






“Objective” measurement and monitoring of cough

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What is objective measure?






Cough intensity

Cough frequency

Cough reflex sensitivity

Future of cough measure and Summary

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What is objective measure?

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Measure and Monitoring

- Basic of evaluation of disease
- From understandable evidence
- Reliable information that can be shared by physicians or patients
- Affected by disease characteristics

For examples,

- COPD

- High symptom group: CAT \geq 20 → Subjective
- PFT definition: FEV1/FVC $<$ 0.7 post bronchodilator → Objective

- Asthma

- Asthma Control Test: 3-5-1-2-4 → Subjective
- Hyper-responsiveness: FEV1 decrease 15% by mannitol → Objective

- Lung cancer

- RECIEST PR: \geq 30% decreased → Objective

Lack of objective measures in our guideline

- Definition of chronic cough: ≥ 8 weeks
- Cough VAS/NRS: severity
- Cough Symptom Score: frequency
- COAT: QoL

→ Patient-reported, not objective

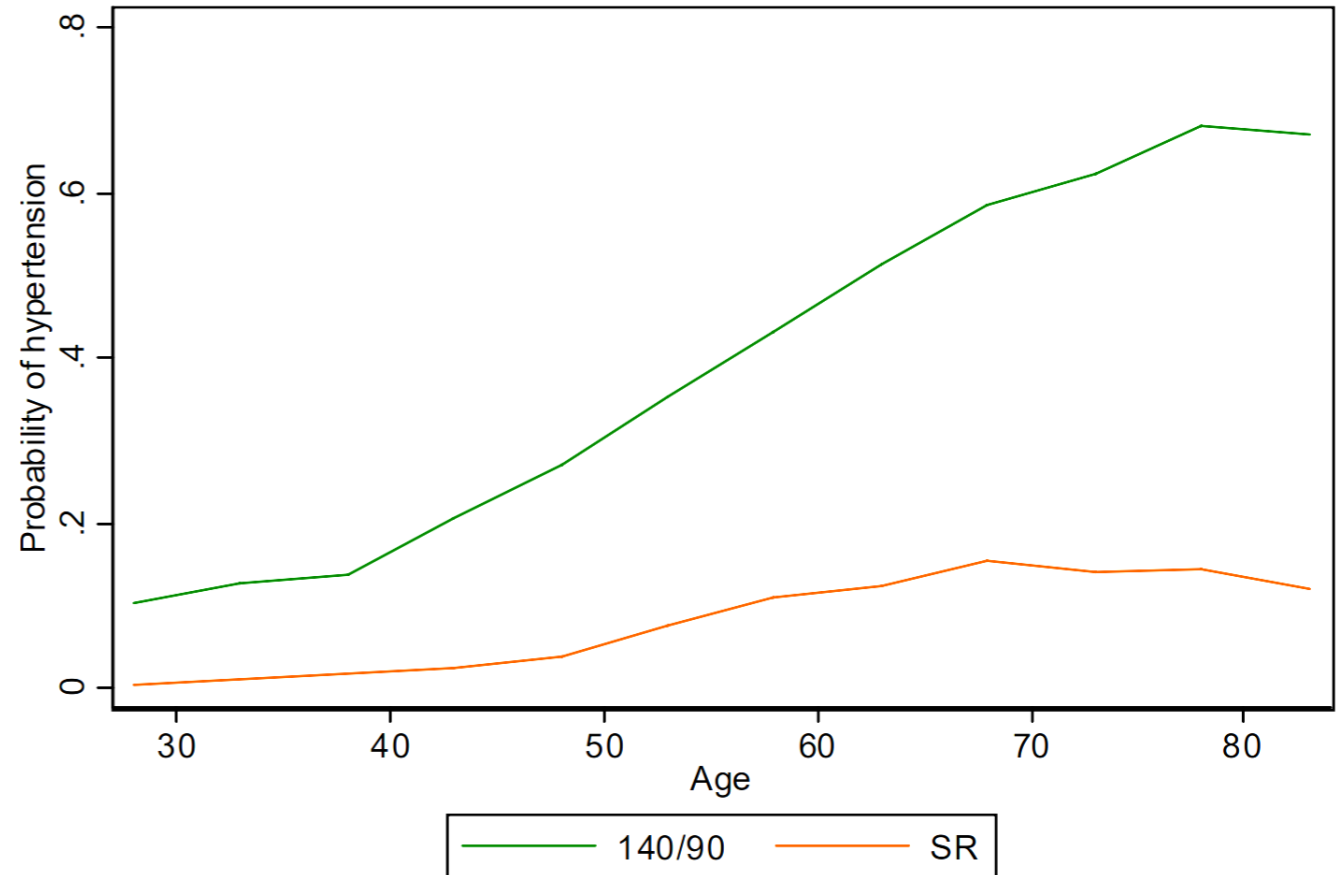
What is objective measure of cough?

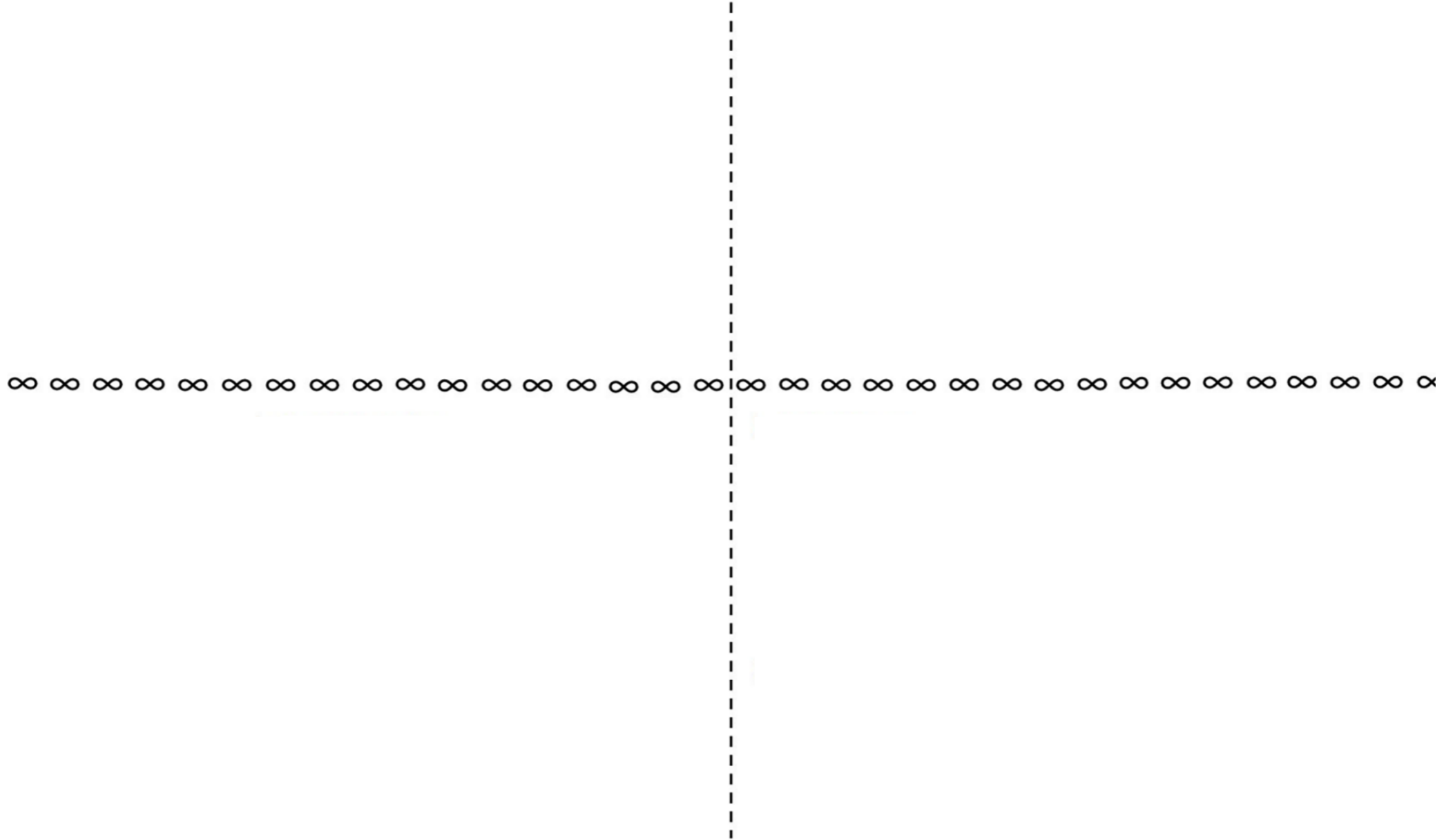
- Subjective
 - “decided by personal judgement, feeling, or opinions”
 - Patient reported
 - e.g.: Severity (NRS/VAS), frequency, diary, questionnaire (LCQ, COAT etc.)
- Objective
 - “not influenced by personal factor”
 - Quantifiable, consistently replicable
 - e.g.: frequency, intensity, sensitivity

Subjective vs. Objective

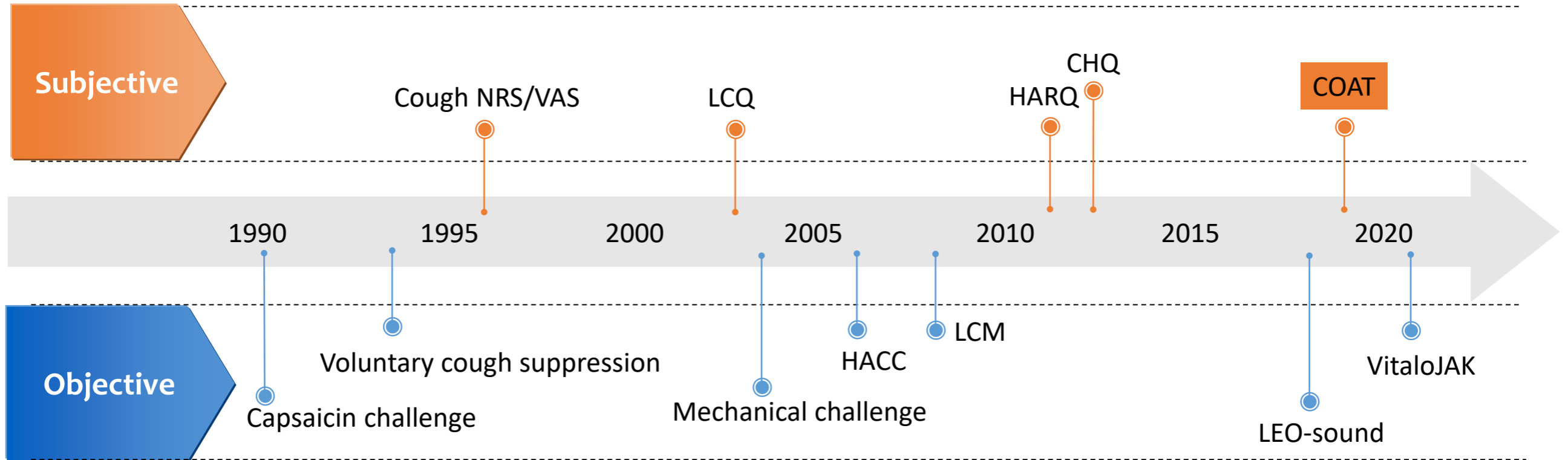
- Not quantifiable
- Lack of consistency
- Personal aspect
- Not truly represent reality

Figure 1: Self-Reported Chronic Hypertension and Objective Hypertension by Age

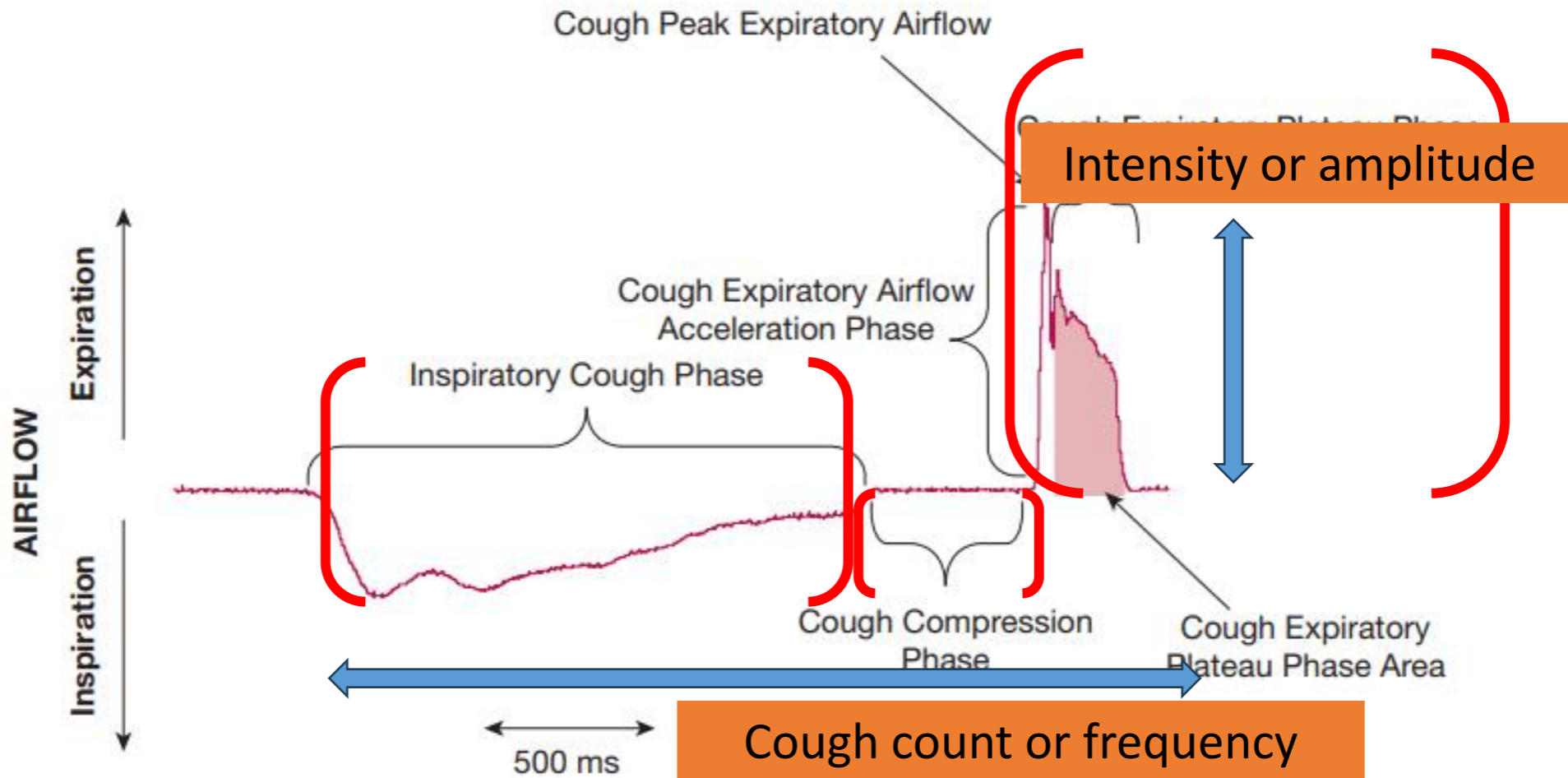




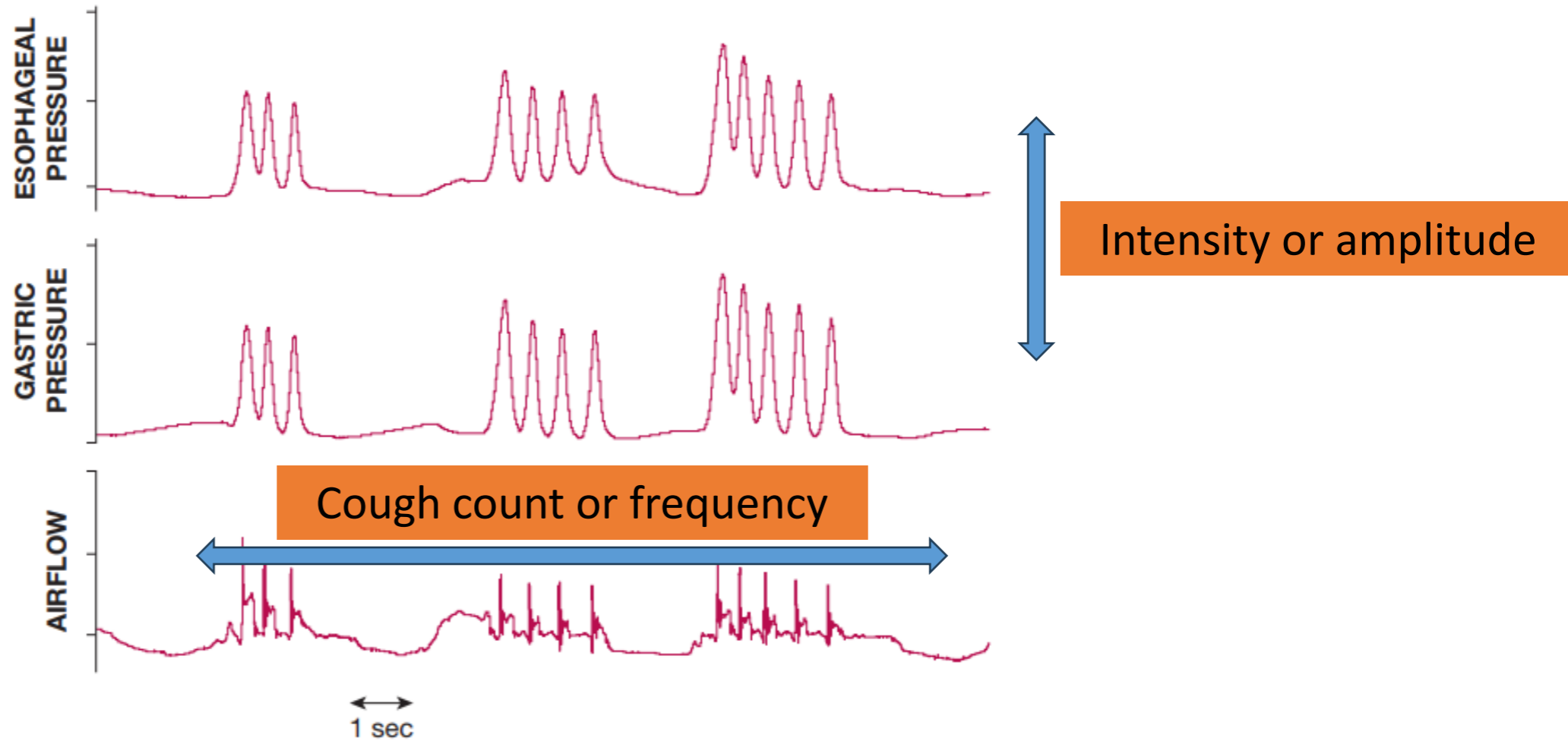
History of Subjective/Objective measures of cough



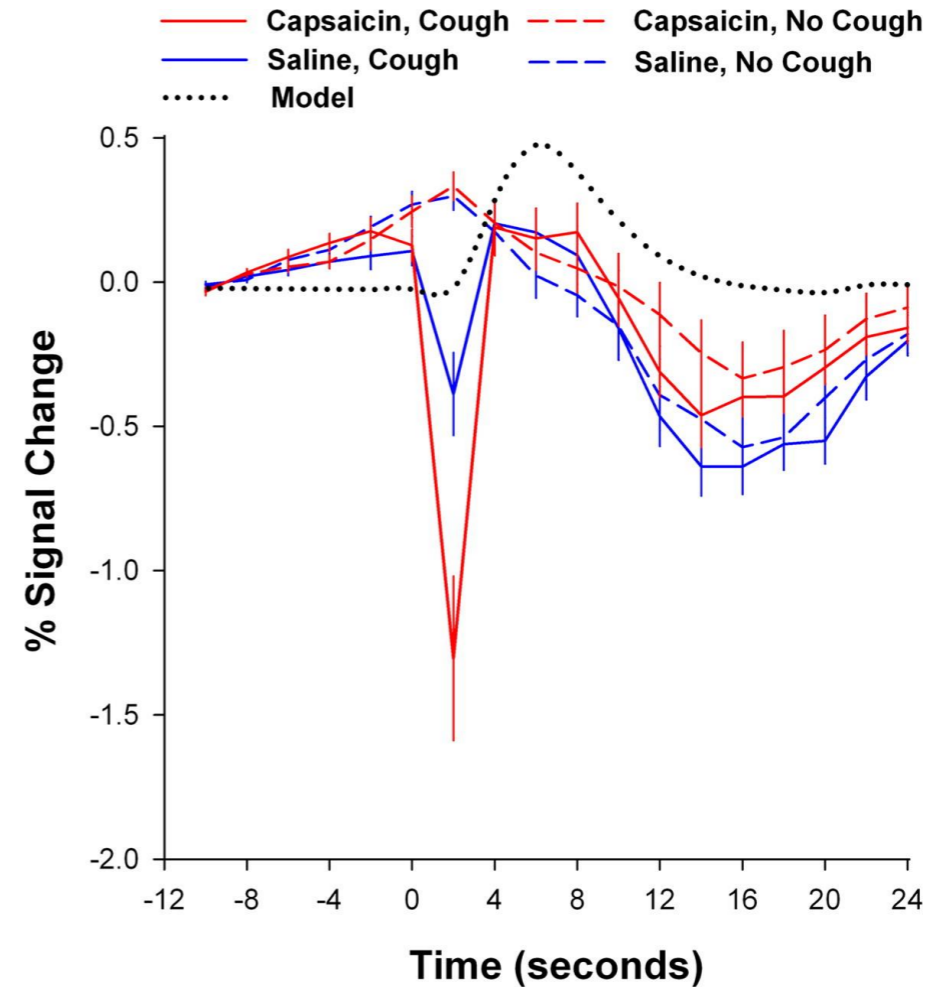
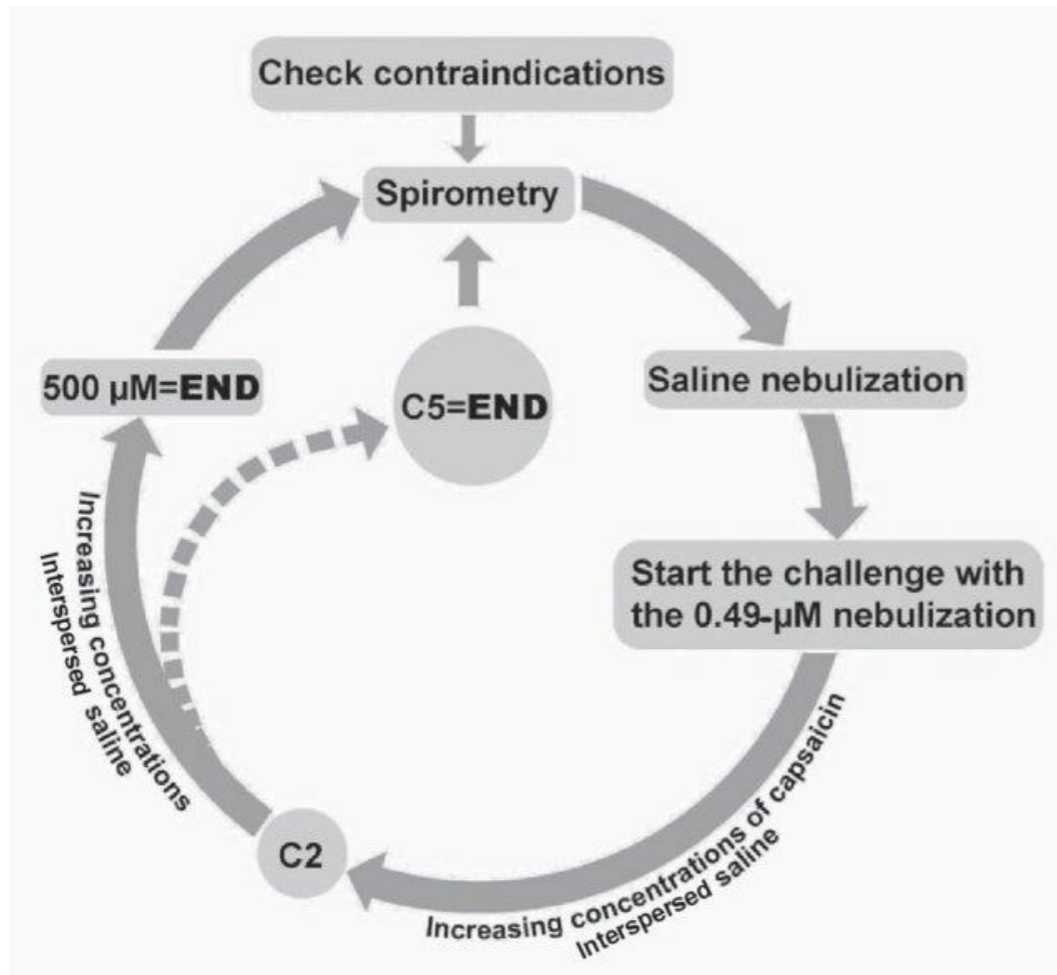
Cough: Airflow








Cough: Gastric and Esophageal pressure



Cough: threshold of trigger



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Cough frequency

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Future of cough measure and Summary

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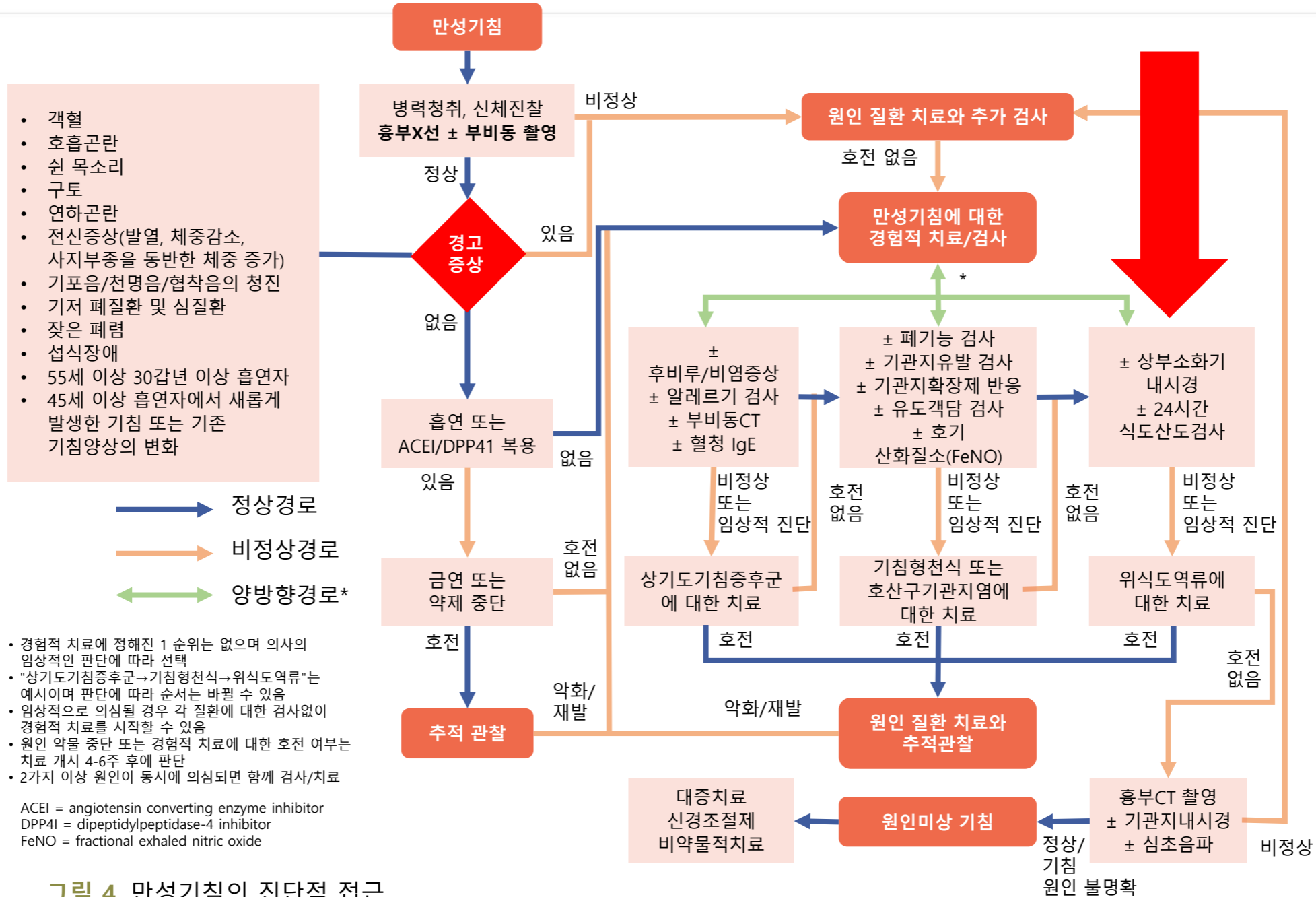
What is objective measure?

Cough intensity – Gastric / Esophageal Pressure

Cough frequency

Cough reflex sensitivity

Future of cough measure and Summary



- 경험적 치료에 정해진 1 순위는 없으며 의사의 임상적인 판단에 따라 선택
- "상기도기침증후군→기침형천식→위식도역류"는 예시이며 판단에 따라 순서는 바뀔 수 있음
- 임상적으로 의심될 경우 각 질환에 대한 검사없이 경험적 치료를 시작할 수 있음
- 원인 약물 중단 또는 경험적 치료에 대한 호전 여부는 치료 개시 4-6주 후에 판단
- 2가지 이상 원인이 동시에 의심되면 함께 검사/치료

대증치료
신경조절제
비약물적치료

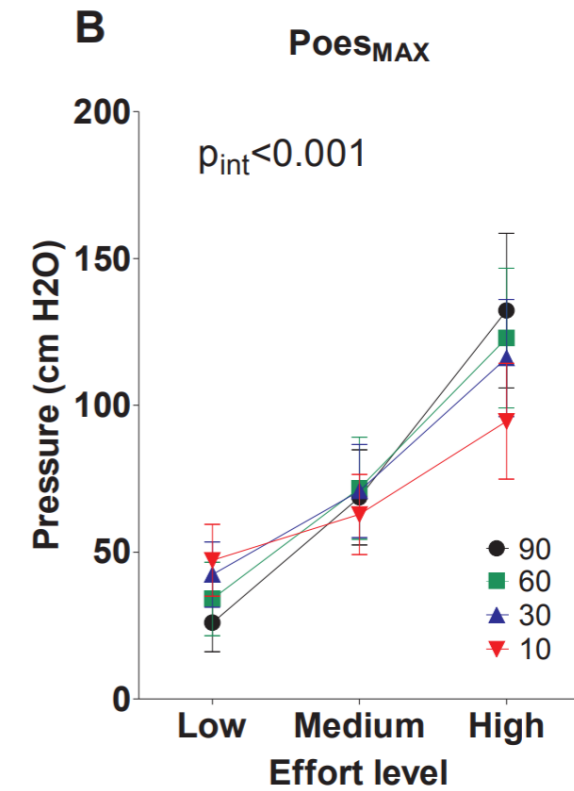
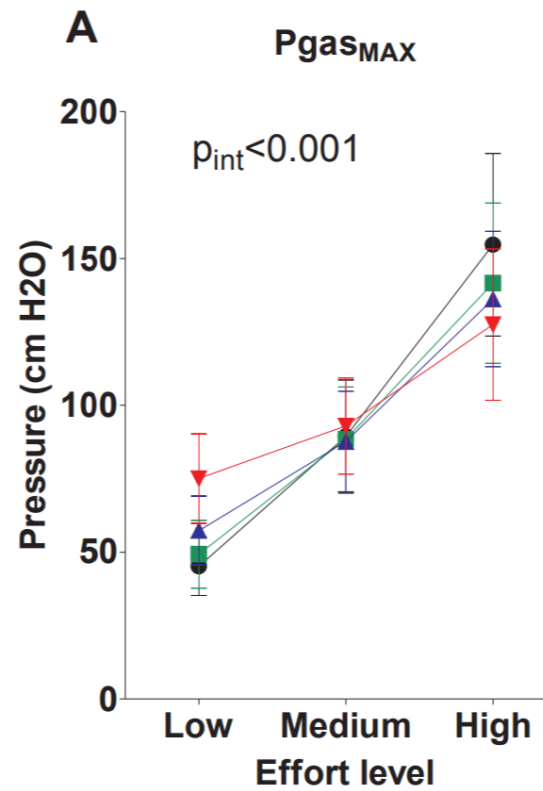
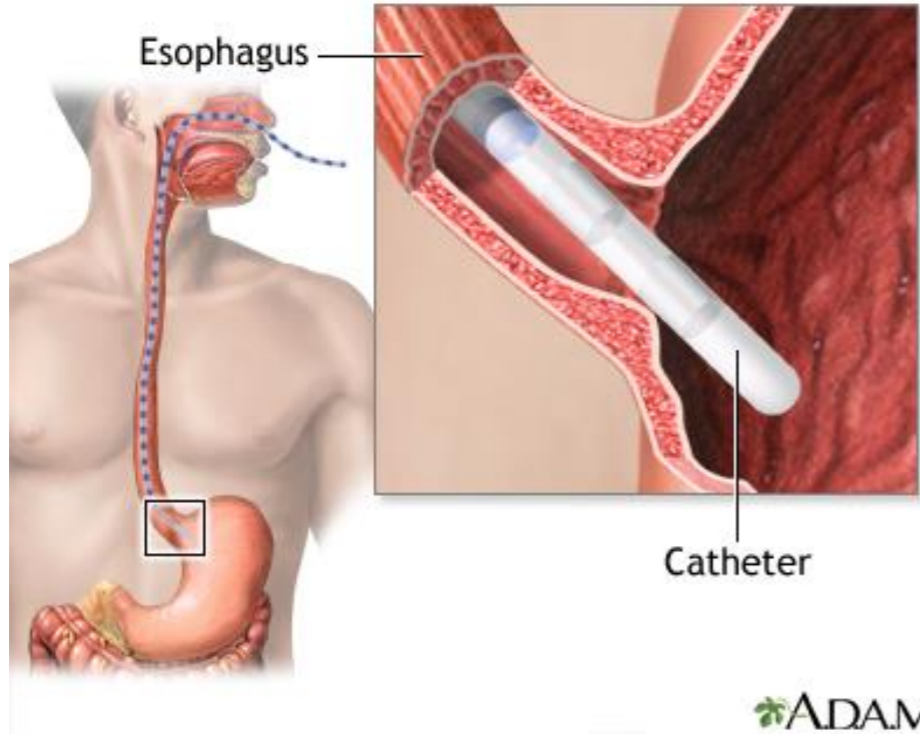
원인미상 기침

홍부CT 촬영
± 기관지내시경
± 심초음파

정상/
기침
원인 불명확

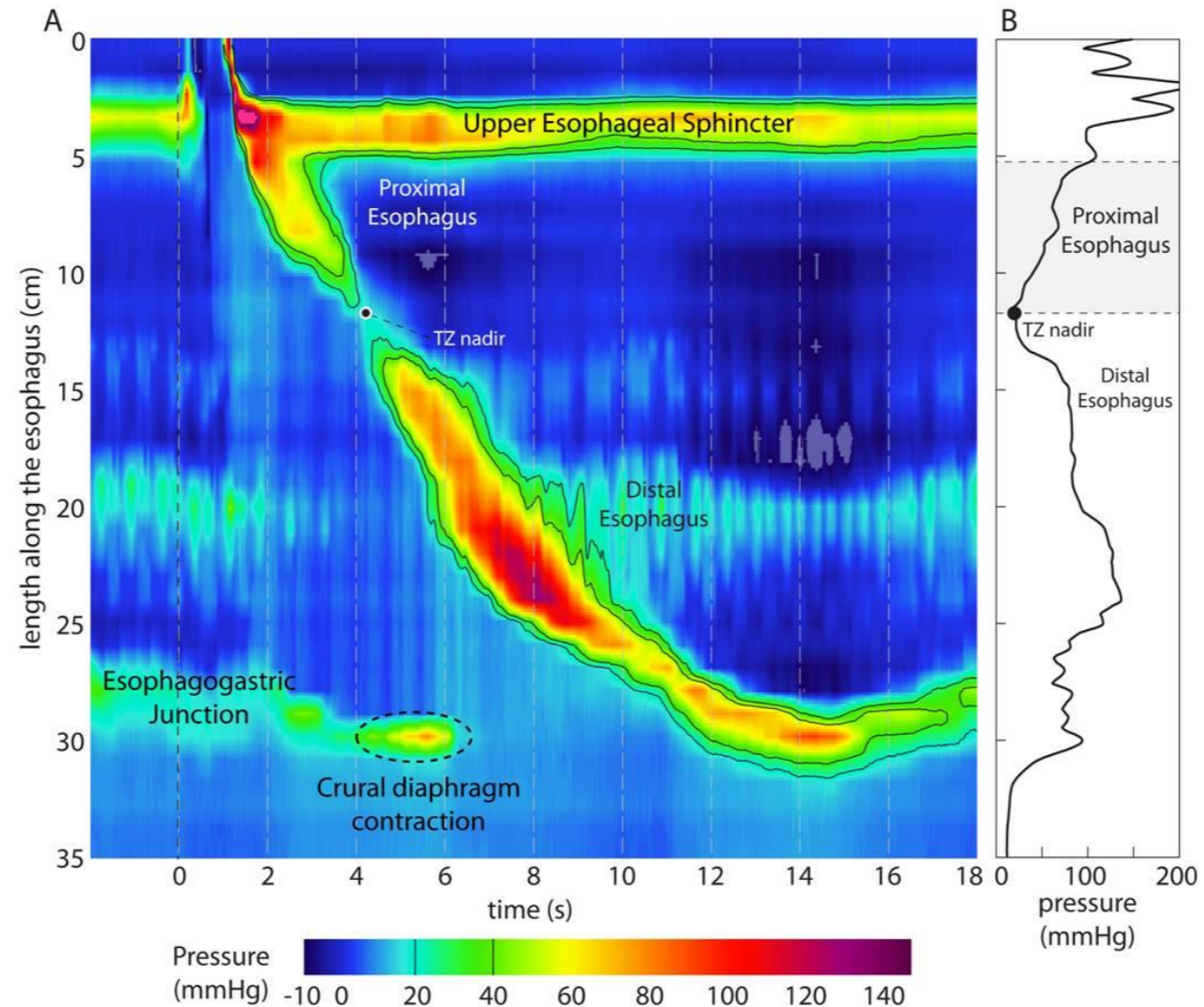
비정상

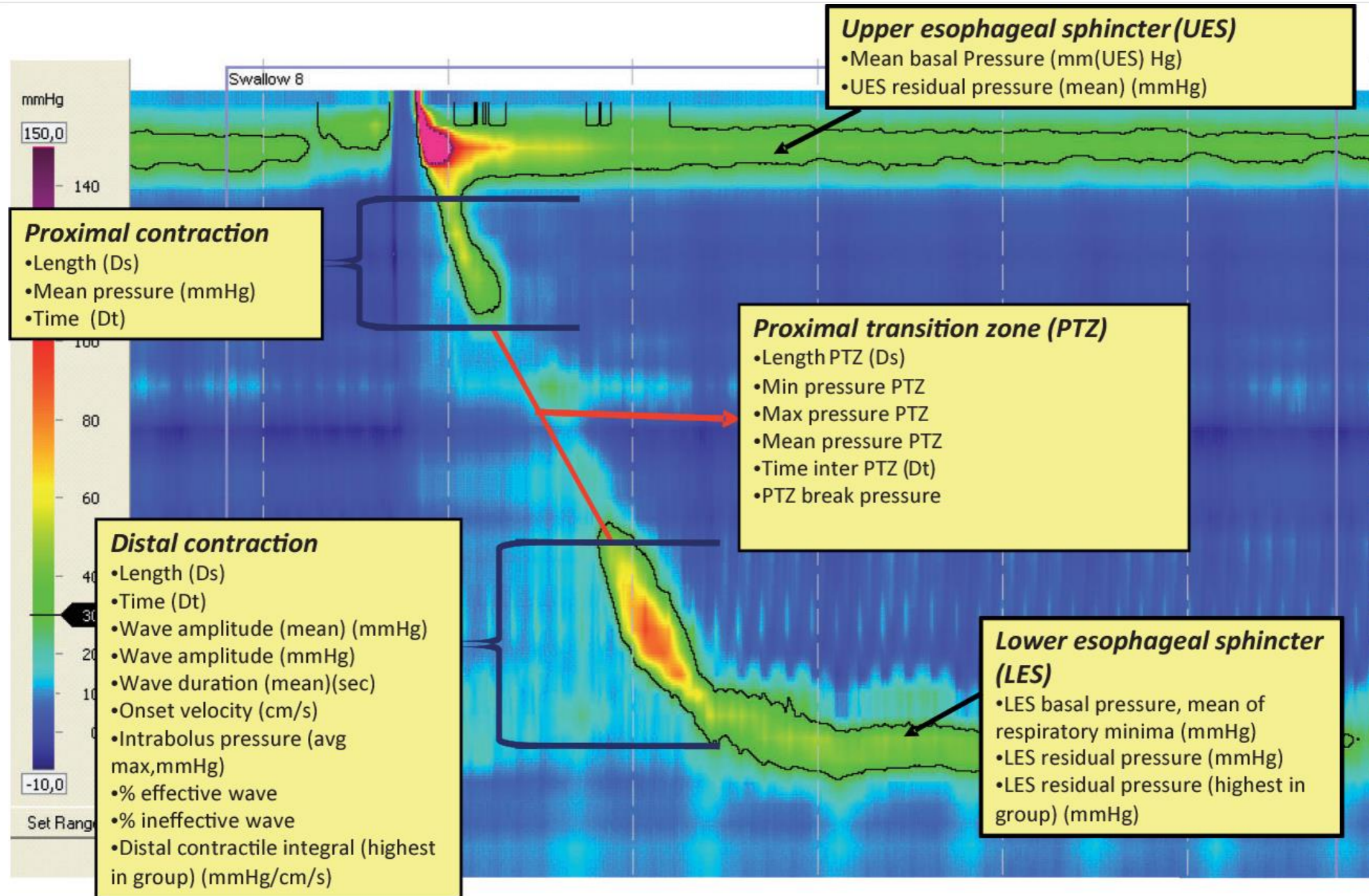
Gastric / Esophageal pressure - Manometry



Gastric (P_{ga}) and oesophageal pressure (P_{oes})

Gastric / Esophageal pressure - High Resolution Manometry (HRM)





HRM

- Objective marker for weak peristalsis

- Figure C: Long-break = weak peristalsis ($\geq 5\text{cm}$)

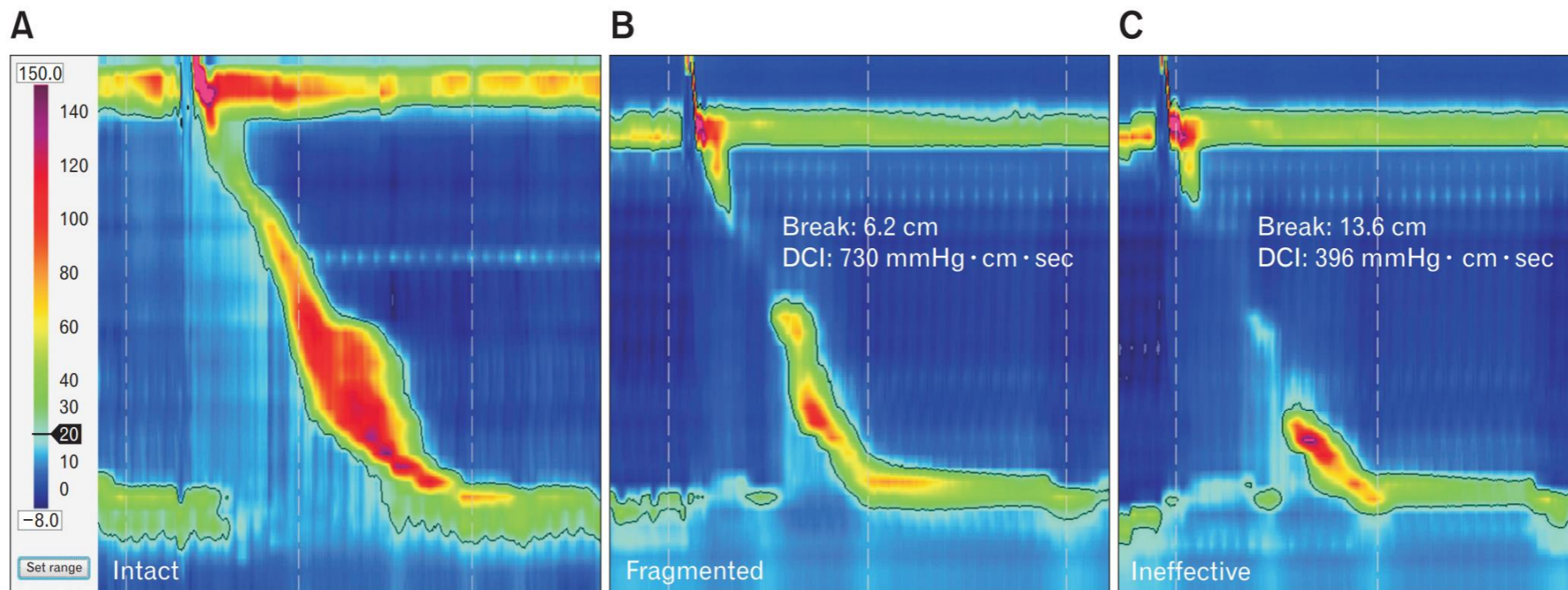
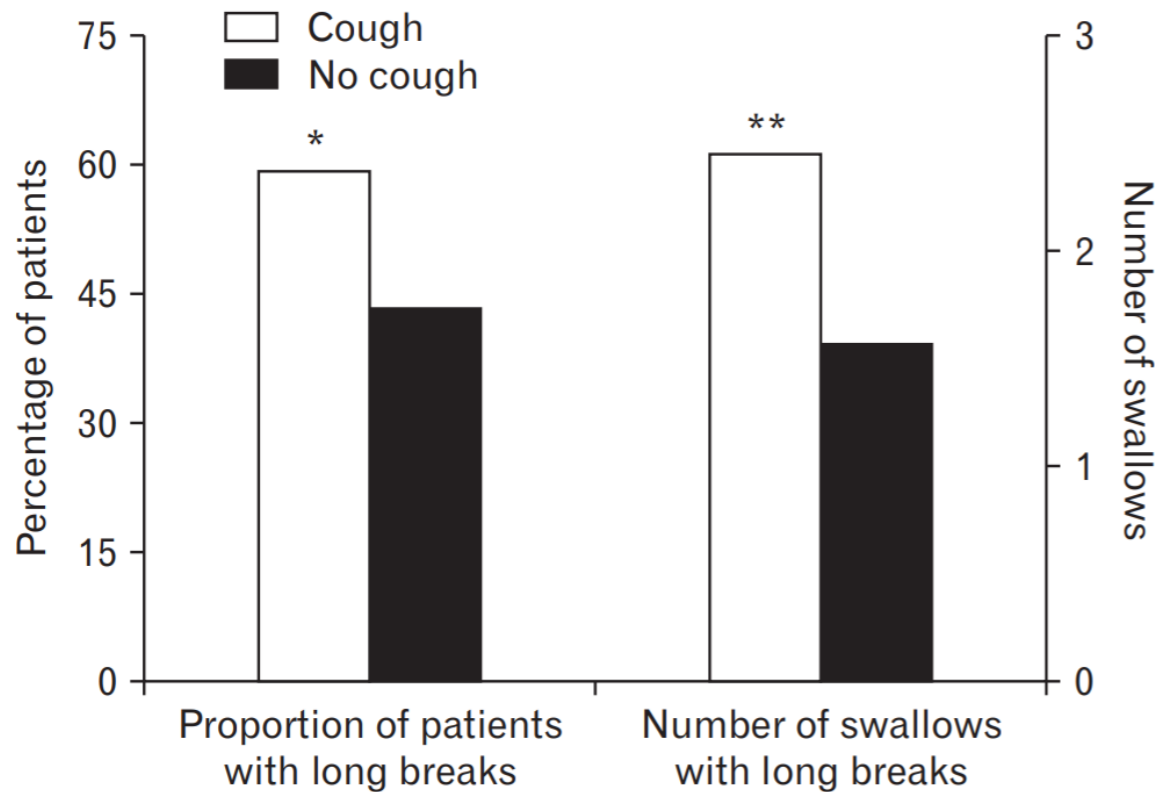


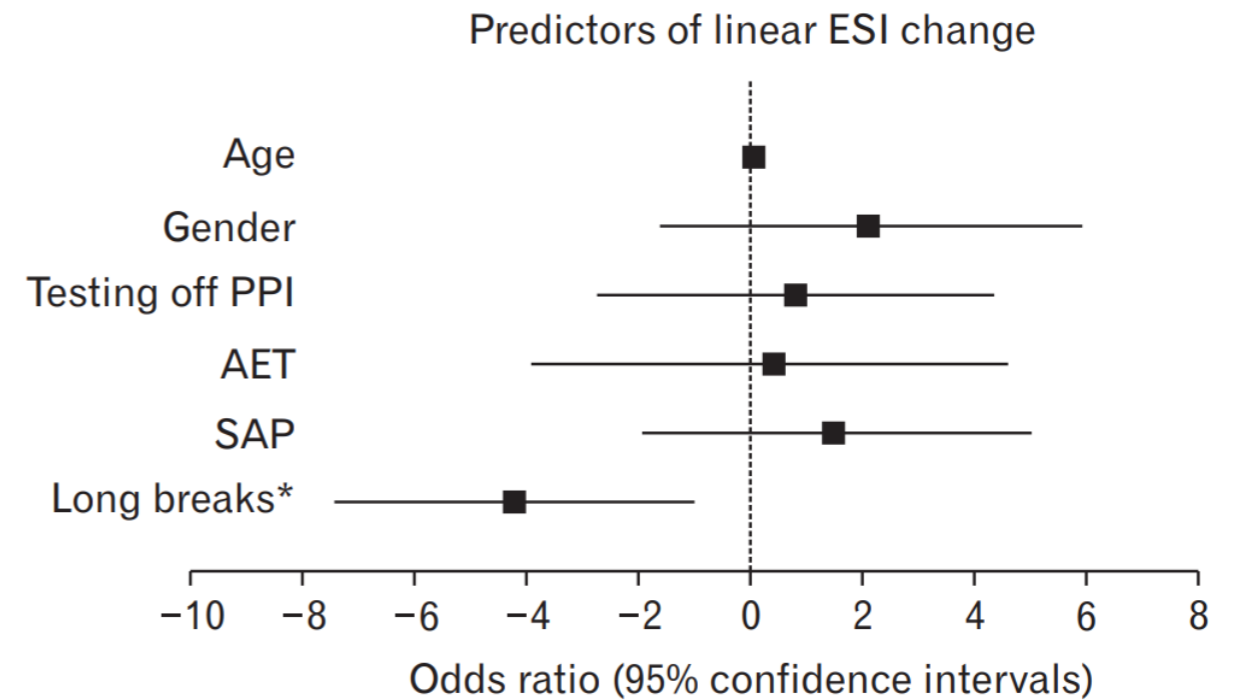
Figure 1. High-resolution manometry Clouse plots demonstrating (A) intact peristaltic contour in an effective swallow, (B) fragmented sequence with a long ($> 5\text{ cm}$) break, and (C) ineffective sequence with a long break.

Long break in HRM






- Higher in Cough patient, Predictor of poor outcome



Outcome of anti-reflux treatment in Cough patients



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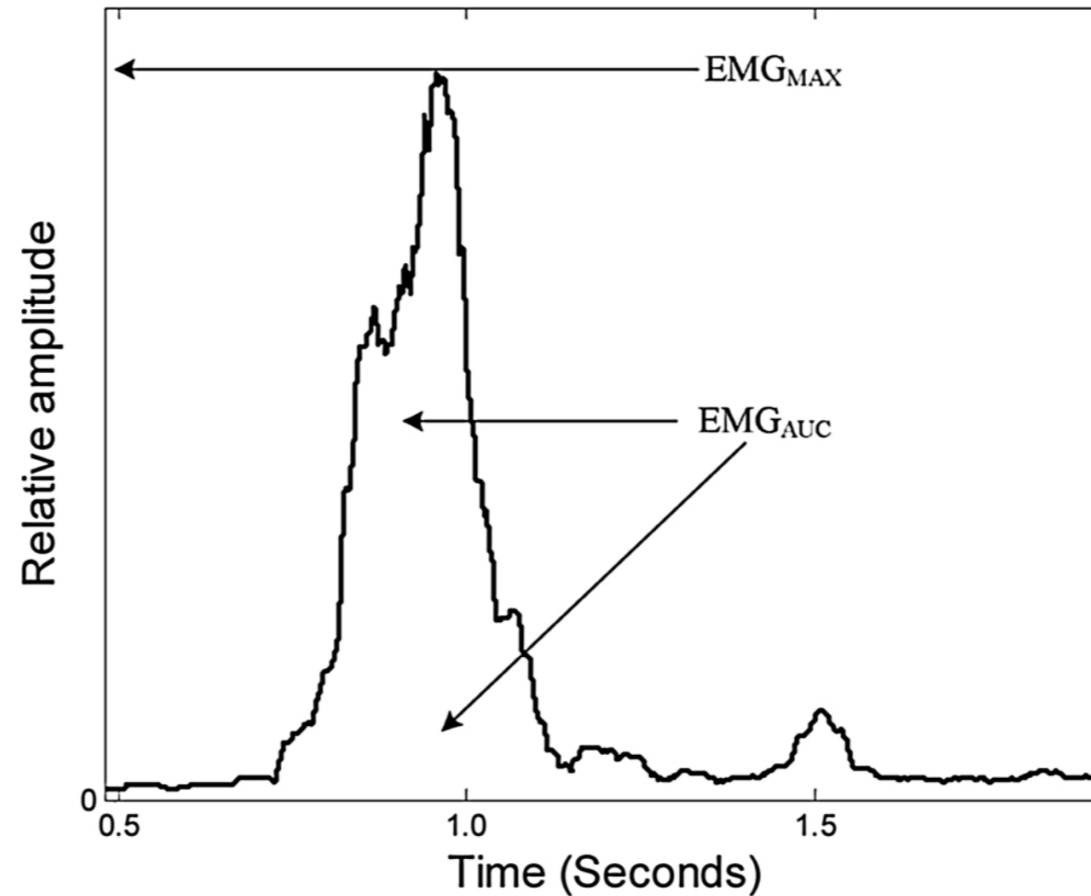
Cough intensity – EMG

Cough frequency

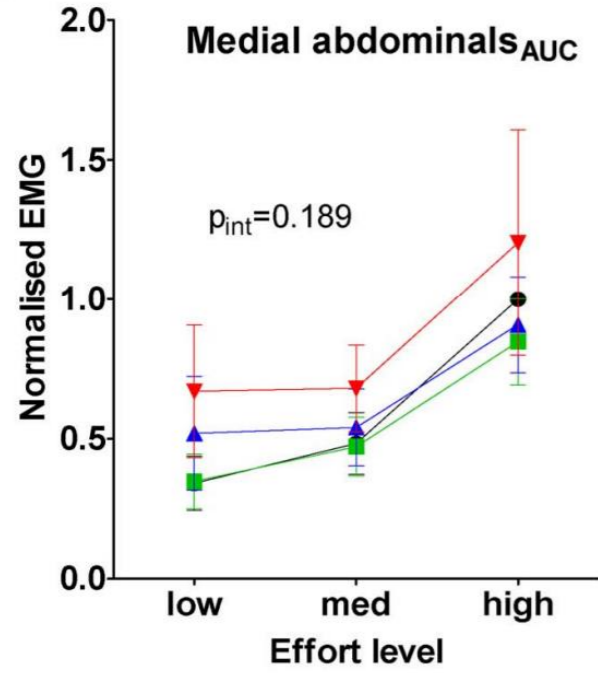
Cough reflex sensitivity

Future of cough measure and Summary

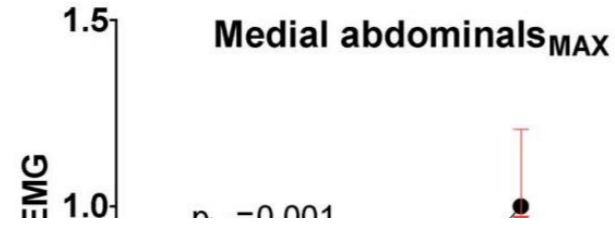
EMG for cough effort level



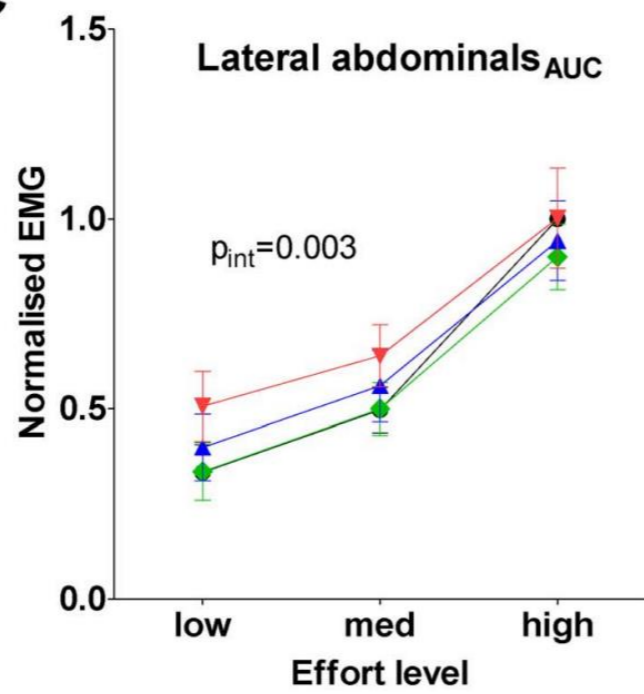
A



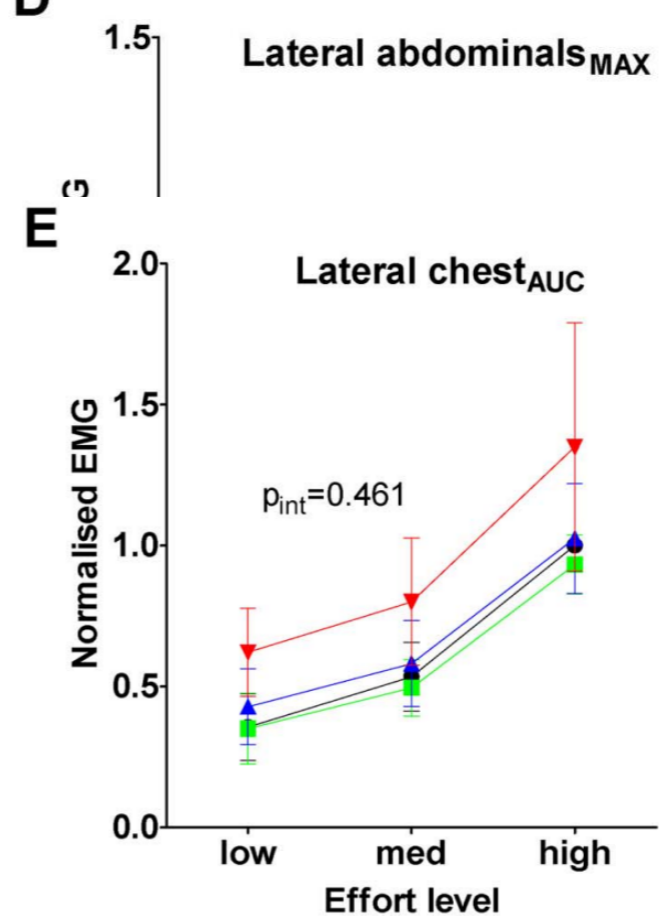
B



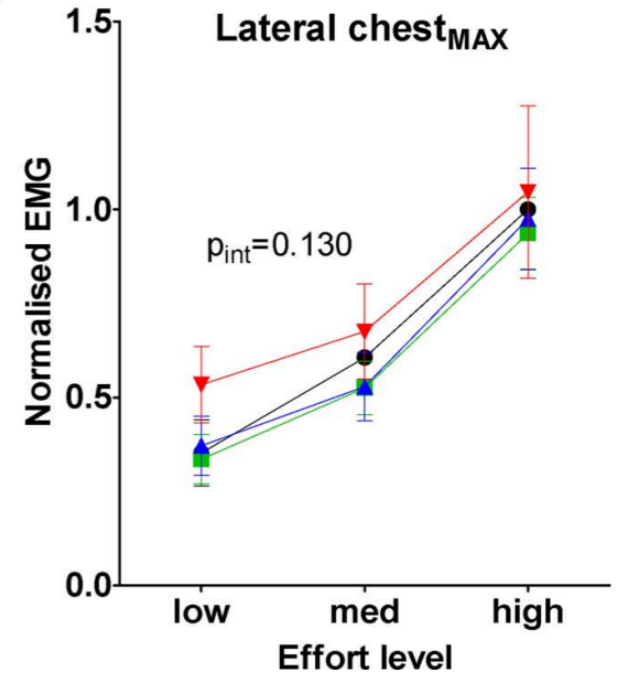
C



D



F



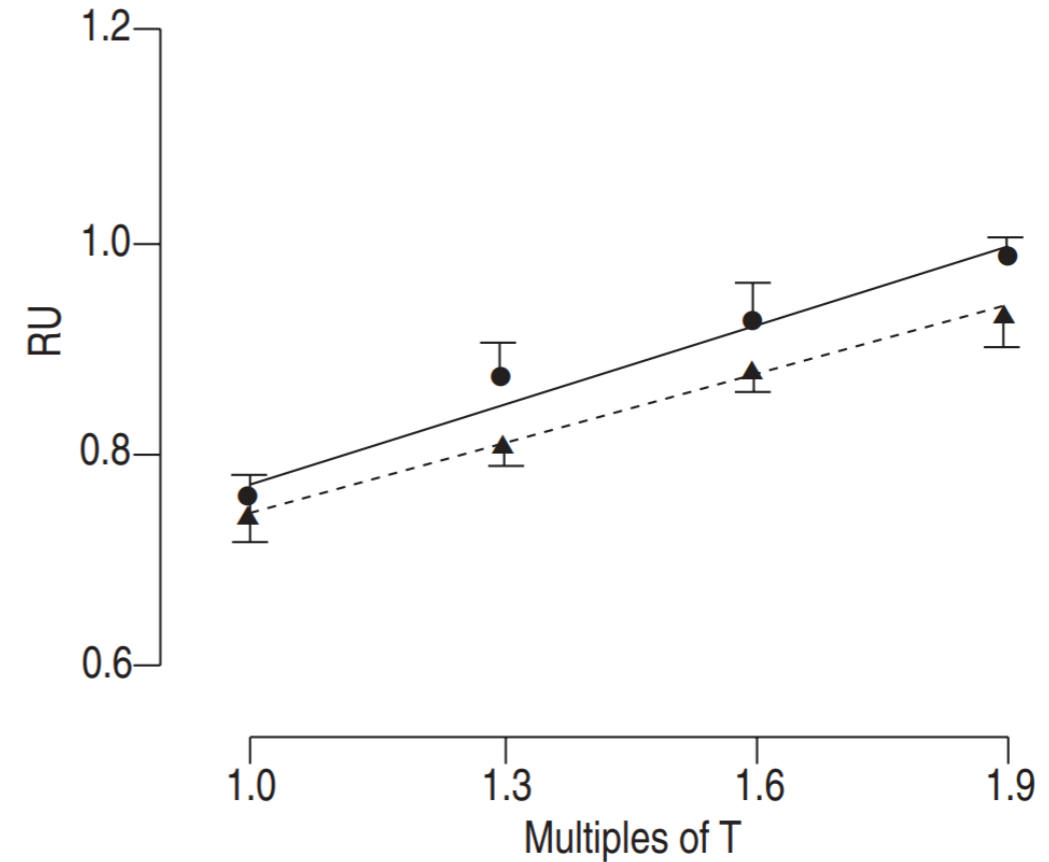
EMG for cough muscle threshold

Eur Respir J 1997; 10: 983-989
DOI: 10.1183/09031936.97.10050983
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European Respiratory Journal
ISSN 0903 - 1936

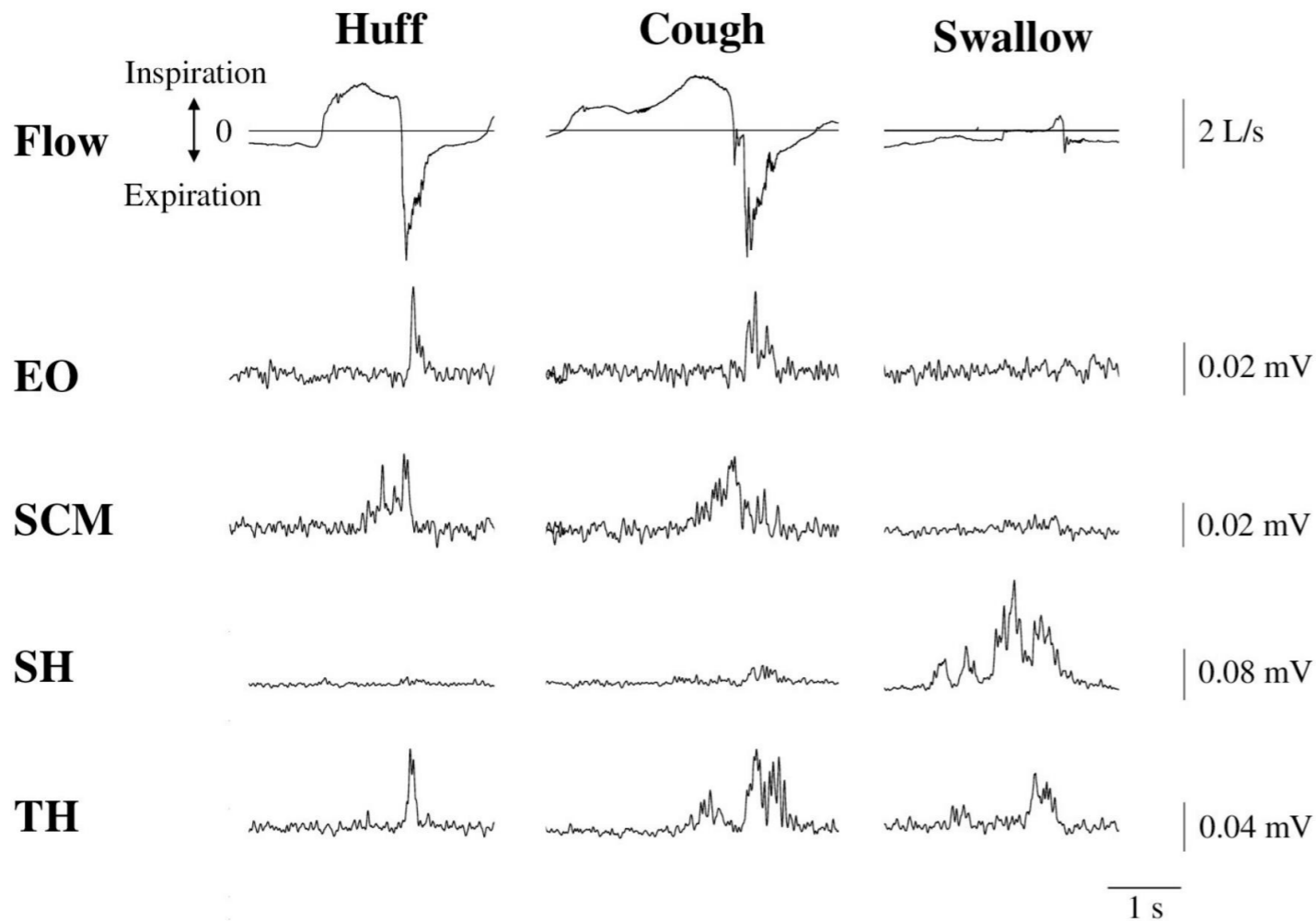
A noninvasive electromyographic study on threshold and intensity of cough in humans

G.A. Fontana*, T. Pantaleo**, F. Lavorini*, V. Boddi+, P. Panuccio*



Relationship of IEMGp (●) and IEMGp/tEC (▲) and cough stimulus intensity (cough threshold values (T)), $r^2=0.754$; $p<0.01$

EMG for distinguishing cough, huff, and swallowing



EO, external oblique muscle

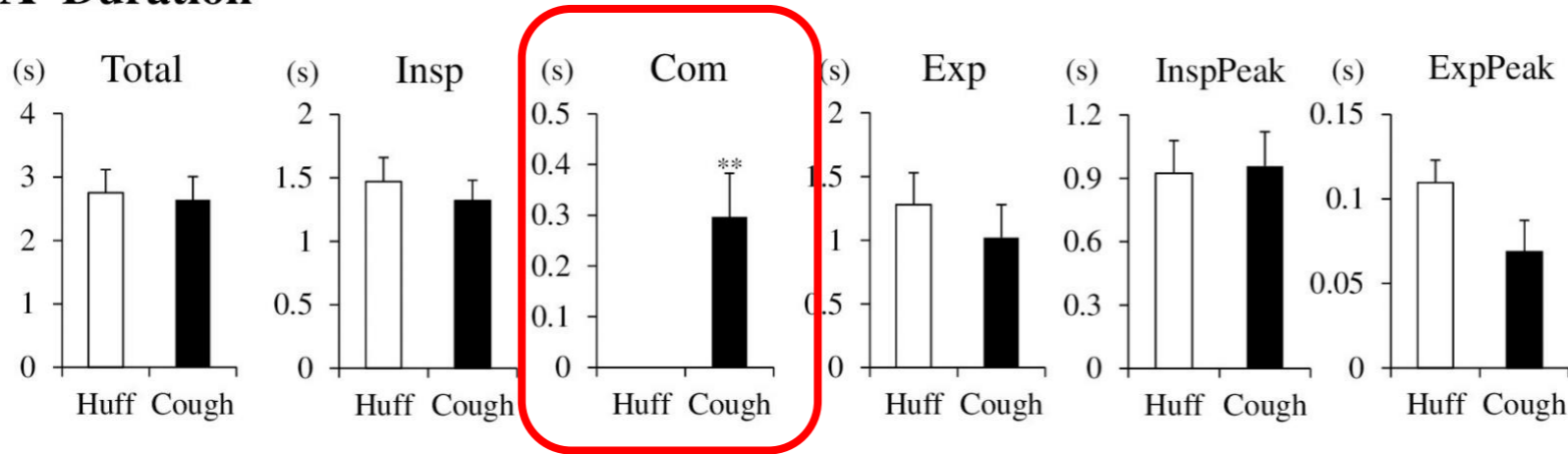
SCM, sternocleidomastoid muscle

SH, suprahyoid muscles

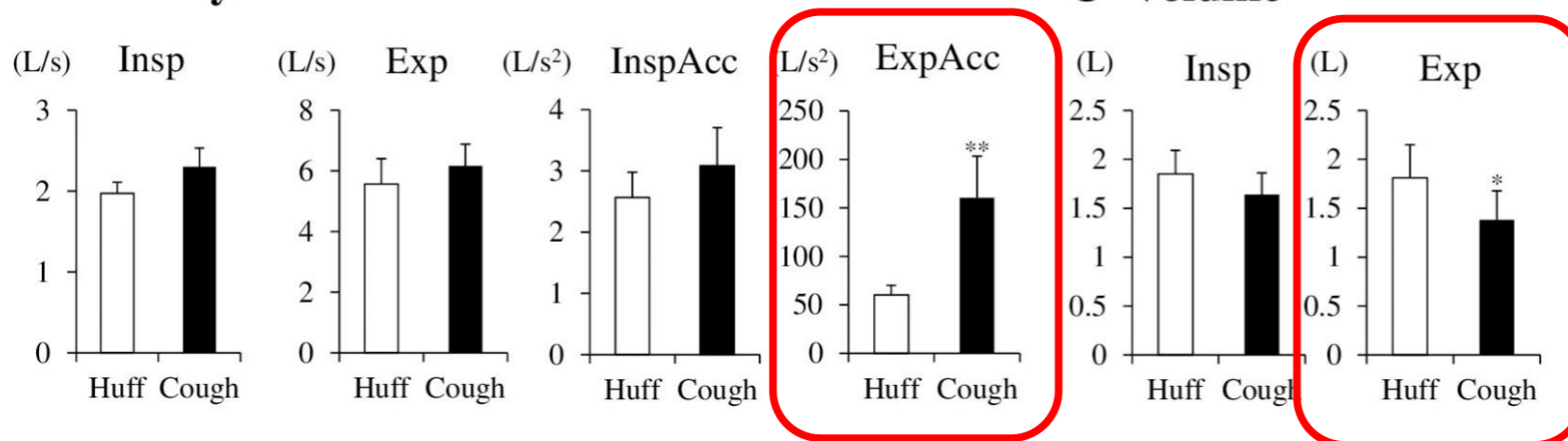
TH, thyrohyoid muscle

EMG for distinguishing cough, huff, and swallowing

A Duration








B Velocity



Com: Compression phase

ExpAcc: Expiratory Acceleration

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What is objective measure?

Cough intensity – Peak Cough Flow

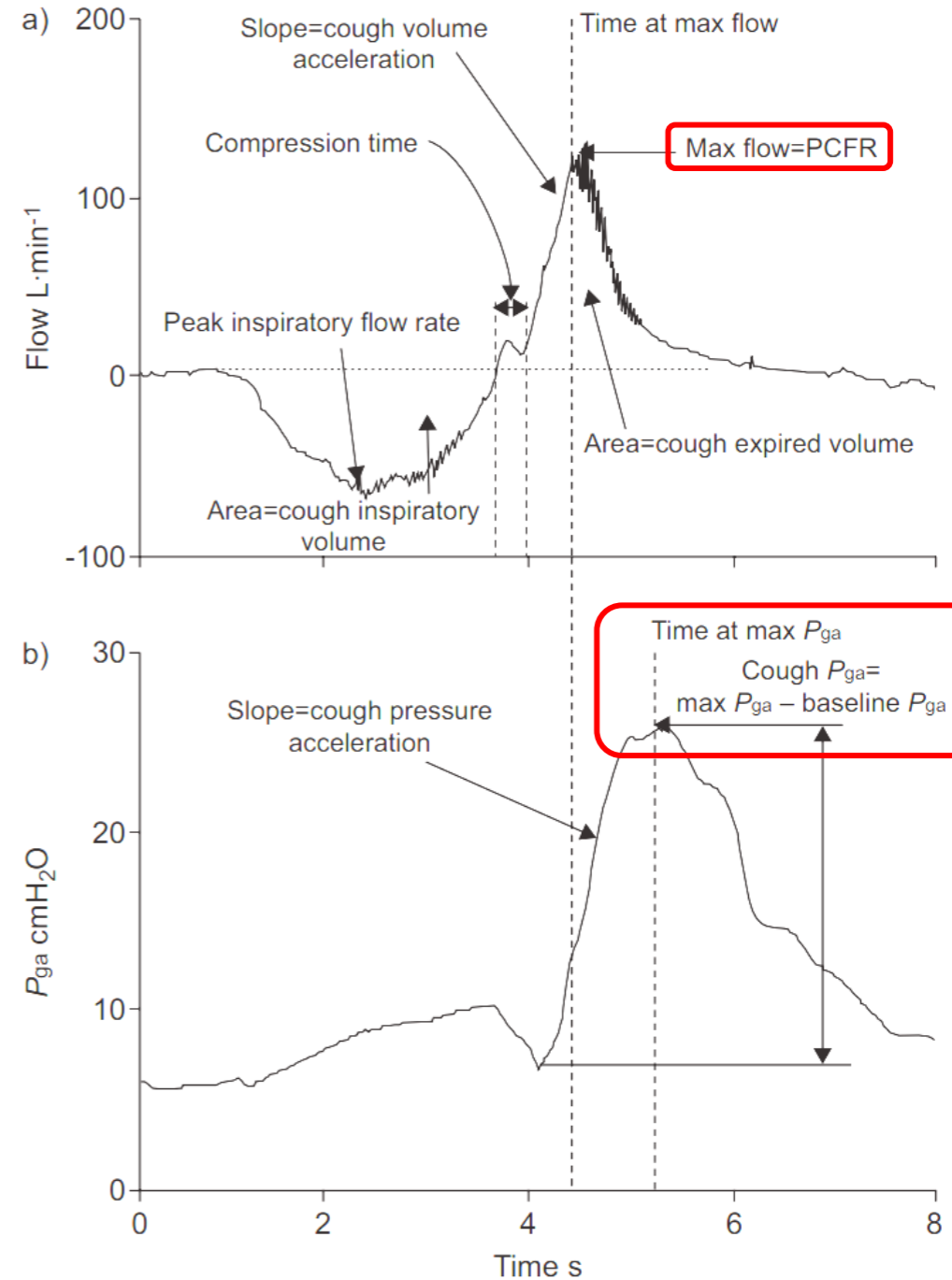
Cough frequency

Cough reflex sensitivity

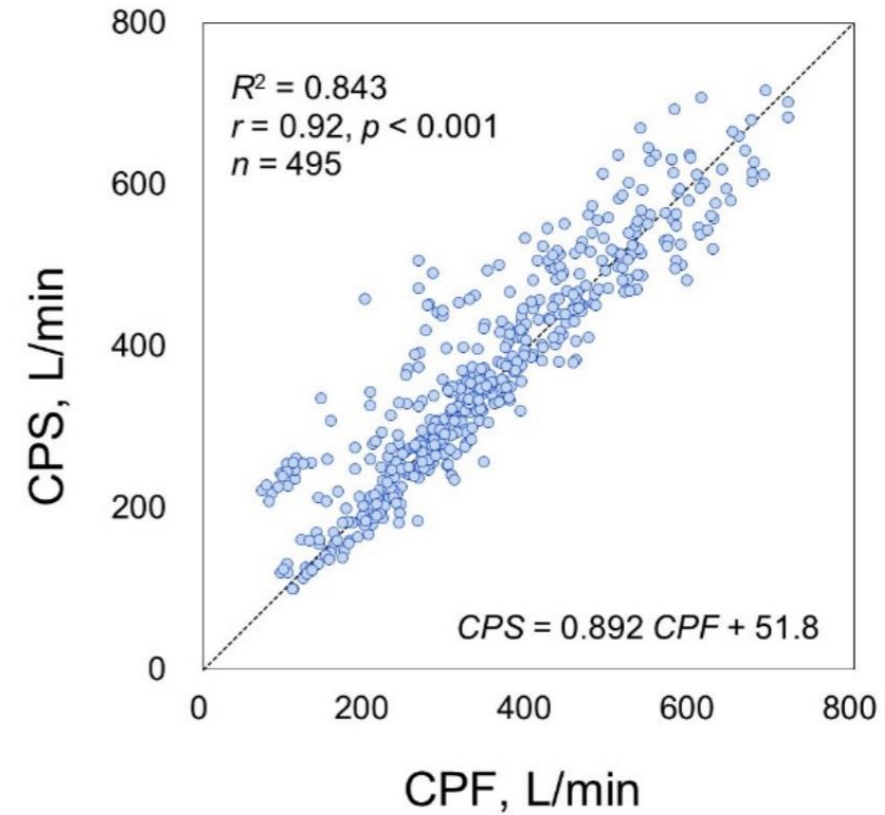
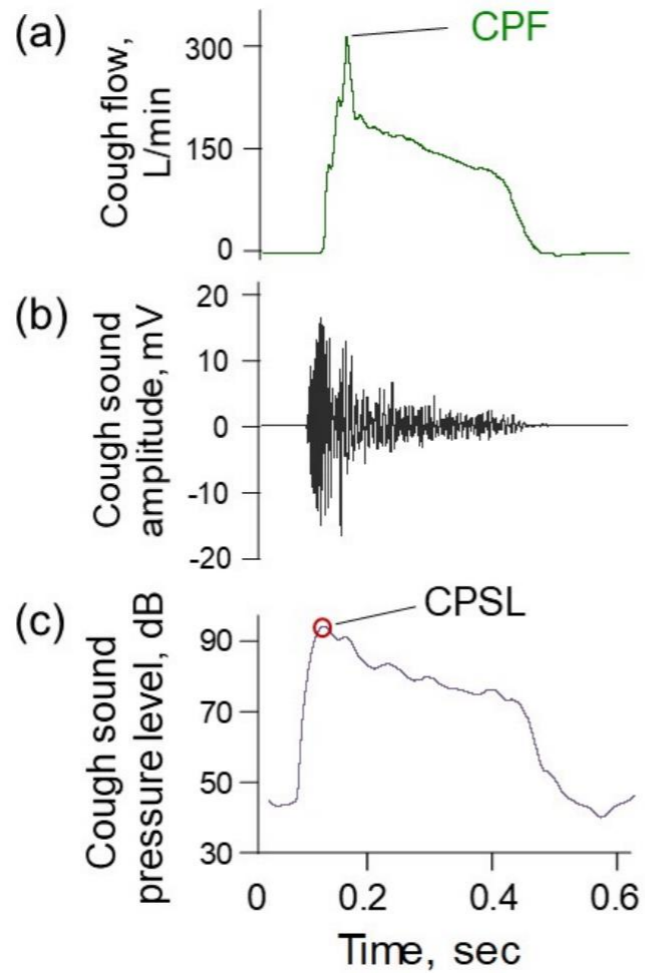
Future of cough measure and Summary

Peak cough flow






- Evidence with peak expiratory flow
- Other chronic disease
- Lack of evidence with cough as result



PCF with other measures



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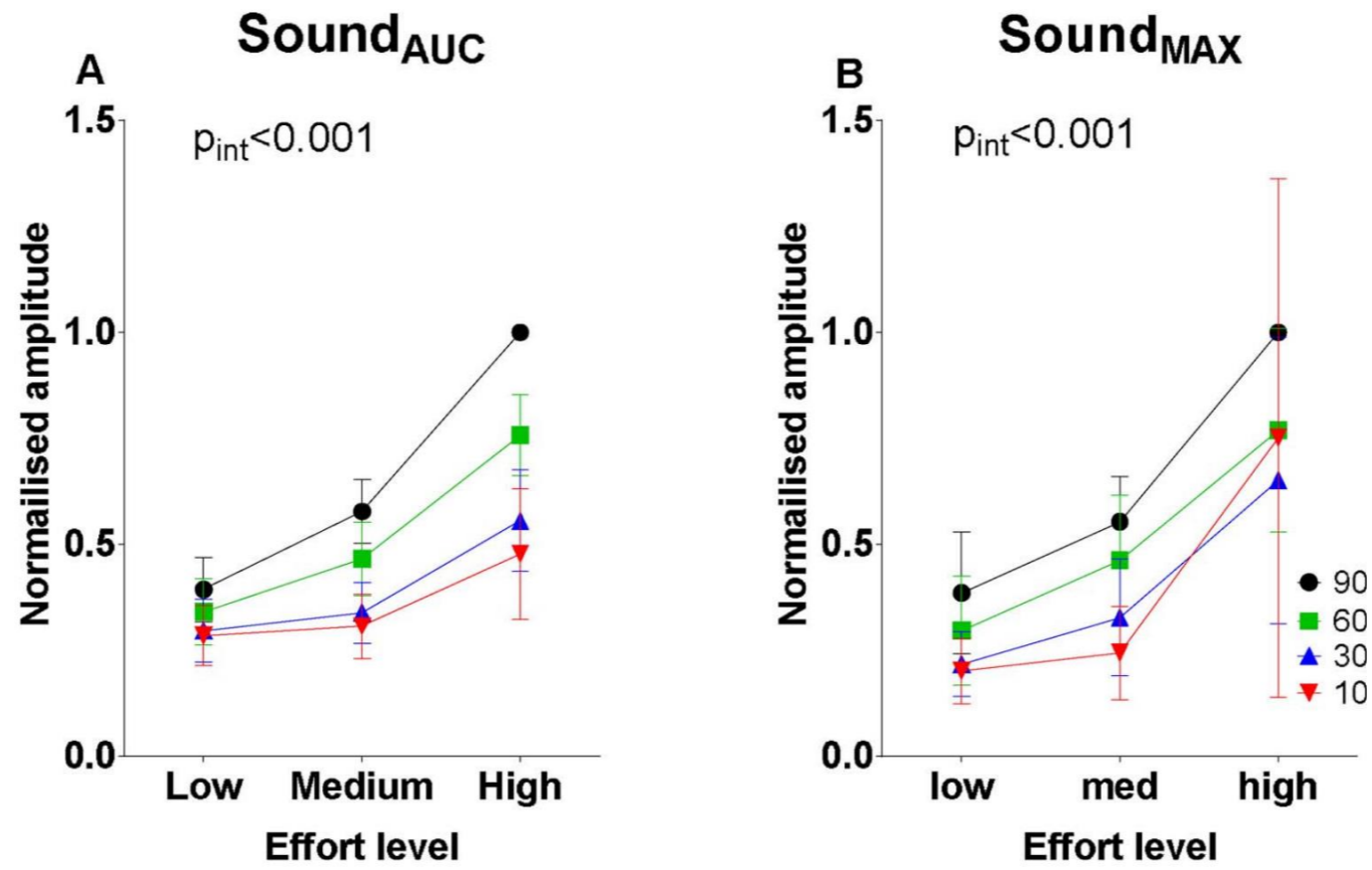
Cough intensity – Cough Sound

Cough frequency

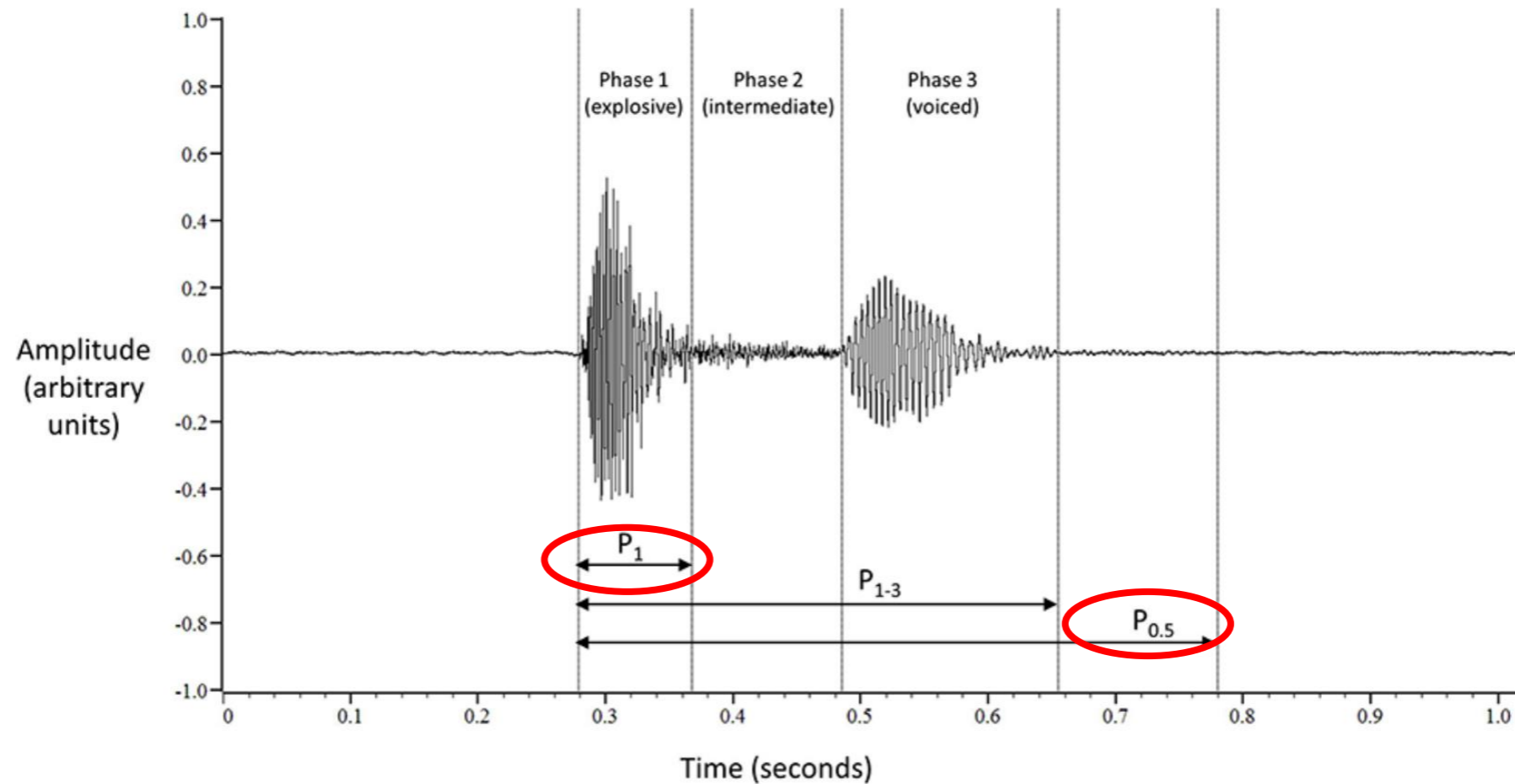
Cough reflex sensitivity

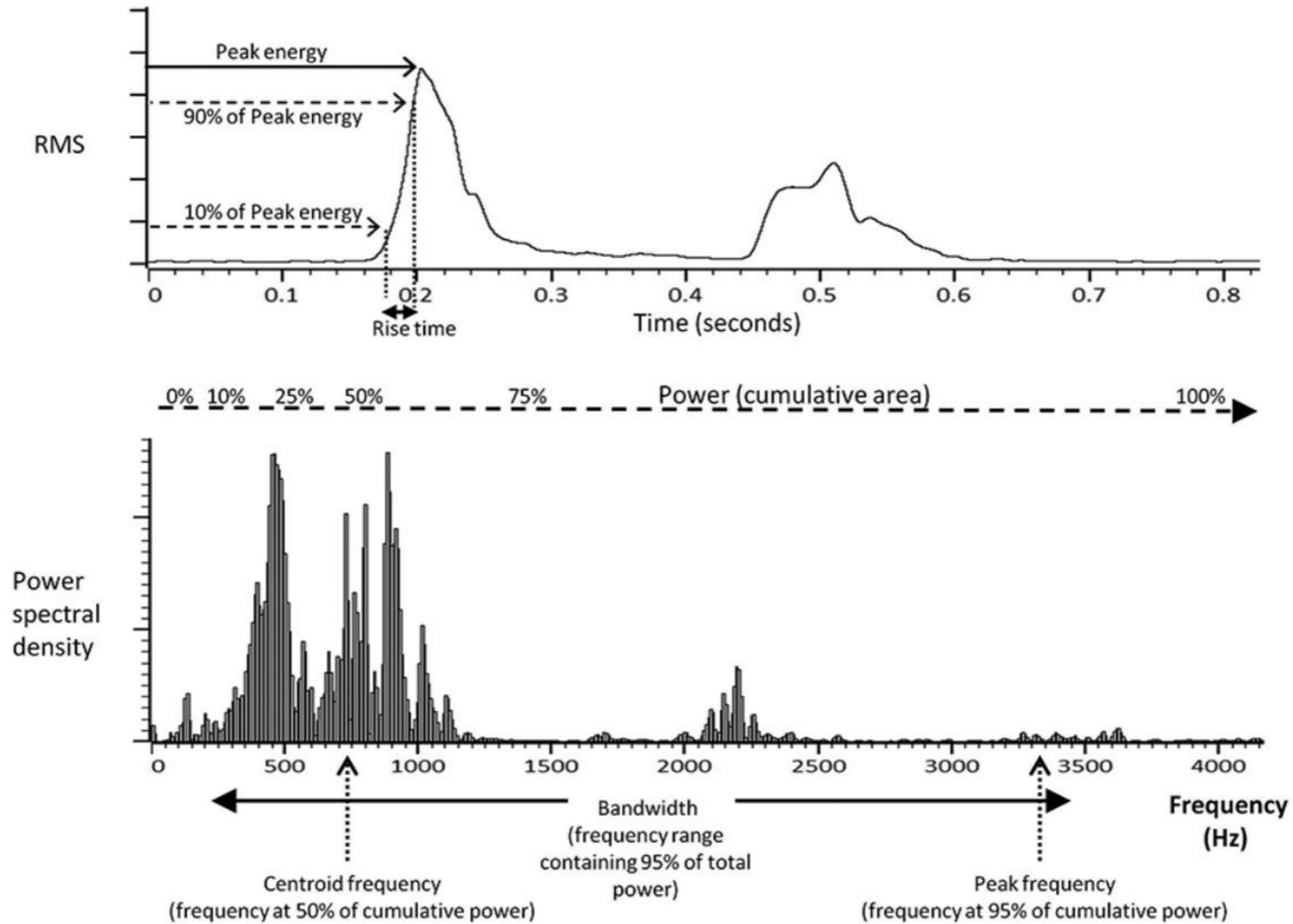
Future of cough measure and Summary

Cough sound and cough efforts

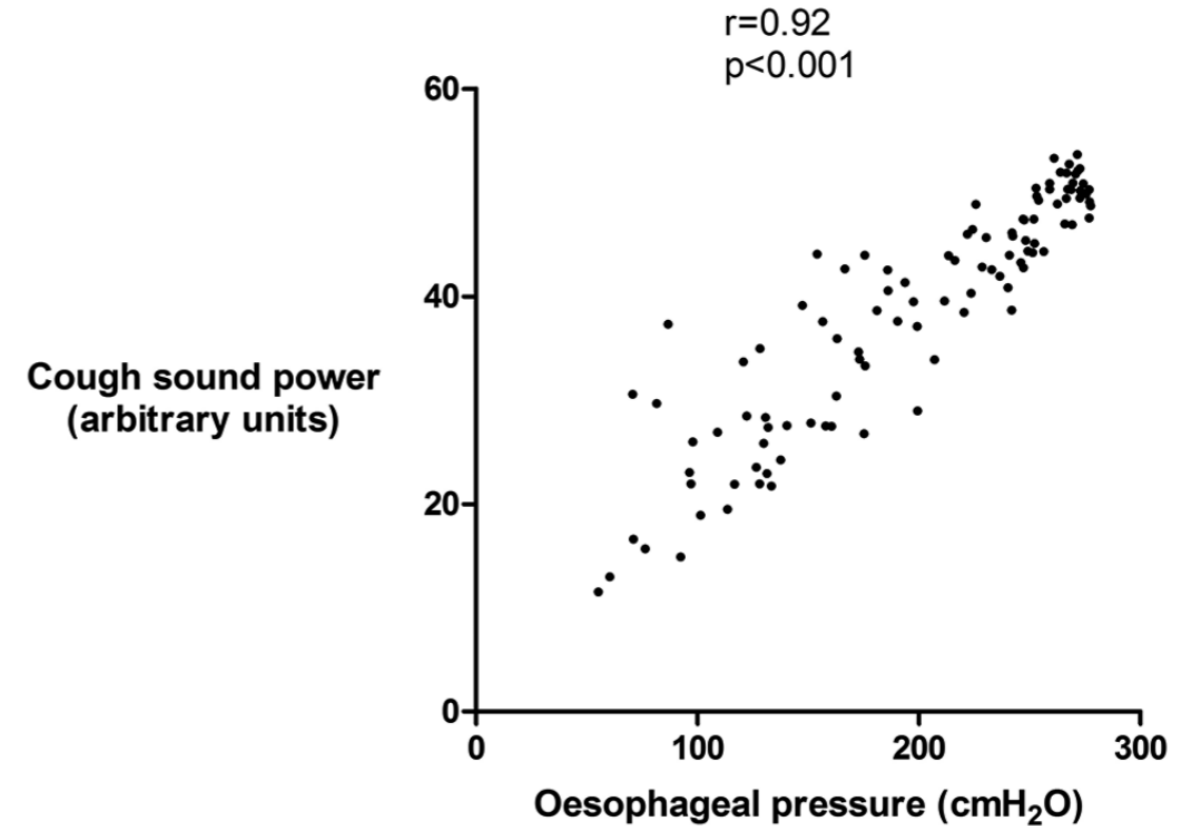
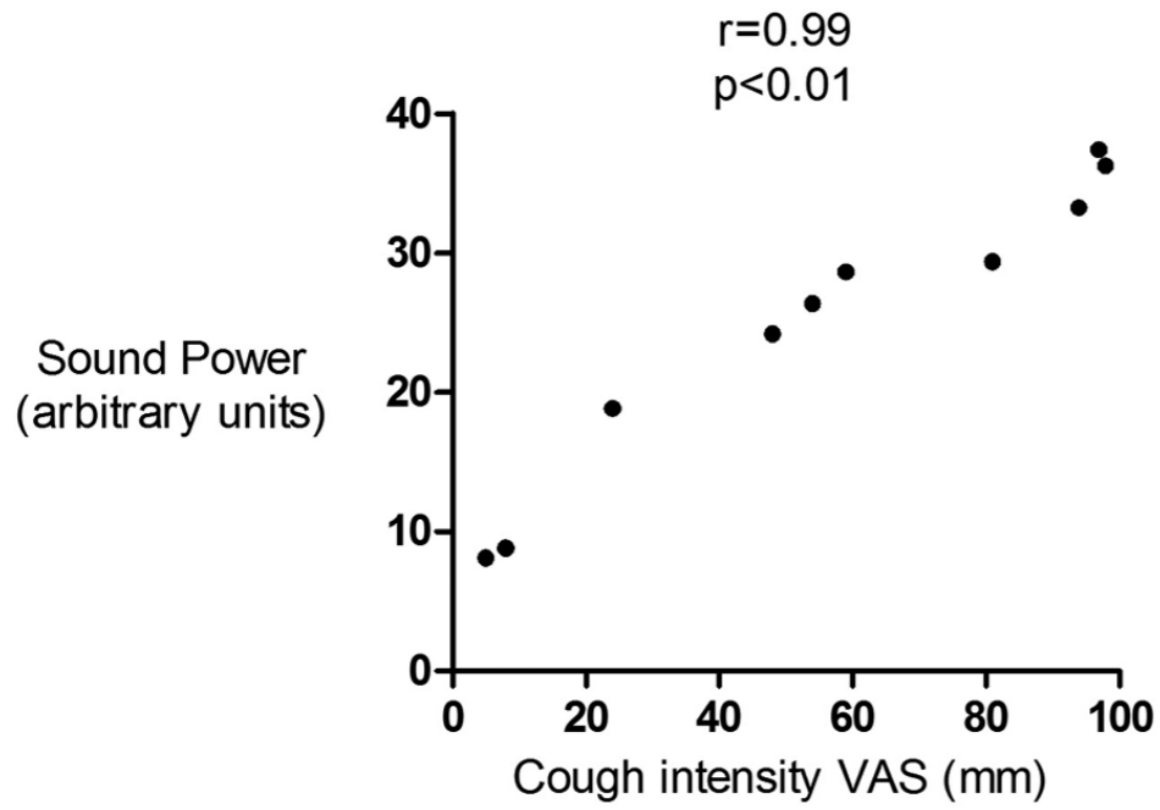


Phase of Cough Sound



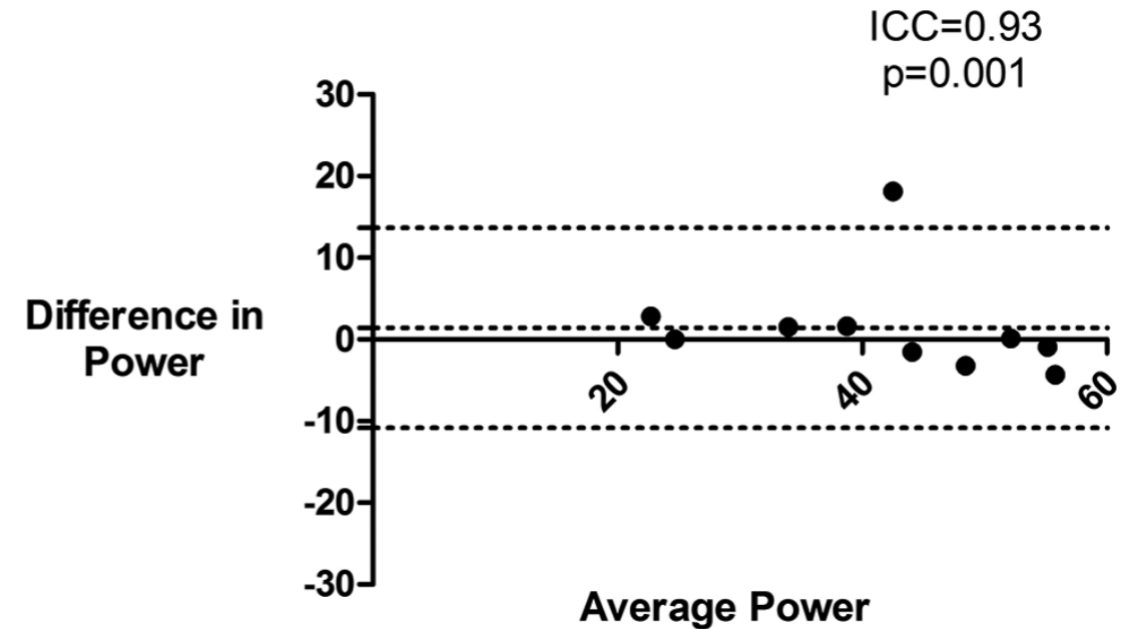


Cough Sound vs. VAS (subjective) and Esophageal pressure (Objective)



Cough sound has good repeatability

- ICC of Power and Frequency
 - P1 (ICC 0.93 and 0.94)
 - P0.5 (ICC 0.93 and 0.94)








Intraclass correlation coefficients (ICC)

Objective measures of cough intensity - limitation

- Little is known to patient's outcome
- No continuous measure or monitoring
- No study in ambulatory setting
- Not much comparing with subjective measure

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Cough intensity

Cough frequency

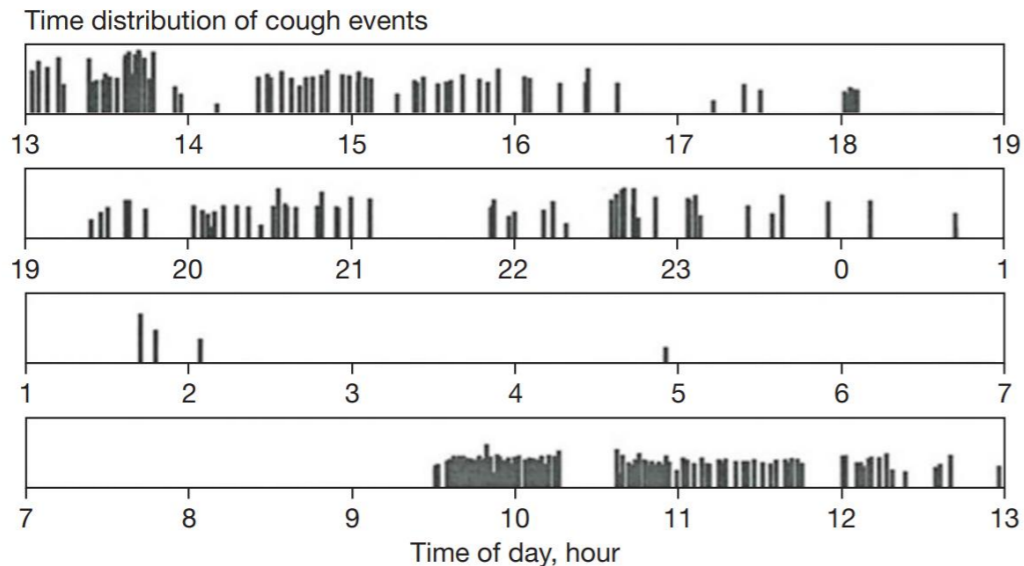
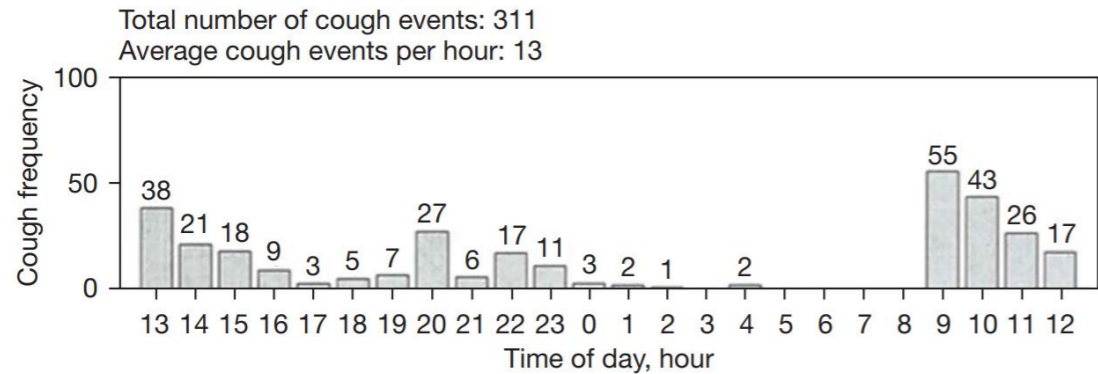
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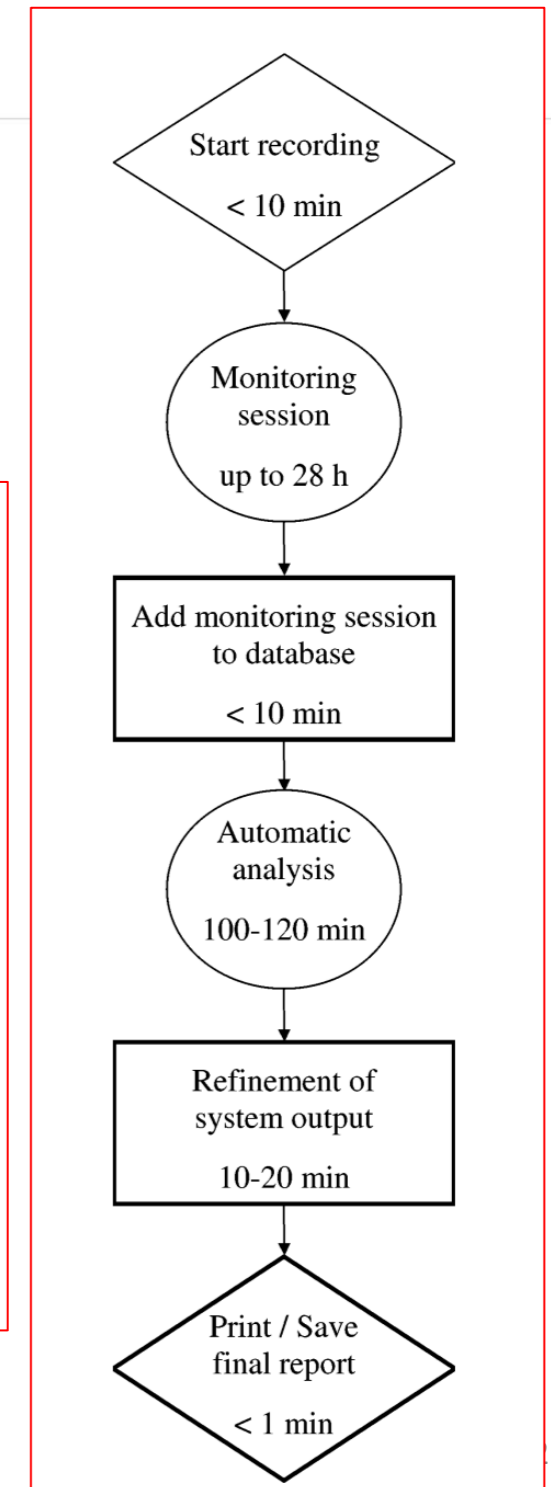
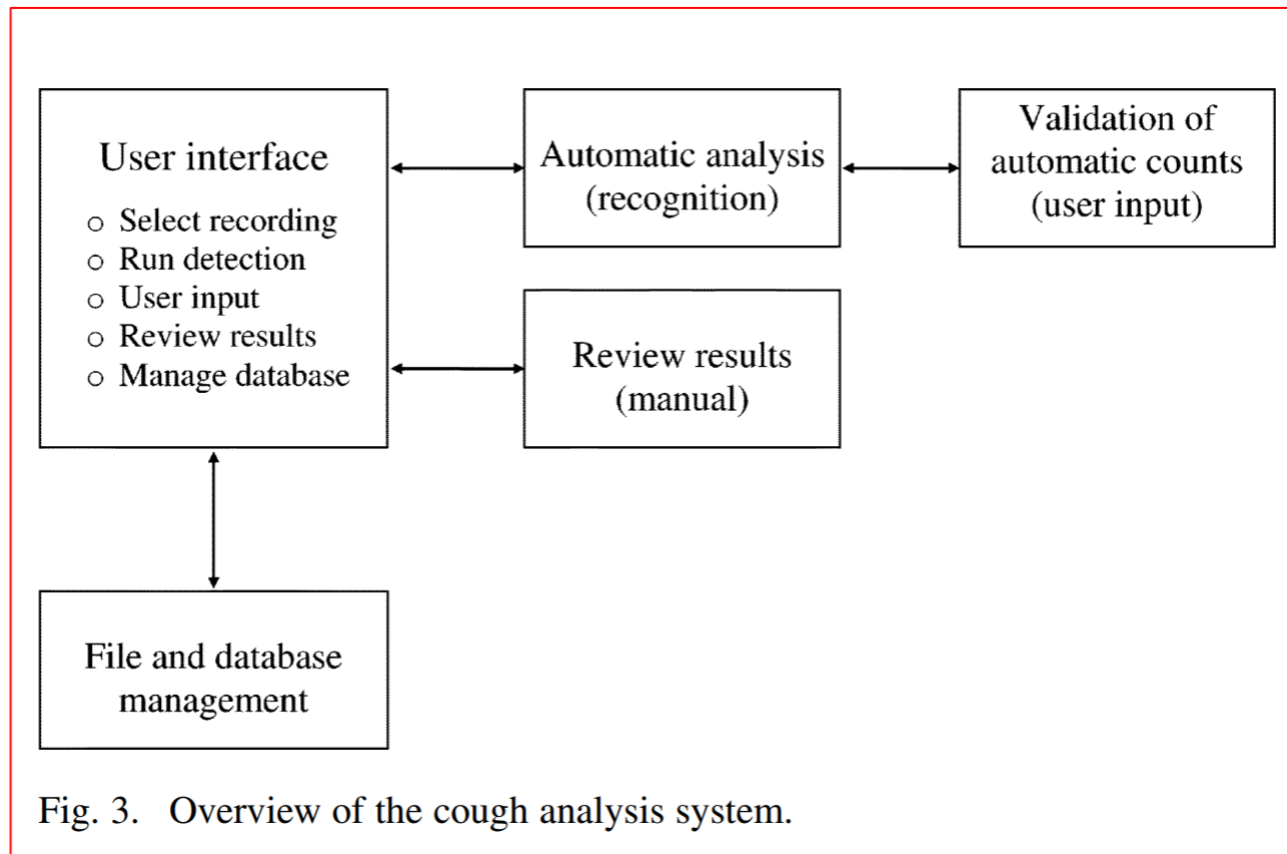
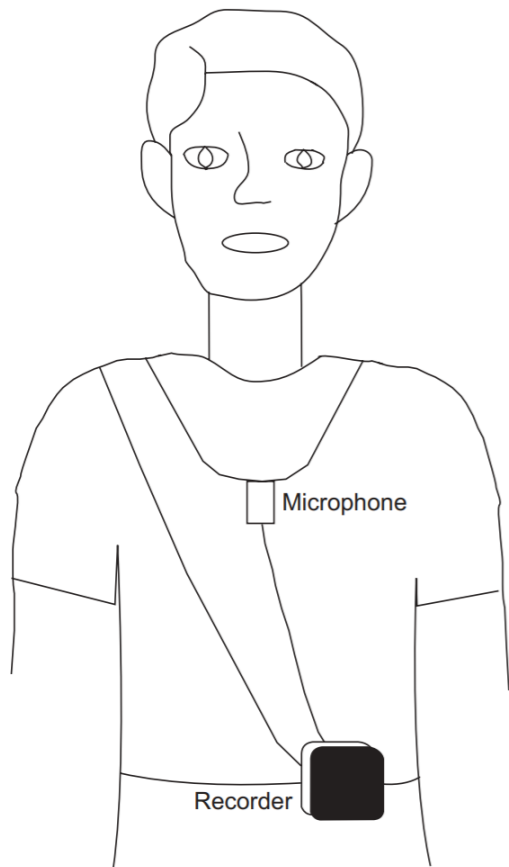
- Not only as severity or frequency → Outcomes
- Recent advance in Technology
 - Development of mobile device, IoT technology, and AI
- e.g.: Leicester Cough Monitor (LCM), VitaloJAK, Hull Automatic Cough Counter (HACC), and LEO sound syndrome etc.

Cough frequency



- Benefit of device
 - Cough attacks anytime
 - Nocturnal cough
 - Behavior associated cough
 - Ambulatory evaluation
 - 24 hours

Leicester Cough Monitor



Leicester Cough Monitor – 24hr, Ambulatory

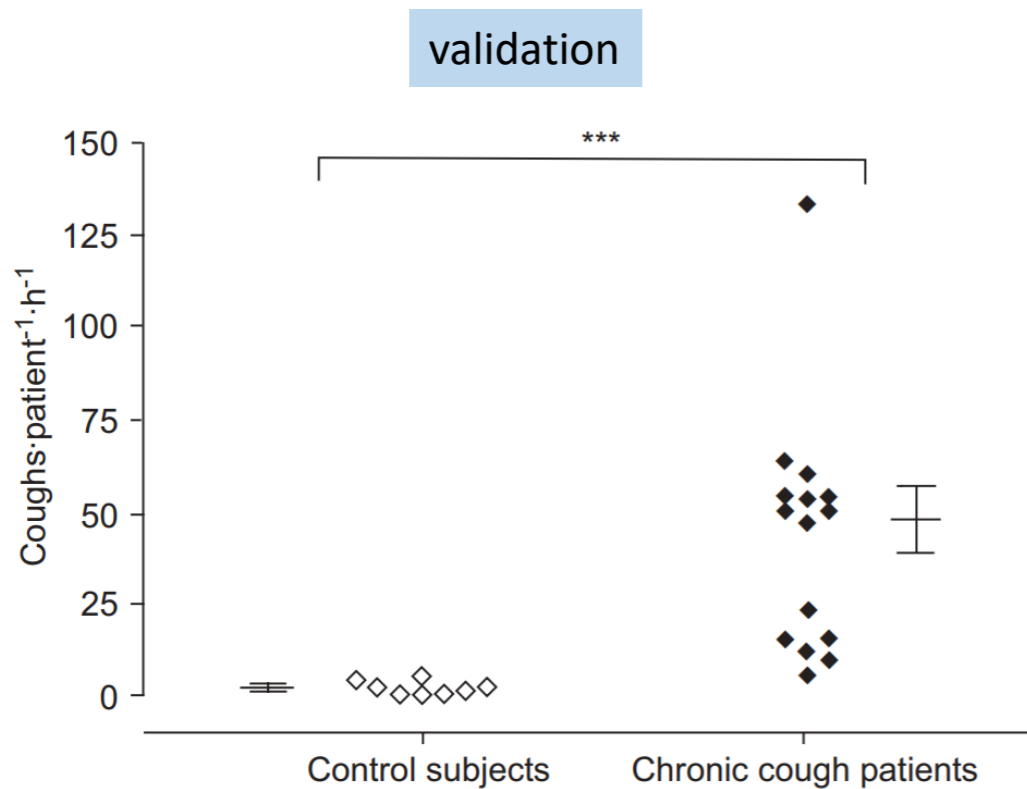


FIGURE 4. Mean ± SEM automated cough counts · patient⁻¹ · h⁻¹ in control subjects and chronic cough patients (6-h recordings). ***: p < 0.001.

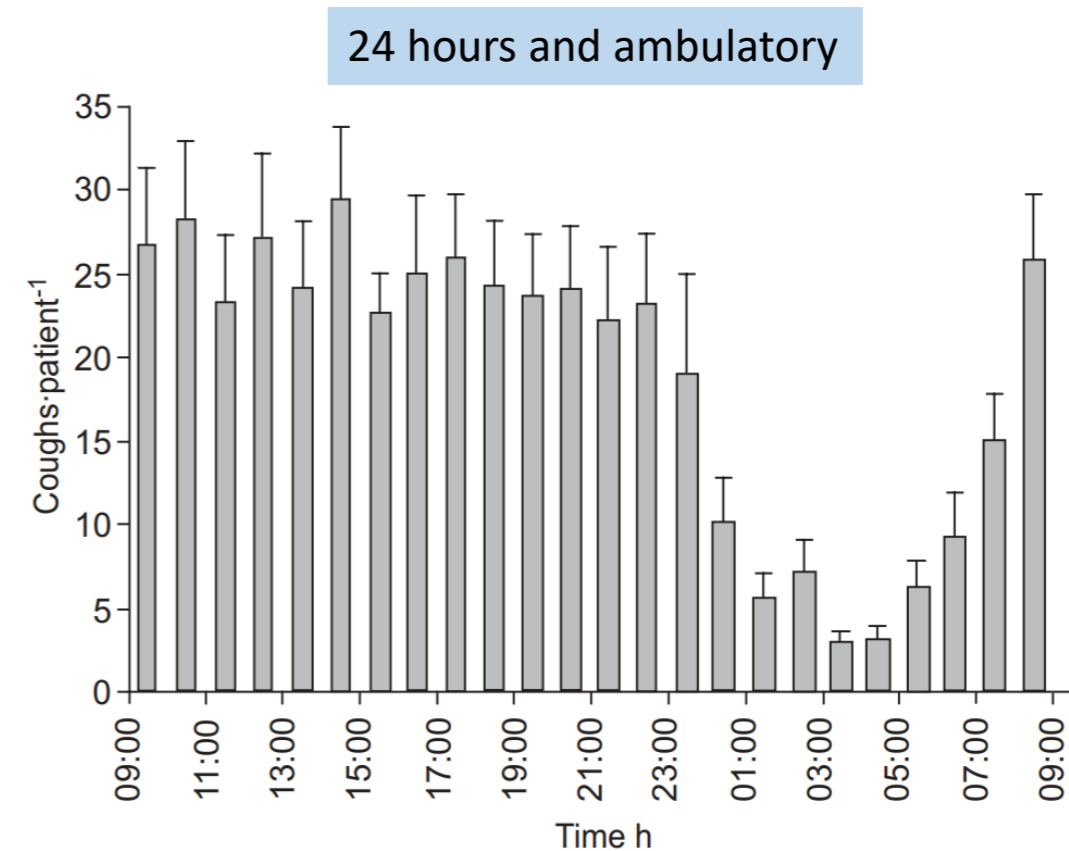


FIGURE 6. 24-h ambulatory, automated cough frequency recordings in 50 chronic cough patients. Data are presented as mean ± SEM.

Leicester Cough Monitor - Performance

	Median	IQR
Sensitivity	85.7 %	72.5 – 97.8 %
Specificity	99.9 %	99.6 – 100 %
PPV	94.7 %	85.0 – 99.6 %
FP rate	0.8	0.1 – 2.2

VitaloJAK

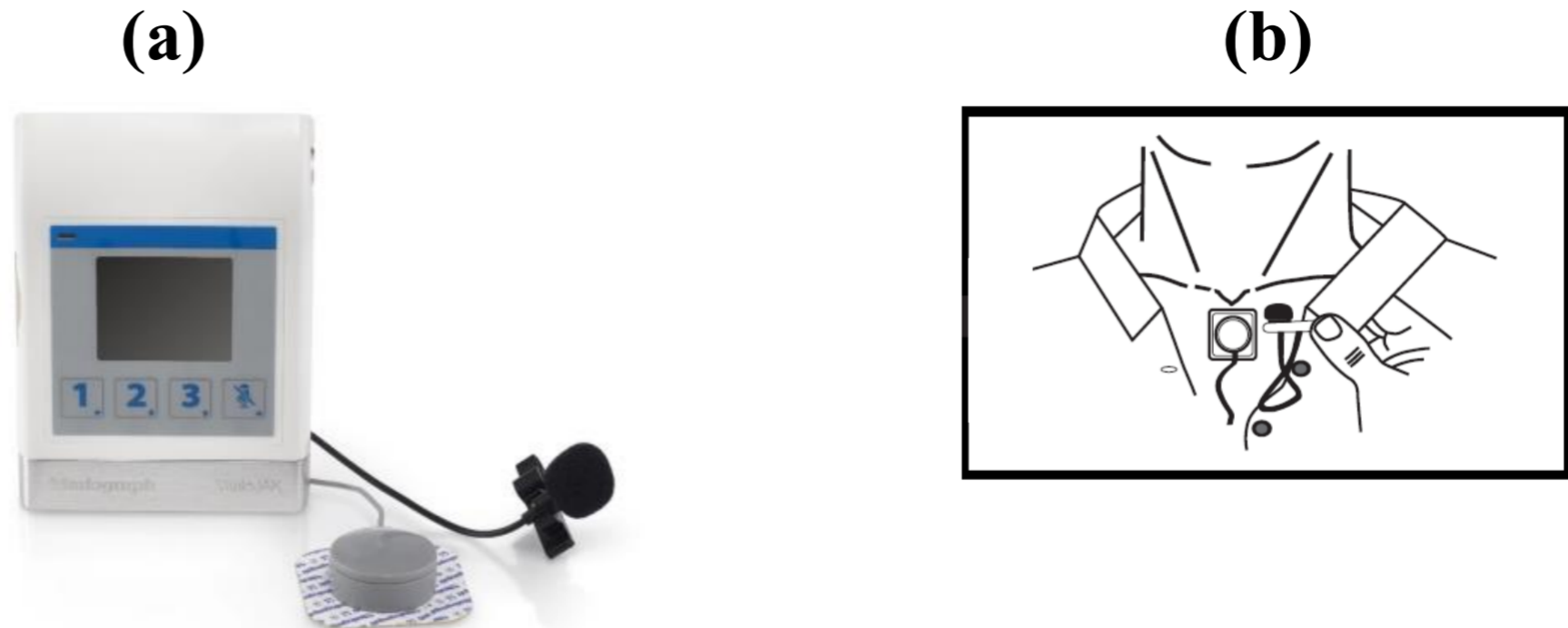
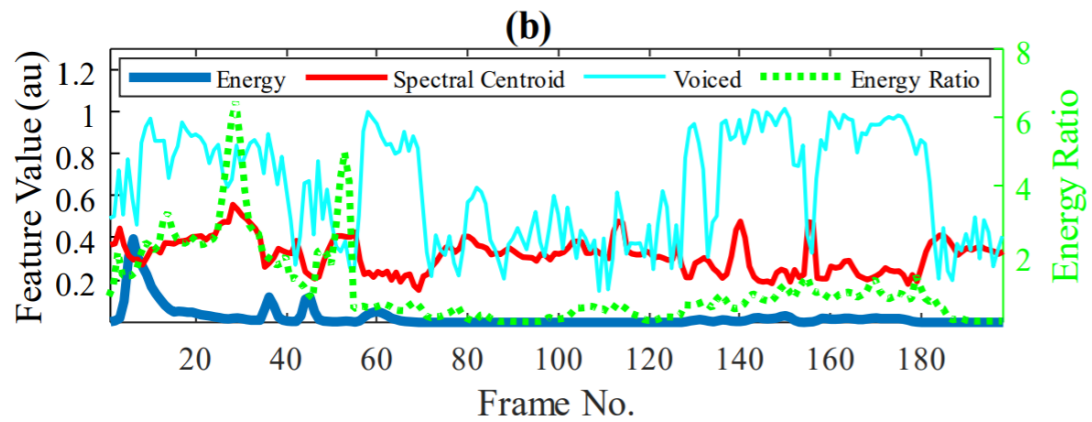
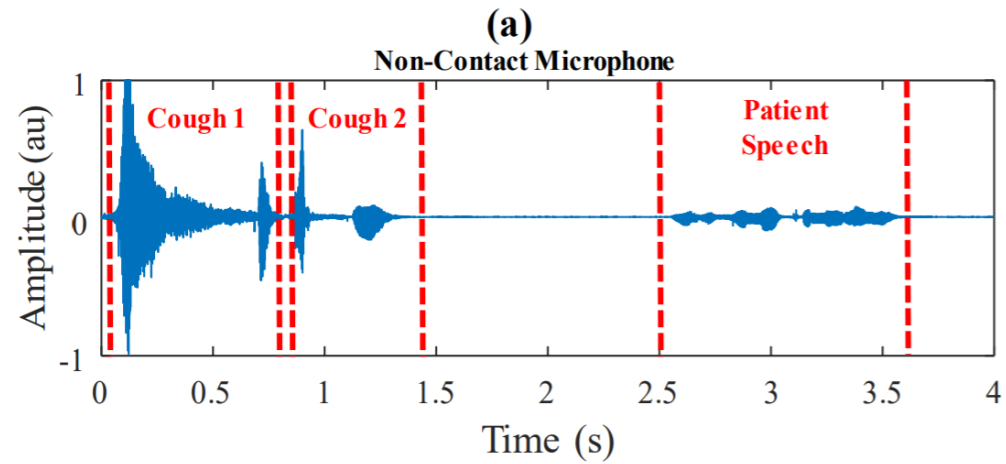


Fig. 2. (a) VitaloJAK® 24-hour cough audio recording device and (b) illustration of placement of non-contact and contact microphones.

VitaloJAK



Cough Monitoring



Vitalograph
Web Portal



Cough Analysis

VitaloJAK – Use in RCC RCT

Lung (2021) 199:121–129
<https://doi.org/10.1007/s00408-021-00437-7>

COUGH

Characterization of Patients With Refractory or Unexplained Chronic Cough Participating in a Phase 2 Clinical Trial of the P2X3-Receptor Antagonist Gefapixant






Lung (2021) 199:121–129

Clinical Practice and applicable federal regulations. All patients provided written informed consent before enrollment and all sites received approval from institutional review boards or independent ethics committees.

Analysis Measures

Baseline cough-related characteristics included objective awake cough frequency and patient-reported outcomes. Objective cough frequency was measured at baseline in a 24-hours sound recording using a VitaloJAK (Vitalograph[®]; Vitalograph Ltd, Buckingham, United Kingdom) acoustic

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Cough intensity

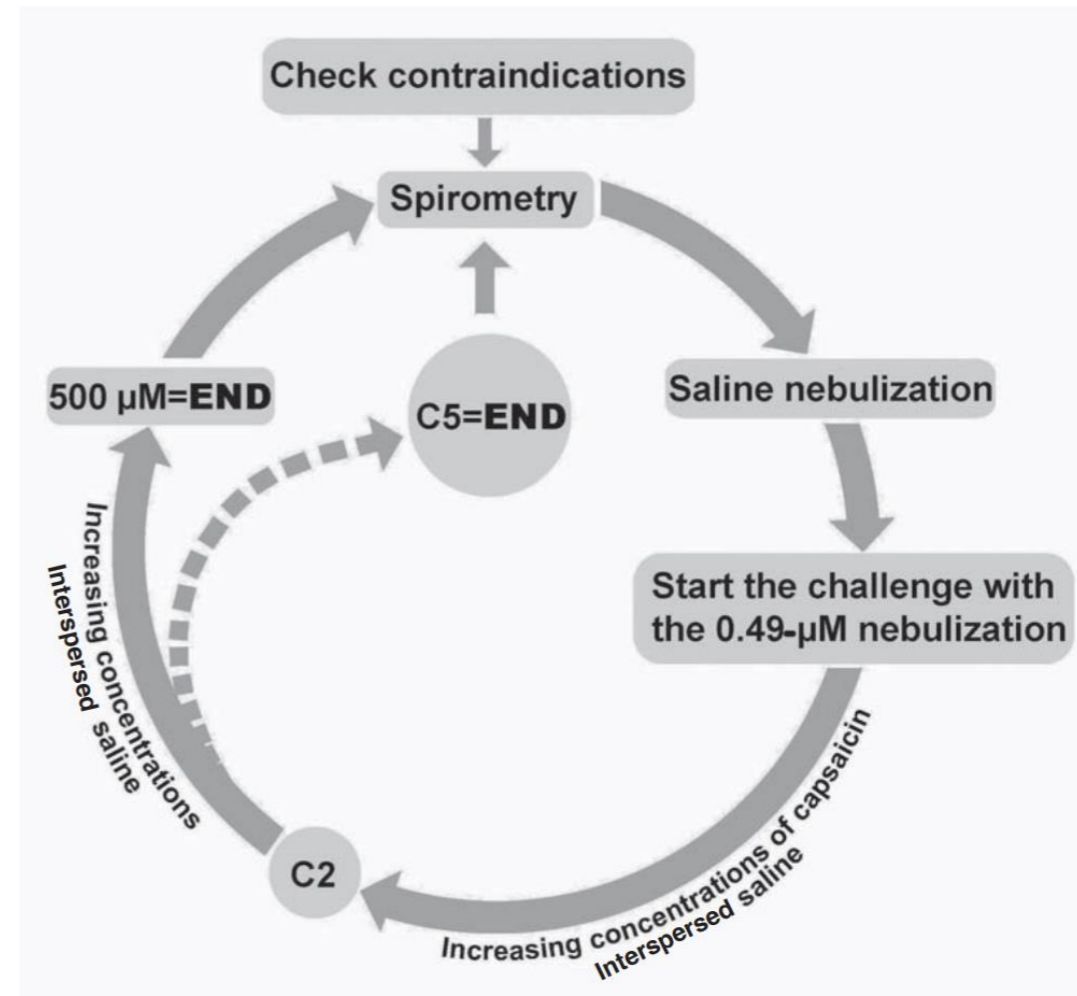
Cough frequency

Cough reflex sensitivity

Future of cough measure and Summary

Peripheral Cough reflex sensitivity

- e.g.: capsaicin, citric acid, ATP
- Gradient escalation
 - C2: Solution inducing 2 cough
 - C5: Solution inducing 5 cough



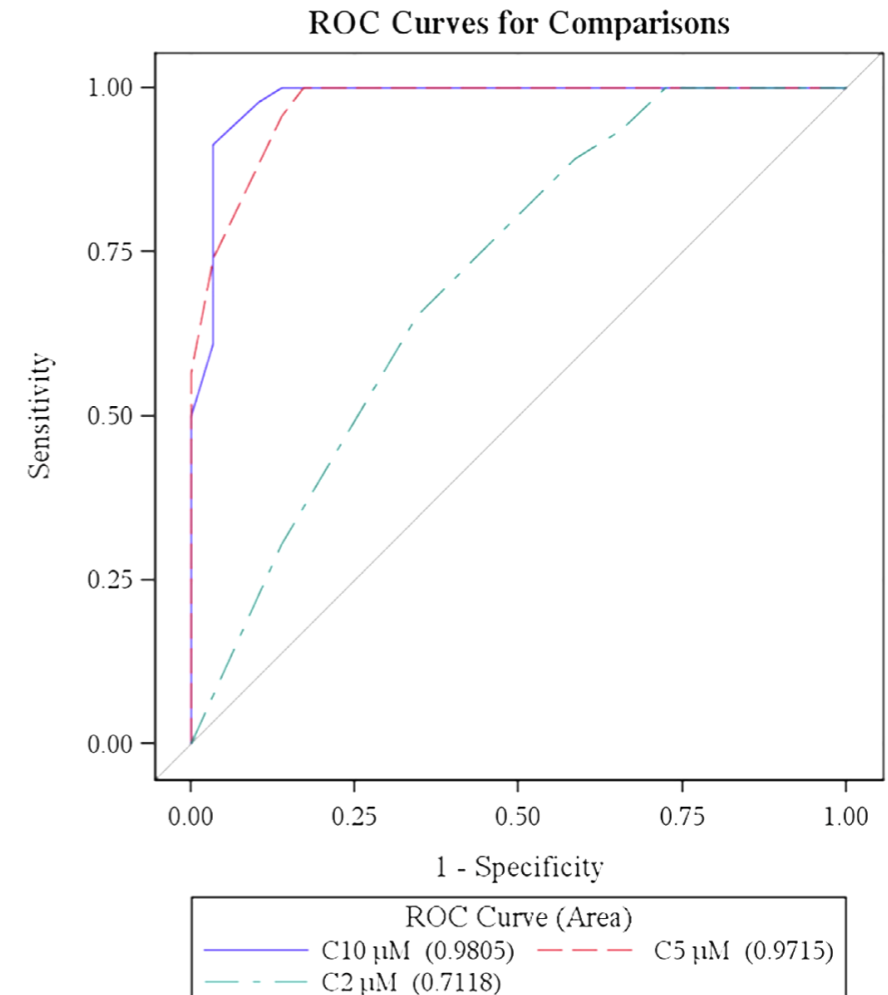
Peripheral Cough reflex sensitivity

Capsaicin cough threshold test in diagnostics



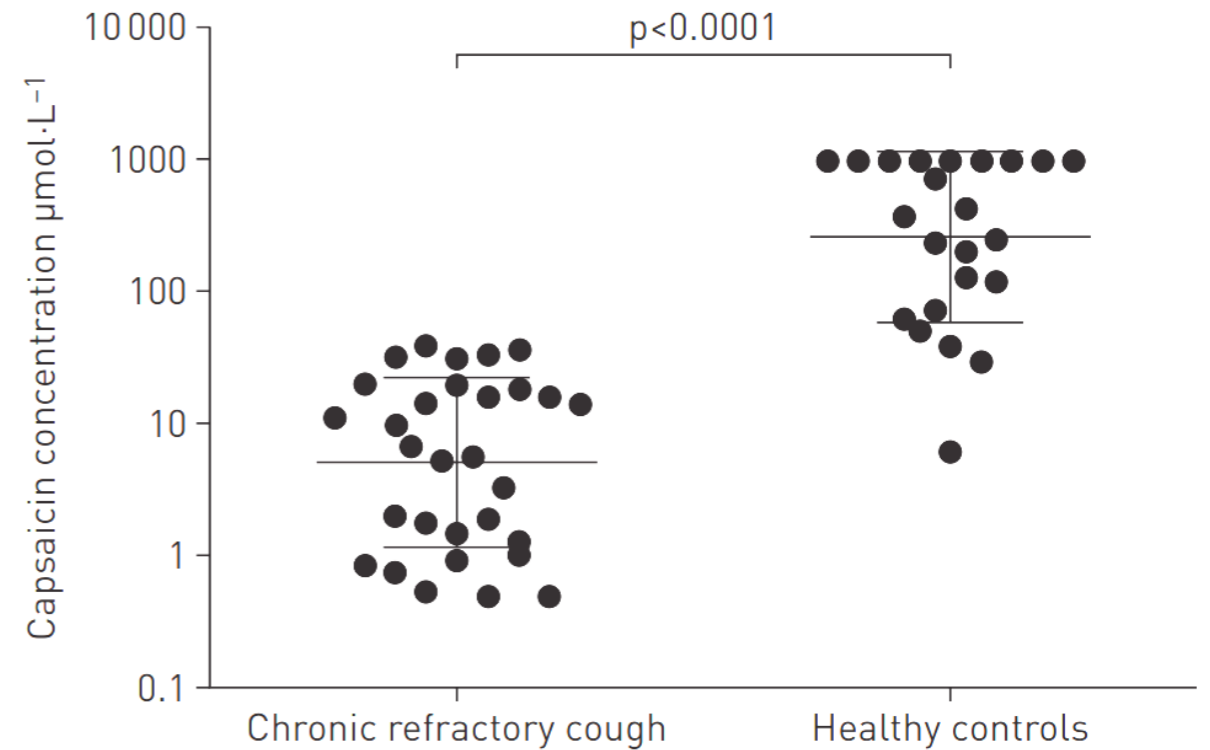
Teet Pullerits ^a, Ewa Ternesten-Hasséus ^a,
Ewa-Lena Johansson ^{b,c}, Eva Millqvist ^{a,*}

- Control vs. Chronic Cough patient (n=46)
- C5 reasonable cut-off



Central Cough reflex sensitivity

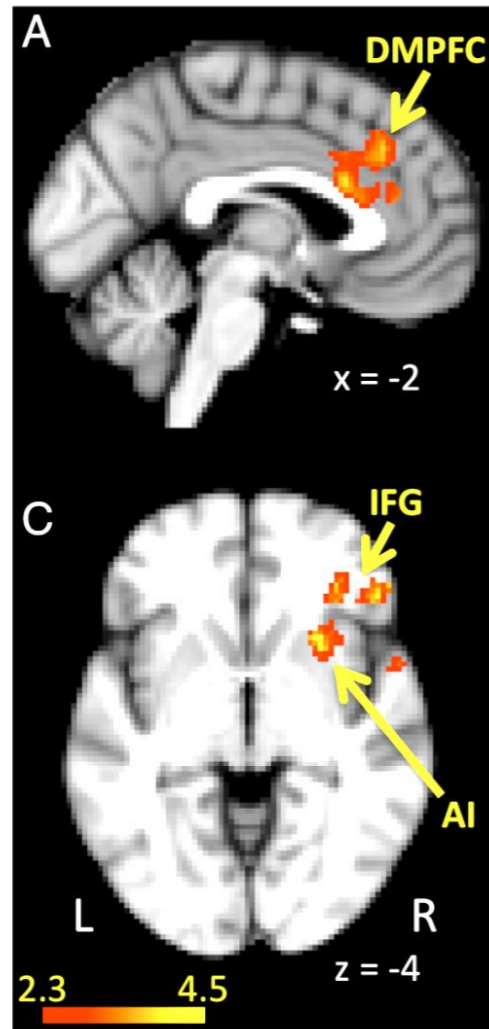
- Voluntary Cough Suppression Test
 - Modifying from capsaicin challenge test
 - “try not to cough”
 - CS5: moderately correlated with objective cough frequency
 - In RCC: sensitivity (100%) and specificity (91.3%) when 39 $\mu\text{mol/L}$ as threshold



Central Cough reflex sensitivity






- Brain functional magnetic resonance imaging (fMRI)
 - CC: Activation of the midbrain during airway irritation
 - but not in healthy subjects
 - Healthy: Activation in the medial prefrontal cortex during airway irritation
 - but not in CC subjects

Central Cough reflex sensitivity



- A: dorsomedial prefrontal cortex (DMPFC) in healthy subject after capsaicin inhalation
- C: right anterior insula (AI) and right inferior frontal gyrus (IFG) in cough patient

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Future of cough measure

- Objective + Subjective
- Smaller, AI, anywhere
- Needs of validated objective measure for cough diagnosis, severity, and monitoring
- In various chronic respiratory disease

Summary - Objective measure and monitoring of cough

- Cough intensity
 - Esophageal/Gastric pressure – Manometry, High resolution manometry
 - About cough muscle - EMG
 - Peak Cough Flow
 - Cough sound: Sound power or intensity

Summary - Objective measure and monitoring of cough

- Cough frequency
 - 24 hours, Mobile, and automated
 - Measure/monitoring value + outcome
 - Leicester cough monitor, VitaloJAK, HACCC, LEO sound etc.
- Cough sensitivity
 - pph: capsaicin, citric acid, ATP
 - Central: Voluntary cough suppression test, brain function MRI

Thank you for listening