MANAGEMENT OF BREATHLESSNESS IN PATIENTS WITH LIFE LIMITING DISEASE

Helen Armstrong
Dr Helen Bonwick
Dr Clare Jeffries
Dr Martin Ledson
Dr Kate Marley
Mrs Sue Oakes
CURRENT STANDARDS AND GUIDELINES

GUIDELINES
• Current standards and guidelines
• Literature review – pharmacological and non-pharmacological
• Audit results
• Proposed new standards and guidelines
• Current management of cough
Non pharmacological options (Level 4)

- These are important and should not be overlooked. They may be used alone or in conjunction with medication.
- They include
  - Reassurance and explanation
  - Use of fan or cool air across face
  - Adequate positioning of the patient to aid breathing
  - Breathing exercises and relaxation training
  - Advice on modifying lifestyle
  - Acupuncture, aromatherapy and reflexology
Pharmacological options

Benzodiazepines (Level 3)

- Benzodiazepines may be useful especially if there is coexisting anxiety and/or fear.
- Lorazepam is suggested for episodes of paroxysmal breathlessness. Dose: 0.5mg-1mg sublingually as required (max dose 4mg daily).
- In patients unable to tolerate oral medication or those in the dying phase, subcutaneous Midazolam 2.5mg-5mg as required may be appropriate. If effective this can be incorporated into a 24hour subcutaneous infusion via syringe driver.
Nebulised Medication (Level 4)/(Level 1)

NB: The first medication of any nebulised medication, including saline, must be monitored for adverse effect such as bronchospasm.

• Nebulised non opioids
  – Nebulised sodium chloride 0.9% may help as a mucolytic. Consider trial for 24 hours. Dose: 5ml via a nebuliser 4 hourly as required.
  – A trial of nebulised bronchodilator should be considered if there is evidence of airways obstruction (Level 4) commonly prescribed bronchodilators are Salbutamol and Ipratropium Bromide.

Dose: Salbutamol 2.5mg-5mg up to 4 times in 24 hours.
Dose: Ipratropium Bromide 500mcgs up to 4 times in 24 hours

• There is no current evidence to support the use of nebulised lignocaine in the management of intractable breathlessness therefore it is not recommended for use at present (Level 4)

• Nebulised opioids
  – Current evidence does not support the use of nebulised opioids in the management of intractable breathlessness (Level 1)
Systemic opioids (Level 4)

- Morphine is the most commonly prescribed oral opioid in the management of intractable breathlessness.
- The prescribing of oral opioids on a ‘as required basis’ may be appropriate for paroxysmal breathlessness.
- A trial of morphine sulphate solution should be considered for patients who are opiate naive. Dose: Morphine Sulphate solution 2.5mg-5mgs every 4 hours, or as required.
- There is some evidence that the use of short acting opioid is more effective at relieving breathlessness. It may be necessary to prescribe on a regular basis in addition to any long acting opioid that the patients may be taking. If a patient is already established on opioids it may be appropriate to increase the dose of the long acting opioid by 25-50%. This would not be appropriate if the patient is experiencing intermittent periods of breathlessness as they may then get an increase in side effects.
- Diamorphine/ morphine are the strong opioids of choice in patients who are unable to swallow. Dose: Morphine 1.25mg-5mg as required subcutaneously if the patient is opioid naïve. If diamorphine is unavailable then morphine may be used as an alternative. Dose: Morphine 2.5mg-10mg as required subcutaneously. If effective, the appropriate dose can be incorporated into a 24hours infusion via a syringe driver.
Oxygen (Level 3)

- The evidence for efficacy is limited.
- A trial of oxygen should be considered in patients known to be hypoxaemic (i.e. oxygen saturation less than 90%). Care is required in patients with known COPD and Type 2 respiratory failure. Dose: oxygen 24 - 28% in patients with known COPD. Oxygen 24 - 60% for other patients.
- The use of continuous oxygen should be avoided if possible as this may lead to patient dependence, reduced mobility and give limited benefit. Intermittent use is the preferred modal of administration.
- Oxygen administered via a mask may be claustrophobic, cause a barrier between the patient and family and result in dryness of the mouth. Nasal prongs are often better tolerated than masks. Humidified oxygen may be more comfortable for the patient.
Corticosteroids (Level 3)

- Corticosteroids may be help in patients with tumour compression or lymphangitis carcinomatosis. They are also used in exacerbations of obstructive airways disease. There is no evidence of their benefit in non-specific dyspnoea. If there is no improvement, they should be discontinued. Dose: Dexamethasone 4mg-8mg daily administered before 2pm. Occasionally higher doses (8mg-16mg) are used e.g. lymphangitis, superior vena cava obstruction.
Anti-cholinergic medications (Level 4)

- Anti-cholinergic medications are the drugs of choice in the management of respiratory secretions in the dying phase. Hyoscine hydrobromide and glycopyrronium are the two most commonly used drugs.

Hyoscine hydrobromide: 400mcgs subcutaneously as required. Prescribe 1.2mgs - 2.4mgs subcutaneously via syringe driver over 24 hours.

Glycopyrronium: 200mcgs subcutaneously as required. Prescribe 0.6mgs - 2.4mgs subcutaneously via syringe driver.

Other medication (Level 4)

- There is anecdotal evidence that phenothiazines, antihistamines, cannabinoids and nebulised frusemide may be useful in the management of intractable breathlessness.
Reversible causes of breathlessness should be identified and treated where appropriate (grade D)

Patients with anxiety should be considered for a trial of relaxation therapy and/or anxiolytics (grade C)

All patients with breathlessness should have access to non-pharmacological interventions (grade C)
Standards

• Breathlessness should be controlled in all dying patients (grade D)
• All patients prescribed nebuliser medication should first receive a test dose (grade D)
• Any adverse reactions to nebulised medication should be clearly documented in the clinical notes (grade D)
Diamorphine/ morphine are the opioids of choice if patients are unable to swallow (grade D)

Midazolam is the benzodiazepine of choice in patients who are unable to swallow (grade D)

Nebulised opioids should not be used in the management of intractable breathlessness (grade C)
Literature Review
OPIOIDS
Cochrane review

- Statistically significant improvements in dyspnoea with both oral and parenteral opioids
- No evidence to support the use of nebulised opioids

Controlled Release Preparations

- Trial involving use of sustained release morphine 20mg in 24 hours in opioid naive patients with breathlessness compared with placebo.
- Intervention group reported improvement in breathlessness and significantly better sleep compared with placebo group.

Benzodiazepines

- Cochrane review: no evidence that benzodiazepines improve breathlessness in advanced disease.
- Analysis revealed a small non significant benefit which is not significant but indicates could be recommended as a third line option.

Midazolam plus Morphine

- RCT involving 101 patients estimated to be in the last week of life
- Randomized to receive 2.5mg morphine sc 4hrly or 25% increase in their current opioid, midazolam 5mg 4 hourly sc or both together
- All regimes improved breathlessness
- Morphine and midazolam together group had fewer breakthrough episodes of breathlessness

Oxygen

- Commonly used in advanced disease but is it beneficial?
- Do patients who are not hypoxic benefit?
- Is oxygen better than air for these patients?
Patient’s Perceptions of Oxygen

- Qualitative study of 8 patients on oxygen in community palliative care setting
- Only 3 were hypoxic
- Saw oxygen as their ‘lifeline’ and some thought they would be dead without it
- Did not admit to any disadvantages at first – but sore ears and nose, restricted life etc.

Risks of Oxygen

- NSPA received 281 reports of serious incidents relating to oxygen and inappropriate administration and management
- Oxygen now required to be prescribed
- Pulse Oximetry is required to be available in all locations where O2 is used

Reviewing previous work

- Cochrane review: failure to demonstrate a consistent beneficial effect of oxygen inhalation over air inhalation in advanced cancer or heart failure.
- Small study in hypoxaemic patients showed these patients had reduced intensity in breathlessness.

- Bruera E, de Stoutz N, Velasco-Leiver, Scoeller T, Hanson J. Effects of oxygen in hypoxic terminal-cancer patients. The Lancet 1993; 342, 13-14
Abernethy et Al 2010

• Randomized controlled trial on patients with advanced disease: oxygen 2L/min versus air via a concentrator for 15 hours of the day

• Inclusion criteria:
  – Over 18 yrs
  – paO2 > 7.3 kPa
  – Refractory dyspnoea related to life limiting illness
  – Maximum treatment for underlying disease
  – Dyspnoea at rest or minimal exertion

Abernethy et Al 2010

- Primary outcomes breathlessness ‘right now’ within 30 mins of waking and 30 mins of going to bed
- No significant difference between O2 and air
- Moving gas across nasal passages via nasal specs can improve dyspnoea but the gas need not be O2
- Maximum effect in first 24 hours

Non-pharmacological treatments for breathlessness
What’s the current evidence?

Dr Clare Jeffries
Specialty Registrar (LAT)
Marie Curie Hospice, Liverpool.
# Summary (SIGN grading/recommendation)

## High strength evidence
- Pulmonary Rehabilitation in COPD (1+/-A)

## Moderate strength evidence
- Non-invasive Ventilation In Motor Neuron Disease (Amyotrophic lateral sclerosis) (1/-B)
- Walking Aids (1/-B)
- Breathing Training (1/-B)

## Low strength evidence
- Acupuncture/Acupressure (1-)

## No evidence
- Distractive Auditory Stimuli /Music (1-)

## Not enough evidence
- Non-invasive Ventilation In COPD (1-)
- Fan (1-)
- Relaxation (1-)
- Counselling and support (1-)
- Counselling/support with breathing-relaxation training (1+)
- Case management (1-)
- Menthol (2-)

## High strength evidence but not routinely available.
- Neuromuscular electrical stimulation in COPD (1+/A)
- Chest wall vibration in COPD and MND (1+/A)

- Cochrane meta analysis
- 31 RCTs of rehabilitation in patients with COPD
- Intervention - at least four weeks exercise training +/- education and/or psychological support.
- Control groups - received conventional community care without rehabilitation.
- Outcomes - quality of life (included dyspnoea) and/or functional or maximal exercise capacity were measured.
- Statistically significant improvements for all the outcomes.
Analysis 01.04. Comparison 01 Rehabilitation versus usual care, Outcome 04 QoL - Change in CRQ (Dyspnea)

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 01 Rehabilitation versus usual care

Outcome: 04 QoL - Change in CRQ (Dyspnea)

<table>
<thead>
<tr>
<th>Study</th>
<th>Rehab</th>
<th>Usual care</th>
<th>Weighted Mean Difference (Random)</th>
<th>Weight (%)</th>
<th>Weighted Mean Difference (Random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behnke 2000a</td>
<td>N=15, Mean(SD)=2.42 (1.24)</td>
<td>N=15, Mean(SD)=0.16 (1.32)</td>
<td></td>
<td>4.6</td>
<td>2.26 [ 1.34, 3.18 ]</td>
</tr>
<tr>
<td>Cambach 1997</td>
<td>N=14, Mean(SD)=1.20 (1.20)</td>
<td>N=8, Mean(SD)=0.00 (0.80)</td>
<td></td>
<td>5.5</td>
<td>1.20 [ 0.36, 2.04 ]</td>
</tr>
<tr>
<td>Goldstein 1994</td>
<td>N=40, Mean(SD)=0.68 (1.14)</td>
<td>N=39, Mean(SD)=0.02 (1.30)</td>
<td></td>
<td>11.8</td>
<td>0.66 [ 0.12, 1.20 ]</td>
</tr>
<tr>
<td>Gosselink 2000</td>
<td>N=34, Mean(SD)=0.80 (1.28)</td>
<td>N=28, Mean(SD)=-0.02 (1.32)</td>
<td></td>
<td>8.6</td>
<td>0.82 [ 0.17, 1.47 ]</td>
</tr>
<tr>
<td>Griffiths 2000</td>
<td>N=93, Mean(SD)=1.00 (1.28)</td>
<td>N=91, Mean(SD)=-0.18 (1.00)</td>
<td></td>
<td>24.3</td>
<td>1.18 [ 0.85, 1.51 ]</td>
</tr>
<tr>
<td>Güell 1995</td>
<td>N=29, Mean(SD)=1.20 (1.40)</td>
<td>N=27, Mean(SD)=-0.10 (1.10)</td>
<td></td>
<td>8.5</td>
<td>1.30 [ 0.64, 1.96 ]</td>
</tr>
<tr>
<td>Güell 1998</td>
<td>N=18, Mean(SD)=0.80 (1.20)</td>
<td>N=17, Mean(SD)=-0.20 (1.20)</td>
<td></td>
<td>6.0</td>
<td>1.00 [ 0.20, 1.80 ]</td>
</tr>
<tr>
<td>Hernandez 2000</td>
<td>N=20, Mean(SD)=1.08 (1.14)</td>
<td>N=17, Mean(SD)=0.30 (1.20)</td>
<td></td>
<td>6.6</td>
<td>0.78 [ 0.02, 1.54 ]</td>
</tr>
<tr>
<td>Simpson 1992</td>
<td>N=12, Mean(SD)=1.20 (1.14)</td>
<td>N=10, Mean(SD)=0.00 (0.84)</td>
<td></td>
<td>5.6</td>
<td>1.20 [ 0.37, 2.03 ]</td>
</tr>
<tr>
<td>Singh 2003</td>
<td>N=20, Mean(SD)=0.96 (0.88)</td>
<td>N=20, Mean(SD)=0.08 (0.84)</td>
<td></td>
<td>12.1</td>
<td>0.88 [ 0.35, 1.41 ]</td>
</tr>
<tr>
<td>Wijkstra 1994</td>
<td>N=28, Mean(SD)=0.86 (1.02)</td>
<td>N=15, Mean(SD)=-0.04 (1.32)</td>
<td></td>
<td>6.4</td>
<td>0.90 [ 0.13, 1.67 ]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>N=323</strong></td>
<td><strong>N=287</strong></td>
<td><strong>Weighted Mean Difference (Random)</strong></td>
<td><strong>100.0</strong></td>
<td><strong>1.06 [ 0.85, 1.26 ]</strong></td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=11.60 df=10 p=0.31 I² =13.8%
Test for overall effect z=10.13  p<0.000001
Non-invasive Ventilation
Non-invasive ventilation in MND


RCT
MND with orthopnoea with maximum inspiratory pressure less than 60% of that predicted or symptomatic hypercapnia.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>NIV (n=22)</th>
<th>Standard care (n=19)</th>
</tr>
</thead>
</table>

Primary Outcomes:
- Survival
- Quality-of-life outcome measures

Dyspnoea was a secondary outcome measure
NIV in MND Continued


All showed improvement in dyspnoea. *Significance In poor bulbar group?*

**Chronic Respiratory Disease Questionnaire - dyspnoea**

<table>
<thead>
<tr>
<th></th>
<th>NIV</th>
<th>Standard care</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n=41)</td>
<td>199 (41–1287)</td>
<td>52 (0–730)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Good bulbar function (n=20)</td>
<td>204 (73–610)</td>
<td>4 (0–90)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Poor bulbar function (n=21)</td>
<td>131 (41–1287)</td>
<td>115 (2–730)</td>
<td>0.57 *</td>
</tr>
</tbody>
</table>

* (not sufficiently powered for this subgroup)

(Main Study Findings)

NIV improved symptoms, quality of life and survival in all patients and in the subgroup with better bulbar function (n=20). This subgroup showed improvement in several measures of quality of life and a median survival benefit of 205 days (p=0.006) with maintained quality of life for most of this period. NIV improved some quality-of-life indices in those with poor bulbar function, including _sym (p=0.018), but conferred no survival benefit.)
Non-invasive ventilation in COPD


6 RCT and 9 non RCT Severed COPD and respiratory failure on NIV

Casanova n=44 1year duration, Clini n=47 2year duration, Garrod n=37 8weeks duration, Renston n=17 <1week duration

### TABLE 10
Dyspnoea ratings with bilevel noninvasive positive pressure ventilation use in chronic obstructive pulmonary disease

<table>
<thead>
<tr>
<th>First author [Ref.]</th>
<th>Scale used</th>
<th>Trial length</th>
<th>Before/after Rx/CL</th>
<th>Outcome data</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RCTs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Casanova [11]</td>
<td>BORG/MRCD</td>
<td>1 yr</td>
<td>Rx</td>
<td>5±1.63±2*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CL</td>
<td>4±1.63±2</td>
<td></td>
</tr>
<tr>
<td>Clini [23]</td>
<td>MRCD at 0 months/12 months/24 months</td>
<td>2 yrs</td>
<td>Rx</td>
<td>3.3±0.3/2.7±0.8*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RX</td>
<td>2.3±0.72</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CL</td>
<td>2.7±0.6/3.0±0.77/</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Garrod [24]</td>
<td>CRDQ dyspnoea score</td>
<td>8 weeks</td>
<td>Rx</td>
<td>13.1 to 18.0***</td>
<td>Data from the dyspnoea portion of the CRDQ instrument</td>
</tr>
<tr>
<td>Renston [22]</td>
<td>BORG</td>
<td>5 days</td>
<td>Rx</td>
<td>2.0±1.2 to 0.7±0.9**</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CL</td>
<td>1.8±1.13 to 1.3±1.13</td>
<td></td>
</tr>
<tr>
<td><strong>Non-RCTs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strumpf [30]</td>
<td>Dyspnoea scale of Mahler</td>
<td>6 months</td>
<td>Before</td>
<td>0.6±1.7</td>
<td>Functional impairment dyspnoea rating</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>After</td>
<td>0.3±1.3</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean±so. Rx: treatment; CL: control; BORG: Borg dyspnoea scale; MRCD: Medical Research Council dyspnoea scale; CRDQ: Chronic Respiratory Disease Questionnaire. *: p=0.048 at 12 months; †: p=0.013 at 24 months. *p<0.05; **: p<0.01; ***: p<0.001.
Non-invasive ventilation in COPD continued


These two longer-term randomised controlled trials of NIV + LTOT versus LTOT alone involving larger patient samples reported small benefits in favour of NIV. Casanova et al showed a small improvement in patient dyspnoea scores, while Clini et al reported improved dyspnoea and health-related QOL using MRF(28) questionnaire but not using SGRQ.


A recent randomised trial n=144 (intervention NIV and LTOT vs control LTOT) showed improved survival but decreased self reported quality of life and no improvement in dyspnoea using SGRQ.
Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.


4. Gupta R et al. Effect of rollator use on health related quality of life in individuals with COPD. Chest 2006;130:1089-95


Walking Aids
Bausewein C, Booth S, Gysels M, Higginson IJ.
Non-pharmacological interventions for breathlessness in advanced stages of malignant
and non-malignant diseases.

7 Studies (6 RCT, Cross Over and 1 RCT)

Participants: n=202, Moderate to very severe COPD

Intervention:
Six studies - 6MWT with Rollator vs 6MW unaided/stick
One study - Integrated rollator in daily activities for 8 weeks vs no rollator.

Outcomes: Included Dyspnoea
(6 Modified Borg, 1 CRQ)

6 high quality studies.
4 showed significant improvement in dyspnoea, one showed a non-significant improvement (latter was underpowered)
Strength of evidence was graded as moderate.
Breathing Training

Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

Breathing Training
Bausewein C, Booth S, Gysels M, Higginson IJ.
Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.


Breathing Training
Bausewein C, Booth S, Gysels M, Higginson IJ.
Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

- 3 studies, 2 RCT, 1 RCT cross over
- 129 participants, 2 studies COPD, 1 study mixed cardiopulmonary
- 2 studies pursed lip breathing, 1 study breathing technique
- Outcomes Borg/modified Borg/VAS

- All 3 studies were of high quality. 2 showed a significant difference in the intervention group, therefore the strength of evidence was classified as moderate.
- (One study although showing no significant difference in dyspnoea during walking did show improved recovery time using purse lip breathing).
Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

Acupuncture and Acupressure
Bausewein C, Booth S, Gysels M, Higginson IJ.
Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.


Acupuncture and Acupressure
Bausewein C, Booth S, Gysels M, Higginson IJ.
Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

• 5 Studies - 3RCT, 2RCT cross over
• 109 participants included in the acupuncture
• 75 participants included in the acupressure studies.
• Mainly COPD, 1 study in cancer patients one study with COPD and 8% non-malignant pulmonary disease.
• Meta analysis was not possible.

• Four studies were of high quality of which 2 showed significant improvement in breathlessness.

• Overall Cochrane Systematic review graded evidence as low.
Hand Held Fan

Very few studies.
Some short term benefit possibly, no evidence on long term effect.
Hand Held Fan


Method: RCT, crossover
Participant: n=49 (48 completed study)
Stable chronic dyspnoea from any cause, dyspnoea >2 on dyspnoea exertion scale
Intervention: Fan directed to cheeks for 5mins (washout period 10mins)
Control: Fan directed to legs for 5mins (washout period 10mins)
Outcome: Significant reduction in breathlessness on VAS score (p=0.003).
Study adequately powered. But no long term follow up.

Authors comments: This study supports the hypothesis that a handheld fan directed to the face reduces the sensation of breathlessness. The fan was acceptable to participants: it is inexpensive, portable, enhances self-efficacy, and available internationally. It should be recommended as part of a palliative management strategy for reducing breathlessness associated with advanced disease.

Method: RCT crossover
Participant: n=17 COPD, FEV1 predicted 28%

Intervention: Fan blowing on face nasal cannulae with O2 flow to maintain sats >90% during controlled 6MWT; testing during 2 trials/day for 3 days.

Control: O2 flow only to maintain sats >90% during controlled 6MWT; testing during 2 trials/day for 3 days.

Outcome: VAS dyspnoea at baseline and every 2 mins
first day difference 0.4 (CI 0.12-0.63, p=0.01),
subsequent 2 days 0.15 (CI -0.39 -0.78, p=0.53)

Authors comments: Half the patients declared a preference for the fan without any association with reduction in dyspnoea. The fan may provide a small and transient or placebo effect to reduce exercise induced dyspnoea.

Method: RCT embedded within a longitudinal study
Participants: n=70. Breathless due to advanced cancer or COPD III/IV. (data available for n=36, high attrition rate – death and lost missing postal questionnaire). Not sufficiently powered due to final sample size

Intervention: Use of hand held fan
Control: Use of wrist band

Outcome: Use of fan after 2 months 50%. Use of wrist band after 2 months 20%. p=0.2 No difference in mean breathlessness change scores on Modified Borg between the fan and the wristband after two months (p = 0.90). 9/23 felt fan helpful and 4/12 felt wrist band helpful.

Authors Conclusions: The preliminary evidence of effectiveness of the HHF could not be proved. Patients often stopped using the HHF but a small group seemed to benefit which was not necessarily related to a relief in breathlessness. Therefore, more work is necessary on selecting and identifying those who might benefit from the HHF.
Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

Relaxation


Progressive muscle relaxation (PMR)


Stress management technique to reduce muscular tension that accompanies anxiety. Participants are trained to voluntarily relax certain muscles to reduce anxiety. Needs to be practiced daily.

**Studies with PMR and daily home practice seem to have a positive effect over four weeks.**

**Long term effect is unclear.** No positive effect in the study which measured breathlessness and other symptoms after 14 weeks (Yu 2007).

**Guided imagery**

There was only one study on guided imagery without any home practice which showed no difference in breathlessness after six sessions.
Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

Counselling and support


Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

Counselling/support with breathing-relaxation training


Intervention based on pulmonary rehabilitation programmes used in COPD patients but specifically tailored to the needs of lung cancer patients.

One was a feasibility study (Corner 1996). The other an adequately powered multi-centre RCT (Bredin 1999).

Both studies showed an improvement in breathlessness in the intervention group. Corner described a lasting effect of the three week intervention after 12 weeks.
Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

Case management


11 normal participants asked to rate respiratory discomfort on VAS while breathing on a device with a flow restrictive load.

Also 8 of the subjects were assessed with strawberry flavoured air

Inhalation of menthol caused a significant reduction in sensation of respiratory discomfort p < 0.01) without a significant change in breathing pattern and ventilation.

Strawberry no effect
Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

Distractive Auditory Stimuli /Music
Bausewein C, Booth S, Gysels M, Higginson IJ.
Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.


Distractive Auditory Stimuli /Music

• 6 Studies conducted in COPD patients.
• 3 RCT and 3 cross over trials.
• Four studies of high quality.
• Three of them did not show an improvement in breathlessness when using DAS during exercise.
• No evidence currently to support DAS to relieve dyspnoea
Coming soon…

- Neuromuscular electrical stimulation in COPD (or magnetic stimulation)
- Chest wall vibration in COPD and MND
Neuromuscular electrical stimulation in COPD

Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.

Neuromuscular electrical stimulation in COPD
Bausewein C, Booth S, Gysels M, Higginson IJ.
Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.


3 studies, 50 participants, moderate to severe COPD
At home, outpatient and inpatient setting

High strength of evidence that NMES over 4-6 weeks helps to relieve dyspnoea in patients with COPD.
Chest wall vibration in COPD and MND

Bausewein C, Booth S, Gysels M, Higginson IJ.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.
**Chest wall vibration in COPD and MND**

**Bausewein C, Booth S, Gysels M, Higginson IJ.**  
**Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.**  


**CWV has been tested in two conditions COPD and MND, showing high strength of evidence in the whole group and also in subgroup of COPD.**
### Summary

<table>
<thead>
<tr>
<th>High strength evidence</th>
<th>Not enough evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pulmonary Rehabilitation in COPD</td>
<td>• Non-invasive Ventilation In COPD</td>
</tr>
<tr>
<td>• Non-invasive Ventilation In Motor Neuron Disease (Amyotrophic lateral sclerosis)</td>
<td>• Fan</td>
</tr>
<tr>
<td></td>
<td>• Relaxation</td>
</tr>
<tr>
<td></td>
<td>• Counselling and support</td>
</tr>
<tr>
<td></td>
<td>• Counselling/support with breathing-relaxation training</td>
</tr>
<tr>
<td></td>
<td>• Case management</td>
</tr>
<tr>
<td></td>
<td>• Psychotherapy</td>
</tr>
<tr>
<td></td>
<td>• Menthol</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate strength evidence</th>
<th>Low strength evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Walking Aids</td>
<td>• Acupuncture/Acupressure</td>
</tr>
<tr>
<td>• Breathing Training</td>
<td></td>
</tr>
<tr>
<td>• Aerobic training in CHF</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low strength evidence</th>
<th>No evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acupuncture/Acupressure</td>
<td>• Distractive Auditory Stimuli /Music</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No evidence</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Neuromuscular electrical stimulation in COPD</td>
</tr>
<tr>
<td></td>
<td>• Chest wall vibration in COPD and MND</td>
</tr>
</tbody>
</table>
PROPOSED NEW STANDARDS AND GUIDELINES
REVISED GUIDELINES

• To remain in the standards and guidelines

• Suggest that this should be removed

• Suggest this should be added
Non pharmacological options (Level 4)

- These are important and should not be overlooked. They may be used alone or in conjunction with medication
- They include
  - Reassurance and explanation
  - Use of fan or cool air across face
  - Adequate positioning of the patient to aid breathing
  - Breathing exercises and relaxation training
  - Advice on modifying lifestyle
  - Acupuncture, aromatherapy and reflexology

- See table of suggested non pharmacological interventions
Pharmacological options

**Benzodiazepines (Level 3)**

- Benzodiazepines may be useful especially if there is coexisting anxiety and/or fear
- Lorazepam is suggested for episodes of paroxysmal breathlessness Dose: 0.5mg-1mg sublingually as required (max dose 4mg daily)
- In patients unable to tolerate oral medication or those in the dying phase, subcutaneous midazolam 2.5mg-5mg as required may be appropriate. If effective this can be incorporated into a 24hour subcutaneous infusion via syringe driver.

- See table of pharmacological interventions
Nebulised medication (Level 4)/(Level 1)

NB The first medication of any nebulised medication, including saline, must be monitored for adverse effect such as bronchospasm

- **Nebulised non opioids**
  - Nebulised sodium chloride 0.9% may help as a mucolytic. Consider trial for 24 hours. **Dose:** 5ml via a nebuliser 4 hourly as required
  - A trial of nebulised bronchodilator should be considered if there is evidence of airways obstruction (Level 4) commonly prescribed bronchodilators are Salbutamol and Ipratropium Bromide.
  
  **Dose:** Salbutamol 2.5mg-5mg up to 4 times in 24 hours.
  **Dose:** Ipratropium Bromide 500mcgs up to 4 times in 24 hours
  see table of pharmacological interventions

- **Nebulised opioids**
  - Current evidence does not support the use of nebulised lignocaine in the management of intractable breathlessness therefore it is not recommended for use at present (Level 4)

- **Nebulised opioids**
  - Current evidence does not support the use of nebulised opioids in the management of intractable breathlessness (Level 1)
Systemic opioids (Level 4),

- Morphine is the most commonly prescribed oral opioid in the management of intractable breathlessness.
- The prescribing of oral opioids on a ‘as required basis’ may be appropriate for paroxysmal breathlessness.
- A trial of morphine sulphate solution should be considered for patients who are opiate naive. Dose: Morphine Sulphate solution 2.5mg-5mgs every 4 hours, or as required see table of pharmacological interventions.
- The opioid of choice is morphine. If the patient is currently taking an alternative strong opioid for pain control then this should be used to relieve breathlessness. The immediate release form is the preferred choice.
- There is some evidence that the use of short acting opioid is more effective at relieving breathlessness. It may be necessary to prescribe on a regular basis in addition to any long acting opioid that the patients may be taking. If a patient is already established on opioids it may be appropriate to increase the dose of the long acting opioid by 25-50%. This would not be appropriate if the patient is experiencing intermittent periods of breathlessness as they may then get an increase in side effects.
- Diamorphine/ morphine are the strong opioids of choice in patients who are unable to swallow. Dose: Morphine 1.25mg- 5mg as required subcutaneously if the patient is opioid naïve. If diamorphine is unavailable then morphine may be used as an alternative. Dose: Morphine 2.5mg-10mg as required subcutaneously. If effective, the appropriate dose can be incorporated into a 24hours infusion via a syringe driver.
- Strong opioids may need to be prescribed via the subcutaneous route if the patient is unable to swallow. Where patient are unable to swallow use the appropriate dose of strong opioid subcutaneously and then incorporate into a continuous subcutaneous infusion as needed (see Guidelines for the use of drugs in the last hours and days of life).
Oxygen (Level 3)

- The evidence for efficacy is limited
- A trial of oxygen should be considered in patients known to be hypoxaemic (i.e. oxygen saturation less than 90%). Care is required in patients with known COPD and Type 2 respiratory failure. Dose: oxygen 24 - 28% in patients with known COPD. If oxygen is not felt to be beneficial then it should be discontinued
- The use of continuous oxygen should be avoided if possible as this may lead to patient dependence, reduced mobility and give limited benefit. Intermittent use is the preferred modal of administration. Oxygen should be used for the shortest period of time which provides relief.
- Oxygen administered via a mask may be claustrophobic, cause a barrier between the patient and family and result in dryness of the mouth. Nasal prongs are often better tolerated than masks. Humidified oxygen may be more comfortable for the patient.
- Continuous long term oxygen therapy should be avoided in most patients
Corticosteroids (Level 3)

- Corticosteroids may be help in patients with tumour compression or lymphangitis carcinomatosis. They are also used in exacerbations of obstructive airways disease. There is no evidence of their benefit in non specific dyspnoea. If there is no improvement, they should be discontinued. **Dose:** Dexamethasone 4mg-8mg daily administered before 2pm. Occasionally higher doses (8mg-16mg) are used e.g. lymphangitis, superior vena cava obstruction. **For suggested doses see table of pharmacological intervention (steroid guideline)**
Anti-cholinergic medications (Level 4)

- Anti-cholinergic medications are the drugs of choice in the management of respiratory secretions in the dying phase. Hyoscine hydrobromide and glycopyrronium are the two most commonly used drugs.

  Hyoscine hydrobromide: 400mcgs subcutaneously as required. Prescribe 1.2mgs-2.4mgs subcutaneously via syringe driver over 24 hours.

  Glycopyrronium: 200mcgs subcutaneously as required. Prescribe 600mcgs -2.4mgs subcutaneously via syringe driver.

Other medication (Level 4)

- There is anecdotal evidence that phenothiazines, antihistamines, cannabinoids and nebulised frusemide may be useful in the management of intractable breathlessness.
REVISED STANDARDS

• To remain in the standards and guidelines
  • Suggest that this should be removed
  • Suggest this should be added
Standards

• Reversible causes of breathlessness should be identified and treated where appropriate (grade D)
• Patients with anxiety should be considered for a trial of relaxation therapy and/or anxiolytics (grade C)
• All patients with breathlessness should have access to non pharmacological interventions (grade C)
Standards

- Breathlessness should be controlled in all dying patients (grade D)
- All patients prescribed nebuliser medication should first receive a test dose (grade D)
- Any adverse reactions to nebulised medication should be clearly documented in the clinical notes (grade D)
Standards

- Diamorphine/ morphine are the opioids of choice if patients are unable to swallow, if the patient is not already prescribed an alternative strong opioid. If this is the case then that opioid should be used initially in the short acting form (grade D).
- Midazolam is the benzodiazepine of choice in patients who are unable to swallow (grade D).
• Nebulised opioids should not be prescribed in the management of breathlessness (grade C)

• When oxygen is given in an inpatient setting it should be prescribed on the medicine chart

• Pulse oximetry should be used to measure oxygen saturation and only if the patient is hypoxic should prescribed oxygen therapy be commenced
• All patients with cough should have their medication reviewed and any medications which precipitates cough should be discontinued (grade D)
• Underlying causes of cough should be sought and treated where applicable (grade D)
• Where medications are used to treat cough their effect should be documented and the drug withdrawn where they are ineffective (grade D)
## Drugs Used in the Management of Breathlessness

<table>
<thead>
<tr>
<th>Drug</th>
<th>Suggested dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>Oramorph 2.5 to 5mg every 4 hours or as required in opioid naïve patients.</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Start at 2 mg b.d. to t.d.s. (could go up to 5mg t.d.s)</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>500 micrograms to 1mg as required (max 4mg daily)</td>
</tr>
<tr>
<td>Salbutamol</td>
<td>2.5mg to 5mg nebs regularly and/or p.r.n. for bronchospasm</td>
</tr>
<tr>
<td>Saline nebs</td>
<td>2.5ml to 5ml regularly and/or p.r.n. for tenacious secretions</td>
</tr>
<tr>
<td>Midazolam</td>
<td>2.5mg to 5 mg p.r.n where patients cannot swallow</td>
</tr>
<tr>
<td>Oxygen</td>
<td>In hypoxaemic patients according to saturations and response of patient. Stop if no benefit</td>
</tr>
</tbody>
</table>
Cough

Martin Ledson
Liverpool Lung Cancer Unit
What is the highest peak in the Alps?

A: Sweat  B: Panic  C: Cheat  D: Run away
Major Charles Ingram, Tecwen Whittock and Alyn H Morice
BTS GUIDELINES. Recommendations for the management of cough in adults.
A H Morice, L McGarvey, I Pavord, on behalf of the British Thoracic Society
What is a cough?

• Defensive reflex to protect and clear the bronchial tree.

• Inspiratory gasp, close glottis, valsala, expiratory blast.
Cough is initiated when the rapidly adapting receptors found in the mucosa of the pharynx, trachea, large airways, pleura are stimulated.

- Afferent-vagus to brainstem
- Efferent-to vagus, phrenic, and glossopharyngeal
- No discrete central cough center
Men prefer pictures!

FIGURE I. Cough Receptors involved in the normal cough mechanism. (From Irwin RS, et al., Cough: A comprehensive review. Arch Intern Med. 1977; 137:1186-91)
Acute cough

- 120,000,000 episodes a year in UK
- 24 million self medicate
Chronic cough

- 15% adults Female > Male
- 10% secondary care referrals
- OAD/Drugs/PND/Smoking/GOR/Heart failure
- Hx/Exam/Bloods/cxr/spirometry/Bronchoscopy/provocation tests/Tracheo-oesophageal pH testing/VQ scan
Medical text book

Table 1: Treatment of Persistent Cough

<table>
<thead>
<tr>
<th>Cause</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post nasal drip and Sinusitis</td>
<td>Antihistamine, nasal decongestant steroid nasal spray ± antibiotics</td>
</tr>
<tr>
<td>Asthma</td>
<td>Steroid inhaler</td>
</tr>
<tr>
<td>Gastro-oesophageal reflux</td>
<td>Antacids, $H_2$ antagonist proton pump inhibitors</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>stop treatment</td>
</tr>
</tbody>
</table>
Men like it when it's simple!

3. Find x.

Here it is...
Cough and Advanced Malignancy

• 48%-80% Hospice patients
• Direct
  • Endobronchial tumour
  • Lymphatic spread and nodes
• Indirect
  – Infection
  – PE
  – Atelectasis
  – Effusions
  – SVCO
  – Oesophageal strictures/fistula
  – Rx induced i.e. radiotherapy
Specific Treatments

- Stop ACE
- Nasal/inhaled/oral steroids
- B2 agonists
- PPI
- Anti-histamines
- Manage central tumour/effusions
Empirical Treatments

- Centrally acting antitussins
  - Codein
  - Dextromethophan
  - Hydrocodein
  - Morphine/methadone/hydromorphone

- Peripherally acting antitussins
  - Benzonatate
  - Nebulised morphine
  - Sodium chromoglycate
  - Lidocaine
Other Treatments

- Benzodiazepines
- Humidification
- Bronchodilators
- Glycoprolate/hyoscyamine
- Marshmellow/sundew/cottsfoot/thyme
- Relaxation
- Psychogenic cough
Evidence

• Chochrane review ‘Interventions for cough in cancer’ 2009.
  • No practice recommendations could be drawn from this review.
• ACCP ‘Cough suppressant and Pharmacologic protussive therapy’
  • Most effective for short term cough
  • Relatively few drugs are effective as cough suppressants
That's a nasty cough you've got there!