



ResMed

*Changing lives
with every breath*



KENTUCKY
— SLEEP SOCIETY —



Longitudinal Assessment and Latest Clinical Evidence for PAP Therapy

Dr Adam Benjafield

Vice President Medical Affairs



Overview

- Past
- Changes in Technology
- Present
- Latest Clinical Evidence
- Future



> Past

**REVERSAL OF OBSTRUCTIVE SLEEP APNOEA
BY CONTINUOUS POSITIVE AIRWAY
PRESSURE APPLIED THROUGH THE NARES**

COLIN E. SULLIVAN
MICHAEL BERTHON-JONES

FAIQ G. ISSA
LORRAINE EVES

*Department of Medicine, University of Sydney, New South Wales
2006, Australia*

Lancet 1981

OSA Treatment



> Lancet – Background

- Severe OSA with excessive daytime sleepiness
- Sealed nasal prongs style mask
- Vacuum-cleaner blower motor

Patient	Age	AI - NREM	AI - REM
1	40	62 (range 33-97)	64 (range 48-85)
2	52		
3	55		
4	48	35sec length	45sec length
5	13		

> Lancet – Results

Patient	CPAP	AI - NREM	AI - REM
1	10	0	0
2	4.5		
3	6		
4	7		
5	4.5		

- “Immediate clinical response to 1 night of unobstructed sleep was remarkable”
- Patients alert and remained awake all day

CPAP through the nares is a fail-safe system for treating OSA



Inherent simplicity and safety suggest that home use will be possible



PULMONARY PERSPECTIVE

Nasal Positive Airway Pressure and Sleep Apnea

Reflections on an Experimental Method That Became a Therapy

Colin E. Sullivan

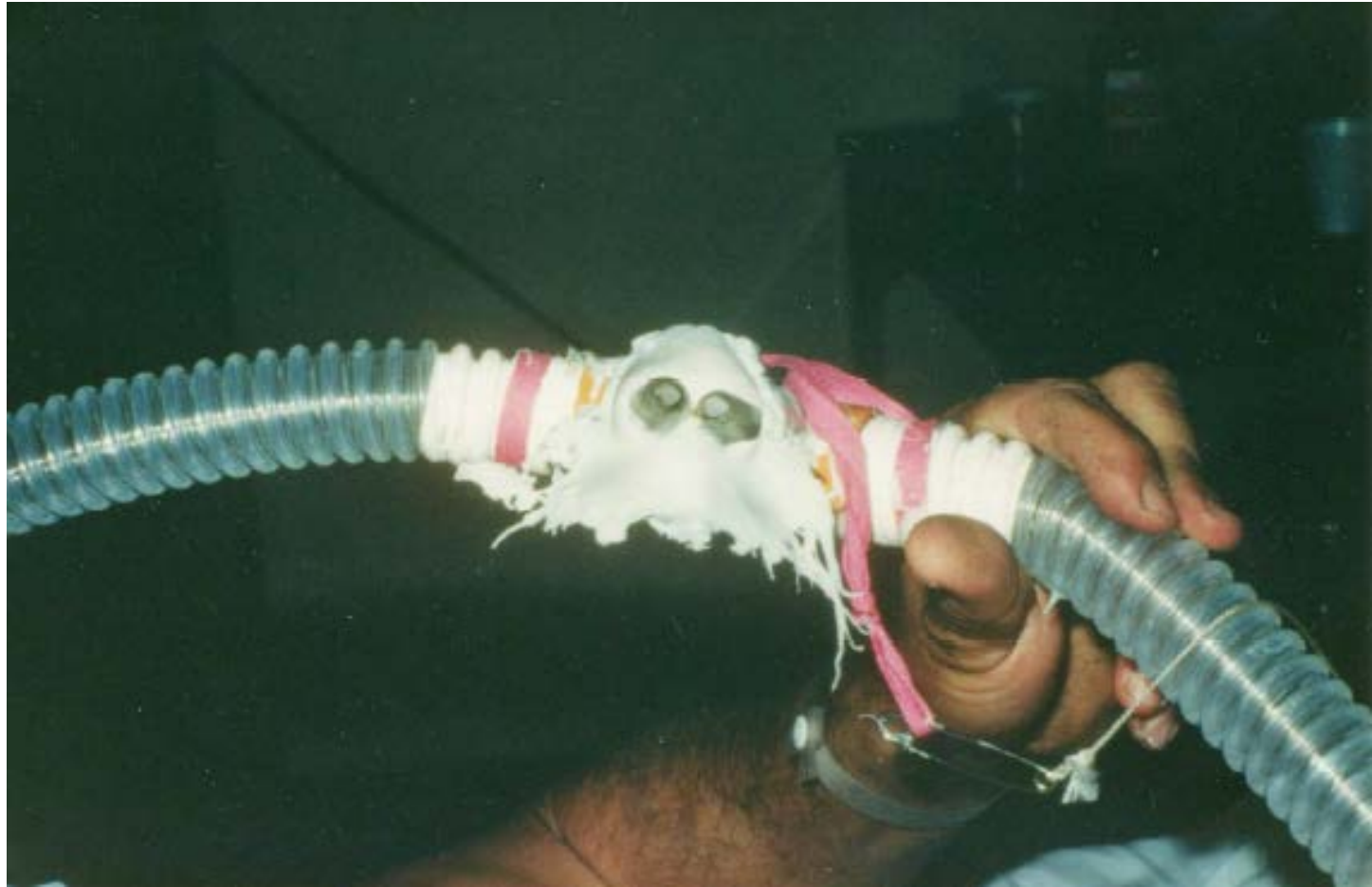
Department of Medicine, University of Sydney, Sydney, Australia

Am J Respir Crit Care Med 2018

> Original CPAP Circuit



➤ Nasal Tubes and Mask After Removal



➤ First Home CPAP System

Mask



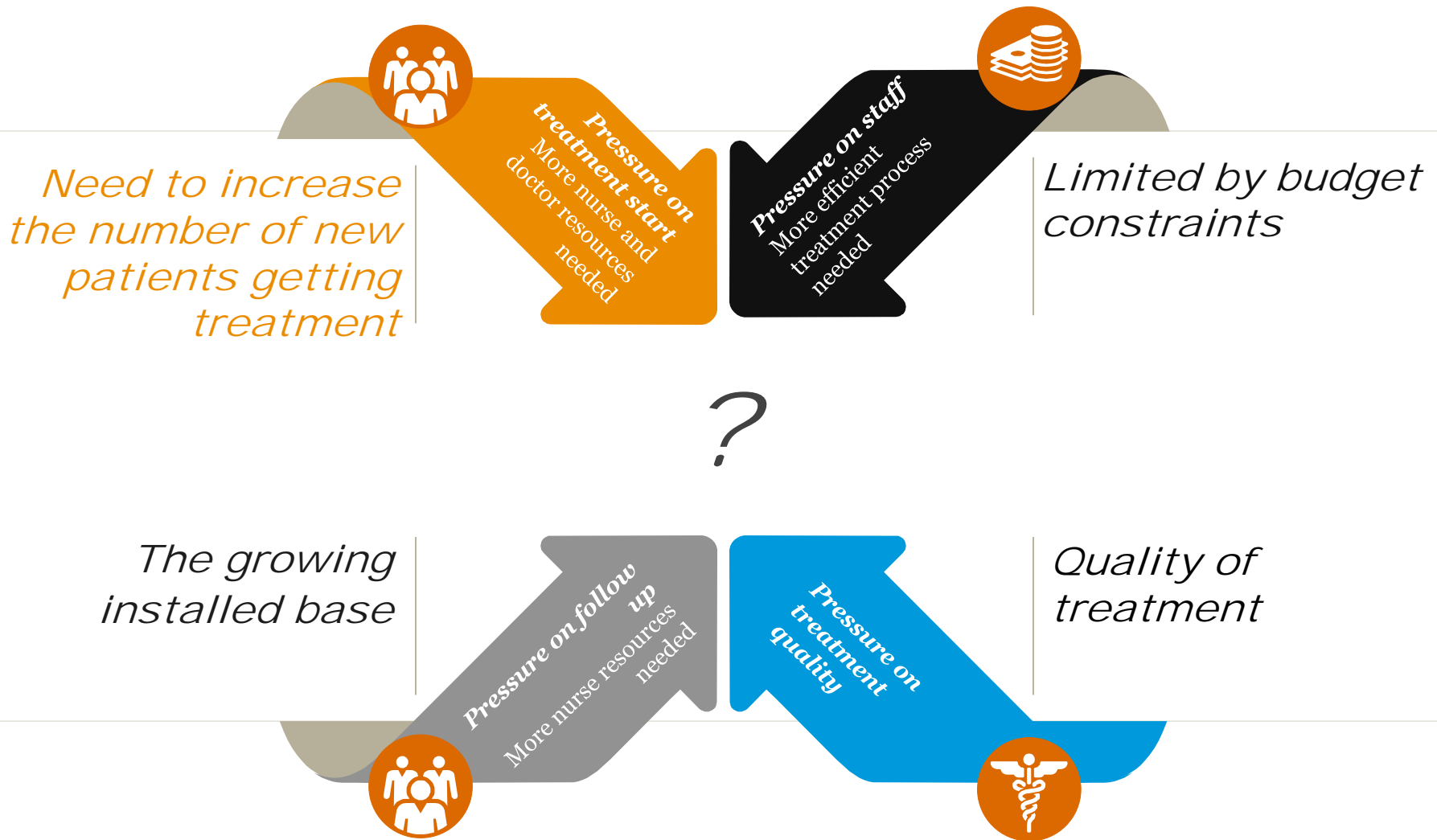
Glue On Mask – NO LEAK!

Device

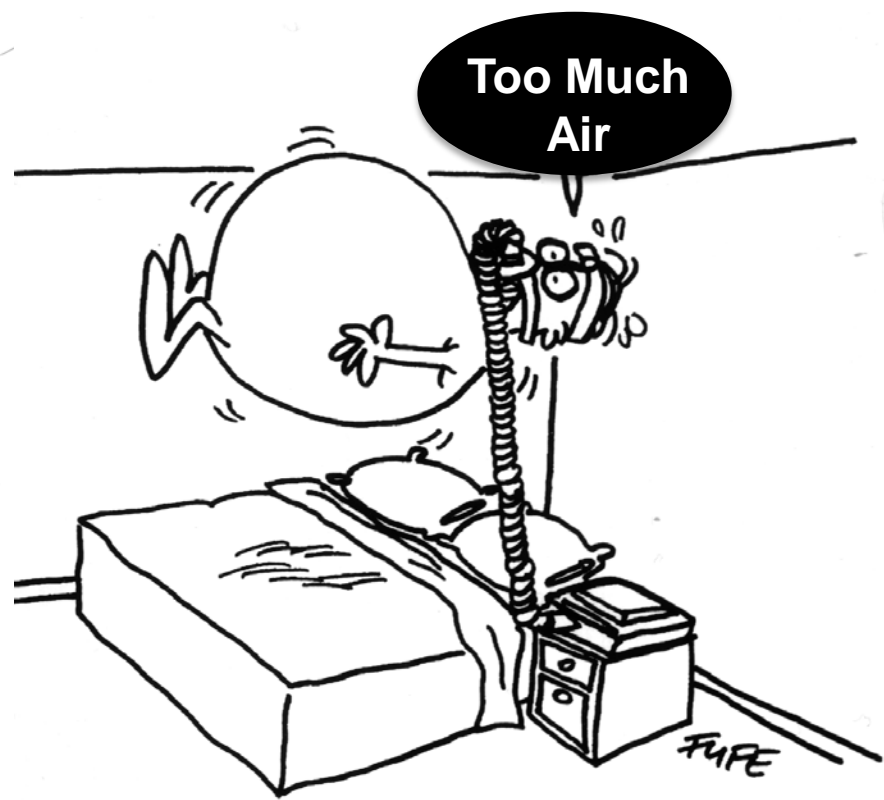


> Present

➤ Sleep Medicine – Facing Challenges



> Major Challenge – Adherence





Adherence in Major Studies

PREDICT

Continuous positive airway pressure in older people with obstructive sleep apnoea syndrome (PREDICT): a 12-month, multicentre, randomised

POSITIVE

Alison McMillan, Daniel J Bratton, Rita Faria, Magda Renata L Rihat, Mary J Morrell, on behalf of the PREDICT Investigators, Andrew Nunn, John R Stradling.



CPAP usage = 2.4 hrs Lancet Respir Med 2014

MOSAIC

Continuous positive airway pressure improves sleepiness but not calculated vascular risk in patients with minimally symptomatic obstructive sleep apnoea: the MOSAIC randomised controlled trial

NEUTRAL

Sonya Elizabeth Craig, on behalf of the MOSAIC Investigators, coll, Daniel J Bratton, Andrew Nunn, Robert Davies, John Stradling

CPAP usage = 2.7 hrs Thorax 2012

SAVE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

R. Doug McEvoy, M.D., Nick A. Antic, M.D., Ph.D., Emma Heeley, Ph.D., Yuanming Luo, M.D., Qiong Ou, M.D., Xilong Zhang, M.D., Olga Mediano, M.D., Rui Chen, M.D., Luciano F. Drager, M.D., Ph.D., Zhibong Liu, M.D., Ph.D., Guofang Chen, M.D., Peter J. McArdle, M.D., Sutapa Mukherjee, M.D., Laurent Billot, M.Sc., Qiang Li, M.B., Brian R. Bhanu, M.D., Susan R. Arora, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Bruce Neal, M.D., Ph.D., David P. White, M.D., Ron R. Grunstein, M.D., Ph.D., Nanshan Zhong, M.D., and Craig S. Anderson, M.D., Ph.D., for the SAVE Investigators and Coordinators*

NEUTRAL

CPAP usage = 3.3 hrs NEJM 2016

HeartBEAT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

CPAP versus Oxygen in Obstructive Sleep Apnea

Daniel J. Gottlieb, M.D., Ph.D., Reena Mehra, M.D., Denise C. Babineau, Ph.D., Roger S. Blumenthal, M.D., Ph.D., and Susan Redline, M.D., M.P.H., Quan, M.D., Rueschman, M.P.H., Bhatt, M.D., M.P.H.,

POSITIVE

CPAP usage = 3.5 hrs NEJM 2014



Adherence in Major Studies

CATNAP

Continuous Positive Airway Pressure Treatment of Sleepy Patients with Milder Obstructive Sleep Apnea

Results of the CPAP Apnea Trial North American Program (CATNAP) Randomized Clinical Trial

Terri E. Weaver^{1,2,3}, Cristina Mancini², J. Richard Landis⁵, Kathleen A. Ferguson⁶, Harly Greenberg⁸, David M. Rapoport⁹, Indira Gurubhagavata³, and Samuel

POSITIVE

Bethany Staley³, Schulman⁷, and Hwang¹⁰,

CPAP usage = 4.0 hrs

AJRCCM 2012

APPLES

EFFECTS OF CPAP ON NEUROCOGNITIVE FUNCTION IN OSA PATIENTS: APPLES

<http://dx.doi.org/10.5665/sleep.2226>

Effects of Continuous Positive Airway Pressure on Neurocognitive Function in Obstructive Sleep Apnea Patients: The Apnea Positive Pressure Long-term Efficacy Study (APPLES)

Clete A. Kushida, MD, PhD¹; Deborah A. Nichols, MS¹; Richard D. Simon Jr., MD⁶; Christian Guilleminault, MD²; Pamela R. Hyde, MA¹; Max Hirshkowitz, PhD⁷; Sylvan

NEUTRAL

Alan K. Walsh, PhD³; Daniel J. Gottlieb, MD, MPH^{4,5}; Lisa K. Schweitzer, PhD³; Eileen B. Leary, RPSGT¹; Alan Gevins, DSc⁸; Gary G. Kay, PhD⁹;

CPAP usage = 4.2 hrs

SLEEP 2012

GLYCOSA

The Effect of Treatment of Obstructive Sleep Apnea on Glycemic Control in Type 2 Diabetes

Jonathan E. Shaw¹, Naresh M. Punjabi², Matthew T. Naughton³, Leslee Willes⁴, Richard M. Bergenstal⁵, Peter A. Cistulli⁶, Greg R. Fulcher⁷, Glenn N. Richards⁸, and Paul Z. Zimmet¹

¹Baker IDI Heart and Diabetes Institute, Melbourne; ²University School of Medicine, Baltimore, Maryland; ³Willems Consulting Group, Inc., Encinitas, California; ⁴Willems Consulting Group, Inc., Encinitas, California; ⁵Willems Consulting Group, Inc., Encinitas, California; ⁶Department of Respiratory and Sleep Medicine and ⁷Department of Respiratory and Sleep Medicine and ⁸ResMed Science, New South Wales, Australia; and ⁹ResMed Science, New South Wales, Australia

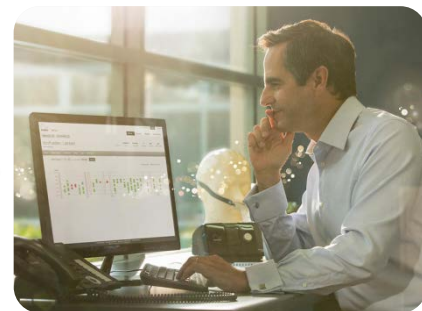
NEUTRAL

¹Willems Consulting Group, Inc., Encinitas, California; ²Willems Consulting Group, Inc., Encinitas, California; ³Willems Consulting Group, Inc., Encinitas, California; ⁴Willems Consulting Group, Inc., Encinitas, California; ⁵Willems Consulting Group, Inc., Encinitas, California; ⁶Department of Respiratory and Sleep Medicine and ⁷Department of Respiratory and Sleep Medicine and ⁸ResMed Science, New South Wales, Australia

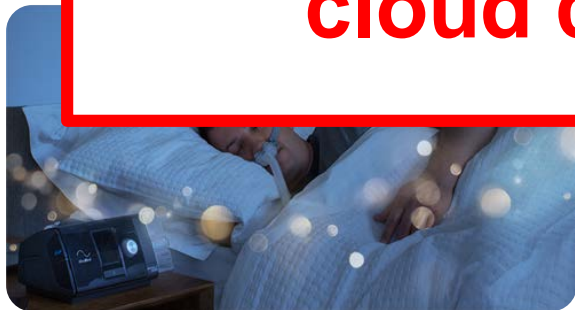
CPAP usage = 4.9 hrs

AJRCCM 2016

Changes in Technology



Currently ResMed has over 6 million cloud connected PAP devices



Patient

**Clinician Notifications
(Action Groups / U-Sleep)**



**Patient Engagement and Notifications
(myAir / U-Sleep)**



Medical Experts in Clinical Outcomes
Using Data Science

***Building clinical learnings through advanced analytics from
AirView and other data sources***



Atul Malhotra
UC San Diego



Peter Cistulli
University of Sydney



Jean-Louis Pepin
Grenoble Alpes
University



Holger Woehrle
Sleep and Ventilation
Center Blaubeurben

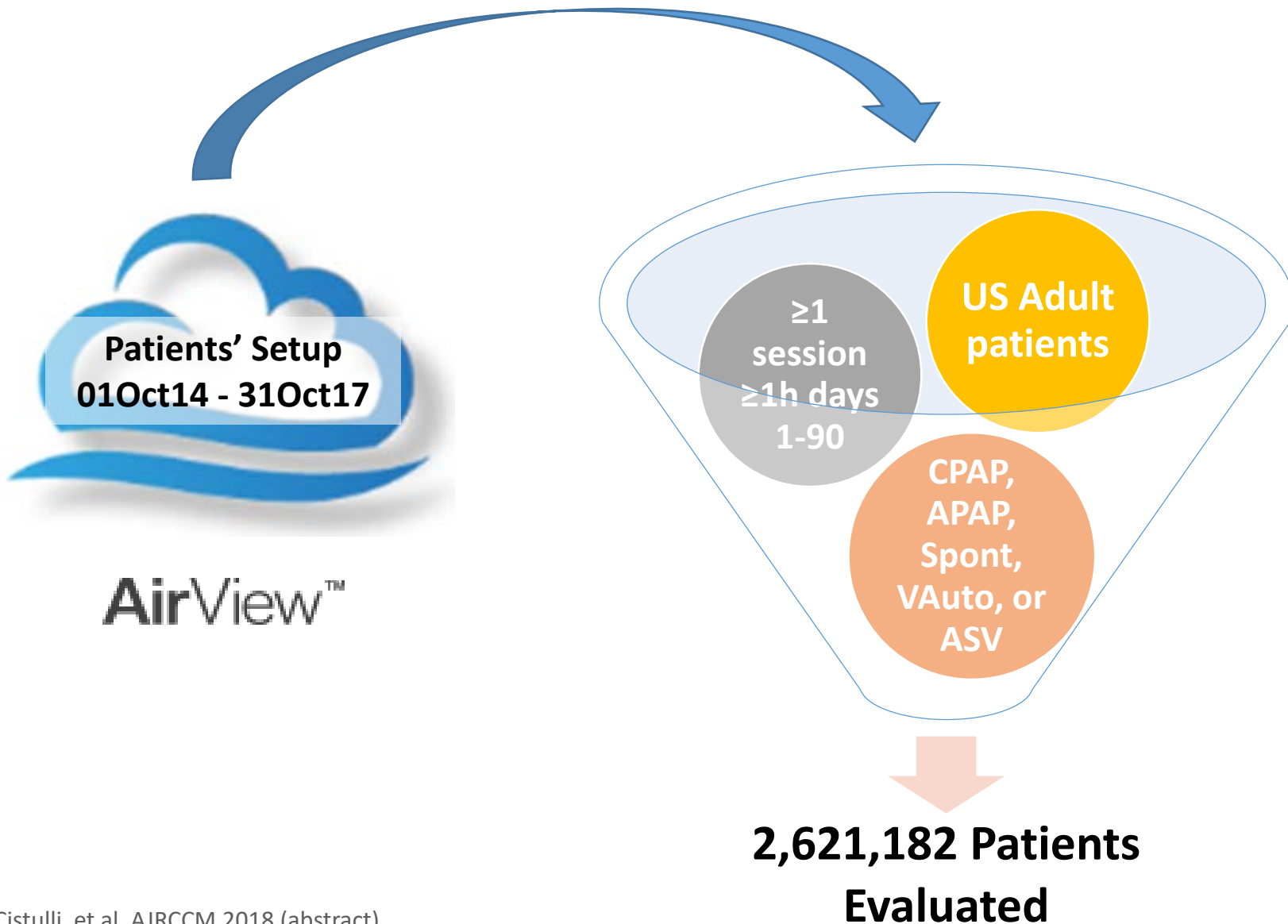
Medical Affairs leaders and Advanced Analytics (data scientists and statisticians) from RMD



Latest Clinical Evidence



Real-World PAP Adherence

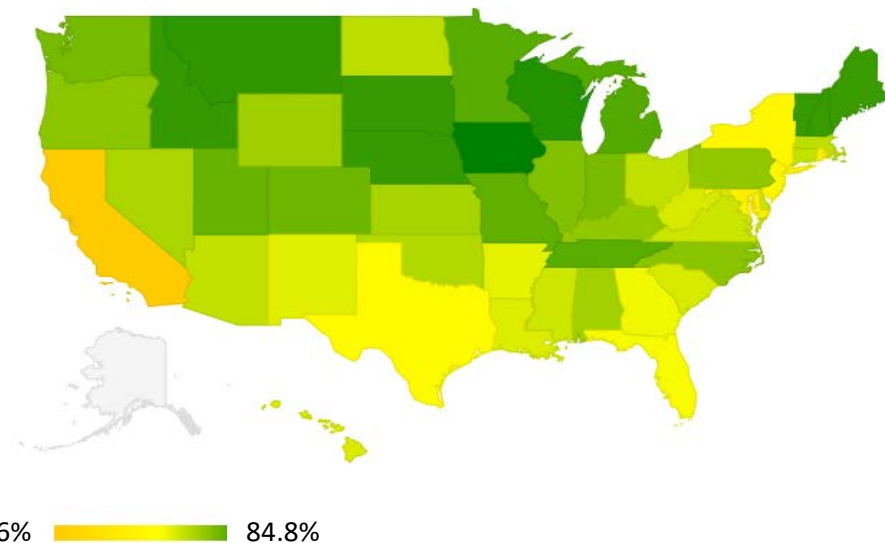


> Real-World PAP Adherence

Over 2.6 million US
AirView patients,
CMS compliance in the
first 90 days

75%

% Met 90-day CMS Compliance by State



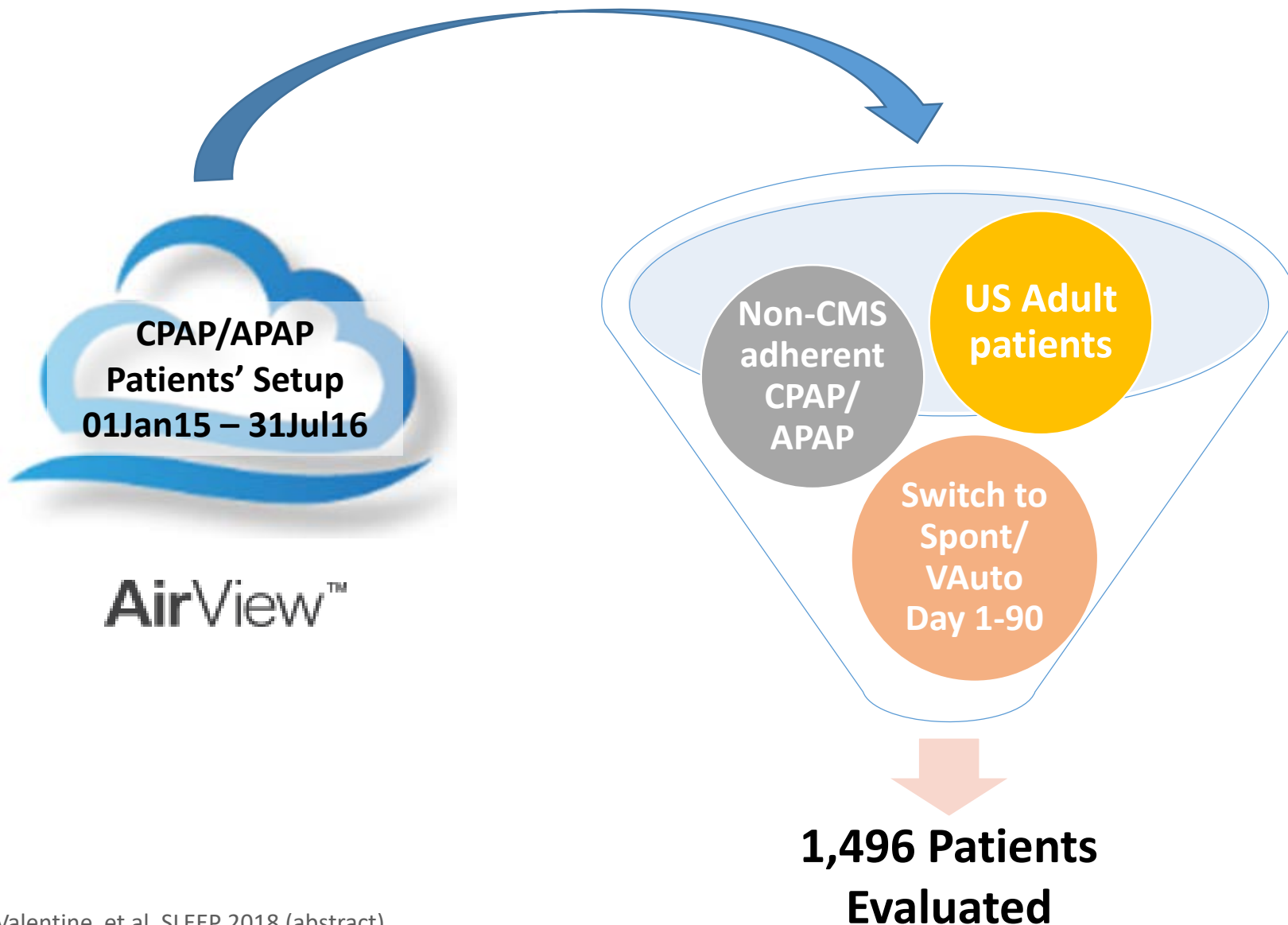
Overall mean daily usage

5.1 hours

Median percentage of days used

93%

> ncOSA Bilevel Rescue





ncOSA Bilevel Transition

Efficacy Metrics (first 90 days)	Before switch (CPAP/APAP)	After switch (Spont/VAuto)
	Median	Median
Avg. AHI	4.93	4.02
Avg. Median Leak (L/min)	5.00	4.14

Usage Metrics (first 90 days)	Before switch (CPAP/APAP)	After switch (Spont/VAuto)	Change	P-Value
	Median	Median		
Percentage of days compliant (≥ 4 hrs) (%)	52.7	68.9	+16.2 (+30.8%)	<0.001
Avg. daily usage (hrs)	3.85	4.75	+0.90 (+23.3%)	<0.001

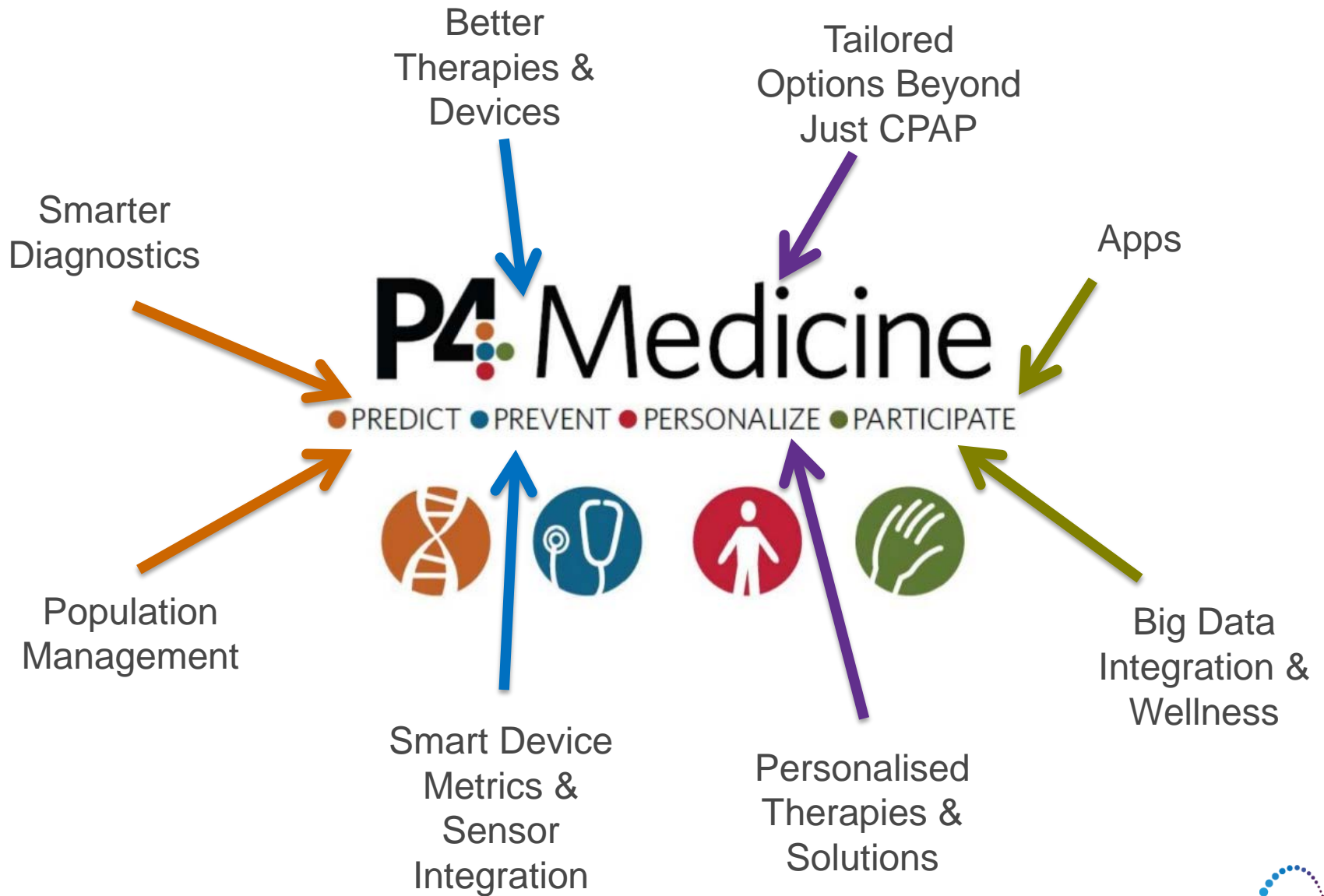
Overall rescue to CMS Compliance with Bilevel = 56.8%

> Future

The world's most valuable resource



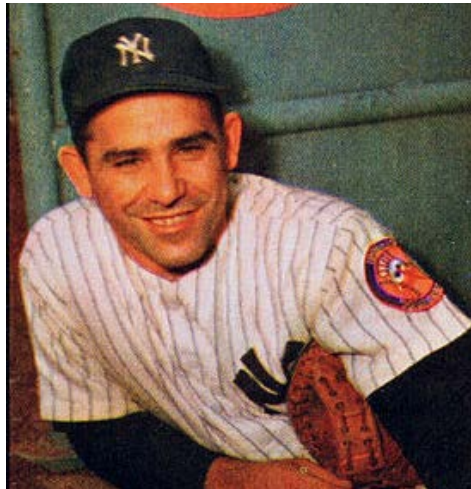
> One Paradigm for the Future of Healthcare





Machine Learning and Prediction in Medicine — Beyond the Peak of Inflated Expectations

Jonathan H. Chen, M.D., Ph.D., and Steven M. Asch, M.D., M.P.H.



Yogi Berra:
“It’s tough to make predictions,
especially about the future.”





➤ Future NIH Major Studies

> Pregnancy and OSA (SLEEP)



Multi-site study (Pregnancy)

PI: Prof. Francesca Facco (Obstetrics),
Prof. Sanjay Patel (Sleep)
UPMC

- **Primary Aim:** Hypertensive disorders of pregnancy
 - Study n=2700
 - Mild to moderate OSA
 - Other outcomes: gestational diabetes, fetal, maternal cardiovascular (VTE, onset HF, MI, onset AF)
- CT.gov Identifier: NCT0348718

ACTIVE



Eunice Kennedy Shriver National Institute
of Child Health and Human Development

> Stoke and OSA (Sleep SMART)



Multi-site study (Stroke)

PI: Prof. Ron Chervin, Prof Devin Brown
University of Michigan

- **Primary Aim:** Recurrence of stroke, ACS or all-cause mortality at 6 months
 - Study n=3062
 - Acute ischaemic stroke or high risk TIA and OSA
 - Functional neurologic status at 3 months
- CT.gov Identifier: pending

Planning Phase



National Institute of
Neurological Disorders
and Stroke



Pre-diabetes and OSA



JOHNS HOPKINS
MEDICINE

Multi-site study (Pre-Diabetes)

PI: Prof. Naresh Punjabi
Johns Hopkins

- **Primary Aim:** Conversion to type 2 diabetes
 - Study n=1200
 - Insulin insensitivity and OSA
- CT.gov Identifier: pending

Early Planning Phase



➤ Conclusions

- CPAP has gone from an experimental apparatus (1981) to commercially available (1985-) long term therapy over the last nearly 40 years
- With growth of Sleep Medicine, we have seen a rapid development of medical devices to treat SDB and adoption of cloud connectivity
- P4 medicine has emerged as a useful paradigm to approach SDB
- Big Data bring new insights and the potential for further innovation
- There are still with many important challenges but





Thank You

