

Breathlessness in patients with heart failure: A critical appraisal of opioid therapy.

Prof. Dr. Jan Gärtner

1 Evidence-base: Examples from breathlessness

2 Heart failure: Meta-Analysis*

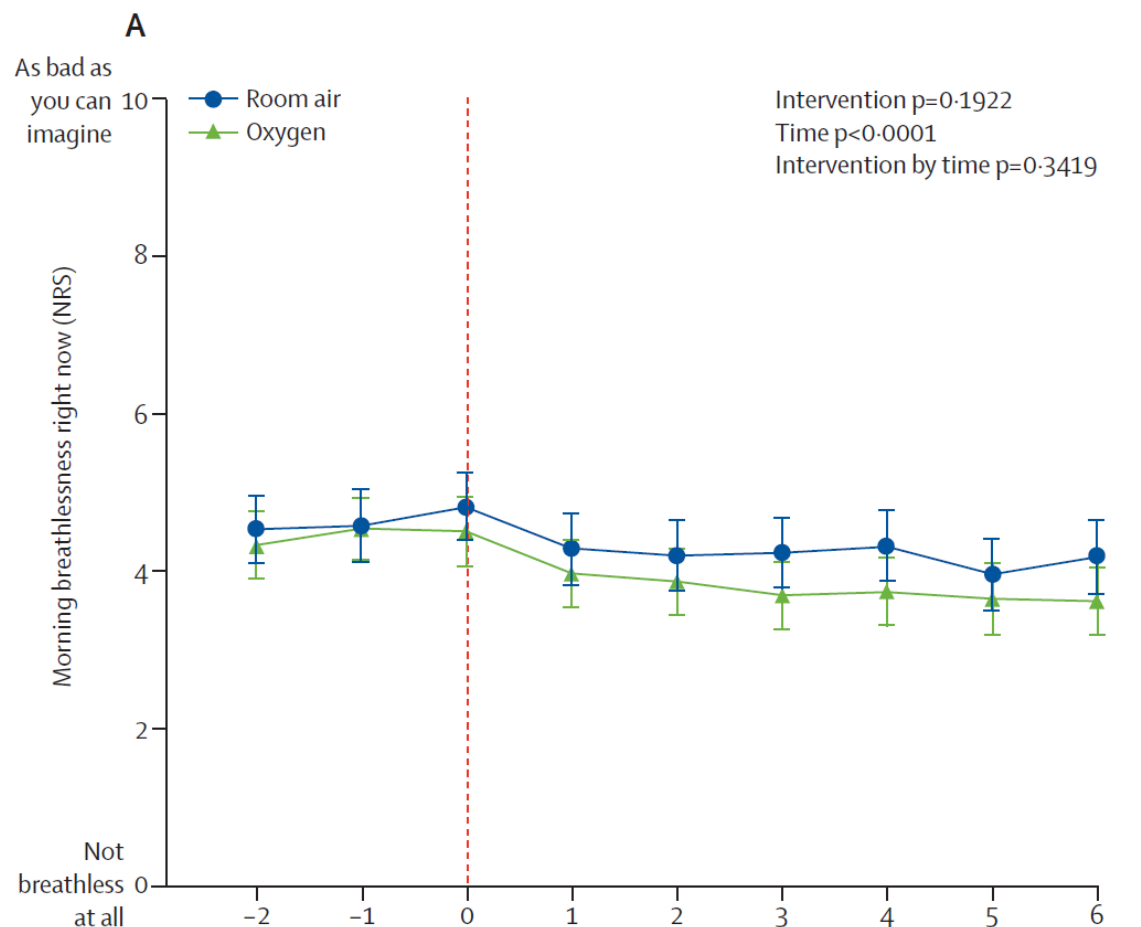
3 Thoughts: It is confusion, how proceed ?

4 Discussion

Oxygen:
Used to be state of the art....

1. Evidence-base, examples

RCT:
Oxygen vs room air
Non-hypoxic Patients



COPD RCT 2022*

1. Evidence-base, examples

Effect of Regular, Low-Dose, Extended-release Morphine on Chronic Breathlessness in Chronic Obstructive Pulmonary Disease The BEAMS Randomized Clinical Trial

Magnus Ekström, MD, PhD; Diana Ferreira, MD, PhD; Sungwon Chang, PhD; Sandra Louw, BSc; Miriam J. Johnson, MD, MBChB;
Danny J. Eckert, PhD; Belinda Fazekas, GDip; Katherine J. Clark, PhD; Meera R. Agar, PhD; David C. Currow, MPH, PhD;
for the Australian National Palliative Care Clinical Studies Collaborative

Conclusion:
-No significant effect

Guideline



1. Evidence-base, examples

Practice Guideline

> Eur Respir J. 2024 Jun 28;63(6):2400335. doi: 10.1183/13993003.00335-2024.

Print 2024 Jun.

European Respiratory Society clinical practice guideline on symptom management for adults with serious respiratory illness

Anne E Holland^{1 2 3}, Anna Spathis⁴, Kristoffer Marsaa⁵, Claudia Bausewein⁶, Zainab Ahmadi⁷,
Angela T Burge^{2 8}, Amy Pascoe², Adelle M Gadowski², Phil Collis^{9 10}, Tessa Jelen¹⁰,
Charles C Reilly^{11 12}, Lynn F Reinke¹³, Lorena Romero¹⁴, Anne-Marie Russell^{15 16},
Ravijyot Saggu¹⁷, John Solheim^{18 19}, Guido Vagheggin^{20 21}, Chantal Vandendungen^{18 22},
Marlies Wijsenbeek²³, Thomy Tonia²⁴, Natasha Smallwood^{2 25 26}, Magnus Ekström^{7 26}

COPD RCT 2022*

1. Evidence-base, examples

Individual patient data analysis (IPD)

Ferreira DH et al. ERJ Open Res 2023;

But....

Is being able to walk to the letterbox life-changing? A qualitative assessment of measures of improvement in persistent breathlessness

Here: Super-responder !

Two patients report, that opioid-therapy was “life-changing” for them

*Ekström.... Currow Morphine on chronic breathlessness in COPD JAMA 2022

Advanced heart failure: Opioids against breathlessness

2. Meta-Analysis

(Palliative Care) Textbooks:

In breathlessness, opioids are drugs of choice,
regardless of underlying disease

Meta-Analysis

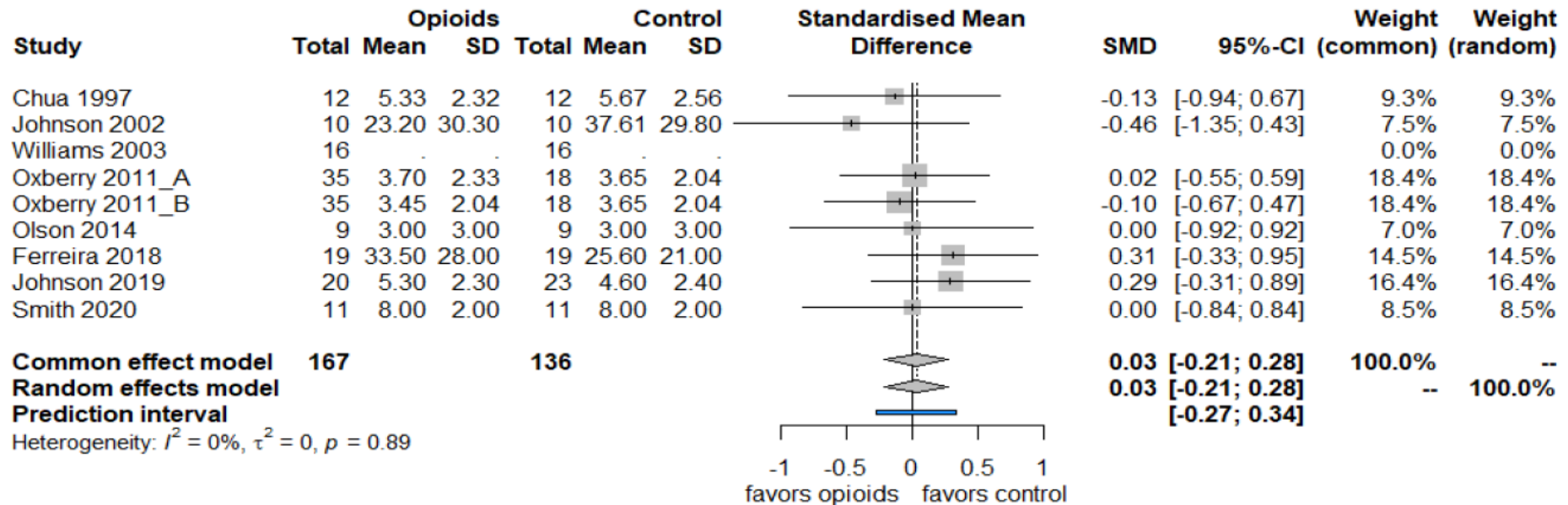
2. Meta-Analysis

1180 Hits
8 RCTs *randomized controlled trials*
271 Patients

Meta-Analysis

2. Meta-Analysis

Primary endpoint: breathlessness



Meta-Analysis

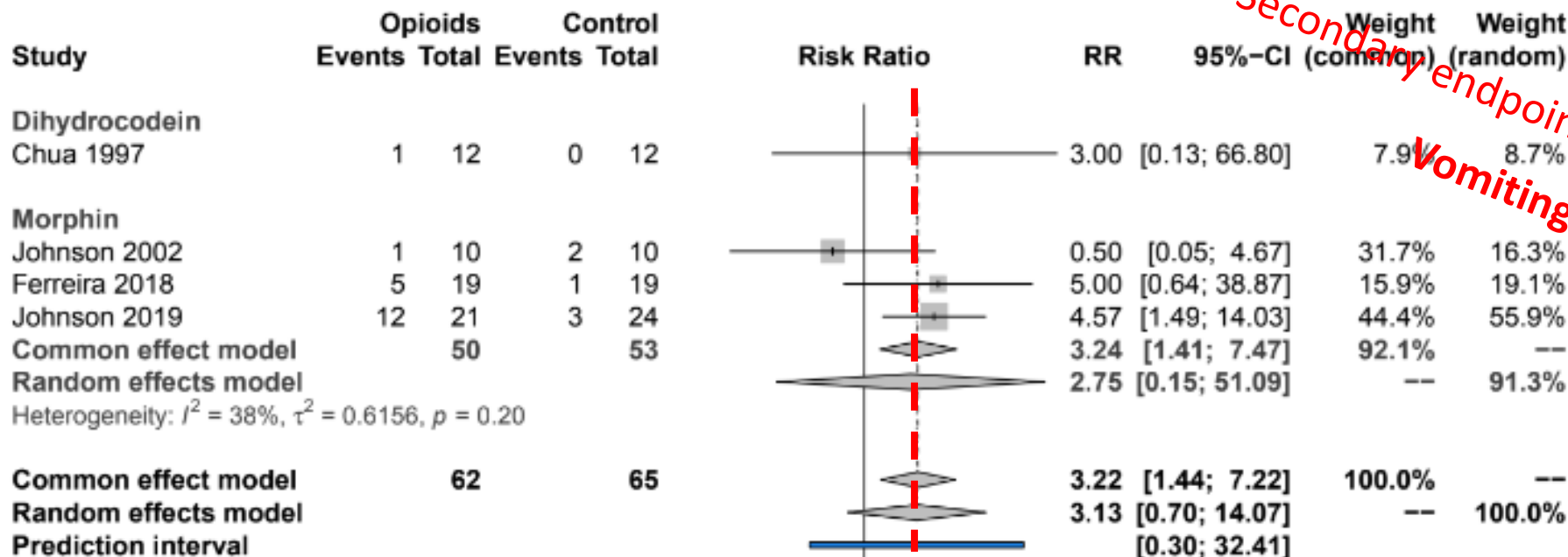
2. Meta-Analysis

Even despite de-facto unblinding !



Meta-Analysis

2. Meta-Analysis



Heterogeneity: $I^2 = 7\%$, $\tau^2 = 0.0720$, $p = 0.36$

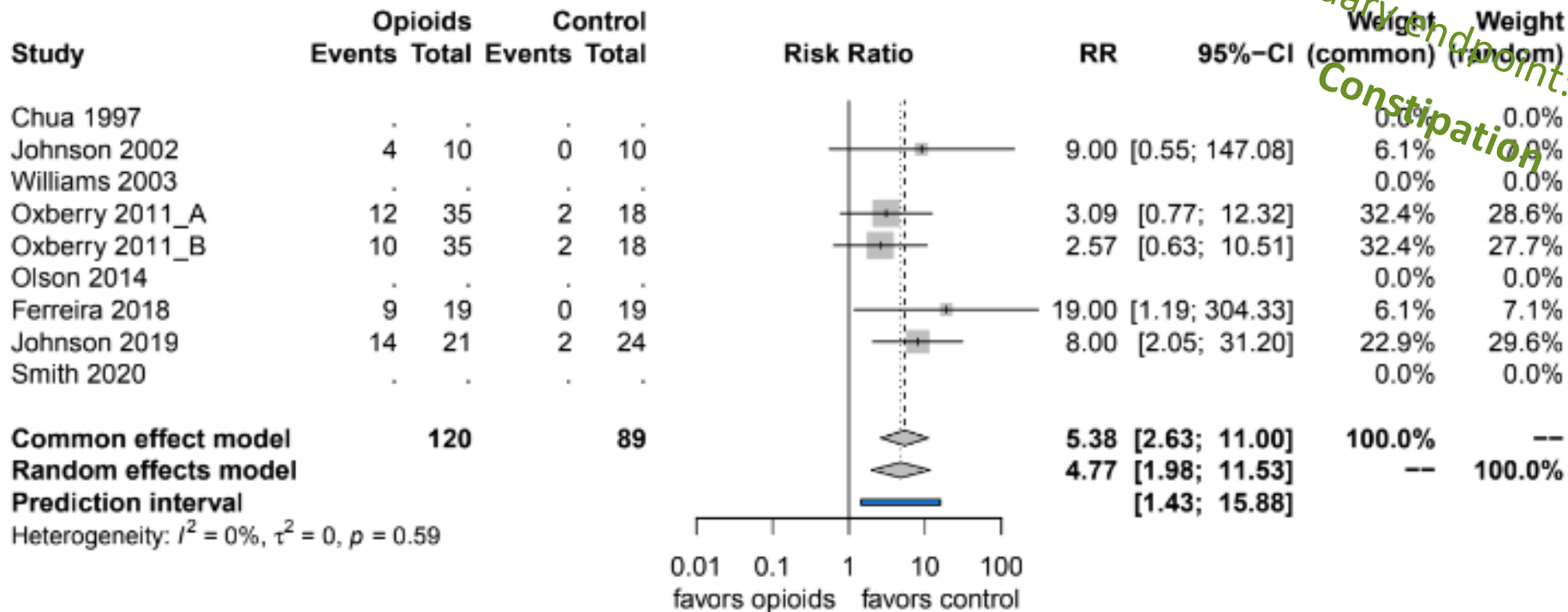
Test for subgroup differences (fixed effect): $\chi^2_1 = 0.00$, $df = 1$ ($p = 0.96$)

Test for subgroup differences (random effects): $\chi^2_1 = 0.00$, $df = 1$ ($p = 0.96$)

Meta-Analysis

2. Meta-Analysis

Secondary endpoint:
 Constipation



Meta-Analysis

2. Meta-Analysis

Patients on opioids withdrew from the study more often

The longer the study, the more pronounced the effect

Example: 12 Wochen follow- up by Johnson et al (2019)

Median time to withdrawal: 12 days for morphine
48 days for placebo.

Breathlessness is scary. Anxiety generates breathlessness

3. How proceed ?

ANNALS OF PALLIATIVE MEDICINE 
AN OPEN ACCESS JOURNAL FOR HIGH-QUALITY RESEARCH IN PALLIATIVE MEDICINE

**Interaction of panic and episodic breathlessness
among patients with life-limiting diseases: a cross-
sectional study**

Key findings

- Most patients suffer from panic during a breathlessness episode.

Vicious circle

Breathlessness is scary. Anxiety generates breathlessness

3. How proceed ?

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Kognitive Verhaltenstherapie ?

Only I Know Now, of Course, How to Deal With it, or
Better to Deal With it: A Mixed Methods Phase II
Study of a Cognitive and Behavioral Intervention for
the Management of Episodic Breathlessness

Karlotta Schloesser ¹, Anja Bergmann ², Yvonne Eisenmann ¹, Berenike Pauli ¹, Martin Hellmich ³,
Max Oberste ³, Stefanie Hamacher ³, Armin Tuchscherer ⁴, Konrad F Frank ⁵, Winfried Randerath ⁶,
Simon Herkenrath ⁶, Steffen T Simon ⁷

Conclusion:

The intervention was safe
 accepted
 breathlessness mastery improved

*

Vicious circle

Breathlessness is scary. Anxiety generates breathlessness

3. How proceed ?

Cognitive behavioural therapy

Musictherapy ? Relaxation ? Hypnosis ?

*

Vicious circle

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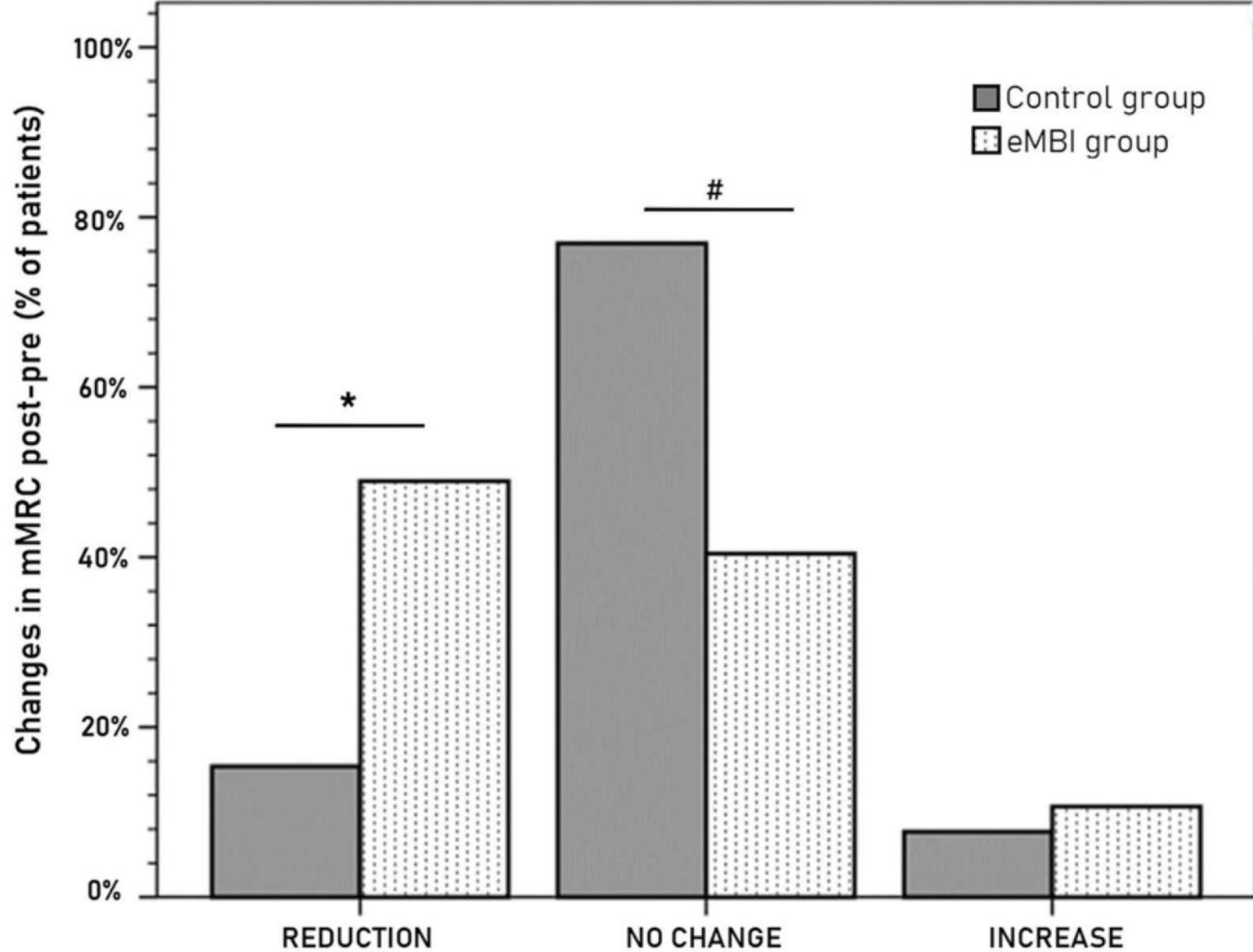


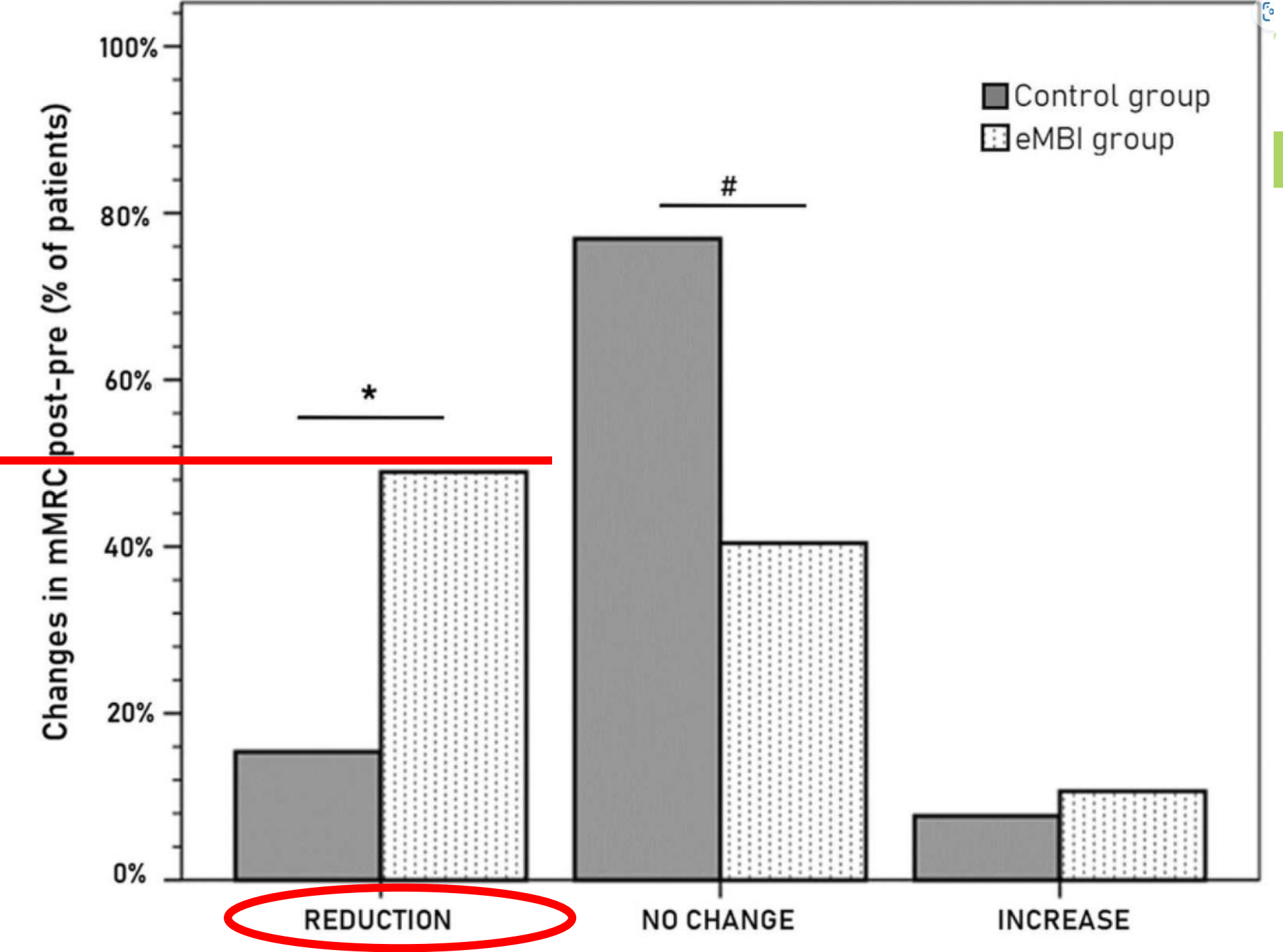
➤ [Complement Ther Med. 2024 Oct 30:103106. doi: 10.1016/j.ctim.2024.103106.](#)
Online ahead of print.

Online Mindfulness-Based Intervention (eMBI) in management of dyspnea in patients with interstitial lung disease: A randomized clinical trial

Siliana Maria Duarte Miranda ¹, Sara de Pinho Cunha Paiva ², Luiz Fernando Ferreira Pereira ³,
Gabriela Patrus Ananias de Assis Pires ⁴, Andrew Nogueira Albuquerque Leal ⁵,
Giane Amorim Ribeiro-Samora ⁶, Eliane Viana Mancuzo ⁷

Vicious circle





Clinical hypnosis “hypnosis”



Palliative Care Nursing, Palliative and Supportive Care Service



Lüthi FT et al. Home-based hypnosis: a feasibility study for end-of-life patients and their relatives. J Pain Symptom Manage. 2025 Mar

Clinical hypnosis *“hypnosis”*

Aim:

To assess the feasibility and acceptability of a home-based hypnosis intervention for

- i) managing end-of-life symptoms and
- ii) enhancing relatives' coping resources.



Table 2 Symptoms and coping resources chosen by the patients or relatives at each session.

Participants	Session 1	Session 2	Session 3	Session 4
	N (%)	N (%)	N (%)	N (%)
Patients				
Pain	12 (38.7%)	10 (43.5%)	8 (42.1%)	3 (16.7%)
Anxiety	9 (29%)	5 (21.8%)	2 (10.5%)	4 (22.2%)
Nausea	1 (3.3%)	1 (4.3%)	1 (5.3%)	-
Fatigue	5 (16.1%)	2 (8.7%)	-	-
Depression	3 (9.6%)	1 (4.9%)	2 (10.5%)	4 (22.2%)
Other	1 (3.3%)	4 (17.4%)	6 (31.6%)	7 (38.9%)
Relatives				
Serenity	7 (53.8%)	8 (72.7%)	3 (37.5%)	3 (37.5%)
Energy	2 (15.4%)	1 (9.1%)	2 (25%)	1 (12.5%)
Distance	2 (15.4%)	-	-	1 (12.5%)
Other	1 (7.7%)	2 (18.2%)	3 (37.5%)	3 (37.5%)



Breathlessness is scary. Anxiety generates breathlessness

3. How proceed ?

Cognitive behavioural therapy

Musictherapy ? Relaxation ? Hypnosis ?

.....

Benzodiazepine: Yes, but the evidence...

Vicious circle

....

Breathlessness is scary. Anxiety generates breathlessness

3. How proceed ?

Cognitive behavioural therapy

Musictherapy ? Relaxation ? Hypnosis ?

.....

Benzodiazepines: Yes, but the evidence...



Authors' conclusions*

There is no evidence for or against benzodiazepines

Benzodiazepines caused more drowsiness compared to placebo, but less compared to morphine.

Vicious circle

Breathlessness is scary. Anxiety generates breathlessness

3. How proceed ?

Cognitive behavioural therapy

Musictherapy ? Relaxation ? Hypnosis ?

.....

Benzodiazepines: Yes, but the evidence

Side effects *Delirium, amnesia, tiredness, daytime functioning*

Physical dependence

Receptor downregulation

Pregabalin *Lyrica®* ?

Attacs/Episode «out of the nothing»

Episode with massive panic ?

➤ [Ann Palliat Med.](#) 2024 Jan;13(1):200-201. doi: 10.21037/apm-23-547. Epub 2023 Nov 24.

Potential role of pregabalin in the treatment of episodic breathlessness

.... [Jan Gaertner](#)¹, [Klaus K Witte](#)²

Look ahead?

3. How proceed ?

Home care: 24/7 diuretic infusion ?

Home care: Inotropics via pump ? *Dobutamin, Milrinon*

Review

➤ [Cardiology](#). 2024;149(5):423-437. doi: 10.1159/000536373. Epub 2024 Jan 18.

Use of Inotropic Agents in Advanced Heart Failure: Pros and Cons

Benjamin Lautrup Hansen ¹, Søren Lund Kristensen ¹, Finn Gustafsson ¹

The cause of breathlessness in normoxic heart failure patient?

3. How proceed ?

The cause of breathlessness in normoxic heart failure patient?

3. How proceed ?

Baroreceptors in the atrium ?

> Eur J Heart Fail. 2023 Jun;25(6):792-802. doi: 10.1002/ejhf.2821. Epub 2023 Mar 13.

Disproportionate exercise-induced pulmonary hypertension in relation to cardiac output in heart failure with preserved ejection fraction: a non-invasive echocardiographic study

Yuki Saito ^{1 2}, Masaru Obokata ¹, Tomonari Harada ¹, Kazuki Kagami ^{1 3}, Hidemi Sorimachi ¹, Naoki Yuasa ¹, Toshimitsu Kato ¹, Naoki Wada ⁴, Yasuo Okumura ², Hideki Ishii ¹

In preserved ejection fraction (HFpEF) under exercise:
Pulmonal hypertonus and breathlessness....

PD III Inhibitors ?

P2x3 Inhibitors ?

Lidocain s.c./i.v. ?

Most important question at the end:

3. How proceed ?

Why do the patients in non-controlled palliative care studies benefit from opioids against breathlessness in heart failure ?

Because Palliative Care is effective !

Multi-professional team !

Attitude !

Psychosocial, existential issues !

Dignity !

Feeling secure ! Feeling secure ! Feeling secure !

Non-pharmacologic measures !

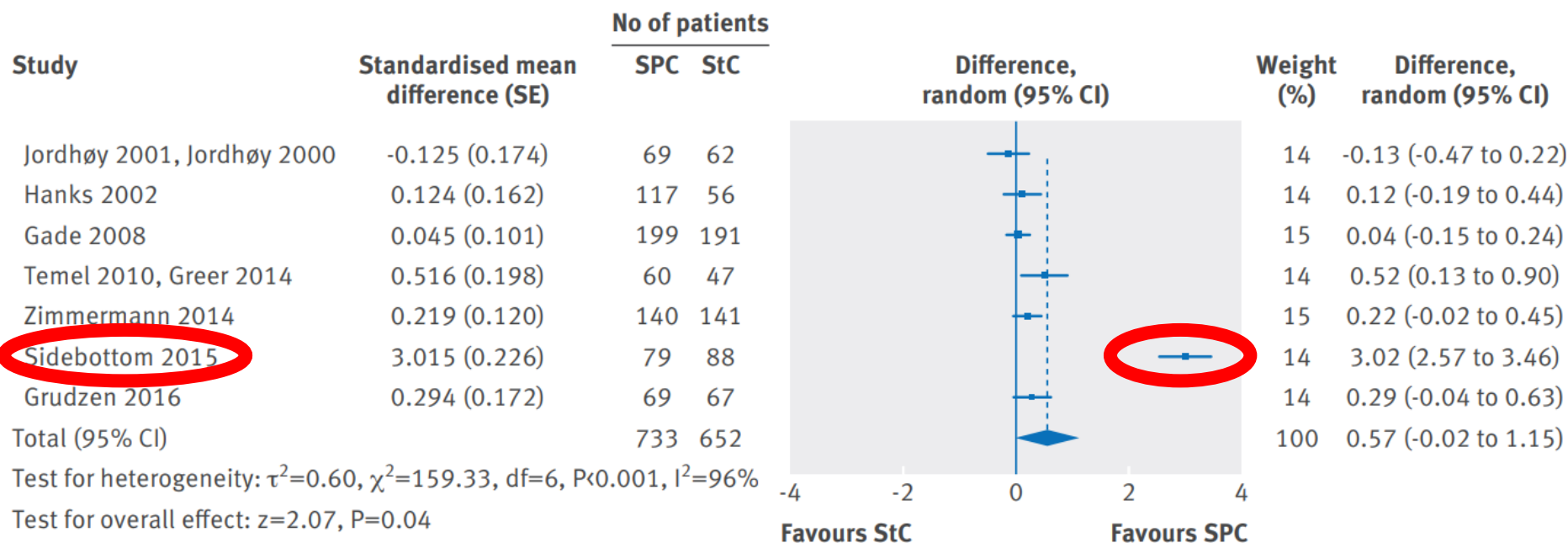
Self-effectiveness !

Unit of care...

And many more...

Meta-Analysis: Effect of specialist Palliative Care on Quality of Life

3. How proceed ?



Personal Conclusion:

Let`s make good Palliative Care !

Your team is the drug !

Recognize our patients anxiety *“will I suffocate”* !

Identify “super-responders” for opioids in this indication !

Be open for future developments *Pumps, ionotropics etc*

Be careful with opioid in this indication*, but NOT in the dying patients !

*similar: Benzodiazepines...

Personal Conclusion:

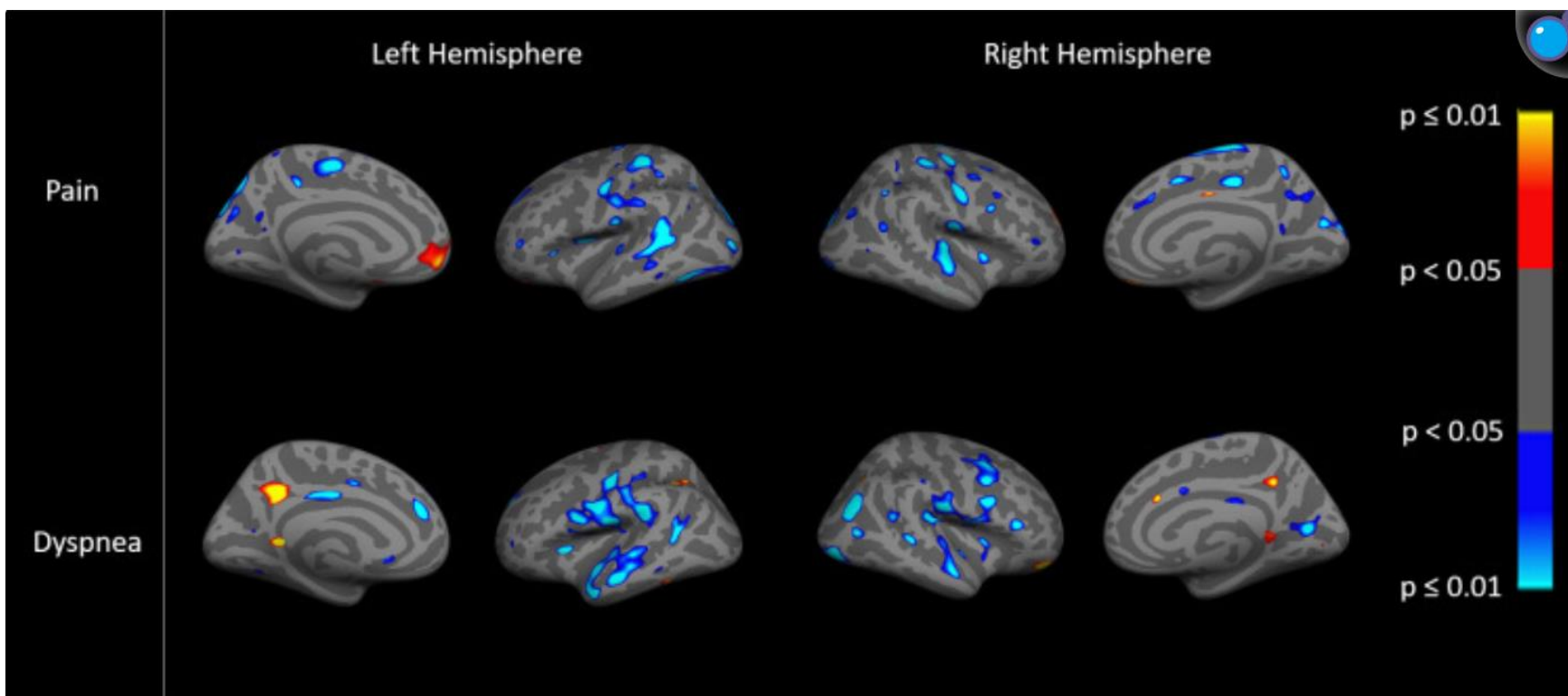
Diuretics:

Consider i.v./s.c. 24/7 at home

Consider high dose: Nephroplasty and congestive (or venous) gastritis

Keep (almost) to the end !

Breathlessness is not equal breathlessness: fMRI Projekt *Ethik eingereicht...*



LVAD ?



BMC Palliative Care 2024

RESEARCH



Multicenter exploration of specialist palliative care in patients with left ventricular assist devices – a retrospective study

Theresa Tenge^{1,2}, Shaylin Shahinzad², Stefan Meier¹, Manuela Schallenburger², Yann-Nicolas Batzler², Jacqueline Schwartz^{2*}, Anja Coym³, Johannes Rosenbruch⁴, Mitra Tewes⁵, Steffen T. Simon⁶, Carmen Roch⁷, Ute Hiby⁸, Christian Jung⁹, Udo Boeken¹⁰, Jan Gaertner^{11,12} and Martin Neukirchen^{1,2}

