

Connecting a Global Community in Clinical Chest Medicine





Sleep Diagnostics

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Conflicts of Interest



- Royalties from UPTODATE as an author and editor
- Received grant monies and was on advisory council for Jazz Pharmaceuticals (2017-2018)



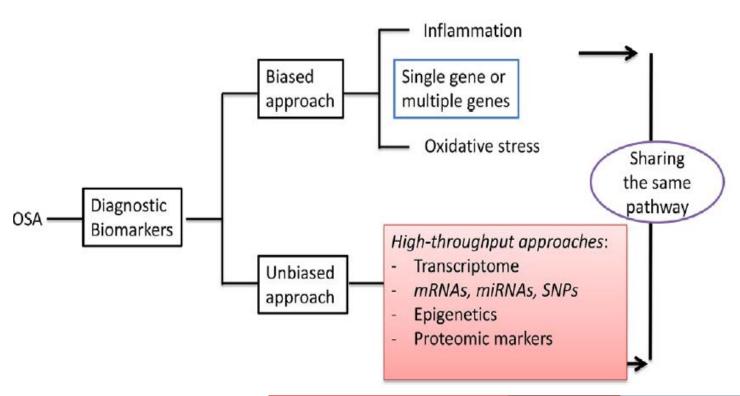
- Biomarkers
- Consumer Devices
 - Assessing sleep
 - Sleep disorders
- PSG intensity

Ideal Biomarker



- disease specificity
- mandatory presence in all affected patients
 - high sensitivity and specificity
- reversibility following proper treatment
- detectability before patients develop clinical manifestations
- reflect severity of the disease and provide indicative information over the cumulative history of the disease,
- enable a cut-off value with minimal overlap between normal and disease
- Minimize the total cost and burden of diagnosing a patient





| Potentia I. Bio mairlærs | Children | Adiul |
|--------------------------|-------------|----------|
| 8-isoprostane | 1 | |
| Adiponectin | 1 | |
| ACB: | | 1 |
| ብጋ ቦቦ | | 1 |
| APOEe4 | 1 | |
| Calproc tectin | | 1 |
| Caltecholamines | ₹. | |
| | 4 | . 1 |
| CRP | 1 | 1 |
| Cystatin C | | 1 |
| FA. | | 1 |
| RAP RAS | | 1 |
| rioci Pruciosamine | | 1 |
| DCT | | <i>-</i> |
| 16.6 | | |
| 1L-8 | 4 | 7 |
| HOMA | - / | |
| I(L-5 | | 1 |
| Lep tin | | 1 |
| Lipid profiles | | 1 |
| MR/8/14 | 1 | |
| MP | | 1 |
| Resistin | | 1 |
| sTN P-RI | | 1 |
| S100 B | | 1 |
| sVCAM-1 | | 1 |
| TAC | | 1 |
| TBARS | | 1 |

 $TNP_{-}\alpha$

Urina ru Neurotra nami Itera





OSA

- Types:
 - Blood
 - Urine
 - Exhaled breath condensate
 - Saliva
- Diagnostic and Prognostic

Interleukin - 6



- 18 studies
- Studied in both adults and children
- Cytokine in macrophages and lymphocytes
- May be more associated with obesity as some studies that showed higher levels were less positive or even not significant after correction for BMI
- Levels do change with CPAP in some but not all studies

OSA versus controls



Thailand

2019

Bangkok | 10-12 April

| tudy name | | Statistics for e | each study | | Differe | ence in mea | ns and 99 | % CI |
|-----------------------------|------------------------|------------------|----------------|---------|---------|-------------|-----------|------|
| | Difference In means | Lower | Upper fimit | p-Value | | | | |
| Alberti et al 2003 | 1.500 | -0.603 | 3.603 | 0.162 | 1 | 1 + | - | |
| Arlas et al 2008 | 0.600 | -1.244 | 2.444 | 0.524 | | - | _ | |
| kavo et al 2007 A | 1.680 | 1.567 | 1.793 | 0.000 | | 1 1 | | |
| ravo et al 2007 B | 1.360 | 1.193 | 1.527 | 0.000 | | 1 1 | | |
| ravo et al 2007 C | 1.940 | 1.787 | 2.093 | 0.000 | | 1 1 | | |
| Offici et al 2004 | 5.590 | 1.273 | 9.907 | 0.011 | | 1 1 | = | - |
| onstantinidis et al 2008 A | 0.420 | 0.357 | 0.483 | 0.000 | | 1 1 | | |
| Constantinidis et al 2008 B | 0.400 | 0.336 | 0.464 | 0.000 | | | i | |
| ornadi et al 2012 | 0.020 | -0.144 | 0.184 | 0.611 | | 1 | ī L | |
| larsch et al 2007 | 3700.000 | 3306.116 | 4093.884 | 0.000 | | ΙТ | 80 | |
| lu et al 2000 | 37.980 | 35.401 | 40.559 | 0.000 | | 1 1 | | |
| iu et al 2011 A | 0.700 | 0.460 | 0.940 | 0.000 | | 1 1 | | |
| lu et al 2011 R | 2.016 | 0.775 | 3.245 | 0.001 | | ΙГ | - | |
| oytblat et al 2000 A | 4.300 | 3.755 | 4.845 | 0.000 | | 1 | | |
| oytblat et al 2000 B | -2.110 | -5.092 | 0.872 | 0.165 | - 1 | - | - F | |
| oytblat et al 2000 C | -37.550 | -51.268 | -25.832 | 0.000 | k | 1 - 1 | | |
| shiman et al 2010 | 0.220 | -0.509 | 0,949 | 0.554 | 1 | l # | | |
| telropolus et al 2010 | 0.370 | -0.276 | 1.016 | 0.262 | | 1 | | |
| homopoulos et al 2009 | 0.976 | 0.246 | 1.706 | 0.009 | | I Ta | | |
| gontzas et al 1997 | 2.230 | 1.701 | 2.759 | 0.000 | | 11 1 | | |
| | 2.160 | 1.623 | 2.697 | 0.000 | | | • | |

Citation: Nadeem R; Molnar J; Madbouly EM; Nida M; Aggarwal S; Sajid H; Naseem J; Loomba R. Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. J Clin Sleep Med 2013;9(10):1003-1012.

TNF - alpha



- Pro-inflammatory cytokine released during acute inflammation
- Participates in cell signaling leading to necrosis or apoptosis
- Associated with excessive daytime sleepiness, nocturnal sleep disturbance, hypoxia
- Higher levels noted in morning and after SDB events in OSA patients
- Conflicting studies on whether it is reduced after CPAP
- Interaction may also be related to degree of obesity

Figure 3—TNF-α, one group standardized mean difference, OSA versus controls





| Study name | | Statistics for | each study | | Std diff in means |
|-----------------------------|----------------------|----------------|----------------|---------|-------------------|
| | Std diff in means | Lower limit | Upper limit | p-Value | and 95% CI |
| Alberti et al 2003 | 0.545 | -0.103 | 1.194 | 0.099 | |
| Arias et al 2008 | 0.545 | -0.085 | 1.175 | 0.090 | |
| Bravo et al 2007 A | -1.185 | -2.072 | -0.298 | 0.009 | - |
| Bravo et al 2007 B | 2.349 | 0.955 | 3.743 | 0.001 | |
| Bravo et al 2007 C | 3.573 | 2.103 | 5.042 | 0.000 | - ■- |
| Ciftcl et al 2004 | 0.433 | -0.087 | 0.952 | 0.102 | |
| Constantinidis et al 2008 A | 0.886 | 0.072 | 1.701 | 0.033 | |
| Constantinidis et al 2008 B | 0.588 | -0.213 | 1.389 | 0.150 | |
| Fornadi et al 2012 | 0.697 | 0.234 | 1.160 | 0.003 | |
| Kanbay et al 2008 | 0.630 | 0.228 | 1.032 | 0.002 | |
| Kobayashi et al 2006 | 1.079 | 0.452 | 1.707 | 0.001 | |
| Li et al 2010 A | 1.002 | 0.714 | 1.289 | 0.000 | |
| Li et al 2010 B | 0.663 | 0.371 | 0.955 | 0.000 | |
| Liu et al 2000 | 5.478 | 4.088 | 6.868 | 0.000 | |
| Ryan et al 2005 | 1.474 | 0.736 | 2.211 | 0.000 | |
| Sahlman et al 2010 | 0.218 | -0.160 | 0.595 | 0.258 | |
| Steiropolus et al 2010 | 0.905 | 0.363 | 1,447 | 0.001 | °T |
| Thomopoulos et al 2009 | 0.495 | 0.148 | 0.842 | 0.005 | |
| Vgontzas et al 1997 | 11.409 | 7.935 | 14.883 | 0.000 | |
| | 1,034 | 0.674 | 1,394 | 0.000 | |

Citation: Nadeem R; Molnar J; Madbouly EM; Nida M; Aggarwal S; Sajid H; Naseem J; Loomba R. Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. *J Clin Sleep Med* 2013;9(10):1003-1012.

Favors control Favors OSA

CRP



- Inflammatory marker, active role in atherogenesis
- Studies in both adults and children
- Mainly produced in the liver
- Multiple studies with varied results
- As with others, relationship is altered by obesity
- High CRP may indicate risk for developing CV events in OSA patients further study needed
- Study in children suggested high levels of HS-CRP may ID children at high risk for cognitive morbidity

Figure 1—CRP, one group standardized mean difference, OSA versus controls

| Study name | | Statistics for | each study | | | | liff in n | | |
|--------------------------|----------------------|----------------|----------------|---------|-------|----------|-----------|--------|---------------|
| | Std diff in means | Lower limit | Upper limit | p-Value | | ar | nd 95% | CI | |
| Barcelo et al 2004 A | 1.426 | 0.743 | 2.109 | 0.000 | 1 | F | | | - 1 |
| Barcelo et al 2004 B | \$.586 | 6.628 | 10.544 | 0.000 | | | | | \rightarrow |
| Barcelo et al 2011 | 0.625 | 0.365 | 0.885 | 0.000 | | | | | - 1 |
| Bhushan et al 2008 A | 1.546 | 1.034 | 2.057 | 0.000 | | | | | |
| Bhushan et al 2008 B | 1.243 | 0.827 | 1.659 | 0.000 | | | | | |
| Carneiro et al 2009 | -0.321 | -1.057 | 0.416 | 0.394 | | | | | |
| Chein et al 2011 | 1.213 | 0.662 | 1.763 | 0.000 | | | 7 | | |
| Drager et al 2010 | 2.122 | 1.718 | 2.525 | 0.000 | | | | | |
| Oziewas et al 2007 | 0.394 | 0.026 | 0.761 | 0.036 | | | 111 | - 1 | |
| ornadi et al 2012 | 0.335 | -0.120 | 0.790 | 0.149 | | | | | |
| Guasti et al 2009 | -0.502 | -1.281 | 0.277 | 0.207 | | | | | |
| Guilleminault et al 2004 | 0.092 | -0.220 | 0.404 | 0.564 | | | 7 | . | |
| Guven et al 2012 | 0.528 | 0.058 | 0.999 | 0.028 | | | T | | |
| Harsch et al 2007 | 2.826 | 1.939 | 3.714 | 0.000 | | | | ■ . | |
| layashi et al 2006 A | 5.835 | 4.711 | 6.959 | 0.000 | | | 1 2 | 714 | - 1 |
| layashi et al 2006 B | 3.504 | 2.670 | 4.339 | 0.000 | | | | | - |
| layashi et al 2006 C | 5.582 | 4.656 | 6.508 | 0.000 | | | | | • |
| esato et al 2007 | 6.991 | 6.212 | 7.771 | 0.000 | | | | . 17 | - |
| Capsimalis et al 2008 A | 0.409 | -0.232 | 1.051 | 0.211 | | | | | |
| Capsimalis et al 2008 B | 0.646 | -0.004 | 1.297 | 0.052 | | | - | | |
| Ju et al 2011 A | 1.136 | 0.468 | 1.804 | 0.001 | | | | | |
| Ju et al 2011 B | 0.530 | 0.015 | 1.045 | 0.044 | | | | | |
| feng et al 2009 | 2.881 | 2.370 | 3.392 | 0.000 | | | | | |
| Sahlman et al 2010 | 0.146 | -0.231 | 0.523 | 0.447 | | | | 7 | |
| Sarlman et al 2011 | 0.930 | 0.100 | 1.759 | 0.028 | | | Tes | | |
| hamsuzzaman et al 2002 | 3.881 | 2.853 | 4.908 | 0.000 | | | | | |
| harma et al 2008 A | -0.143 | -0.611 | 0.324 | 0.547 | | | | Т | |
| Sharma et al 2008 B | 0.822 | 0.253 | 1.392 | 0.005 | | | | | |
| iteiropolus et al 2010 | 0.166 | -0.352 | 0.685 | 0.530 | | | - | | |
| homopoulos et al 2009 | 0.057 | -0.285 | 0.399 | 0.744 | | | Ŧ | | |
| okoe et al 2003 | 7.988 | 6.203 | 9.774 | 0.000 | | | т. | | - |
| fumino et al 2007 | 0.514 | 0.088 | 0.941 | 0.018 | | | | | Т |
| | 1.774 | 1.284 | 2.263 | 0.000 | | | - □(| | |
| | | | | | -8.00 | -4.00 | 0.00 | 4.00 | 8.0 |
| | | | | | Fa | vors cor | ntrol Fa | vors O | SA. |



Citation: Nadeem R; Molnar J; Madbouly EM; Nida M; Aggarwal S; Sajid H; Naseem J; Loomba R. Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. *J Clin Sleep Med* 2013;9(10):1003-1012.

CRP/OSA Meta-analysis





- 219 OSA vs 116 controls
 - Adult non-smoking matched for BMI, age, gender
- 5 studies with low heterogeneity

| | Obstructi | ve sleep a | pnea | (| Control | | S | td. Mean Difference | | Std. | Mean Diffe | erence | |
|---|---------------|------------|-------|-------|---------|-------|--------|---------------------|-------------|----------------------|--------------|-------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | I\ | /, Fixed, 95 | % CI | |
| Carneiro et al 2009 | 0.83 | 0.56 | 16 | 0.91 | 1.23 | 13 | 10.2% | -0.08 [-0.82, 0.65] | | _ | | _ | |
| Minoguchi et al 2006 (mild) | 0.09 | 0.09 | 20 | 0.07 | 0.13 | 9 | 8.8% | 0.19 [-0.60, 0.98] | | - | | | |
| Diccone et al 2014 (mild) | 0.132 | 0.048 | 26 | 0.108 | 0.053 | 20 | 15.7% | 0.47 [-0.12, 1.06] | | | + | * | |
| Guven et al 2012 | 0.403 | 0.358 | 47 | 0.241 | 0.195 | 29 | 24.7% | 0.52 [0.05, 0.99] | | | - | - | |
| finoguchi et al 2005 (mild) | 0.15 | 0.11 | 13 | 0.09 | 0.08 | 8 | 6.7% | 0.58 [-0.33, 1.48] | | | - | _ | - |
| finoguchi et al 2006 (moderate severe) | 0.23 | 0.22 | 20 | 0.07 | 0.13 | 9 | 8.2% | 0.79 [-0.03, 1.60] | | | | - | _ |
| finoguchi et al 2005 (moderate-severe) | 0.28 | 0.19 | 23 | 0.09 | 0.08 | 8 | 7.5% | 1.09 [0.23, 1.94] | | | - | | |
| Diccone et al 2014 (moderate-severe) | 0.184 | 0.067 | 54 | 0.108 | 0.053 | 20 | 18.2% | 1.18 [0.63, 1.73] | | | | - | |
| Total (95% CI) | | | 219 | | | 116 | 100.0% | 0.61 [0.38, 0.84] | | | | • | |
| Heterogeneity: Chi ² = 10.46, df = 7 (P = 0. | 16); 2 = 33% | , | | | | | | | + | - | | - | 1 |
| Test for overall effect: Z = 5.11 (P < 0.000 | 01) | | | | | | | | -2 Favou | -1 rs Obstructive | sleep Fav | 1 ours Control | 2 |

Quantitative EEG in OSA



- Examine power spectral analysis by transforming amplitude vs time to amplitude vs frequency; essentially quantifies the amplitude and prevalence of different frequency sine waves
 - Slowing of the EEG associated with sleepiness and fatigue in wake and changes in sleep EEG may be associated with learning and memory
- 24 studies examined qEEG in OSA

Quantitative EEG in OSA



- Waking EEG and severity of OSA: heterogeneous results
- Waking EEG and daytime sleepiness: seems to correlate better with subjective sleep measure than with objective sleep measures
- Waking EEG and performance tasks (PVT, driving simulator) show some correlation but often need more sophisticated signal processing technique
- Waking EEG after CPAP reduction of theta power; variable effects noted on delta power

Quantitative EEG in OSA



- Effect on sleep EEG:
 - reduced slow wave activity with the exception of OHS who may have higher SWA
 - Reduced spindle activity
 - Effect of CPAP may reverse SWA reduction
- Conclusion that more sophisticated and standardized analysis is needed with better controls

REM Sleep Behavior Disorder:

Congress 2019 Thailand Bangkok | 10-12 April

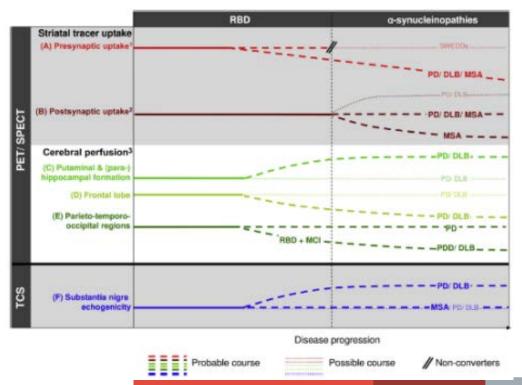
Potential biomarkers

- Might allow early prognostication
- DAT scan (radiotracer that measures presynaptic dopamine transporter density)
- ¹⁸F-FDG Pet scan (metabolic increases in pons, thalamus, medial frontal and sensorimotor areas, hippocampus, temporal gyri, posterior cerebellum)
- Transcranial sonography (echogenicity of brain tissue) see striatal nigra hyperechogenecity
- None of these are quite ready for prime time

REM Sleep Behavior Disorder: Potential biomarkers









Consumer Devices for Sleep and Sleep Disorders





How many times have you heard...

- "my Fitbit says I am having lots of disruptions in my sleep"
- "my sleep tracker says I am not getting enough deep sleep; or dream sleep..."
- "should I go buy a fitness device that monitors my sleep? which one is best?"



Consumer Devices

- Search for sleep terms on smartphones, get about
 2500 apps
- Modalities:
 - Mobile device (smartphones and tablets)
 - Wearable technology
 - Unique physical devices embedded into sleep environment
 - Online programs (desktop or website platforms)
 - Accessory devices that may interact with mobile devices

Consumer Sleep Technologies: A Review of the Landscape

Congress
2019

Thailand
Bangkok | 10-12 April

Ping-Ru T. Ko, MD¹; Julie A. Kientz, PhD²; Eun Kyoung Choe, PhD³; Matthew Kay, MS⁴; Carol A. Landis, PhD, RN, FAAN⁵; Nathaniel F. Watson, MD, MSc⁶

- Very nice review of available types and brands of devices
- Note lack of validation for many
- Do raise consumer awareness of sleep
- Many pros and cons!

Mobile devices



- 77% of adults own a smartphone!!
- Sleep tracking, alarms, sleep and dream logging
- May facilitate sleep with graphics, music or sounds, professional hypnotists
- Often sit on mattress and may be affected by other body sleep (bedpartner, animal) or type of mattress (waterbed, pillowtop)
- "Smart alarm" awaken you from light sleep; require you to do a task so you can't go back to sleep integrate with a lamp that slowly illuminates
- Detect snoring, sleep talking
- Awaken when snoring (vibrates or makes a noise)

Rate My Sleep: Examining the Information, Function, and Basis in Empirical Evidence Within Sleep Applications for Mobile Devices

CONGRESS
CONGRESS
2019

Congress
2019

Congress
2019

Peta A. Lee-Tobin, MProfPsych¹³, Rowan P. Ogeil, PhD¹³, Michael Savic, PhD¹²; Dan I. Lubman, PhD, FRANZCP, FACHAM¹² (Eastern Health Clinical School, Monash University, Box Hill, Victoria, Australia ¹Turning Point, Eastern Health, Fizroy, Victoria, Australia

- Apps in Google Play store
- Primary sleep complaint addressed:
 - OSA (n = 23, 30.3%)
 - insomnia (n = 9, 11.8%)
 - Sleep cycles or circadian rhythms (n = 32, 42.1%)
 - general sleep (n = 8, 10.5%)
- Categorized as either "health & fitness" (n = 46, 60.5%) or "medical" (n = 20, 26.3%) apps
- Most were free to download (n = 61, 80.3%); maximum cost of \$6.82

Rate My Sleep: Examining the Information, Function, and Basis in Empirical Evidence Within Sleep Applications for Mobile Devices

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Congress
2019

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2019

Peta A. Lee-Tokin, MProfPsych^{1,2}, Rowan P. Ogeil, PhD^{1,2}, Michael Savic, PhD^{1,2}; Dan I. Lukman, PhD, FRANZCP, FACHAM^{1,2}
'Eastern Health Clinical School, Monach University, Box Hill, Victoria, Australia 'Turning Point, Eastern Health, Fitzrox, Victoria, Australia

- 10 most downloaded sleep apps
 - rating of 4 or more stars (representing high user satisfaction)
 - only one of these apps was identified as containing evidence
- 10 least downloaded apps
 - 8 /10 were given ratings under 4 stars
 - most of them focusing on OSA

Smartphone Applications to Support Sleep Self-Management: Review and Evaluation

Congress
PhD. RN1 2019



Yong K. Choi, MPH¹; George Demiris, PhD²; Shih-Yin Lin, PhD, MPH, MM¹; Sarah J. Iribarren, PhD, RN¹; Carol A. Landis, PhD, RN¹; Hilaire J. Thompson, PhD, RN, ARNP, CNRN, AGACNP-BC¹; Susan M. McCurry, PhD¹; Margaret M. Heitkemper, PhD, RN¹; Teresa M. Ward, PhD, RN¹

Table 1—MARS items and subscales criteria.

| App Quality Scoring Criteria | Subscales |
|---------------------------------|--|
| 1. Engagement | 1.1 Entertainment 1.2 Interest 1.3 Customization 1.4 Interactivity 1.5 Target group |
| 2. Functionality | 2.1 Performance 2.2 Ease of use 2.3 Navigation 2.4 Gestural design |
| 3. Aesthetics | 3.1 Layout 3.2 Graphics 3.3 Visual appeal: how good does the app look? |
| 4. Information | 4.1 Accuracy of app description 4.2 Goals 4.3 Quality of information 4.4 Quantity of information 4.5 Visual information 4.6 Credibility 4.7 Evidence base |
| 5. Subjective quality | 5.1 Would you recommend this app? 5.2 How many times do you think you would use this app? 5.3 Would you pay for this app? 5.4 What is your overall star rating of the app? |

Smartphone Applications to Support Sleep Self-Management: Review and Evaluation

CHEST Congress 2019



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Table 4—Description of top 5 apps combining MARS and IMS functionality scores.

| Name | Platform | Cost, US \$ | # of Installs* | Star Rating | MARS Score | IMS Score | Tracking Type |
|--------------------------|---------------|-------------|-------------------------|-------------|------------|------------------|---------------|
| Sleep as Android Unlock | Google/Amazon | 3.99 | 500,000-1,000,000 | 5 | 4.0 | 11 | Both |
| Sleep Center Free | Apple | Free | N/R | NA | 4.0 | 10 | Both |
| Good Morning Alarm Clock | Apple/Google | Free | 1,000,000-5,000,000 | 4 | 3.7 | 11 | Automatic |
| Samsung Health | Google | Free | 100,000,000-500,000,000 | 4 | 3.7 | 11 | Manual |
| Snail Sleep | Google/Amazon | Free | 100,000-500,000 | 4 | 3.5 | 10 | Automatic |

Smartphone Applications to Support Sleep Self-Management: Review and Evaluation





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- "However, it is critically important to highlight that such sleep parameters calculated by the custom algorithms of the sleep selfmanagement apps have yet to be successfully validated against results obtained by polysomnography (PSG), the gold standard
- ...only three apps (Sleep Time, 15 MotionX 24/7, 16 Sleep Cycle 17) have been formally evaluated for clinical validity comparing the parameters reported by the apps and those obtained by PSG.
- The validation studies have shown that the sleep parameters by the apps poorly correlated with PSG and failed to accurately reflect the sleep stages and thus deemed not useful as a clinical tool."

Is There a Clinical Role For Smartphone Sleep Apps? Comparison of Sleep Cycle Detection by a Smartphone Application to Polysomnography

Sushanth Bhat, MD¹; Ambra Ferraris, MD¹; Divya Gupta, MD¹; Mona Mozafarian, MD¹; Vincent A. DeBari, PhD²; Neola Gushway-Henry, MD¹; Satish P. Gowda, MD¹; Peter G. Polos, MD, PhD¹; Mitchell Rubinstein, RPSGT¹; Huzaifa Seidu, MD¹; Sudhansu Chokroverty, MD¹

- 20 subjects no history of sleep disorders
- Download app (Azumio) then used at home for 5 nights (so app can become acclimated)
- Underwent PSG study and questionnaire

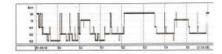




Figure 1



В



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Table 3—Comparison of absolute parameters obtained by polysomnography and provided by the app for subjects in the study (n = 20).

| | PSG | Арр |
|---------------------------------|----------------|-------------------------|
| Sleep efficiency (%) | 86.6 ± 8.0 | 86.5 ± 6.3 |
| Light sleep (%) | 60.7 ± 12.4 | 32.8 ± 13.7° |
| Deep sleep (%) | 39.6 ± 11.9 | 50.6 ± 8.9 ^b |
| Traditional sleep latency (min) | 11.6 ± 14.5 | 27.3 ± 16.2° |
| Sustained sleep latency (min) | 17.3 ± 18.4 | 27.3 ± 16.2° |

Table 7—App performance in awakening patients out of light sleep during the in-laboratory polysomnography.

Number of Subjects

Awake at the time of app alarm

3/20 (15%)

Asleep and in light sleep at the time of app alarm

14/17 (82.4%)

Asleep and in deep sleep at the time of app alarm

3/17 (17.6%)

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| Total number of PSG sleep epochs | Total number of epochs correctly scored by the app as sleep (regardless of stage) | Sensitivity | Specificity | PPV | NPV |
|-------------------------------------|--|-------------------------|--------------------------|-------------------------|-------------------------|
| 473 | 425 | 89.9% (Cl 86.8–92.4) | 50.0% (CI 36.1–63.9%) | 94.0% (Cl 91.4–96.0) | 36.0% (CI 25.2–47.9) |

CI, confidence interval; NPV, negative predicted value; PPV, positive predicted value; PSG, polysomnography.

Table 5—Statistical performance of intrasleep staging by the app based on epoch-by-epoch comparison.

| Sleep stage | Total number of PSG epochs | Total number of epochs correctly staged by the app | Sensitivity | Specificity | PPV | NPV |
|-------------|-------------------------------|---|-------------------------|-------------------------|-------------------------|-------------------------|
| Light sleep | 283 | 96 | 33.9% (CI 28.4–39.8) | 67.6% (CI 61.4–73.5) | 54.9% (CI 47.2–62.4) | 46.9% (Cl 41.6–52.2) |
| Deep sleep | 190 | 119 | 62.6% (CI 55.3–69.5) | 53.1% (CI 47.6–58.5) | 43.0% (Cl 37.1–49.0) | 71.6% (CI 65.6–77.1) |

Cl. confidence interval; NPV, negative predicted value; PPV, positive predicted value; PSG, polysomnography.

Table 6—Stage-wise accuracy of app staging based on epoch-by-epoch comparison.

| | All epochs sleep- wake detection only | All epochs staging | Wake | N1 | N2 | N3 | REM | |
|------------------------|--|-----------------------|-------|-------|-------|-------|-------|--|
| Number of epochs | 527 | 527 | 54 | 11 | 272 | 111 | 79 | |
| Accuracy | 85.9% | 45.9% | 50.0% | 54.5% | 33.0% | 71.2% | 50.6% | |
| N1, stage 1 sleep; N2, | stage 2 sleep; N3, stage | | | | | | | |

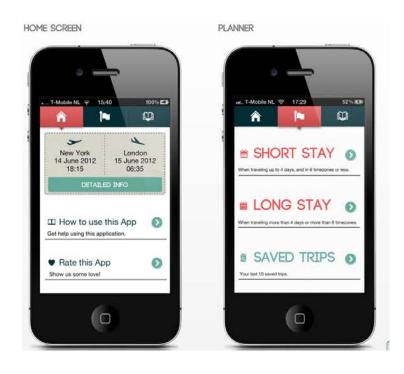
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g a Global Community Clinical Chest Medicine

Apps for Jet Lag











ADVICE



EXPORT TO CALENDAR



ess 019 Bangkok | 10-12 April

Wearable devices



- Usually on wrist but can be in clothing or a pendant
- Track body movements, biometric info
- Often report "light", "deep", "REM" sleep
- Most not well validated or validation data not readily available

Wearable devices

Congress
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Thailand
Bangkok | 10-12 April

- Fitbit
- Jawbone
- Smartwatches
- Sleep Shepherd hat
- SleepImage







Embedded platforms



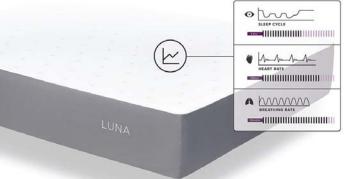


- Physical devices embedded in sleep environment
- May use cameras, microphones
- Examples include:
 - Sleep number bed (remotely raises when snoring)
 - Tanita Sleep scan (Matt under mattress)
 - Luna (mattress cover) can monitor sleep stage, has a smart alarm, change temperature









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Validation of Contact-Free Sleep Monitoring Device with Comparison to Polysomnography

Asher Tal, MD1; Zvika Shinar, PhD2; David Shaki, MD1; Shlomi Codish, MD3; Aviv Goldbart, MD1

Soroka Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negey; *EarlySense Ltd., Ramat Gan, Israel; *Clalit Health Services, Beer Sheva, Israel

- Tested this device during PSG in sleep lab (43) and then at home, one person in bed (7) and two persons in bed (13)
- Device set to distinguish REM, "light" sleep (N1+ N2), deep sleep (SWS)
- Detects RR, HR, movement



The ES sensor (left) is placed under the mattress under the estimated location of the patient's chest. The ES device is considered a nonsignificant risk device because the sensor is placed under the mattress, does not come in contact with the subject, and does not require subject compliance.

Validation of Contact-Free Sleep Monitoring Device with Comparison to **Polysomnography**





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Reference Values (full PSG)

| Α | Piezoelectric contact-free system | Awake | REM | LS | SWS |
|---|-----------------------------------|---------------|---------------|----------------|---------------|
| | Awake | 9,482 (80.4%) | 588 (5.4%) | 3,710 (9.7%) | 114 (1.1%) |
| | REM | 569 (4.8%) | 5,844 (53.7%) | 4,224 (11.1%) | 308 (3.0%) |
| | LS | 1,477 (12.5%) | 4,190 (38.5%) | 24,771 (64.9%) | 4,014 (39.7%) |
| | SWS | 265 (2.2%) | 254 (2.3%) | 5,471 (14.3%) | 5,684 (56.2%) |

PSG Reference

| В | Piezoelectric contact-free system | Wake | Asleep |
|---|-----------------------------------|---------------|----------------|
| _ | Wake | | • |
| | | 9,482 (80.4%) | 4,412 (7.5%) |
| | Asleep | 2,311 (19.6%) | 54,760 (92.5%) |

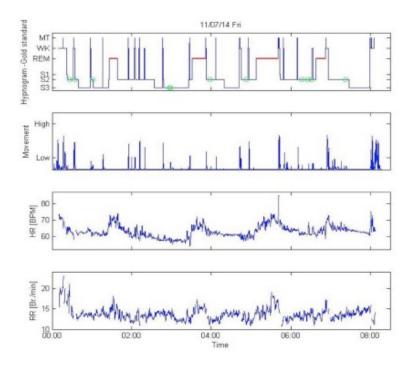
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EXECT Congress 2019



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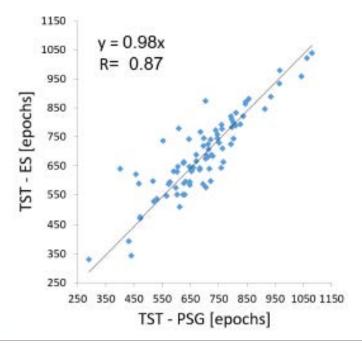
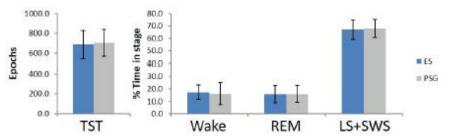


Figure 5 — Comparison between data assessed by the EarlySense (ES) sensor (blue bars) and that derived from polysomnography (PSG) data (gray bars) for all nights (h = \$5), including in the sleep laboratory and at home.



Digital Health and Sleep-Disordered Breathing: A Systematic Review **EXECT** and Meta-Analysis





Talita Rosa, MD, MS1; Kersti Bellardi, MS2; Alonço Viana Jr, MD, MS3; Yifei Ma, MS4; Robson Capasso, MD5

Bed/Mattress-Based Sensors

Studies: Cross-sectional studies with one-gate design (Agatsuma et al. 2009, Beattie et al. 2013, Takasaki et al. 2008, Tsukahara et al. 2014) and diagnostic case-control (Norman et al. 2014)

| AHI Threshold | Summary Accuracy (95% CI) | | No. of Participants | Otrodica Nat Included |
|--------------------|---------------------------|----------------------|---------------------|-----------------------|
| Subgroup | Sensitivity | False Positive Rate | (Studies Included) | Studies Not Included |
| Overall | 0.921 (0.870, 0.953) | 0.203 (0.124, 0.314) | 515 (5) | := |
| Cutoff 5 events/h | 0.951 (0.789, 0.990) | 0.395 (0.189, 0.647) | 515 (5) | - |
| Cutoff 15 events/h | 0.944 (0.886, 0.973) | 0.155 (0.055, 0.366) | 515 (5) | - |
| Cutoff 30 events/h | 0.917 (0.833, 0.961) | 0.113 (0.065, 0.191) | 515 (5) | - |

Digital Health and Sleep-Disordered Breathing: A Systematic Review **EXECT** and Meta-Analysis





Talita Rosa, MD, MS1; Kersti Bellardi, MS2; Alonço Viana Jr, MD, MS3; Yifei Ma, MS4; Robson Capasso, MD5

Contactless Devices (Other Than Bed/Mattress-Based Sensors)

Studies: Cross-sectional studies with one-gate design (Abad et al. 2016, Davidovich et al. 2016, Espinoza-Cuadros et al. 2015, Nandakumar et al. 2015, Zaffaroni et al. 2013. Weinreich et al. 2014)

| AHI Threshold | Summary Acc | uracy (95% CI) | No. of Participants | Studies Not Included |
|--------------------|----------------------|----------------------|---------------------|--|
| Subgroup | Sensitivity | False Positive Rate | (Studies Included) | |
| Overall | 0.905 (0.839, 0.946) | 0.217 (0.110, 0.383) | 594 (6) | 5 : |
| Cutoff 5 events/h | 0.976 (0.899, 0.995) | 0.487 (0.137, 0.851) | 498 (5) | Davidovich et al. 2016 |
| Cutoff 15 events/h | 0.876 (0.760, 0.941) | 0.136 (0.075, 0.235) | 594 (6) | - |
| Cutoff 30 events/h | 0.806 (0.695, 0.883) | 0.066 (0.043, 0.101) | 456 (4) | Davidovich et al. 2016, Weinreich et al. 2014 |

Digital Health and Sleep-Disordered Breathing: A Systematic Review **EXECT** and Meta-Analysis





Talita Rosa, MD, MS1; Kersti Bellardi, MS2; Alonço Viana Jr, MD, MS3; Yifei Ma, MS4; Robson Capasso, MD5

Studies: Cross-sectional studies with one-gate design (Benistant 2016), and diagnostic case-control with two-gate design (Al-Mardini et al. 2014)

| AHI Threshold | Summary Accuracy (95% CI) | | No. of Participants | Ctudies Net Included |
|-------------------|---------------------------|----------------------|---------------------|----------------------|
| Subgroup | Sensitivity | False Positive Rate | (Studies Included) | Studies Not Included |
| Overall | 0.771 (0.466, 0.929) | 0.094 (0.029, 0.269) | 24 (2) | _ |
| Cutoff 5 events/h | 0.770 (0.171, 0.982) | 0.134 (0.028, 0.459) | 24 (2) | - |

Contact Devices With Fewer Than Three Sensors

Studies: Cross-sectional studies with one-gate design (Dinc et al. 2014, Ozmen et al. 2011, Levendowski et al. 2015), and diagnostic case-control with two-gate design (Selvaraj et al. 2014)

| AHI Threshold | Summary Accuracy (95% CI) | uracy (95% CI) | No. of Participants | Studies Not Included |
|--------------------|---------------------------|----------------------|---------------------|--|
| Subgroup | Sensitivity | False Positive Rate | (Studies Included) | |
| Overall | 0.713 (0.594, 0.808) | 0.099 (0.058, 0.166) | 169 (4) | - |
| Cutoff 5 events/h | 0.637 (0.392, 0.827) | 0.077 (0.011, 0.392) | 51 (2) | Ozmen et al. 2011, Selvaraj et al. 2014 |
| Cutoff 15 events/h | 0.716 (0.500, 0.865) | 0.122 (0.049, 0.273) | 169 (4) | _ |
| Cutoff 30 events/h | 0.450 (0.191, 0.740) | 0.022 (0.001, 0.268) | 31 (1) | Ozmen et al. 2011, Selvaraj et al. 2014, Levendowski et al. 2015 |

Digital Health and Sleep-Disordered Breathing: A Systematic Review and Meta-Analysis





Talita Rosa, MD, MS1; Kersti Bellardi, MS2; Alonço Viana Jr, MD, MS3; Yifei Ma, MS4; Robson Capasso, MD5

- Devices that were bed/mattress-based were found to have the best sensitivity overall (0.921, 95% confidence interval [CI] 0.870, 0.953)
- The sensitivity of contactless devices to detect mild OSA cases was the highest of all groups (0.976, 95% CI 0.899, 0.995), but provided a high false positive rate (0.487, 95% CI 0.137, 0.851).
- The remaining groups of devices showed low sensitivity and heterogeneous results

Accessory Appliance Platforms



- Separate device that may or may not interact with mobile devices or internet
- Examples:
 - Specialized alarm clocks
 - Wakeup lights
 - EmWave biofeedback device
 - Sense with Sleep pill senses noise, light, temp, humidity, allergens then adjusts sound and light
 - Withings Aura similar but adjust light spectrum





SmartHomeDB.





What should you do when a patient wants to show you their phone app sleep data?



- A. Tell them you don't believe the data so don't bother
- B. Review the data and use it to guide your therapy decisions
- C. Assess their dependence on the data and suggest discontinuation if it is causing anxiety

What should you do when a patient wants to show you their phone app sleep data?



- A. Tell them you don't believe the data so don't bother
- B. Review the data and use it to guide your therapy decisions
- C. Assess their dependence on the data and suggest discontinuation if it is causing anxiety

Consumer Sleep Technology: An American Academy of Sleep Medicine Position Statement





Table 2—General principles of CST engagement.

- Clinicians should have a general awareness of CST and a readiness to discuss CST with patients.
- Clinicians should understand the general framework of devices and apps available and have a basic knowledge of available evidence or lack thereof.
- Most CSTs are not FDA cleared or validated clinical devices/ applications, but widespread accessibility and use by patients (and potential patients) may augment patient engagement.
- Data can be utilized as a tool for opening discussions with patients.
- Clinicians should recognize the patient's use of CST as a commitment to focus on sleep wellness.

Table 4—Guidance for clinicians encountering data in a clinical setting.

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- If/when data are presented by patients, it should be considered in the context of a comprehensive sleep evaluation and should not replace validated diagnostic instruments or treatments that have undergone rigorous scientific investigation.
- Discuss with the patient which biometric the CST is measuring (if known) and how this differs from gold-standard sleep measurement.
- · Encourage the patient to evaluate their sleep based on subjective symptoms, clinical context, and validated diagnostic testing rather than CST data of unclear significance.
- Reconcile the patient's symptoms with the data presented by the CST, emphasizing that CST-derived information must be interpreted carefully in the context of clinical signs and symptoms.
- Present options for ongoing use of the CST (eg, to set personal goals, assess change over time).
- Patients utilizing CST may favor engaging with validated online therapies such as CBT-I
- If the patient has developed anxiety, unreasonable expectations, or inadequate sleep hygiene related to the use of the CST, consider encouraging the patient to discontinue use of the device either temporarily or permanently.





Conclusion – Sleep Tracking Devices

- Consumer sleep tracking devices significantly over estimate total sleep time when compared to PSG (like actigraphy)
- In addition, data for specific parameters such as sleep onset latency, sleep efficiency, and sleep stage analysis are unreliable
- The basis for the sleep score/quality seems to be unclear
- How are they affected by bedpartners, pets, mattress, sleep disorders
- For the consumer is "light sleep" good or bad? How much "deep sleep" is needed? Is REM sleep "light" or "deep"?



Co – morbidity in patients undergoing PSG over time





- Mayo Clinic chart review
- Development of Polysomnogram Clinical Index (PSGCI)
- Premise: the complexity of patients undergoing PSG has increased since HSAT has become more popular
- This may have effects on staffing ratios, staff expertise, facility design and monitoring capabilities





- 43,780 pts studied from 2005 2015
- Examined comorbidity indices (Charlson, Elixhauser)
 - Comorbidity = total burden of illness unrelated to the principal diagnosis
 - Both indices use ICD-9 or ICD-10 diagnosis codes
- Developed a pretest score that could be used to predict fall risk, staff ratio, etc
 - Included pt comorbid conditions + complexity of study being done

Sleep Study Complexity





| Likert Scale Value | Type of study/PAP |
|-----------------------|--|
| 1 | Diagnostic Polysomnogram (PSG) |
| 2 | Polysomnogram with parasomnia protocol (requiring special precautions and monitoring) |
| 3 | PSG with oxygen therapy titration |
| 4 | PSG with CPAP and or BiPAP-S titration |
| 5 | PSG with CPAP and or BiPAP- S with oxygen therapy titration |
| 6 | PSG with advanced PAP therapy (ASV, Auto SV, BiPAP ST, IVAPS, AVAPS) titration |
| 7 | PSG with advanced PAP (other than CPAP or BiPAP-S) and oxygen therapy titration, Study with parasomnia protocol with PAP therapy with or without oxygen therapy titration |
| 8 | Portable PSG (hospital study) |

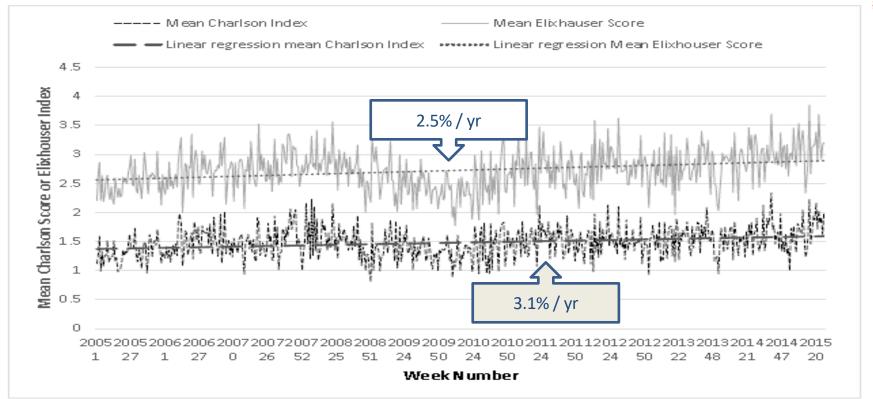




- Mayo Clinic providers "rate" the patients from 0-3
 - 0 = routine patient, no additional requirements
 - 1 = fall precautions
 - 2 = fall precautions + additional assistance (ambulation, re-orientation, nebulizer or medications)
 - 3= requires in hospital study

Figure 2: Slope of the Charlson Comorbidity and Elixhauser Index over a 10-year period



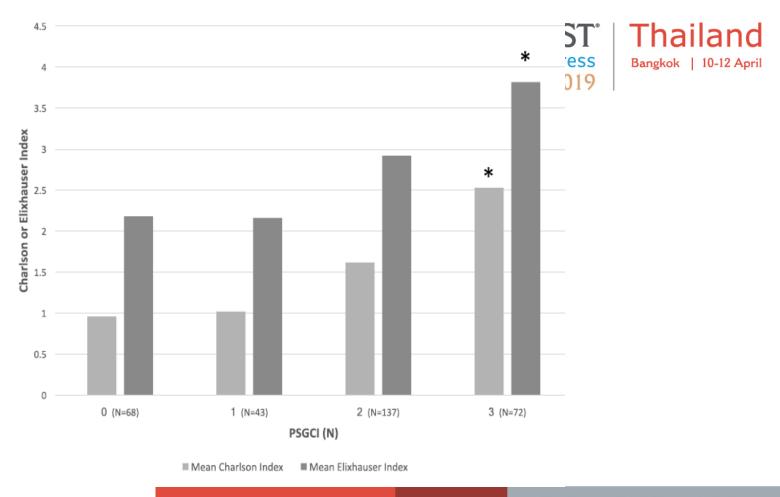






- Overall volumes steady
- 30% increase in comorbidities
 - Differences persisted after adjustment for age, sex, BMI and race
- Pts were older, more female, lower BMI's
- Patients had more peripheral vascular disease, renal disease, liver disease, dementia, MI and hemiplegia (stroke)

Sleep study complexity also increased



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Implications for the future

- Patients in sleep labs are sicker, less mobile and require more complex. titrations
- Labs need to "gear up" for these types of patients fall precautions, more sophisticated monitoring (CO2)
- Technologists need to become more knowledgeable about comorbid diseases
 - Peritoneal dialysis
 - LVAD's (left ventricular assist devices)
 - Continuous infusions
 - HGNS (hypoglossal nerve stimulators)
 - VNS (vagal nerve stimulators)

Conclusions





- The search for biomarkers continues and has great promise to assist with better phenotyping of our patients with sleep disorders
- Consumer sleep technologies are the future, better validation needed
- Beware the MSLT!!
- PSG patients are sicker and require higher intensity management