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BACK TO THE FUTURE IN OSAHS
Therapeutics in the 21st Century

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King's College London

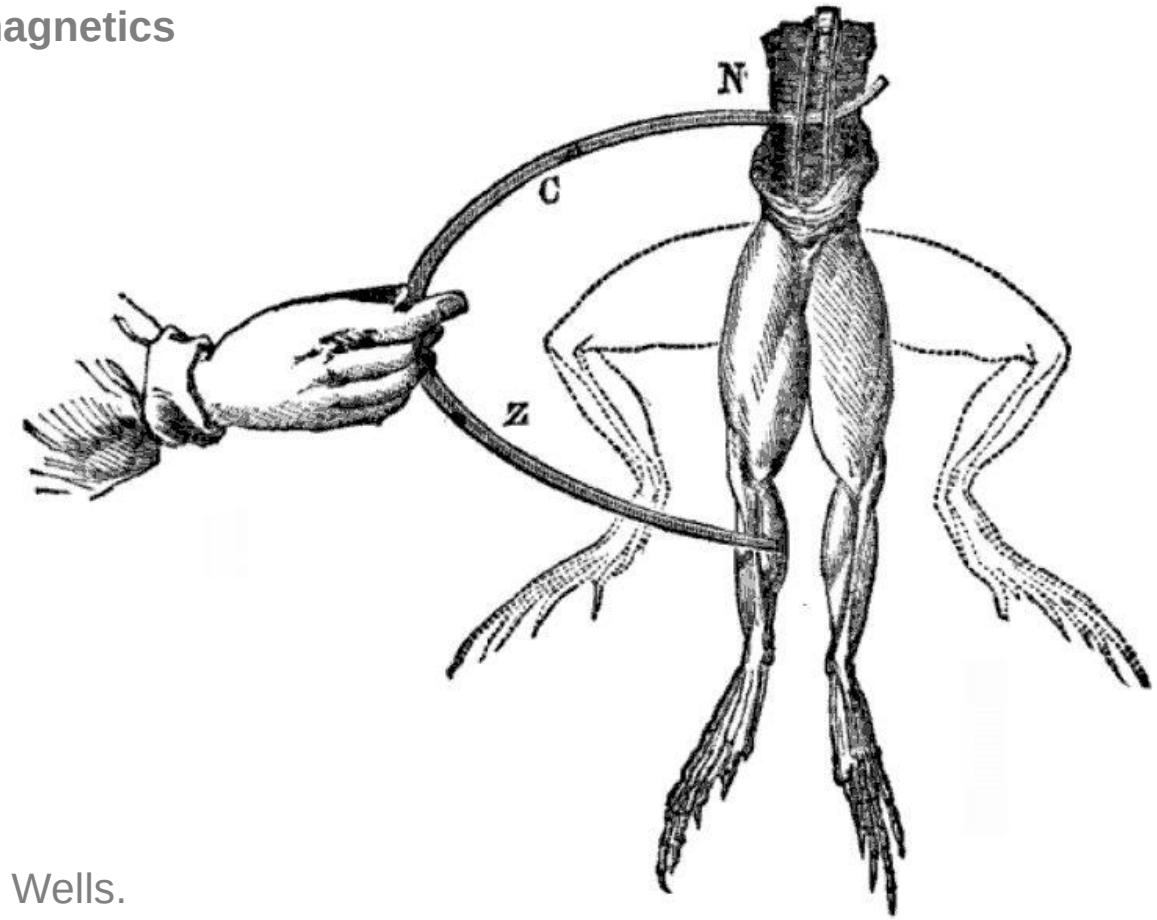
European Respiratory Society Task Force

"…apnoea triggered muscle stimulation cannot be recommended as an effective treatment at the moment (grade C)."

Non-CPAP therapies in obstructive sleep apnoea. *Eur Respir J* ***2011 37:1000***

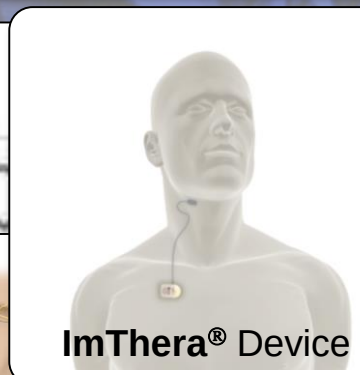
Luigi Galvani (1737-1798)

Bioelectromagnetics

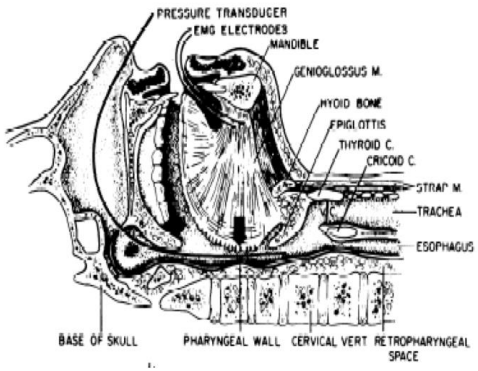


David Ames Wells.
The science of common things: a familiar explanation of the first principles of physical science. Ivison & Phinney, New York 1859

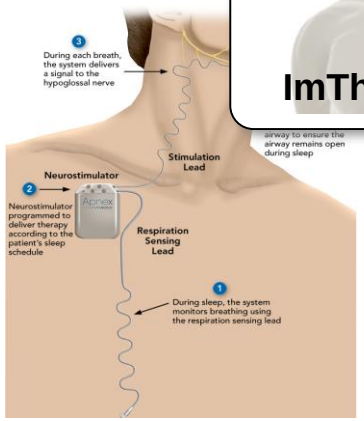
Electrical Stimulation in Obstructive Sleep Apnoea



ImThera® Device

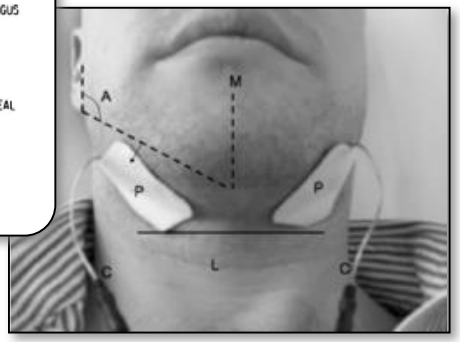


Remmers JE et al,
J Appl Physiol 1978

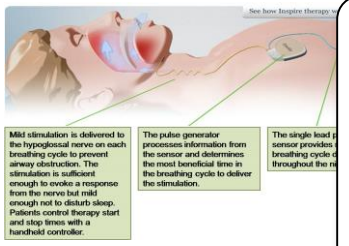


Apnex® Device

Invasive
versus
Noninvasive



Steier J et al,
Chest 2011



Inspire® Device

Nyxoah® Device

Pengo M et al,
Thorax 2016

Transcutaneous Electrical Stimulation

Figure 1a

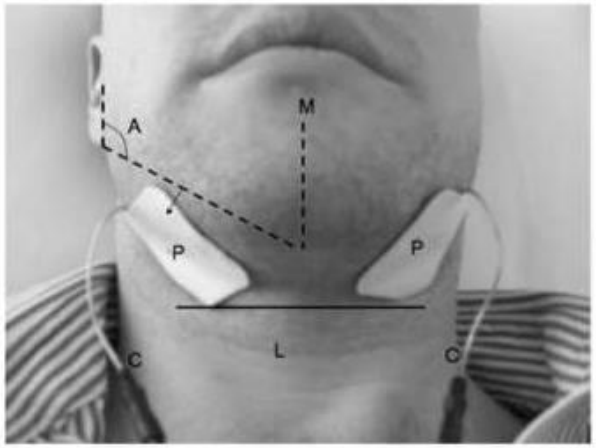
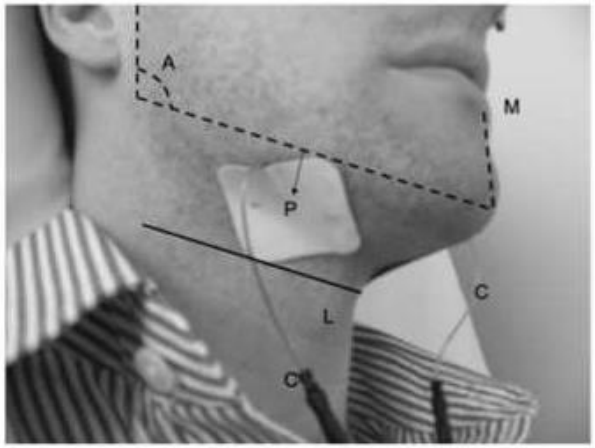


Figure 1b



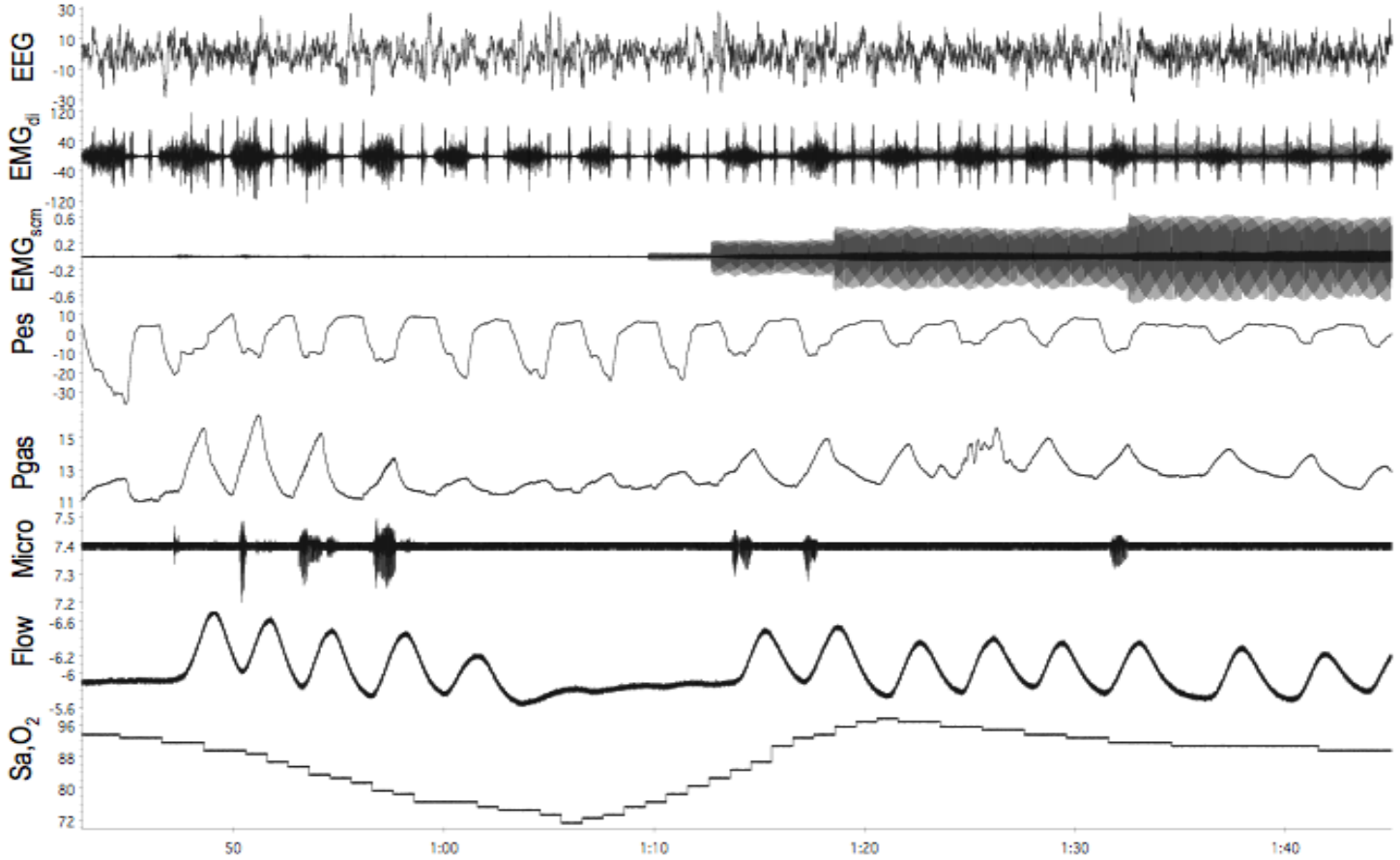
Parameter	Awake	10minutes Pre-Stimulation	10minutes-During Stimulation	10 Minutes Post-Stimulation
Heart Rate (1/min)	84 (26)	79 (22)	69 (18)	74 (20)
Snoring (score[J]; 0-3points)	---	2.1 (0.9)	1.4 (0.9)***	1.7 (0.9)**
Sa,O_2 (%)	---	91.9 (2.1)	93.2 (1.8)**	92.8 (2.1)*
RDI (1/h)	---	28.1 (26.3)	10.2 (10.2)**	26.6 (26.0)
AHI (1/h)	---	26.3 (25.1)	10.0 (9.8)	25.7 (25.1)
Poes (cmH_2O)	14.3 (6.1)*	23.6 (14.1)	18.3 (7.5)*	23.4 (11.3)
Pdi (cmH_2O)	18.7 (6.2)	24.1 (13.5)	19.7 (7.1)*	24.2 (10.8)
EMGdi (μV)	25.5 (8.4)	42.9 (30.5)	26.3 (13.4)**	40.8 (25.7)
EMGdi (%max)	15.0 (4.4)	23.8 (12.6)	15.7 (6.4)***	22.6 (10.4)
Current (mA)	---	---	10.1 (3.7)	---

[J] as described in the methods section on page 10

Steier et al. *Chest* 2011

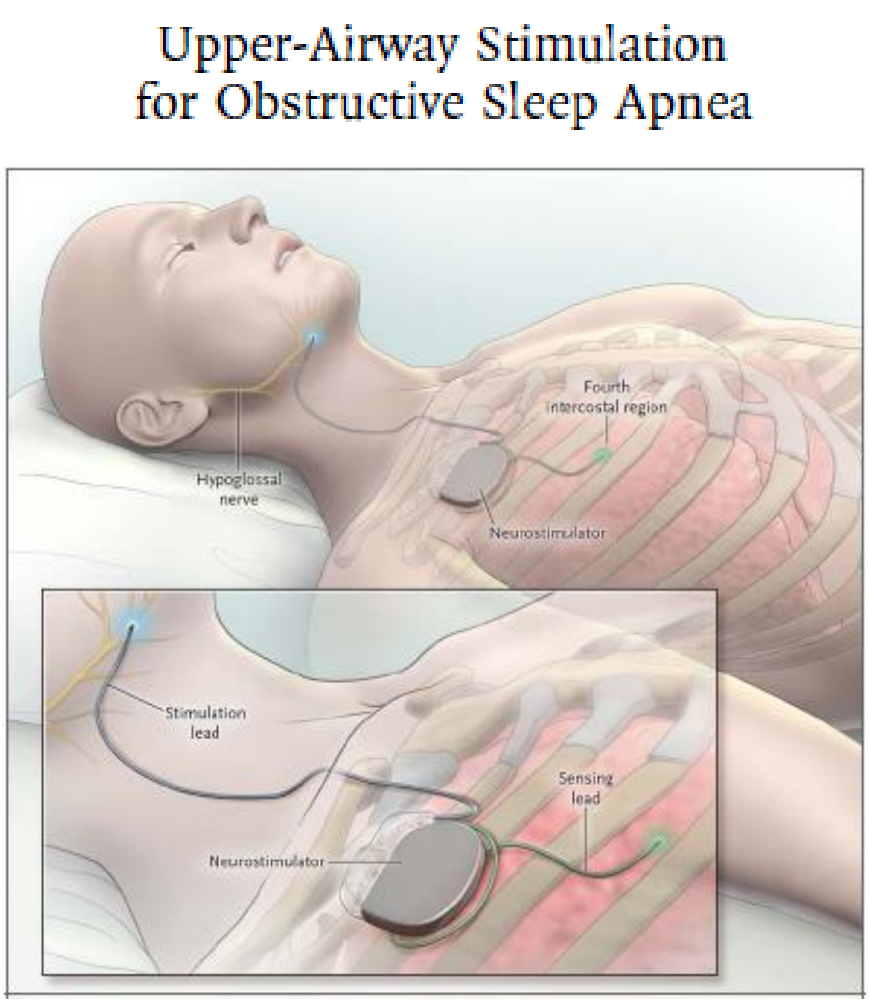
Transcutaneous Electrical Stimulation

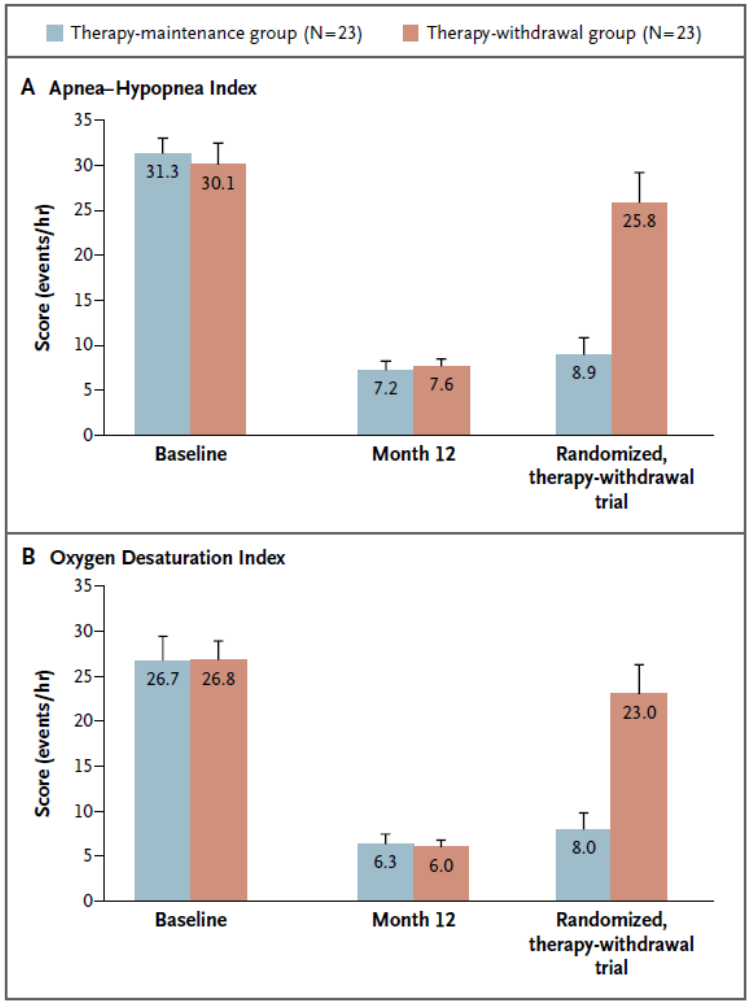
(30Hz, titrating 1-4mA)



Steier J, Seymor J, Rafferty GF, Jolley CJ, Solomon E, Luo YM, Man WDC, Polkey MI, Moxham J. **Continuous Transcutaneous Submental Electrical Stimulation in Obstructive Sleep Apnea: A Feasibility Study.** *Chest* 2011;140:998-1007

Hypoglossal Nerve Stimulation





STAR Trial

Strollo et al. *N Engl J Med* 2014;370:139-49

Patient and Public Involvement

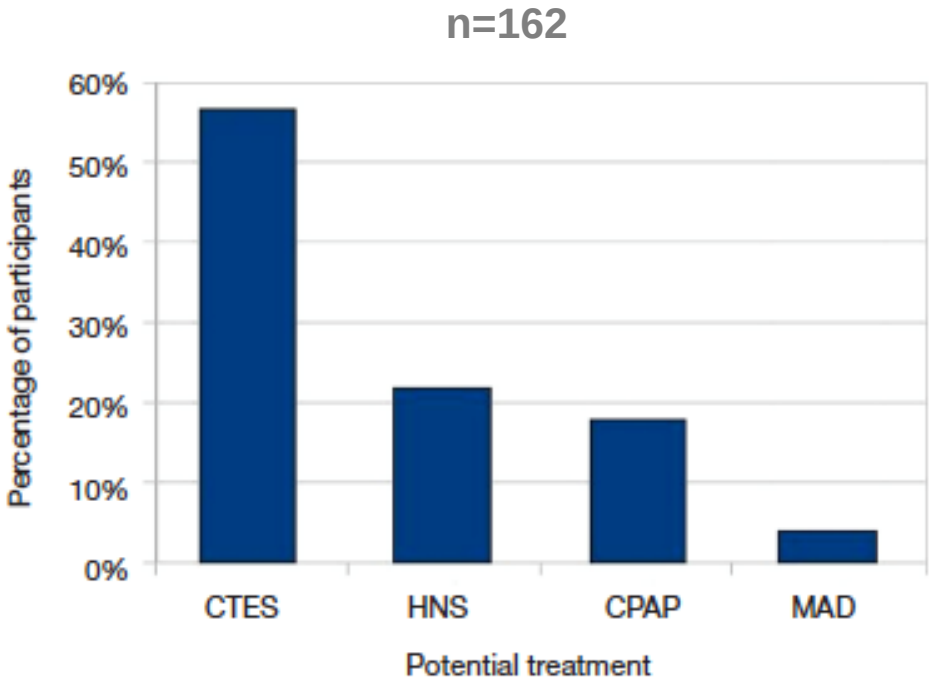
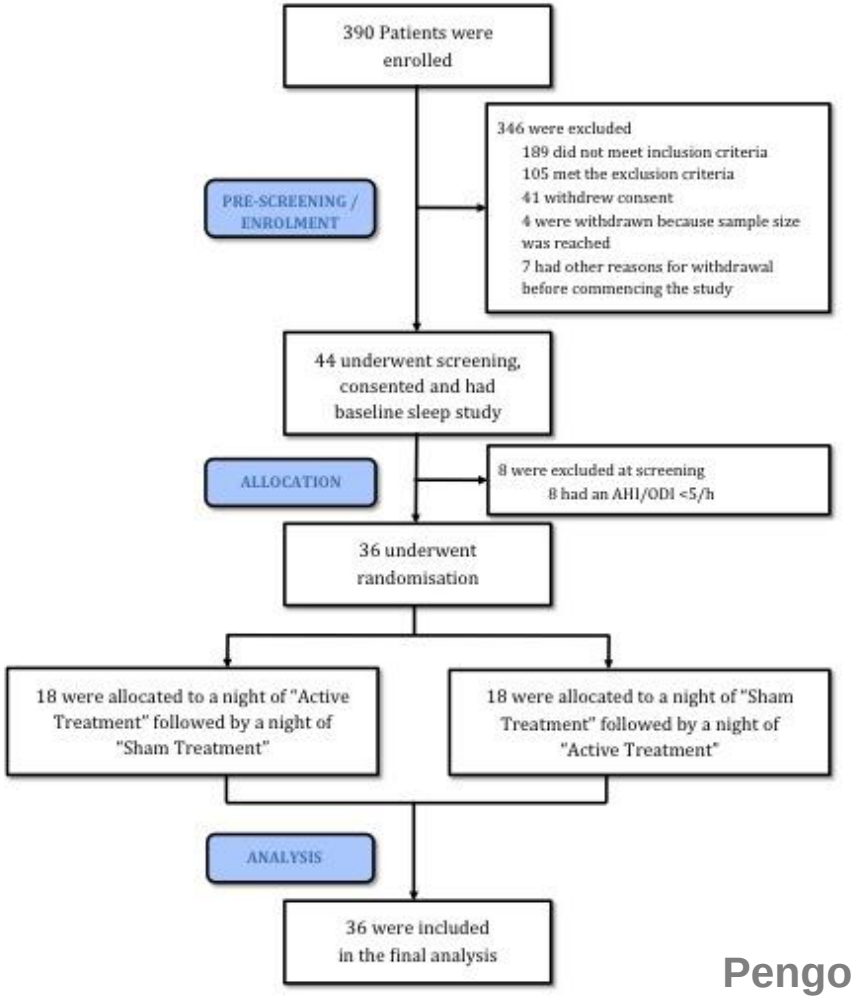


Figure 1 Patients' preferences for potentially available treatments for OSA. CTES, continuous transcutaneous electrical stimulation; HNS, hypoglossal nerve stimulation; CPAP, continuous positive airway pressure; MAD, mandibular advancement device; OSA, obstructive sleep apnoea.

Campbell T et al. *J Thorac Dis* 2015

TESLA Trial, CONSORT diagram

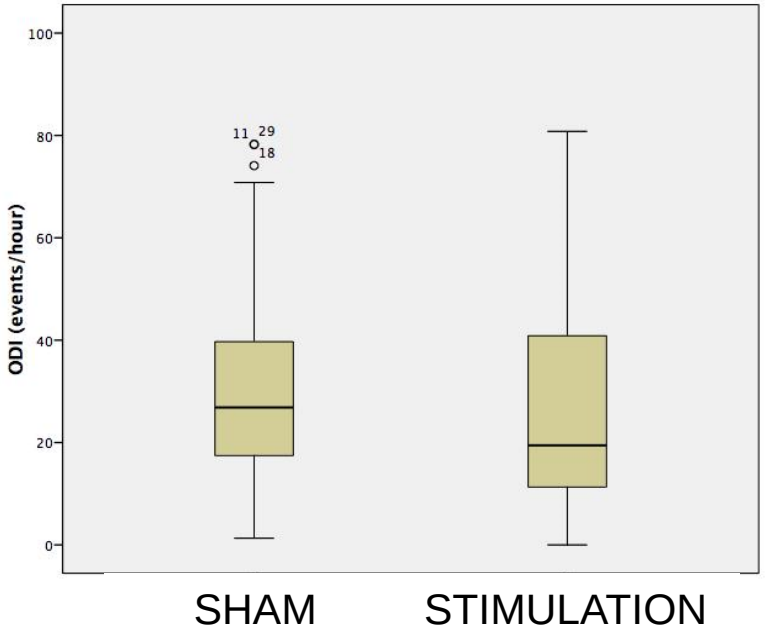


Pengo M et al, *Thorax* 2016

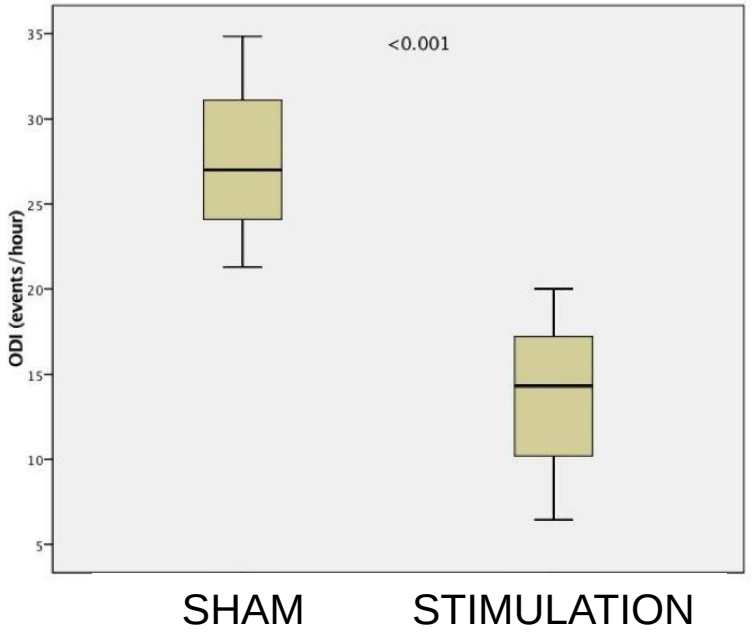
TESLA Trial, Primary Outcome

Oxygen Desaturation Index (4%ODI)

Total Cohort (n=36)



Responder Group (n=17)



Pengo M et al, *Thorax* 2016

TESLA Trial, Secondary Outcome

Parameters	Sham Stimulation	Active Treatment	p-value
Feeling refreshed	5·7 (2·7-7·2)	6·6 (2·2-8·5)	0·40
Sleep quality	5·6 (2·9-7·1)	6·4 (2·4-8·0)	0·28
Mouth dryness	4·4 (2·2-8·5)	7·4 (4·9-9·7)	0·007
Tongue unpleasant sensation	9·9 (9·4-10·0)	9·9 (9·4-10·0)	0·63
Morning headache	9·4 (6·3-10·0)	9·9 (8·1-10·0)	0·27
Skin discomfort	9·9 (9·5-10·0)	9·9 (9·7-10·0)	0·95
Sleepiness	3·0 (2·0-3·5)	3·0 (2·0-3·0)	0·29

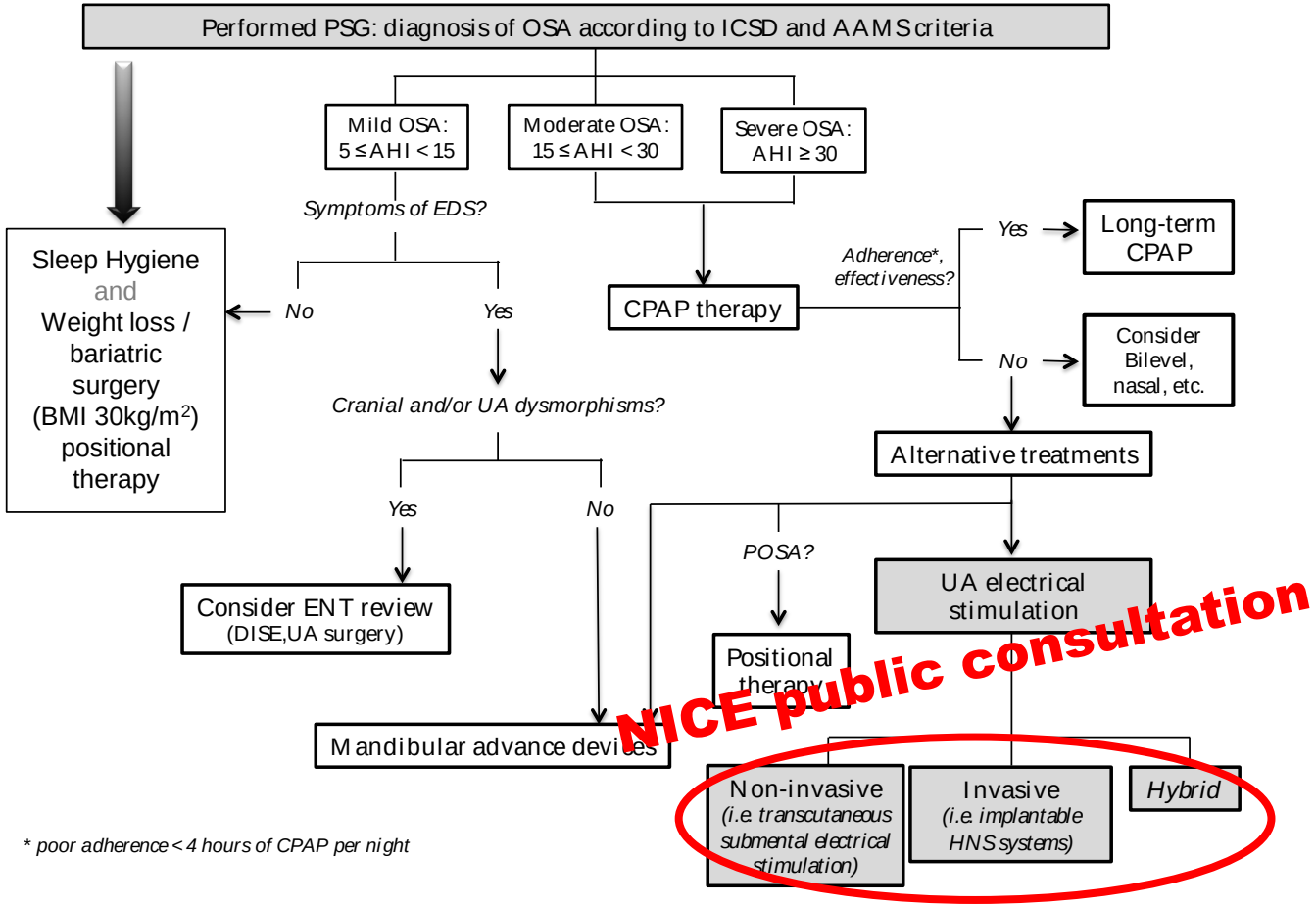
Pengo M et al, *Thorax* 2016

Direct HNS *vs* TESLA: Which Method?

	Non-invasive stimulation	Hypoglossal nerve stimulation
Current intensity	++	++
Efficacy	+	++
Cost	+	+++
Long term follow up	-	+
Effect on cardiovascular parameters	-	+
Application	++	-
Stimulation	Continuous	Triggered, Continuous
Target	unspecific	specific
Type of stimulation	Bilateral	Unilateral
Adverse events	Local skin irritation	+++
Set up	Patches, skin electrodes	Surgical intervention
Current level of evidence according to latest guidelines (48)	C	C

Pengo et Steier. *J Thorac Dis* 2014

Treatment Recommendations



Bisogni V et al, *Exp Rev Resp Med* 2017

Clinical Trials.gov

- **Inspire®**

STAR-trial, current ongoing post-market research and international registry as well as trial in Down-Syndrome.

- **ImThera®**

Targeted hypoglossal nerve stimulation (unilateral), ongoing

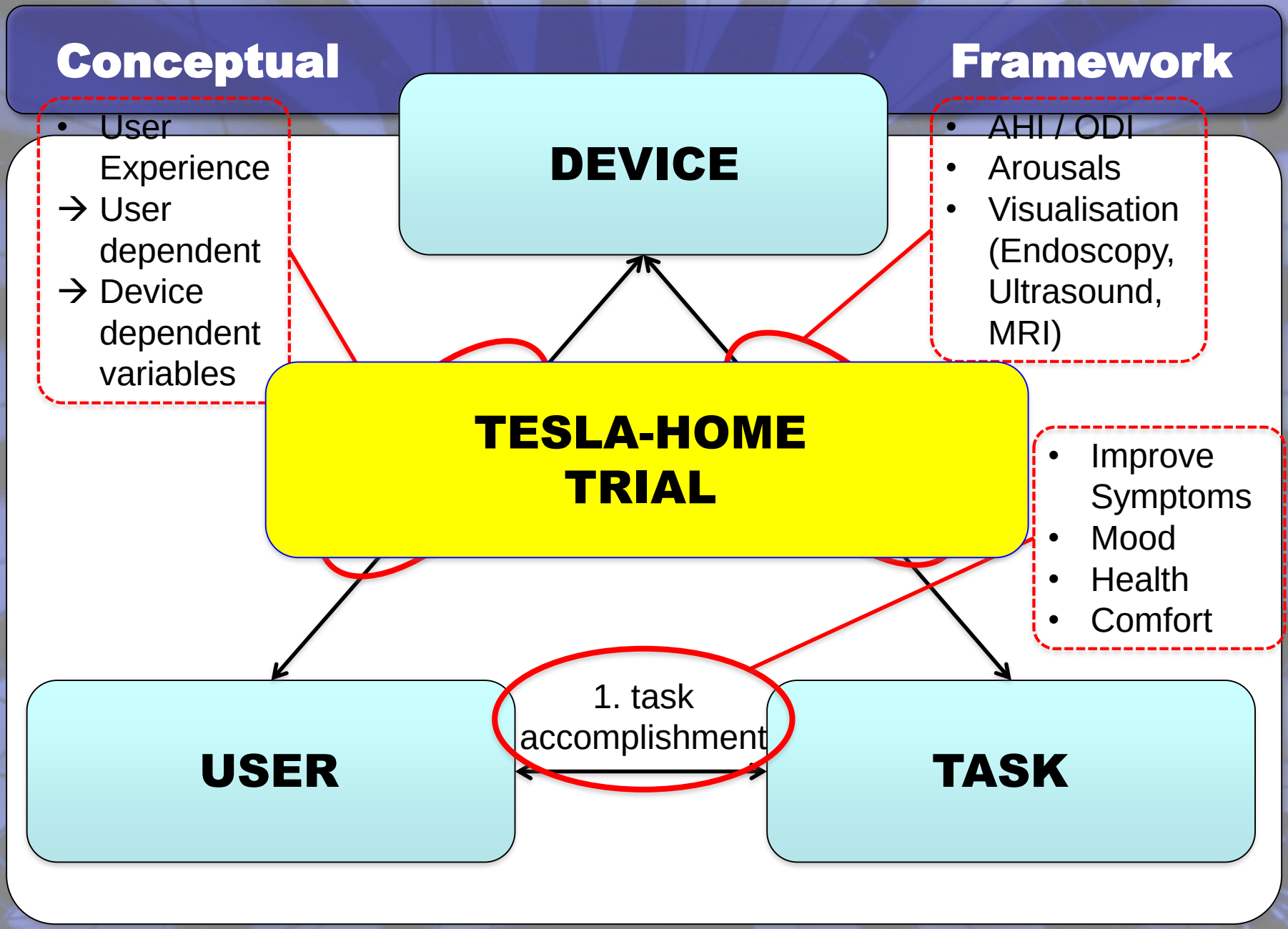
- **Nyxoah®**

Hybrid technology using bilateral hypoglossal nerve stimulation (median), ongoing

- **TESLA/TESLA home**

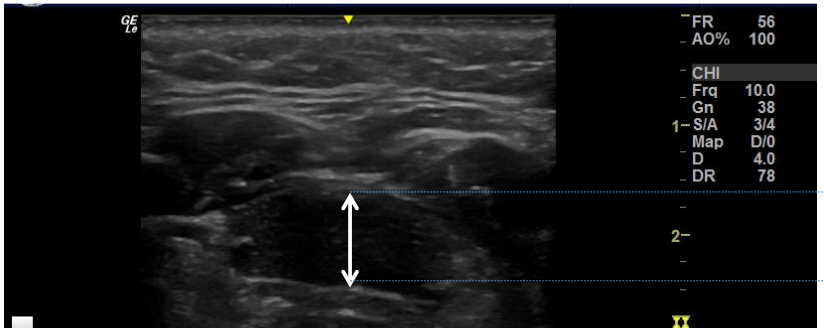
Transcutaneous electrical stimulation using a TENS machine, non-commercial, domiciliary usage (Joerg Steier, GSTT/KCL)

Conceptual Framework

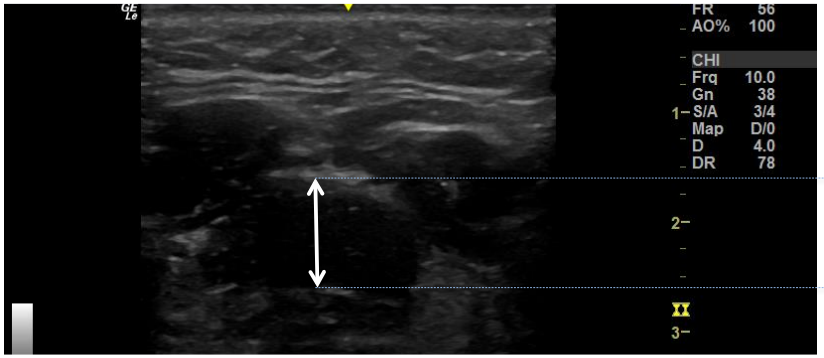


Submental Ultrasound (TESLA-home)

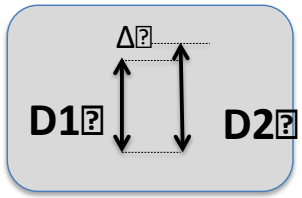
TESLA-home® Ultrasound Genioglossus (001)

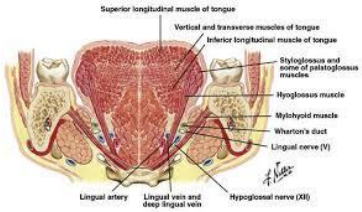


A: Coronal view of the submental area, relaxed



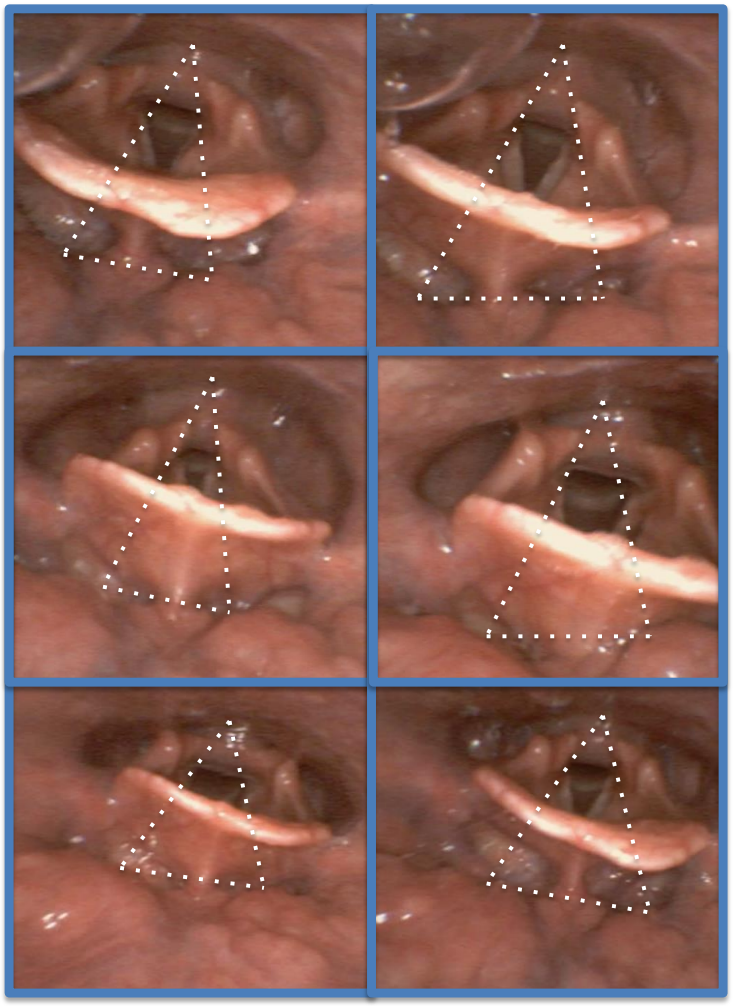
B: Coronal view of the submental area, stimulated (EMS, continuous, 30Hz, 250µs, 11mA)



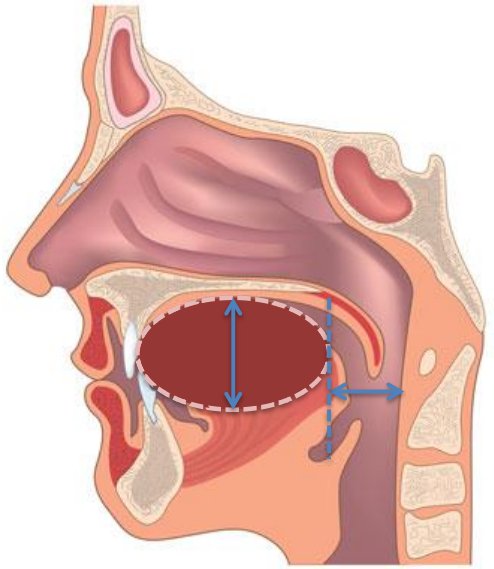


Unpublished data

Video-Endoscopy Stimulation (TESLA-home)

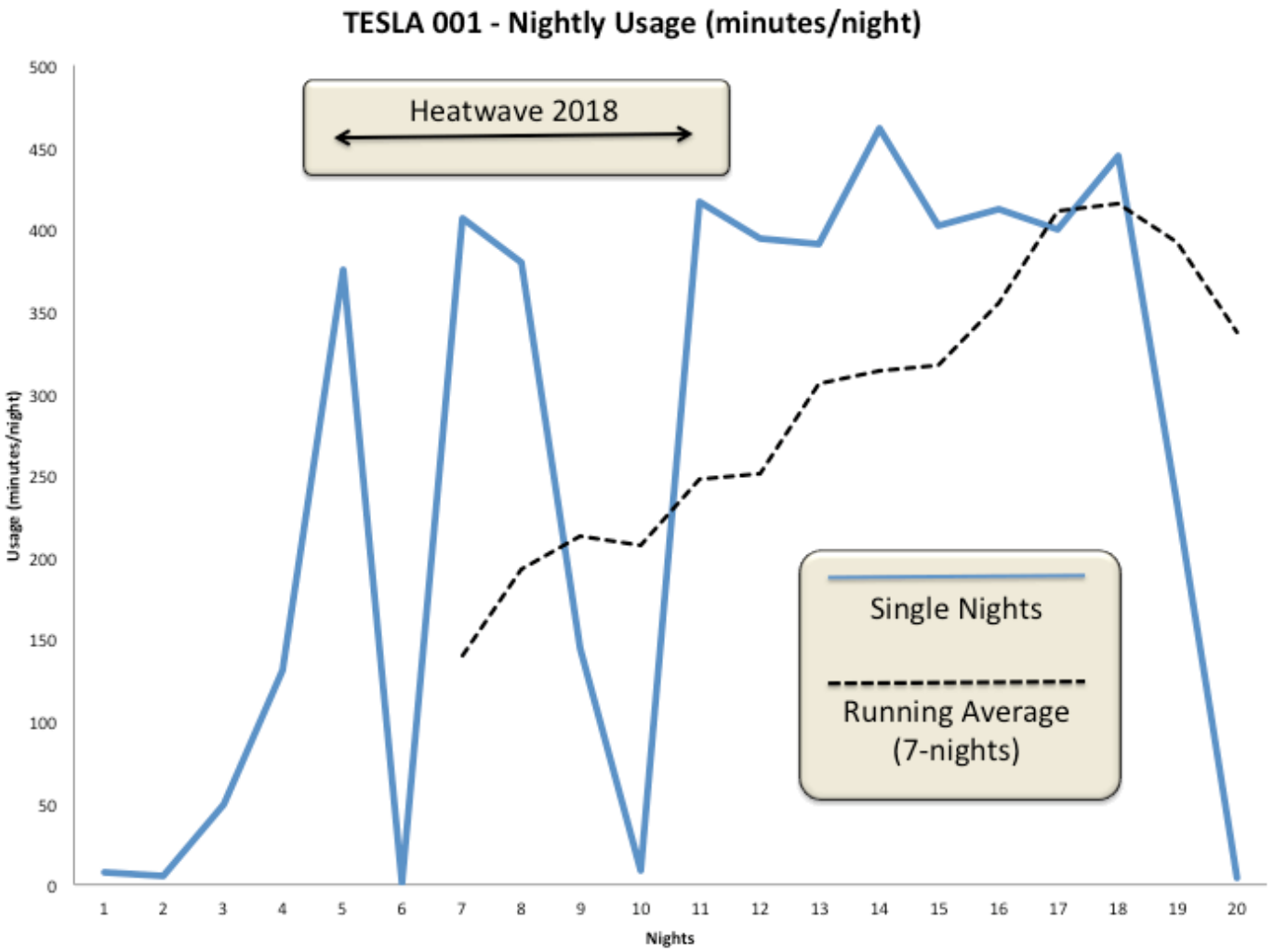


Sagittal View of the Upper Airway



Unpublished data

TESLA-Home, feasibility



Summary Points

- **Key Point**

Electrical current can be delivered to increase the upper airway dilator neuromuscular tone, invasively via hypoglossal nerve stimulation (STAR) and non-invasively via transcutaneous patches (TESLA), for the entire night.

- **Bottom line**

Electrical stimulation of the upper airway dilator muscles delivered throughout the night improves obstructive sleep apnoea.

- **Future work**

It is important to refine the specifications of electrical stimulation of the upper airway dilator muscles, as this method offers a promising and novel approach in the cascade of non-CPAP therapies for patients with obstructive sleep apnoea.

- **National Institute for Health and Care Excellence (NICE)**

NICE have published their public consultation on safety and efficacy of hypoglossal nerve stimulation in OSA.

Thank you for your interest

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