








Better Treatments for Breathlessness in Palliative and End of Life Care

Prof Matthew Maddocks
Cicely Saunders Institute, King's College London
















BETTER-B is funded by the European Union's Horizon2020 research and innovation programme under grant agreement No. 825319. The views expressed in this presentation are those of the author(s) and not necessarily those of the funders.

Follow us on twitter: [#betterbreathe](https://twitter.com/betterbreathe) www.better-breathe.eu

1

DISCLOSURE

- Name: Matthew Maddocks
- Affiliation: King's College London

- Relationships with for-profit and not-for-profit interests: None

- Grants/Research Support: European Commission, UKRI, NIHR
- Consulting fees: None
- Other (including employment): None

www.csi.kcl.ac.uk

2

Why severe breathlessness in advanced illness?

- A **subjective** experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity
- Becomes **chronic** or **refractory** when it persists despite optimal treatment of the underlying condition and results in disability
- Also called dyspnoea/dyspnea
- **Affects >15 million people in Europe, 75 million world wide**
- **Burdensome and common** in advanced COPD and other lung diseases, heart failure, cancer, neurological diseases
- People with breathlessness in advanced illness **typically have 13-14 other symptoms**
- Frequent **cause of** emergency hospital **admission** (1 in 5 ambulance presentations)



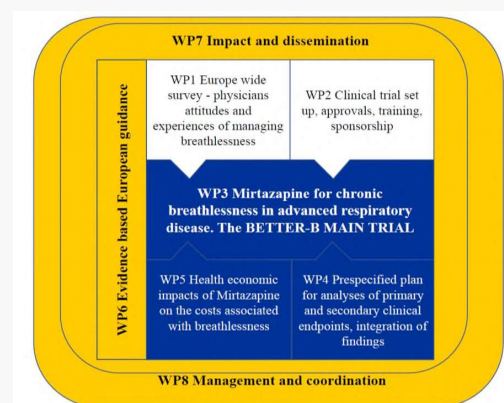
www.csi.kcl.ac.uk

3

The BETTER-B Project

Objectives:

- Explore current practice and experiences of palliative and respiratory clinicians across Europe on the management of breathlessness in lung disease
- Test the effectiveness and cost-effectiveness of mirtazapine for the relief of chronic breathlessness in patients with chronic obstructive pulmonary disease (COPD) or interstitial lung diseases (ILD)
- Produce and disseminate accessible European wide multi-lingual guidance on the management of breathlessness in palliative and end of life care



BETTER-B consortium brings together: respiratory, palliative, geriatric and rehabilitation clinicians; statisticians, trialists, health economists, health service researchers and patient and consumer groups across **Poland, Germany, Italy, Ireland, Switzerland, UK and Australia...**

www.csi.kcl.ac.uk

www.better-breathe.eu

4

Case series and feasibility study: results informed BETTER-B programme

Use of mirtazapine in patients with chronic breathlessness: A case series

Natasha Lovell¹, Sabrina Bajwah¹, Matthew Maddocks¹, Andrew Wilcock² and Irene J Higginson¹

Palliative Medicine
2018, Vol. 32(9) 1518–1521

Patients took mirtazapine for 2 weeks to 5 months, reported feeling more in control of breathlessness, quicker recovery from episodes.

BETTER-B Feasibility Results

- No differences between arms for tolerability or safety
- Worst breathlessness ratings day 28, 7.1 (95%CI 6.2-7.9, placebo), 6.3 (95%CI 5.6-7.0, mirtazapine)

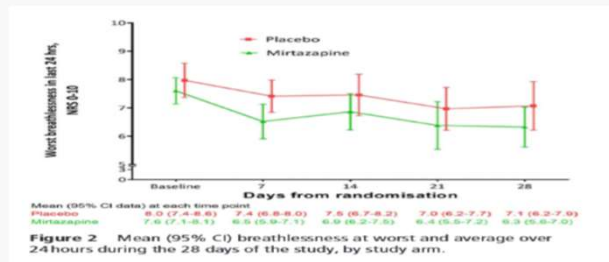
Brief communication



Randomised, double-blind, multicentre, mixed-methods, dose-escalation feasibility trial of mirtazapine for better treatment of severe breathlessness in advanced lung disease (BETTER-B feasibility)

Irene J Higginson¹, Andrew Wilcock², Miriam J Johnson³, Sabrina Bajwah¹, Natasha Lovell¹, Deokhee Yi¹, Simon F Hart⁴, Vincent Crosby⁵, Heather Poole⁶, David Currow⁷, Emma Best⁸, Sarah Brown⁶, on behalf of BETTER-B Feasibility Trial Group

Thorax 2020;75:176-179.



www.csi.kcl.ac.uk

5

Better-B Main Trial Objective

- To determine whether mirtazapine is an effective treatment for the reduction of self-reported worst breathlessness (as measured by a numerical rating scale (NRS)) at 56 days post start of treatment compared to placebo in patients with COPD or ILD.

www.csi.kcl.ac.uk

6

BETTER-B Main Trial

- **Design:** International, multi-centre, randomised, placebo controlled, pragmatic Phase III trial
- **Participants:** COPD, ILD patients with Modified Medical Research Council Dyspnoea Scale grade 3-4
 - Grade 3 (I stop for breath after walking about 100 yards or after a few mins on level ground) or
 - Grade 4 (I am too breathless to leave the house or I am breathless when dressing or undressing)
- **Procedures:** Randomised 1:1 to oral mirtazapine 15mg/day or placebo, assessments at baseline, day 7, 14, 28, 56, 180
- **Clinical end points (at 56 days)**
 - 'Worst' and 'average' breathlessness over the past 24 hours using NRS
 - Chronic Respiratory Questionnaire (CRQ)
 - Integrated Palliative care Outcome Scale (IPOS)
 - Hospital Anxiety and Depression Scale (HADS)
- **Qualitative interviews & health economics**

www.csi.kcl.ac.uk

7

Overview of Progress So Far

- All deliverables and milestones to date have been met.
- WP1 survey has been completed and results disseminated at the EAPC and ERS conferences. The main paper is published (Krajnik et al BMC Pulm Med. 2022; 22, 41)
- Trial recruitment and follow-up ended with **272 UK/EU participants** (205 patients/67 caregivers) and **28 Australian participants** (20 patients/8 caregivers), making this the largest trial of mirtazapine in our patient population.
- We worked collaboratively alongside and through many challenges not least Covid-19 and its recurrent waves:
 - Participating countries de-prioritised non-Covid research
 - Fear of infection by participants/reluctance to visit hospital
 - Staff diversion to COVID-related work/staff shortage/overworked staff

www.csi.kcl.ac.uk

8

<https://betterbreathe.eu/>

The screenshot shows the homepage of the BETTER-B website. The header features the BETTER-B logo and a navigation menu with links for HOME, PROJECT, PARTNERS, RESOURCES, PUBLICATIONS, and CONTACT. Below the header is a search bar and the tagline "IMPROVING THE SITUATION OF PEOPLE AFFECTED BY BREATHLESSNESS". The main content area is divided into two columns. The left column contains a news item titled "Dr J. Randall Curtis" with a sub-header "You are here: Home". The right column features a "HOME" section with a definition of breathlessness and a paragraph about research. Below this is a large image of a dandelion seed head with seeds blowing away. At the bottom of the page, there is a footer with the URL "www.csi.kcl.ac.uk".

BETTER-B HOME PROJECT PARTNERS RESOURCES PUBLICATIONS CONTACT

IMPROVING THE SITUATION OF PEOPLE AFFECTED BY BREATHLESSNESS

Dr J. Randall Curtis
You are here: Home

We are deeply saddened to share the news of the death of our valued colleague Dr J. Randall Curtis, who has recently passed away.

Dr Curtis was a valued member of the BETTER-B programme, acting as scientific advisor. He has greatly supported this first international trial of mirtazapine for breathlessness, and has left a significant personal impact on the field of palliative care and critical care in serious illness.

Our thoughts and sympathies are with Randall's family and those close to him. You can read further about his professional legacy in a special issue in the Journal of Pain and Symptom Management [here](#).

[Click here to subscribe to our newsletter](#)

News

GENERAL

BETTER-B FINAL CONFERENCES 4TH AND 11TH DECEMBER
Category: General


28
New

We would like to cordially invite you to the BETTER-B

HOME

Breathlessness is the feeling of being out of breath as your lungs work harder to draw in more oxygen. Persistent breathlessness is when this persists long-term, despite treatment of the underlying condition. It is a frightening symptom that leads to increased distress for patients, families and carers.

Research has shown it is often neglected or under-treated. Our international partners have worked to improve its visibility by growing the knowledge base for treatments which work to improve breathlessness self-management and quality of life, and those that don't.



Because of its link between mind and body, persistent breathlessness is best targeted with a range of treatments to suit the individual. These can focus on non-drug treatments like breathlessness toolkits, however sometimes optimising treatment of the underlying disease plus non-drug treatments are not enough, and so drug treatments sometimes become necessary.

International breathlessness experts from respiratory, palliative care and rehabilitative specialisms are joining in 2019 for a European Commission funded trial to test whether an antidepressant can be repurposed to help in managing breathlessness where non-drug treatments cannot be effectively used.

www.csi.kcl.ac.uk