep (≥7 hours)	
Chronic condition	**%**	**95% CI**	**%**	**95% CI**
Heart attack	4.8	(4.6–5.0)	3.4	(3.3–3.5)
Coronary heart disease	4.7	(4.5–4.9)	3.4	(3.3–3.5)
Stroke	3.6	(3.4–3.8)	2.4	(2.3–2.5)
Asthma	16.5	(16.1–16.9)	11.8	(11.5–12.0)
COPD (chronic obstructive pulmonary disease)	8.6	(8.3–8.9)	4.7	(4.6–4.8)
Cancer	10.2	(10.0–10.5)	9.8	(9.7–10.0)
Arthritis	28.8	(28.4–29.2)	20.5	(20.2–20.7)
Depression	22.9	(22.5–23.3)	14.6	(14.3–14.8)
Chronic kidney disease	3.3	(3.1–3.5)	2.2	(2.1–2.3)
Diabetes	11.1	(10.8–11.4)	8.6	(8.4–8.8)

Date: 6/1/2016



INSUFFICIENT OR POOR QUALITY SLEEP

ADVERSE HEALTH OUTCOMES

GENERAL HEALTH

CARDIOVASCULAR HEALTH

METABOLIC HEALTH

IMMUNOLOGIC HEALTH

HUMAN PERFORMANCE

Adapted from: Grandner. Sleep, Health, and Society, Sleep Medicine Clinics, Volume 12, Issue 1, 2017

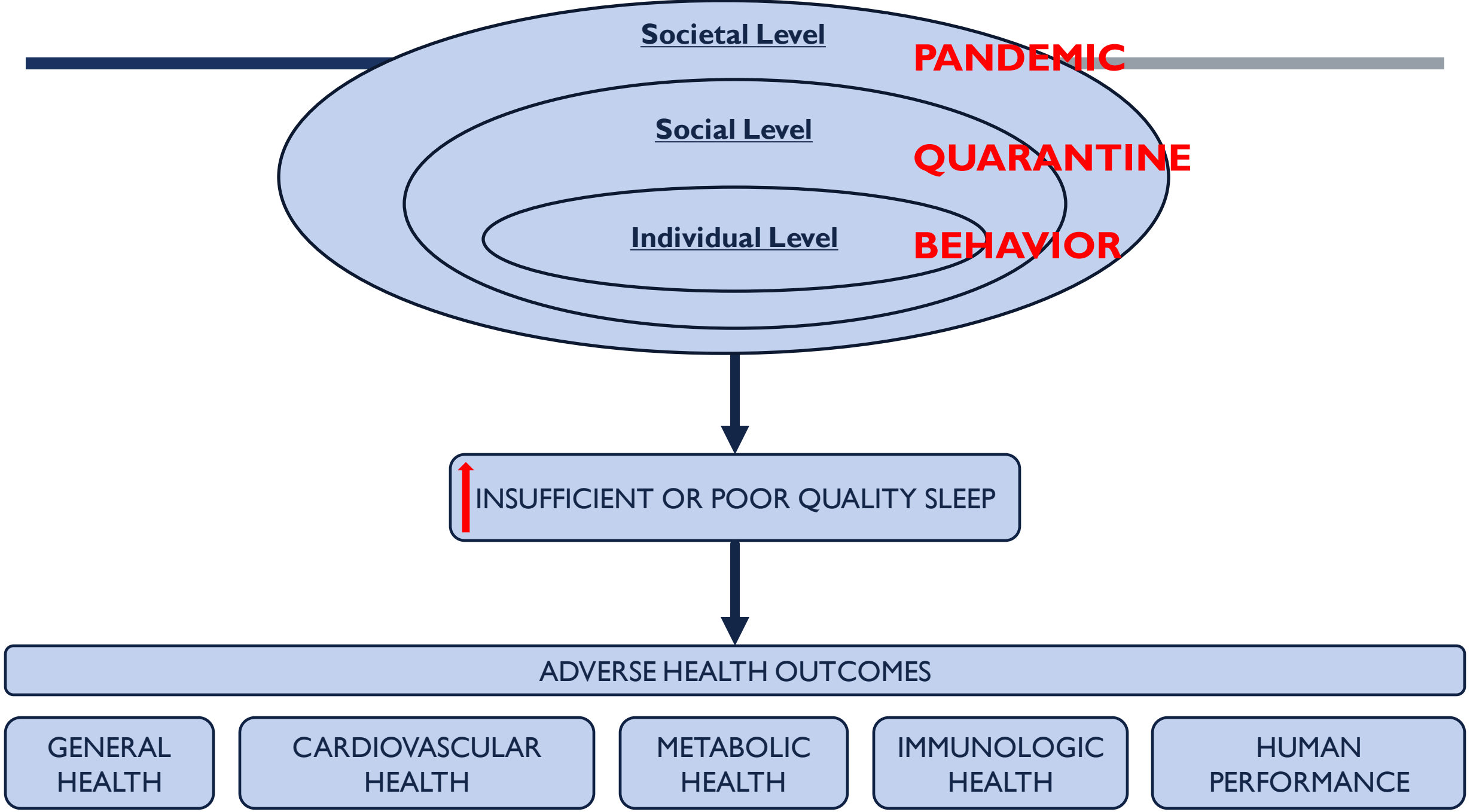
HOW ARE WE CURRENTLY SLEEPING?

COVID-19 PANDEMIC

- Job loss
- Home schooling
- Eviction
- Hospitalization
- Mortality
- Uncertainty

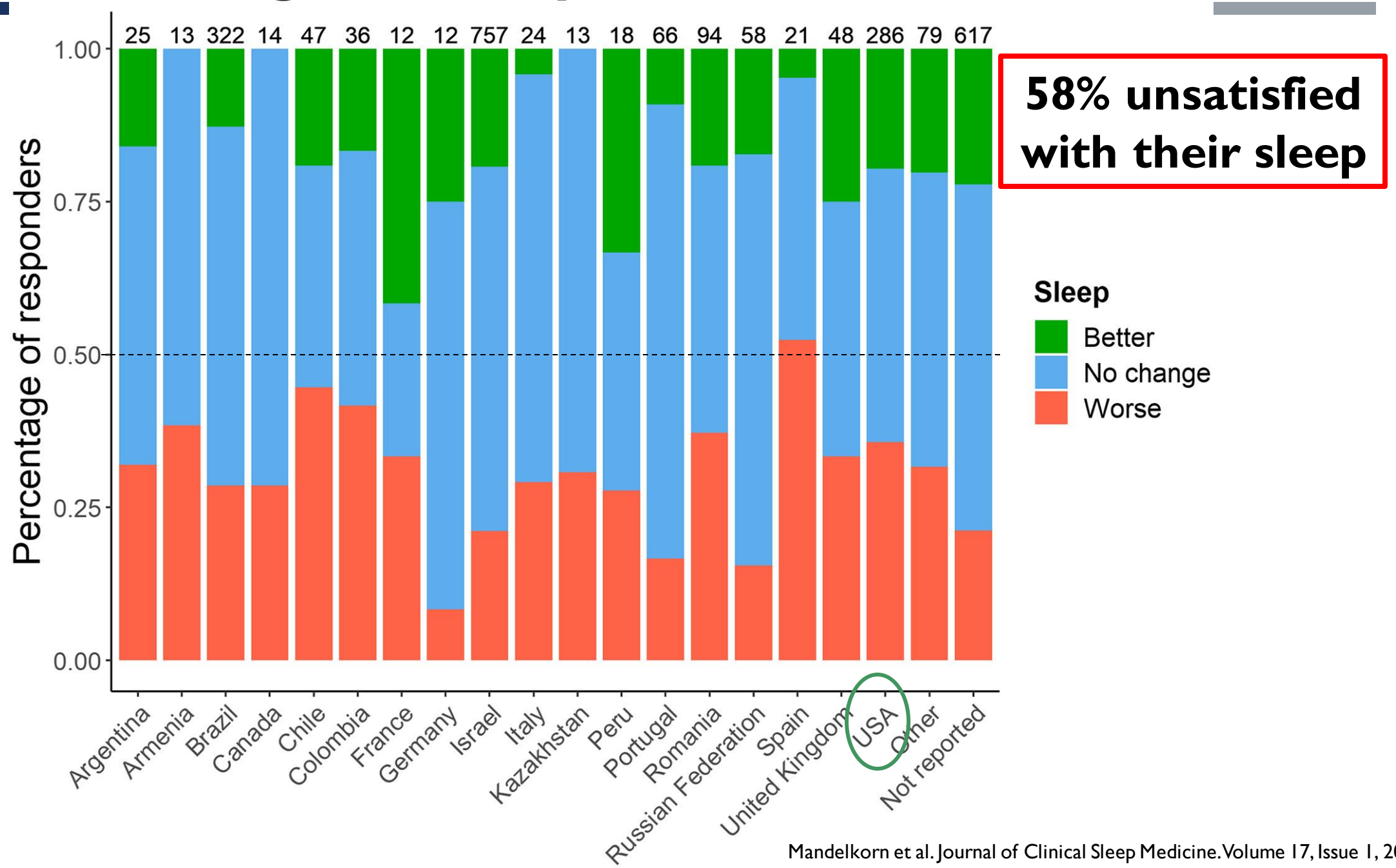
STRESS

POOR SLEEP



Adapted from: Grandner. Sleep, Health, and Society, Sleep Medicine Clinics, Volume 12, Issue 1, 2017

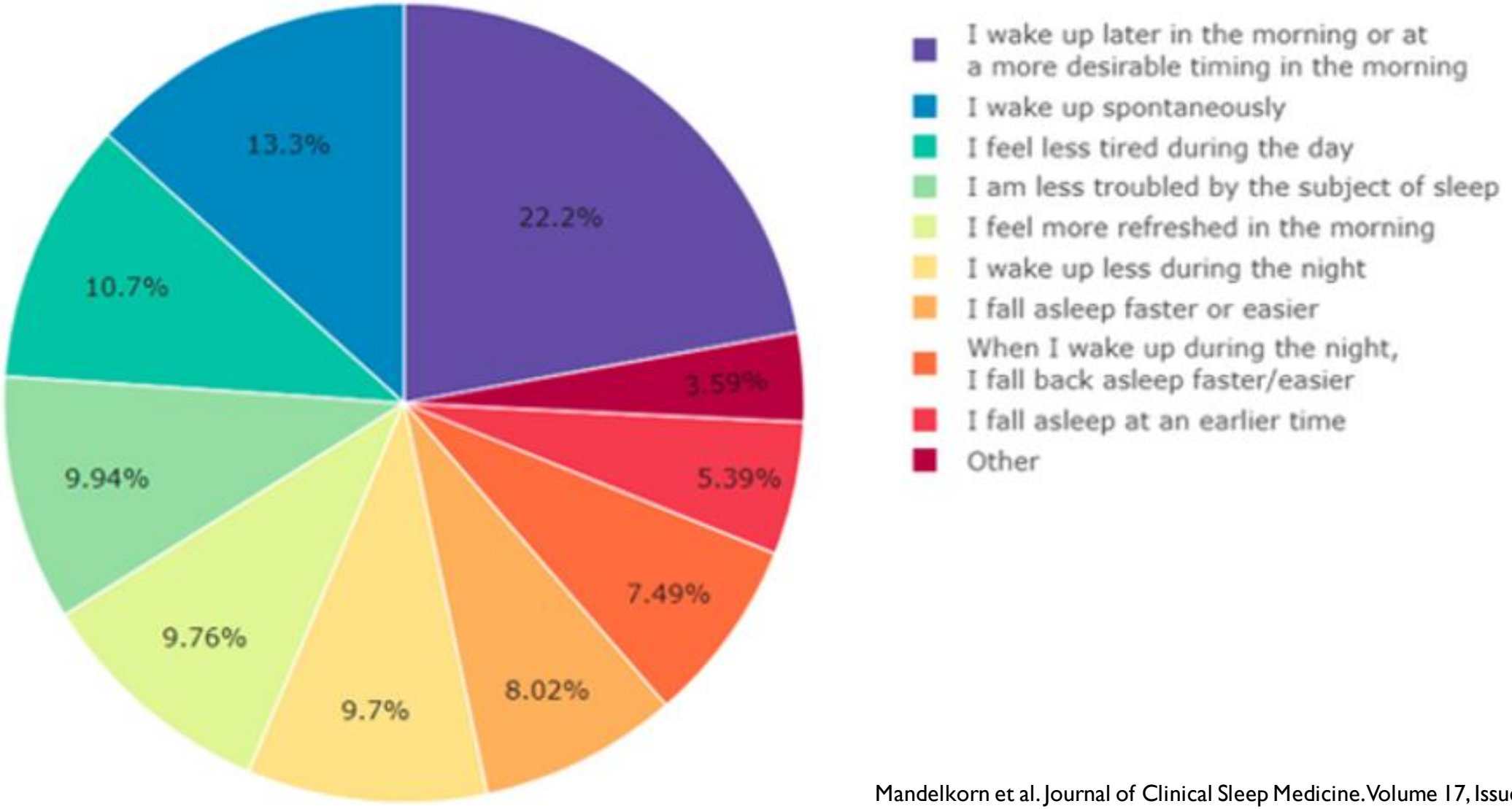
Change in Sleep



58% unsatisfied with their sleep

Mandelkorn et al. Journal of Clinical Sleep Medicine. Volume 17, Issue 1, 2021

Reasons for Sleep Improvement



Mandelkorn et al. Journal of Clinical Sleep Medicine. Volume 17, Issue 1, 2021

Reasons for Sleep Worsening

Mandelkorn et al. Journal of Clinical Sleep Medicine. Volume 17, Issue 1, 2021

Table 4—Multivariable logistic regression demonstrating factors independently associated with worsening sleep quality following COVID-19.

Variable	Study 1 (n = 1,994)			Study 2 (n = 753)		
	Odds Ratios	95% CI	z	Odds Ratios	95% CI	z
Age						
18–30 years	1.02	0.75–1.37	0.13	1.48	0.94–2.34	1.67
31–45 years	1.21	0.93–1.58	1.42	1.63*	1.06–2.52	2.21
46–60 years	–	–	–	–	–	–
>60 years	0.73*	0.53–0.99	–2.00	1.15	0.65–2.02	0.48
Female sex	1.45***	1.17–1.80	3.40	1.82***	1.33–2.50	3.74
Being in quarantine	1.32**	1.08–1.61	2.76	1.31	0.96–1.79	1.73
Having young children	0.97	0.73–1.28	–0.23	1.36	0.90–2.06	1.45
Livelihood affected by COVID-19 pandemic	1.38**	1.11 – 1.71	2.90	1.72***	1.25–2.38	3.33
Less physical activity	1.25*	1.03–1.53	2.21	1.84***	1.36–2.51	3.90

*$P < .05$; **$P < .01$; ***$P < .001$; odds ratio > 1 indicated increased odds for sleep quality change score (SQCS) > 0. CI = confidence interval.

Table 2—Meta-analysis of sleep problems during COVID-19: by population and by research measure.

Component	K	N	Random-Effects Meta-Analysis Pooled Results [95% CI]	Heterogeneity			Moderators		Publication Bias
				I^2	τ^2	Q	Age	Sex (%Male)	
Sleep problems (all populations, all measures*)	40	53,489	35.7% [29.4%–42.4%]	99.5%	0.8	7477 (39)	NS	NS	Kendall's *P* = .70, Egger's *P* = .72
Sleep problems (general population, all measures)	26	46,751	32.3% [25.3%–40.2%]	99.5%	0.8	6137 (25)	NS	NS	Kendall's *P* = .80; Egger's *P* = .90
Sleep problems (health care workers, all measures)	11	4854	36.0% [21.1%–54.2%]	99%	1.6	1048 (10)	NS	NS	Kendall's *P* = .70; Egger's *P* = .80
Sleep problems (COVID-19 patients, all measures)	3	932	74.8% [28.7%–95.6%]	96%	2.7	50 (2)	*P* = .001	*P* = .001	Kendall's *P* = .60; Egger's *P* = .80
Sleep problems (all populations, PSQI only)	18	20,570	39.6% [29.6%–50.6%]	99.5%	0.8	2933 (17)	NS	NS	Kendall's *P* = .80; Egger's *P* = .42
Sleep problems (general population, PSQI only)	9	16,516	37.9% [25.2%–52.4%]	99.6%	0.8	2018 (8)	*P* = .001	NS	Kendall's *P* = .80; Egger's *P* = .42
Sleep problems (health care workers, PSQI only)	8	4854	39.7% [21.2%–61.6%]	99%	1.6	853 (7)	NS	NS	Kendall's *P* = 1.0; Egger's *P* = .96
Sleep problems (general population, SD)	6	8538	25.2% [9.3%–52.6%]	99.7%	2.2	1774 (5)	NS	NS	Kendall's *P* = .85; Egger's *P* = .96
Sleep problems (general population, ISI)	3	7220	29.7% [11.9%–56.9%]	99.6%	1.1	531 (2)	NS	NS	Kendall's *P* = .60; Egger's *P* = .71
Mean sleep quality (all populations, PSQI)	15	9230	7.1 [6.3–8.0]	99.1%	2.4	1716 (14)	NS	NS	Kendall's *P* = .08; Egger's *P* = .045
Mean sleep quality (general population, PSQI)	4	4722	6.0 [5.3–6.8]	98%	0.6	182 (3)	NS	*P* = .04	Kendall's *P* = 1.0; Egger's *P* = .47
Mean sleep quality (health care workers, PSQI)	9	4483	7.7 [6.1–9.2]	99%	5.4	1358 (9)	NS	NS	Kendall's *P* = .14; Egger's *P* = .13

COVID-19 patients (74.8%) > healthcare workers (36.0%) > general population (32.3%)

Jahrami et al. Journal of Clinical Sleep Medicine. Volume 17, Issue 2, 2021

Table 2—Sleep, health, and mental health by working-at-home status.

	Working From Home (n = 539), mean (± SD) or n (%)	Working In-Person (n = 290), mean (± SD) or n (%)	*t* (*P* Value)/χ^2 Test of Independence
Average sleep duration			
Before stay-at-home	7.20 h (±.84)	7.04 h (±1.5)	*t* = –0.200; *df* = 538 *P* = .842
During stay-at-home	7.21 h (±1.2)	6.58 h (± 1.52)	*t* = 5.13; *df* = 289 *P* < .001
Work hours			
More hours	n = 69 (26)	n = 67 (39)	$\chi^2(1) = 7.8$ *P* = .005 n = 440
Fewer hours	n = 197 (74)	n = 107 (62)	
Sleep schedule			
Bedtime later	n = 248 (64)	n = 116 (56)	$\chi^2(2) = 15.1$ *P* = .001 n = 595
Bedtime earlier	n = 40 (10)	n = 46 (22)	
Bedtime same	n = 99 (26)	n = 46 (22)	
Wake time later	n = 287 (74)	n = 72 (35)	$\chi^2(2) = 91.2$ *P* < .001 n = 596
Wake time earlier	n = 51 (13)	n = 85 (41)	
Wake time same	n = 50 (13)	n = 51 (25)	
Exercise/movement			
More	n = 211 (48)	n = 78 (39)	$\chi^2(1) = 4.6$ *P* = .033 n = 636
Less	n = 226 (52)	n = 121 (61)	
Diet			
More food	n = 204 (73)	n = 97 (63)	$\chi^2(1) = 4.2$ *P* = .041 n = 433
Less food	n = 76 (27)	n = 56 (37)	
More healthy	n = 146 (48)	n = 63 (36)	$\chi^2(1) = 6.4$ *P* = .012 n = 480
Less healthy	n = 159 (52)	n = 112 (64)	
Mood change			
Better/same	n = 61 (16)	n = 20 (9)	$\chi^2(1) = 7.7$ *P* = .005 n = 602
Worse	n = 308 (84)	n = 213 (91)	$\chi^2(3) = 9.2$ *P* = .027 n = 31
Much more depressed	n = 0 (0)	n = 2 (20)	
Much more anxious	n = 6 (29)	n = 0 (0)	
Much more irritable	n = 0 (0)	n = 1 (10)	
All of the above	n = 15 (71)	n = 7 (70)	

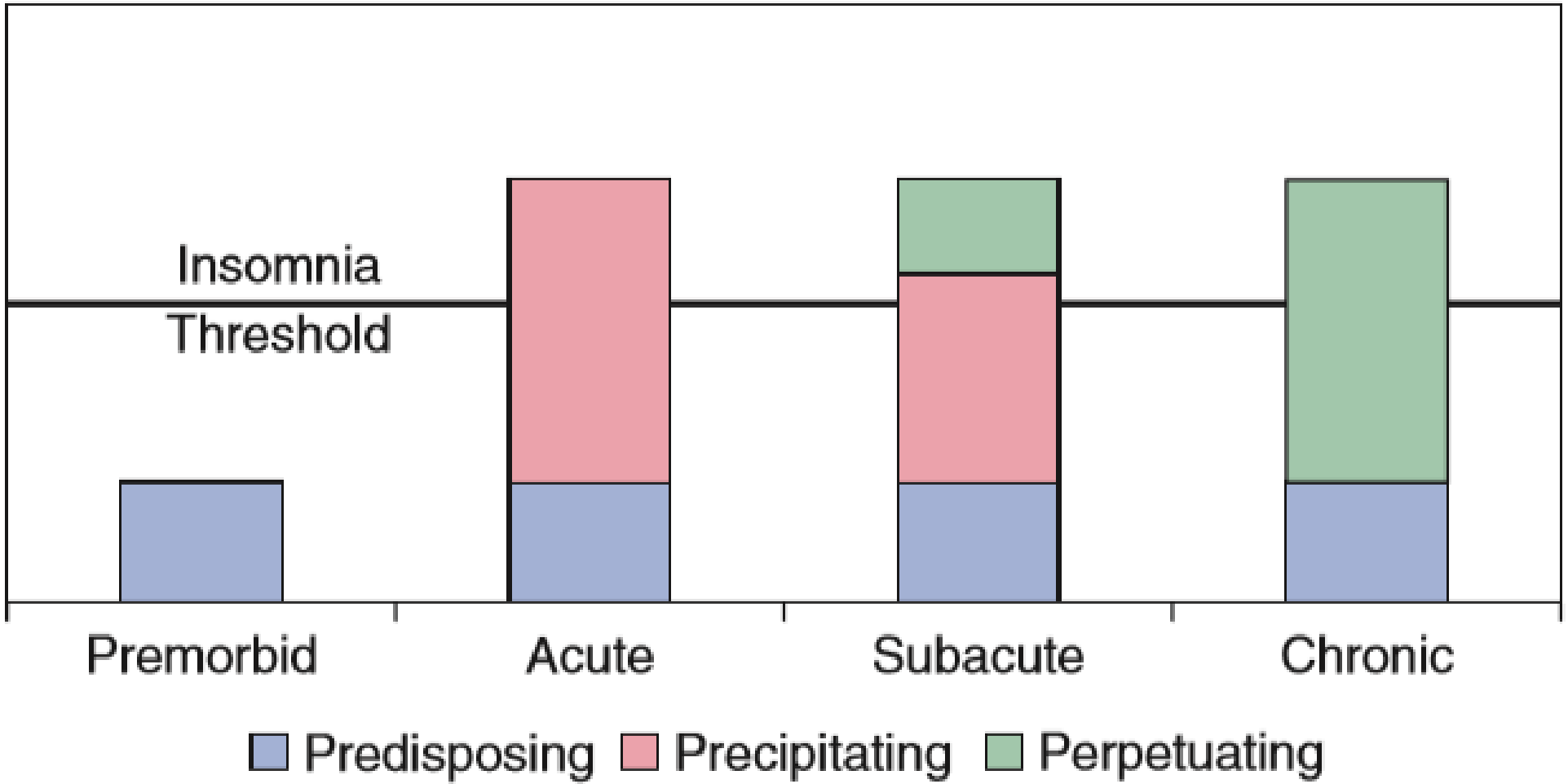
Conroy et al. Journal of Clinical Sleep Medicine. Volume 17, Issue 2, 2021

Table 3—Sleep and working patterns by mood change.

	Mood Same or Better During COVID-19 Pandemic	Mood Worsened During COVID-19 Pandemic	*t* or χ^2 (*P* Value)
Average sleep duration before stay-at-home order	n = 81 6.84 h (SD = 0.99)	n = 522 7.25 h (SD = 1.4)	*t* = 2.6 *P* = .009
Average sleep duration after stay-at-home order	n = 81 7.48 h (SD = 1.4)	n = 521 6.83 h (SD = 1.5)	*t* = –3.6 *P* < .001
Change in sleep duration after stay-at-home order	n = 81 0.64 h (SD = 1.4)	n = 521 –0.42 h (SD = 1.6)	*t* = –5.7 *P* < .001
Conducting job from home	n = 61 (17%)	n = 308 (84%)	$\chi^2(1) = 7.7$ *P* = .005
Wake time moved later	n = 45 (78%)	n = 217 (54%)	$\chi^2(2) = 11.9$ *P* = .003
More screen time before bed	n = 41 (51%)	n = 341 (65%)	$\chi^2(1) = 6.5$ *P* = .011

Conroy et al. Journal of Clinical Sleep Medicine. Volume 17, Issue 2, 2021

Spielman's model for the evolution of chronic insomnia



DEFINITION OF INSOMNIA

- Difficulty initiating sleep OR maintaining sleep
- Cannot be explained purely by inadequate opportunity or circumstances
- Must have daytime consequences – *fatigue, inattention, memory impairment, mood disturbance, irritability, behavioral problems, hypersomnolence, reduced motivation, lack of energy, proneness for errors, dissatisfaction with sleep* – symptoms occur at least 3 times a week

- Present for < 3 months = short term insomnia disorder
- Present for ≥ 3 months = chronic insomnia disorder

International Classification of Sleep Disorders, 3rd edition, American Academy of Sleep Medicine, 2014

RECOMMENDATIONS FOR THE USE OF BEHAVIORAL AND PSYCHOLOGICAL TREATMENTS FOR CHRONIC INSOMNIA IN ADULTS

1.	We recommend that clinicians use multicomponent cognitive behavioral therapy for insomnia for the treatment of chronic insomnia disorder in adults.	STRONG ⊕⊕⊕⊖ B>h
2.	We suggest that clinicians use multicomponent brief therapies for insomnia for the treatment of chronic insomnia disorder in adults.	CONDITIONAL ⊕⊕⊕⊖ B>H
3.	We suggest that clinicians use stimulus control as a single-component therapy for the treatment of chronic insomnia disorder in adults.	CONDITIONAL ⊕⊕⊖⊖ B>H
4.	We suggest that clinicians use sleep restriction therapy as a single-component therapy for the treatment of chronic insomnia disorder in adults.	CONDITIONAL ⊕⊕⊖⊖ B>H
5.	We suggest that clinicians use relaxation therapy as a single-component therapy for the treatment of chronic insomnia disorder in adults.	CONDITIONAL ⊕⊕⊖⊖ B>H
6.	We suggest that clinicians not use sleep hygiene as a single-component therapy for the treatment of chronic insomnia disorder in adults.	CONDITIONAL ⊕⊕⊖⊖ B=H

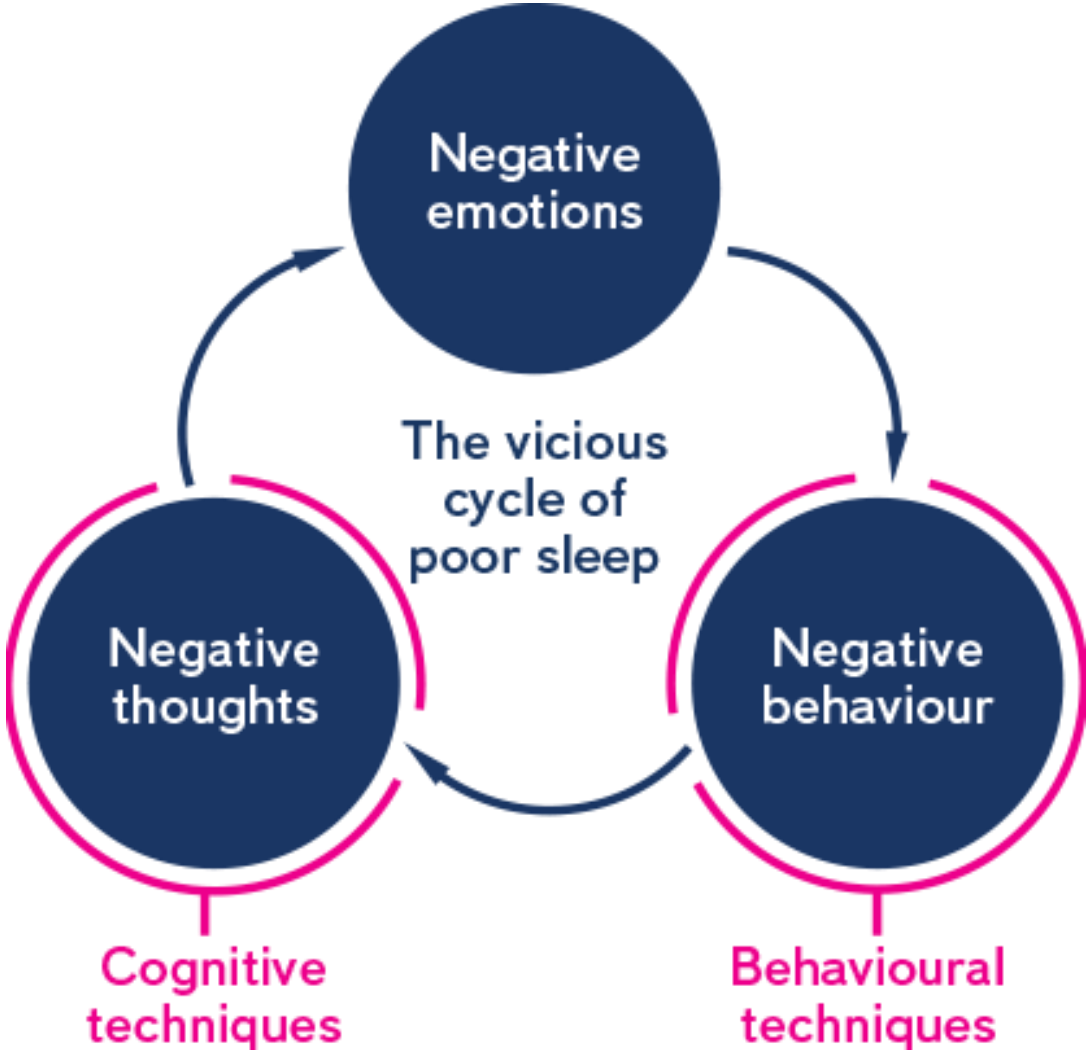
CBT-I

Edinger et al. Journal of Clinical Sleep Medicine. Volume 17, Issue 2, 2021

GOOD SLEEP HYGIENE PRACTICE

- Keep a consistent sleep schedule even on weekends and vacations
- Establish a relaxing bedtime routine
- Keep bedroom quiet, dark, and cool
- Limit bright light exposure in the evenings
- ***Turn off electronics at least 30min before bedtime***
- Don't eat a large meal and reduce fluid intake before bedtime
- Exercise regularly and maintain a healthy diet
- Avoid caffeine consumption in the late afternoon or evening
- Avoid alcohol before bedtime

COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA (CBTI)



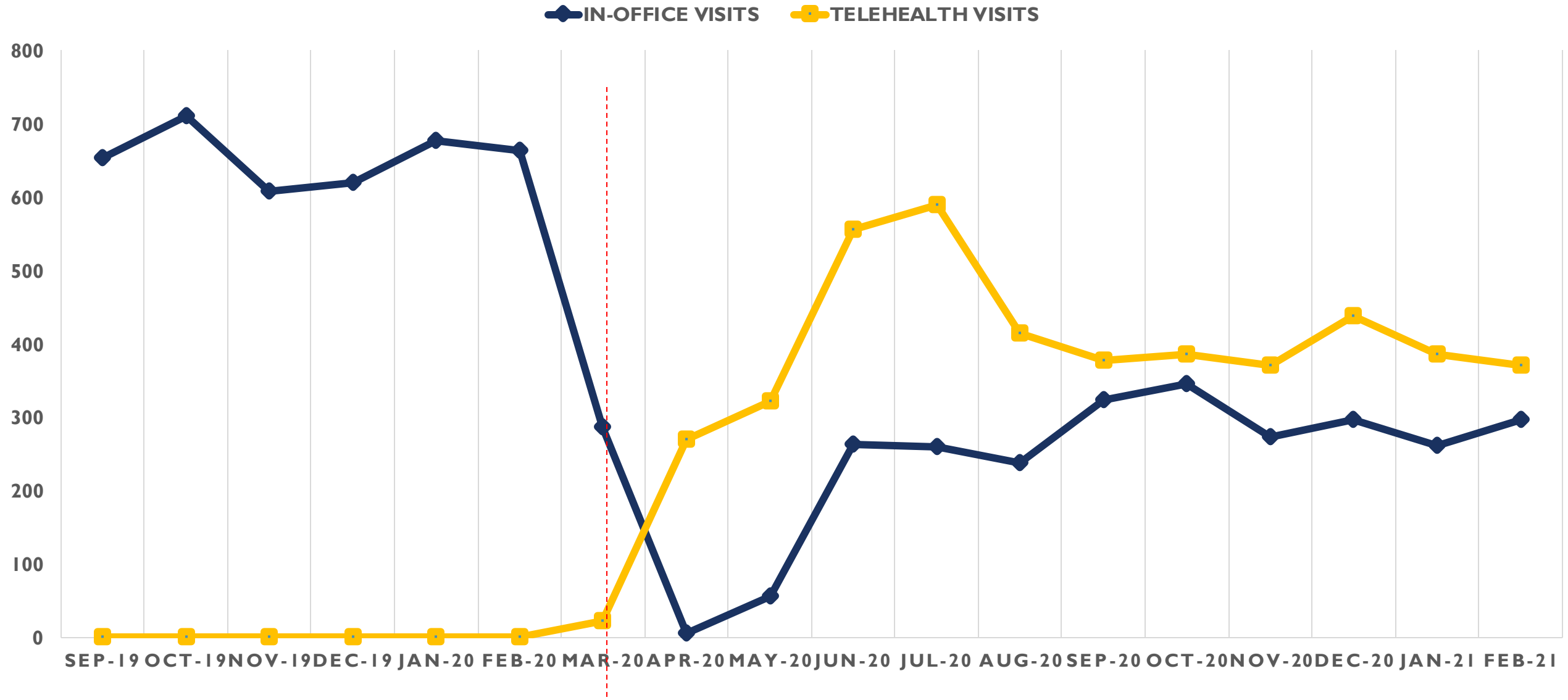
STIMULUS CONTROL THERAPY

1. Go to bed only when sleepy (not just tired).
2. Only use the bed for sleep and sex. Do not use the bed for reading, watching TV, eating or thinking (worrying).
3. If you have not fallen asleep within 20 min or so, leave the bedroom. Stay up until you are sleepy then return to bed. Do not watch the clock.
4. **Repeat step 3 as often as needed.**
5. Get up at the same time every morning irrespective of how much sleep you got during the night.
6. Avoid naps during the day.

SLEEP MEDICINE DURING TIME OF COVID-19 PANDEMIC

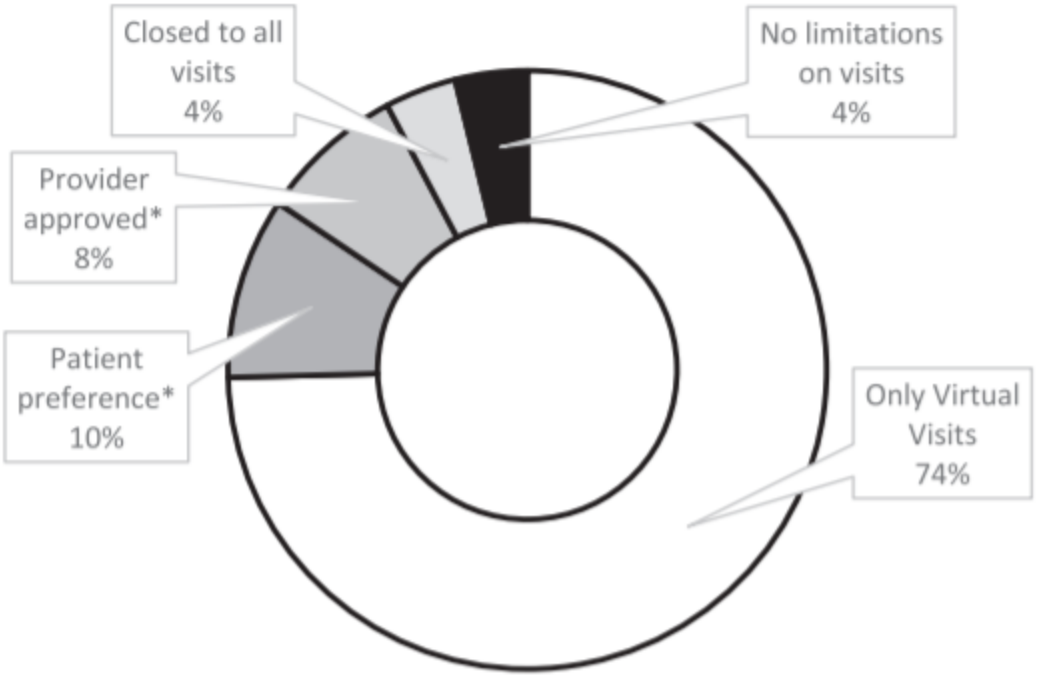
- Increase in insomnia and circadian disorder patients
- Shift in testing modality for underlying sleep-related breathing disorders

CLINIC VISITS AT SLEEP AND BREATHING DISORDERS CENTER



KG Johnson, SS Sullivan, A Nti, et al.

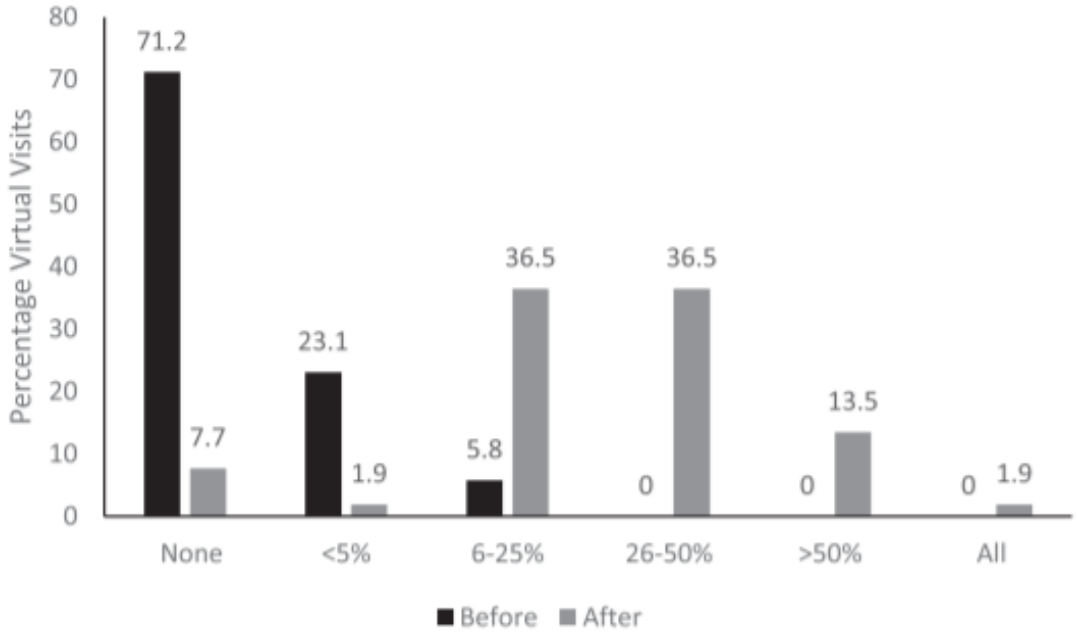
Figure 3—Sleep clinic mitigation strategies.



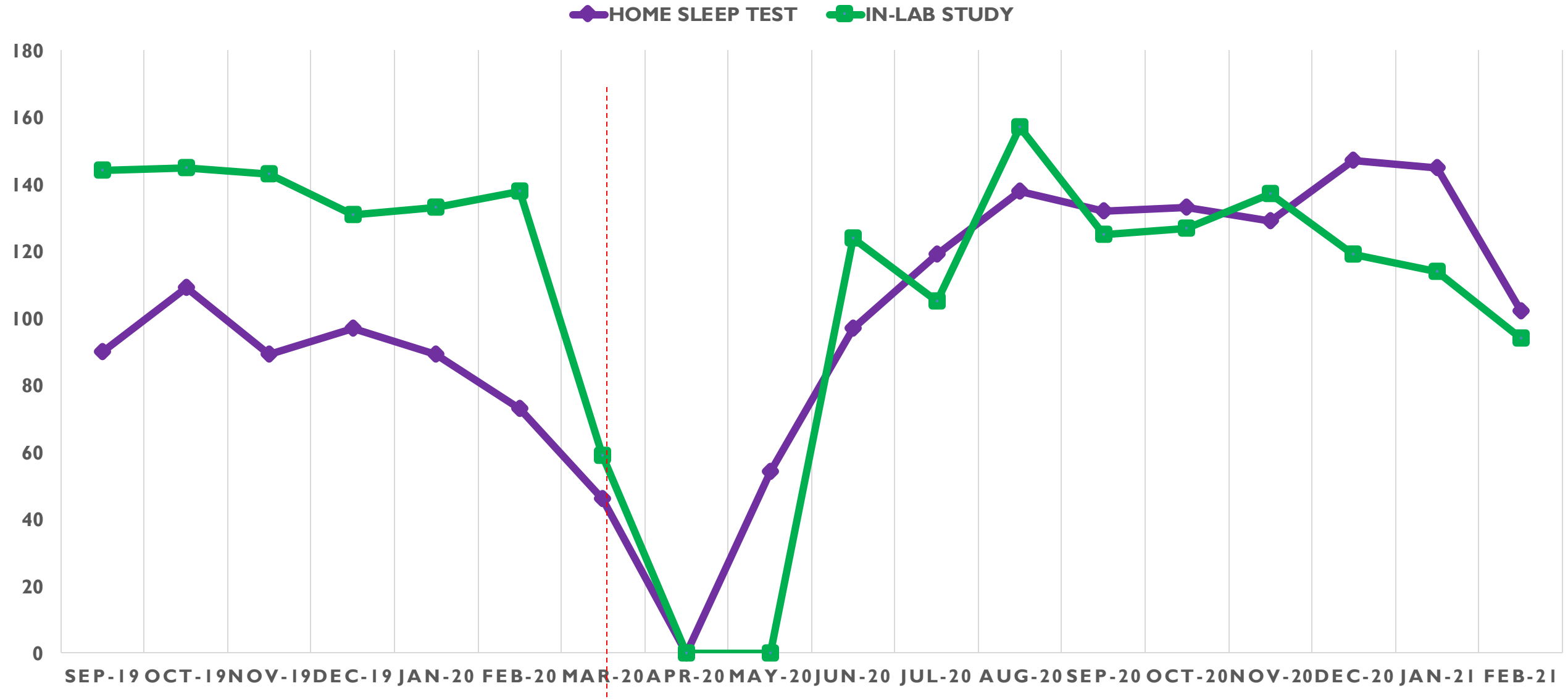
*For in-person visits

KG Johnson, SS Sullivan, A Nti, et al.

Figure 4—Estimated percentage of virtual clinic visits before and after COVID-19.



SLEEP STUDIES AT SLEEP AND BREATHING DISORDERS CENTER

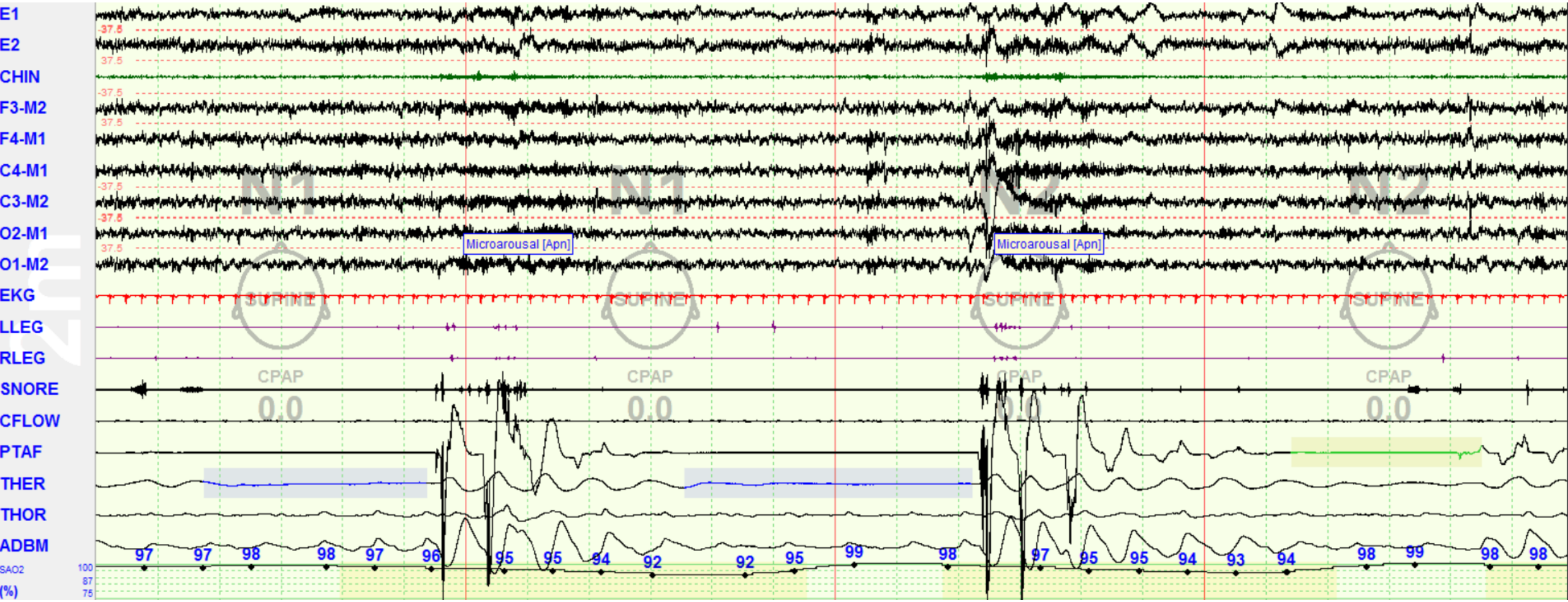


Polysomnogram (PSG)	
Advantages	**Limitations**
• Comprehensive	• First night effect
• Close observation	• Costly

Home Sleep Apnea Test (HSAT)	
Advantages	**Limitations**
• Familiar environment	• Data loss
• More affordable	• Troubleshooting

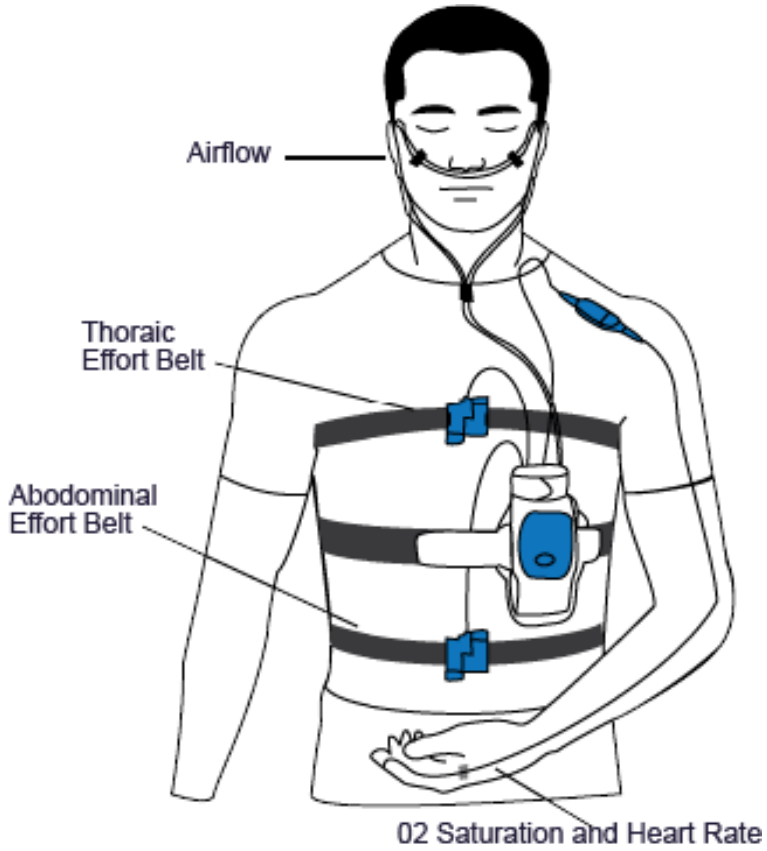
POLYSOMNOGRAM (PSG)

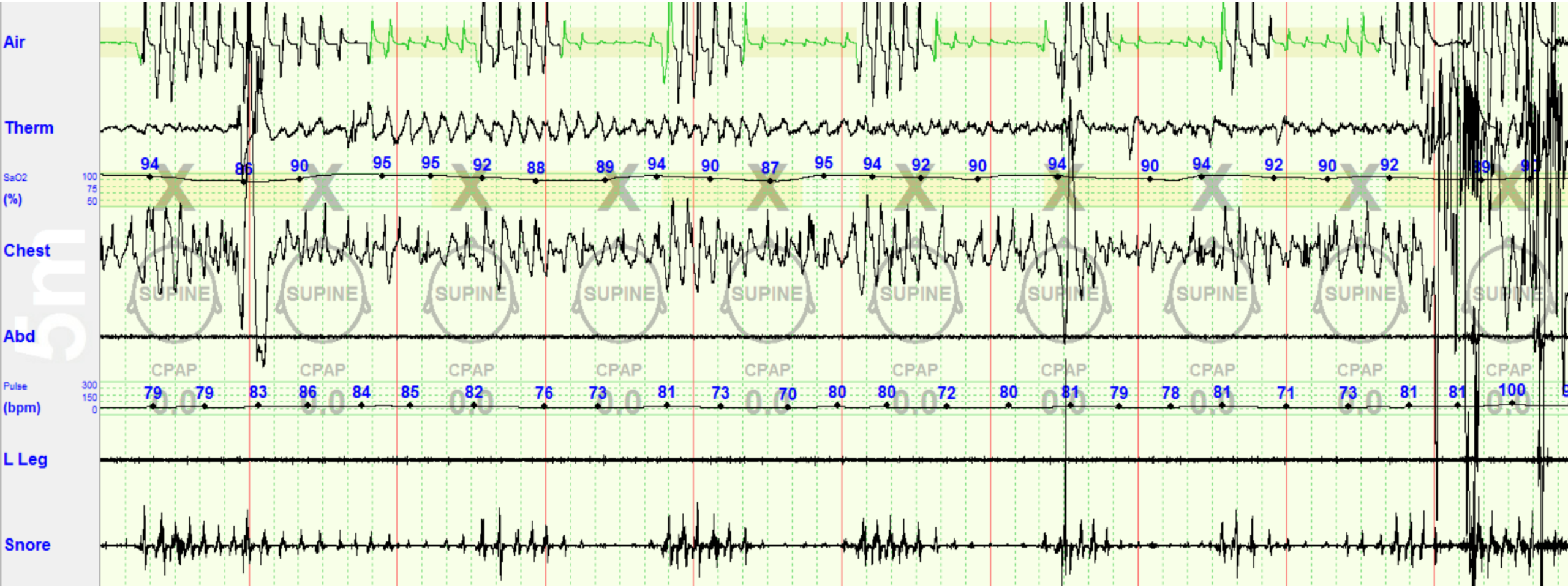
- Comprehensive overnight video-monitored in-lab sleep study
  - Limited EEG
  - Single lead EKG
  - Limb leads
  - Respiratory channels
  - Oximetry
  - Thoracic and abdominal effort belts
  - +/- CO2 monitoring


E1
E2
CHIN
F3-M2
F4-M1
C4-M1
C3-M2
O2-M1
O1-M2
EKG
LLEG
RLEG
SNORE
CFLOW
PTAF
THER
THOR
ABDM
SAO2
(%)
100
87
75
N1
N1
N2
N2
Microarousal [Apn]
Microarousal [Apn]
SUPINE
SUPINE
SUPINE
SUPINE
CPAP
CPAP
CPAP
CPAP
0.0
0.0
0.0
0.0
97 97 98 98 97 96 95 95 94 92 92 95 99 98 97 95 95 94 93 94 98 99 98 98

HOME SLEEP APNEA TEST (HSAT)

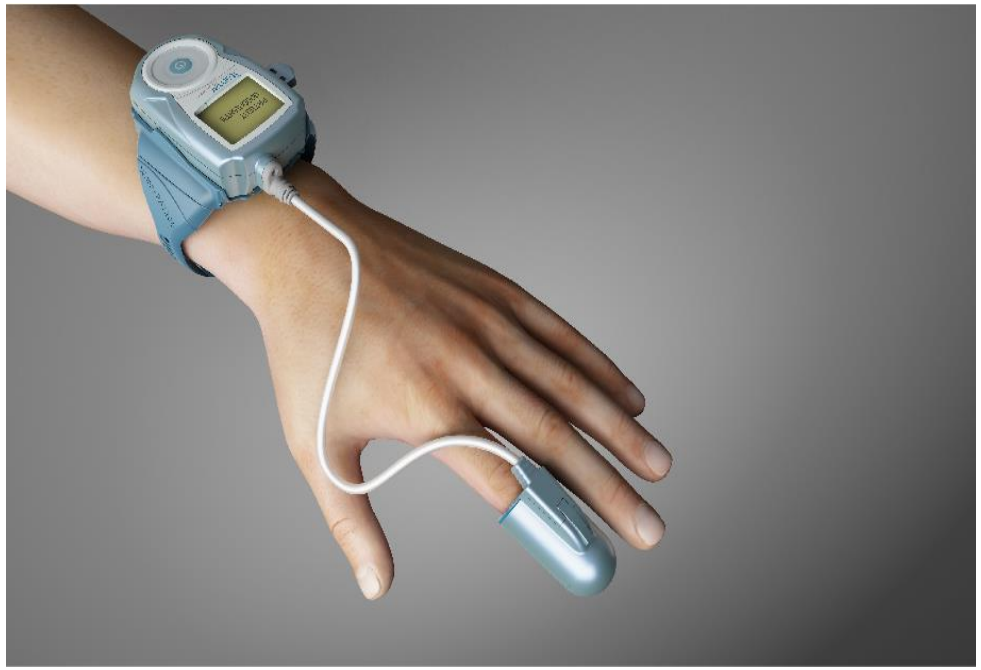
- No EEG – most unable to distinguish sleep
  - May underestimate severity of sleep-disordered breathing
- Indicated in those with high pretest probability without significant comorbidities
  - Severe COPD or CHF
  - Hypoventilation
  - Central sleep apnea
  - Severe insomnia

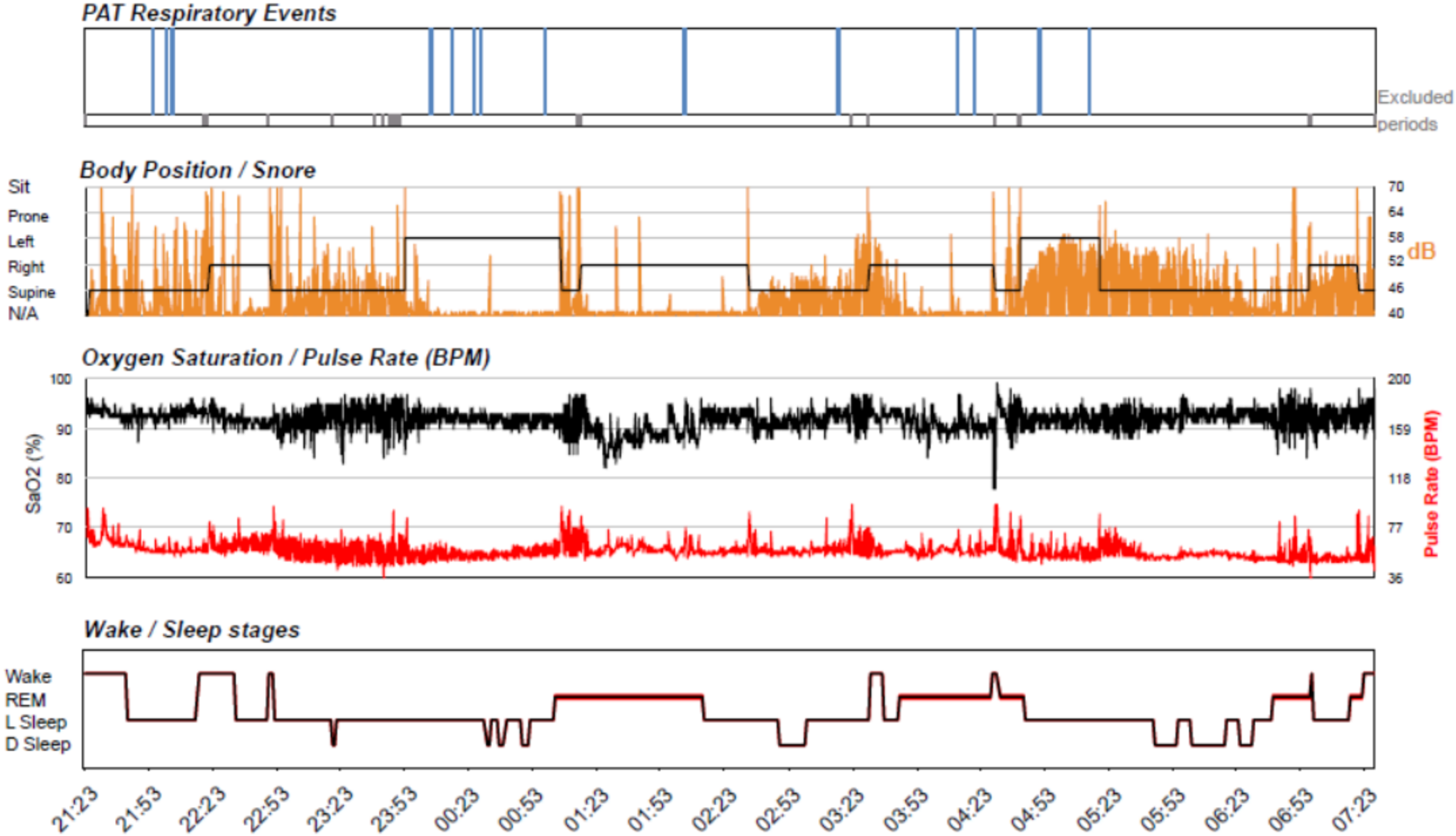



Air
Therm
SaO2
(%)
100
75
50
94 86 90 95 95 92 88 89 94 90 87 95 94 92 90 94 90 94 92 90 92
Chest
SUPINE
Abd
CPAP
Pulse
(bpm)
300
150
0
79 79 83 86 84 85 82 76 73 81 73 70 80 80 72 80 81 79 78 81 71 73 81 81 100
L Leg
Snore

WATCHPAT

- Measures peripheral arterial tonometry (PAT)
- Actigraphy to estimate total sleep time
- Oximetry
- Disposable/Mail-Out versions




PAT Respiratory Events
Excluded periods
Body Position / Snore
Sit
Prone
Left
Right
Supine
N/A
70
64
58
52
46
40
dB
Oxygen Saturation / Pulse Rate (BPM)
SaO2 (%)
100
90
80
70
60
200
159
118
77
36
Pulse Rate (BPM)
Wake / Sleep stages
Wake
REM
L Sleep
D Sleep
21:23
21:53
22:23
22:53
23:23
23:53
00:23
00:53
01:23
01:53
02:23
02:53
03:23
03:53
04:23
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05:23
05:53
06:23
06:53
07:23

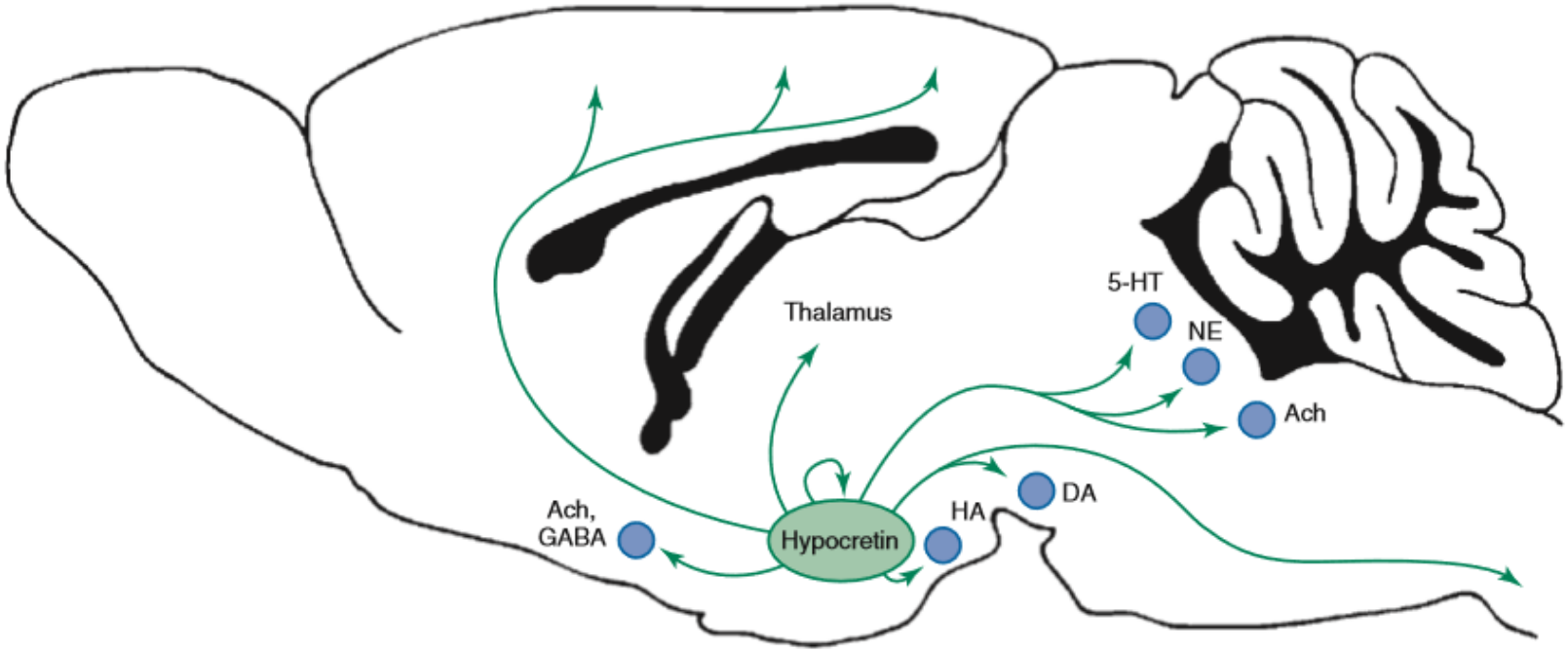
Medication Class	Generic Name	Trade Name	Dose (mg)	Half Life (hours)	Tmax (hours)	Common Side Effects
Anti-histamines	Diphenhydramine	Benadryl	25, 50	7–12	2	Dizziness, somnolence, dry mouth
	Doxylamine	Unisom	12.5, 25	10–12	2–4	Dizziness, somnolence, dry mouth, constipation, urinary retention
BzRAs	Estazolam	Prosom	1, 2	10–24	1.5–2	Somnolence, hypokinesia, dizziness, abnormal coordination
	Flurazepam	Dalmane	15, 30	47–100	1.5–4.5	Dizziness, drowsiness, lightheadedness, staggering, ataxia, falling
	Lorazepam	Ativan	0.5, 1, 2	12	2	Drowsiness, sedation, dizziness, weakness, unsteadiness, fatigue, memory impairment,
	Quazepam	Doral	7.5, 15	39–73		Drowsiness, headache, fatigue, dizziness, dry mouth, dyspepsia
	Temazepam	Restoril	7.5, 15, 30	3.5–18.4		Drowsiness, headache, fatigue
	Triazolam	Halcion	0.125, 0.25	1.5–5.5	1	Drowsiness, dizziness, lightheadedness
Non-BzRAs	Eszopiclone	Lunesta	1, 2, 3	6	1	Headache, somnolence, unpleasant taste
	Zaleplon	Sonata	5, 10, 20	1	1	Headache, dizziness, drowsiness, paresthesia, nausea, abdominal pain, memory impairment
	Zolpidem	Ambien	5, 10	2.6	1.6	Drowsiness, nausea, dizziness, nightmares, agitation
	Zolpidem ER	Ambien CR	6.25, 12.5	2.8	1.6	Drowsiness, nausea, dizziness, nightmares, agitation, anterograde amnesia
	Zolpidem SL	Edluar	5, 10	2.75	0.5–3	Drowsiness, nausea, dizziness, nightmares, agitation
Melatonin Agonist	Ramelteon	Rozerem	8	1- 2.6	0.75	Somnolence, dizziness, fatigue, nausea, exacerbated insomnia
Tricyclic Anti-depressant	Doxepin	Silenor	3, 6	15.3	3.5	Headache, somnolence, sedation, nausea, upper respiratory tract infection
DORA	Suvorexant	Belsomra	5, 10, 20	10–22	2	Daytime somnolence, headache, dizziness

BzRA = benzodiazepine receptor agonist, DORA = dual orexin receptor antagonist

Janto et al. Journal of Clinical Sleep Medicine. Volume 14, Issue 8, 2018

OREXIN/HYPOCRETIN

- Neuropeptide that stabilizes the sleep-wake state
  - discovered in 1998
  - Dr. Yanagisawa – UTSW – "Orexin"
  - Dr. Kilduff – Scripps Research – "Hypocretin"



Janto et al. Journal of Clinical Sleep Medicine. Volume 14, Issue 8, 2018

NEW INSOMNIA MEDICATION

- **Suvorexant (Belsomra)**
  - Dual orexin receptor antagonist
  - Dosages: 5mg, 10mg, 20mg
  - Side Effects: sedation, headaches, abnormal dreams, dry mouth
  - Well tolerated in elderly patients

Janto et al. Journal of Clinical Sleep Medicine. Volume 14, Issue 8, 2018

NEW HYPERSOMNIA MEDICATIONS

- **Solriamfetol (Sunosi)**
  - Dopamine and norepinephrine reuptake inhibitor
  - FDA approved in 2019 for sleepiness in OSA and narcolepsy
  - Dosages: 37.5-150mg (OSA) and 75-150mg (narcolepsy)
  - Side effects: headaches, palpitations, anxiety, may increase BP

Thorpy et al. Annals of Neurology. Volume 85, Issue 3, 2019

NEW HYPERSOMNIA MEDICATIONS

- **Pitolisant (Wakix)**
  - Histamine, H3, receptor antagonist
  - FDA approved in 2019 for sleepiness and cataplexy in narcolepsy
  - Dosages: 8.9mg titrated up to 35.6mg
  - Side effects: headaches, nausea, anxiety

Guevarra et al. Nature and Science of Sleep. 2020

QUESTIONS?