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Results of a pilot investigation into a complex intervention for breathlessness in advanced chronic obstructive pulmonary disease (COPD): Brief report

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ABSTRACT

Objective: Breathlessness is the most common devastating symptom of advanced chronic obstructive pulmonary disease (COPD). The Breathlessness Intervention Service (BIS) is a multidisciplinary service that uses both pharmacological and non-pharmacological evidence-based interventions to reduce the impact of the symptom. The results of a Phase II evaluation of the service are reported.

Method: Pretest - posttest analysis of non-randomized data was performed for 13 patients with severe advanced COPD referred to BIS.

Results: Mean VAS-Distress scores (primary outcome measure) decreased (improved) for the group between baseline and follow up suggesting a clinically significant improvement: 6.88 ($SD = 2.50$) to 5.25 ($SD = 2.99$). At an individual level, 11 of the 13 patients showed a decrease in their distress due to breathlessness, and for eight of these this was clinically significant (range of all decreases 0.3–7.1 cm). Changes in secondary outcome measures are also reported.

Significance of results: The Breathlessness Intervention Service appears to reduce distress due to breathlessness among patients with advanced COPD. A Phase III fully-powered randomized controlled trial is warranted.

KEYWORDS: Breathlessness, Chronic obstructive pulmonary disease, Complex intervention, Feasibility study

INTRODUCTION

Breathlessness is the most common devastating symptom of advanced chronic obstructive pulmonary disease (COPD) affecting both patient and family (Rocker et al., 2007). Breathlessness is underreported by patients, and clinicians are uncertain how to manage chronic intractable breathlessness and do not actively assess it (Roberts et al., 1993; Booth et al., 2003). There is increasing evidence that a multi-professional approach using both pharmacological and non-pharmacological interventions can reduce the impact of the symptom and improve quality of life (Bredin et al., 1999; Booth et al., 2006).

The results of a Phase II evaluation of the Breathlessness Intervention Service (BIS) based on this approach are described here. Although there is an evidence base for each intervention used by the service, the clinical and cost-effectiveness of the complex intervention provided by such a service has not been formally evaluated in patients with COPD. In a Phase I qualitative study of BIS, patients and carers reported liking: the positive, educational approach of the service which emphasised what was possible, not

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what lost; non-pharmacological strategies (some of which were new to them for example a handheld fan); open access to advice; and, being seen in their own homes. Referrers valued its educational role and the opportunity for a second opinion on the management of patients with complex conditions (Booth et al., 2006).

Phase II was a pilot investigation of BIS with patients with advanced COPD. It also tested the feasibility of a single-blind, fast-track, pragmatic, randomized controlled trial (RCT) design of BIS versus standard care (ClinicalTrials.gov: NCT00711438) to enable planning of a definitive, fully-powered RCT. Although BIS cares for people with breathlessness of any etiology, COPD is the most common respiratory disease associated with breathlessness in the United Kingdom. It will be the third most common cause of mortality across the world by 2020 (Murray & Lopez, 1997), and is less researched than advanced cancer; thus Phase II focused on patients with COPD.

METHOD

The feasibility trial's methodology is described in detail in a separate paper (Farquhar et al., 2009a). Ethics and R&D approvals were obtained (REC reference no. 05/Q0108/471), and informed consent was obtained from participants. The fast track trial design (Higginson et al., 2006; Farquhar et al., 2009b) made it possible to combine the baseline pre-intervention data for both arms of the trial (i.e. all t1s) and the follow-up post-intervention data for both arms (i.e. t3 for the fast track arm and t5 for waiting list arm), so converting the data set from a randomized one to a pretest —posttest non-randomized one. This increased the sample receiving the intervention and completing outcome measures from seven to 13.

Table 1. *The Breathlessness Intervention Service*

A multidisciplinary service was established in the Department of Palliative Care in a tertiary referral center in 2004, with the aim of improving the palliation of breathlessness. The service model was developed on the basis of the findings of earlier studies (Booth et al., 1996; Booth & Adams, 2001; Booth et al., 2003; Booth et al., 2006) conducted within the MRC framework for the development and evaluation of complex interventions (Medical Research Council, 2000). A specialist respiratory physiotherapist was recruited to join the Macmillan consultant in palliative medicine to offer a number of evidence-based interventions over a period of weeks, working closely with other clinical services already caring for the patient. The service was given the title Breathlessness Intervention Service[1] (BIS) because it uses an active, focused rehabilitative approach in partnership with patient and carer. A detailed initial assessment of the impact of breathlessness on the patient and family is followed by implementation of an individualized treatment program with emphasis on problem-solving and the enhancement of self-management strategies. Evidence-based interventions are both non-pharmacological (modifying central perception by a range of psychological and physical interventions including a palliative care approach to life-threatening disease and psychosocial issues) and pharmacological, as required. Uniquely, care is flexibly located where the patient chooses. Referrals come from hospital and primary care specialists in medicine, nursing, and the allied health profession.

[1]by PF, first physiotherapist on the team

Table 2. *Reported quantitative outcome measures and clinically significant changes for Phase II evaluation of Breathlessness Intervention Service*

Outcome measure	Clinically significant difference from baseline to follow up
VAS-Distress (Corner et al., 1996) VAS-Breathlessness at Worst (Corner et al., 1996) VAS-Breathlessness at Best (Corner et al., 1996)	A difference between the baseline and follow up measurements of 1 cm on this scale could be regarded as clinically significant for patients with intractable breathlessness (Charles et al., 2008).
Chronic Respiratory Questionnaire (CRQ): Mastery subscale (Guyatt et al., 1987)	Guyatt et al. states that an improvement in 0.5 per domain (e.g. mastery) represents a small but important change in patients' day-to-day lives, changes between 0.75 and 1.25 represent important changes of moderate magnitude and changes >1.5 represent important changes of large magnitude (Guyatt et al., 1987).
Hospital Anxiety and Depression Scale (HADs) (Zigmond & Snaith, 1983)	Scores of 8–10 in each subscale (anxiety and depression) indicate "possible clinical disorder" and of 11–21 indicate "probable clinical disorder" (Zigmond & Snaith, 1983). Puhan et al. reported a minimally important difference for the HADS of $\sim$1.5 in COPD patients corresponding to a change from baseline of $\sim$20% (Puhan et al., 2008).

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Breathlessness Intervention Service (BIS)

The intervention, the Breathlessness Intervention Service (BIS) is described in Table 1.

Outcome Measures

The primary outcome measure was "distress due to breathlessness" measured using a Visual Analogue Scale (VAS-Distress; anchors "no distress"/ "extreme distress"). Existing trials of interventions for patients with COPD (e.g. of pulmonary rehabilitation) focus on physiological outcomes (e.g. clinical measures of breathlessness), however our earlier work suggested the need to look beyond these and consider other outcomes. VAS-Distress was used by Bredin et al.'s multi-center RCT of a breathlessness intervention clinic for patients with lung cancer (Bredin et al., 1999). The outcome measures are summarized in Table 2.

Sample

A cohort of consecutive patients with advanced COPD referred to the pilot BIS.

Analysis

The data set was analyzed as a non-randomized group. Descriptive statistics were computed for baseline (pre-intervention) and follow up (post-intervention) data across the entire sample. Data are presented as summary statistics and plots of individual scores to show within-patient changes. No statistical testing was conducted due to the small sample size. Plotting scores against time is recommended for serial measurements in small samples (Matthews et al., 1990). As this was a feasibility study and comparative analysis was not our primary objective, it was not powered for statistical testing. Missing data are reported elsewhere (Farquhar et al., 2009a). Extracts of qualitative follow-up interviews are presented in two illustrative case studies.

RESULTS

Response Rates

Twenty consecutively referred patients met the inclusion criteria, 16 agreed to participate, two were withdrawn before recruitment due to acute deterioration, and 13 completed the protocol (one died on protocol). Data are reported for the 13 patients who completed the protocol.

Demographics

The age range of responding patients was 53–80 years (median 69 years). The majority of patients were male (8/13); three lived alone. Most recent FEV1s ranged from 0.68–1.28 L/min and % predicted ranged from 12.6–28.9% (indicating severe COPD). Four patients had probable clinical anxiety disorders and three had probable clinical depression disorders at baseline, per Hospital Anxiety and

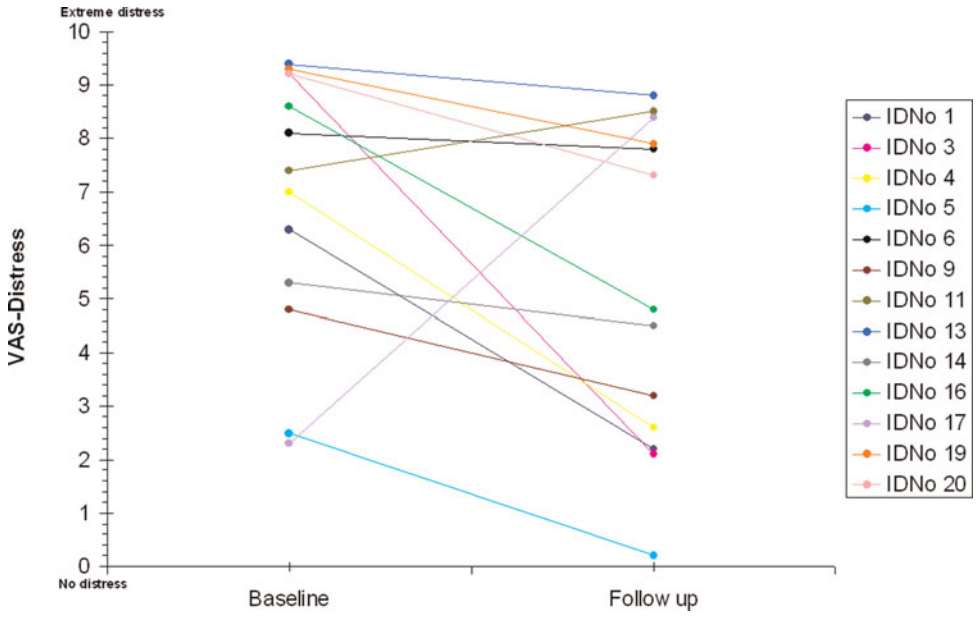

Fig. 1. (Color online) Changes in individuals' scores on VAS-Distress due to Breathlessness from baseline to follow up (Phase II Evaluation of Breathlessness Service Intervention).

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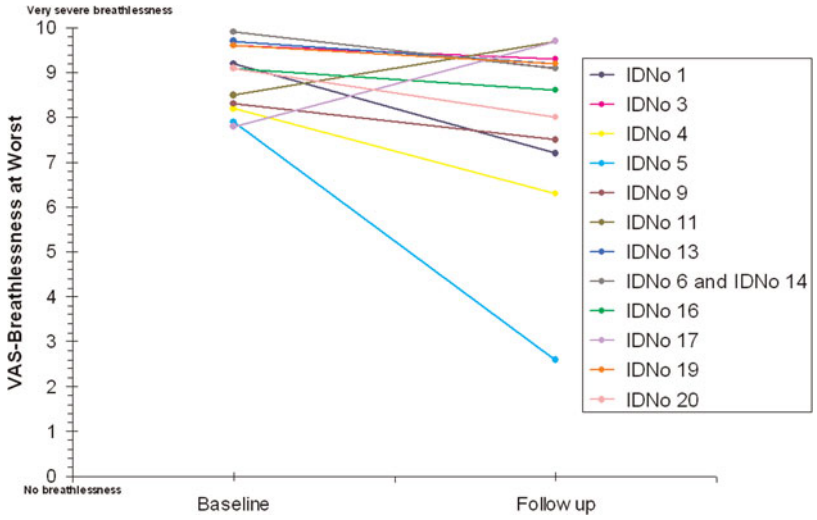

Fig. 2. (Color online) Changes in individuals' scores on VAs-breathlessness at worst from baseline to follow-up (Phase II evaluation of Breathlessness Intervention Service).

Depression Scale (HADS), reflecting a typical pattern for patients with severe advanced COPD (a further seven and three had 'possible' clinical anxiety and depression respectively).

Primary Outcome Measure — VAS-Distress

Group mean VAS-Distress scores decreased (improved) between baseline and follow up from 6.88 ($SD = 2.50$) to 5.25 ($SD = 2.99$): a clinically significant improvement. Figure 1 presents plots of individuals' scores.

For individuals, 11 patients showed a decrease in their distress due to breathlessness, and for eight this was clinically significant (range of all decreases 0.3–7.1 cm).

Secondary Outcome Measures

Group mean VAS-Breathlessness at Worst scores decreased (improved) between baseline and follow up from 8.95 ($SD = 0.76$) to 8.12 ($SD = 1.96$): not a clinically significant improvement. Figure 2 presents plots of individuals' scores.

Table 3. *Clinically significant improvements by individuals from baseline to follow up; Phase II evaluation of Breathlessness Intervention Service*

ID no.	VAS-Distress	VAS-Breathlessness at Worst	VAS-Breathlessness at Best	Mastery CRQ[1]	HADS[2] anxiety	HADS depression
Level of change required for clinically significant improvement:	1 cm+	1 cm+	1 cm+	0.5+	1.5+	1.5+
001	✓	✓	X	✓	✓	X
003	✓	X	X	✓	X	X
004	✓	✓	X	✓	✓	X
005	✓	✓	✓	✓	✓	X
006	X	X	X	X	X	X
009	✓	X	✓	✓	X	X
011	X	X	✓	✓	X	X
013	X	X	X	X	X	X
014	X	X	✓	X	X	X
016	✓	X	✓	X	X	X
017	X	X	X	X	X	X
019	✓	X	X	X	X	X
020	✓	✓	X	✓	✓	X

[1]CRQ = Chronic Respiratory Questionnaire
[2]HADS = Hospital Anxiety and Depression Scale

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For individuals, 11 patients showed improved Breathlessness at Worst scores, and for four this was clinically significant. Two patients' scores deteriorated (range of changes 0.3–5.3 cm for improvers, 1.2–1.9 cm for deteriorators).

Group mean VAS-Breathlessness at Best scores increased (deteriorated) between baseline and follow up from 2.75 ($SD = 1.60$) to 2.92 ($SD = 1.87$); not a clinically significant deterioration. For individuals, seven patients showed improved Breathlessness at Best scores, and for five this was clinically significant. Five patients' scores increased representing deterioration and one showed no change (range of changes 0.6–3.2 cm for improvers, 0.6–4.8 cm for deteriorators).

Group mean Chronic Respiratory Questionnaire (CRQ) Mastery scores improved between baseline and follow up from 3.38 ($SD = 0.97$) to 3.83 ($SD = 1.50$), but not at the level suggesting small but important changes in patients' day-to-day lives. For individuals, eight patients improved their scores: in two instances this represented a small but important change in patients' day-to-day lives (+0.5), in three instances this represented important changes of moderate magnitude (+0.75–1.25) and in two instances changes were of a large magnitude (1.5+). One improver did not reach clinical significance (improvement of 0.25). Four patients' scores decreased: three by 0.5 and one by 2.75. One patient's score remained unchanged.

Table 3 summarizes clinically significant improvements on key quantitative outcome measures, by individual. Four respondents made significant improvements across four or more measures (001, 004, 005 and 020), and three made no significant improvements on any (006, 013 and 017).

Table 4 presents a case study of a patient who made a clinically significant improvement on four of

Table 4. *Case study 001 (clinically significant improvement). This gentleman was able to use relaxation therapy (self-hypnosis training), the handheld fan, and an individual exercise plan very successfully, and was also able to make use of information and education. He had minimal social support and a carer with chronic illness. He had previously had numerous hospital admissions with little apparent change in condition. These attributes seem to be typical of those patients who respond well to the Breathlessness Intervention Service*

ID no. 001	VAS-Distress	VAS-Breathlessness at Worst	VAS-Breathlessness at Best	Mastery CRQ	HADS anxiety	HADS depression
Level of change required for clinically significant improvement	1 cm+	1 cm+	1 cm+	0.5+	1.5+	1.5+
Achieved?	✓	✓	X	✓	✓	X
Baseline-follow up scores	6.3–2.2	9.2–7.8	4.7–3.8	2.25–4.75	9–5	6–6

Extracts from follow up interview:
P [BIS] told me [. . .] that breathlessness. . .. I won't die from breathlessness. [Recently] I knew I was bad. I phoned the doctor. I got an appointment, went to see her and she put me on steroids and antibiotics. Now if it hadn't have been for what [BIS] told me in here I would have said to [my wife] 'get me an ambulance!'. [. . .] That made me less panicky. I knew I was ill. I knew I had to see my doctor. [But] I didn't have to go to [hospital]. Yeah.
I Has nobody ever said that to you before?
P No. Nobody's ever said to me 'you won't die from breathlessness'. I panicked and panicked. I sat in the club one day with my mates playing cards and I'd bought a pint of Guinness, hadn't even touched it. Sat playing cards and I just said to my mate 'phone me. . . phone me an ambulance, can't get me breath'. So that was it. That was the kind of thing that was happening to me.
I Right. But if that happened now. . .
P I would relax, take in a breathing session. Relax. Once I was a bit [calmer] say 'get me a taxi. Don't get me an ambulance, get me a taxi, I'm going home' [and use my machine].
[. . .]
P The paperwork that [BIS] gave me. . . it gave me a lot to think about and it also gave me a lot of relief. It stopped me panicking. It really helped (taps side of head) up here. [. . .] on the leaflet. . . if I'm going up the stairs, find somewhere sort of half way up where I could take a rest and things like that. [. . .] how to sit up and relax your shoulders, get your breath and then if I am walking, when I want to stop, lean against the wall or something and relax. But I think the biggest thing she's done for me, setting my mind at rest, is saying to me I'm not going to die. If I'm going to die it's going to be a heart attack or something. It's not going to be because of me breathing. That has always been my panicking. [. . .] The symptoms are still there, but I can manage them better I think.
I Right. So it's your ability to cope with them that's improved?
P Yeah.
I And has that made life better in general?
P Yeah I think so. It's stopped me panicking. It's stopped. . . I can sense it and say 'hey relax, calm down'. Yeah.

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Table 5. *Case study 013 (no clinically significant improvement). This lady, supported but socially isolated and well known to respiratory services, did not use the information or handheld fan and was poorly motivated to exercise on her own. At that time there was poor provision of rehabilitation in her area. With review, her psychological status was a barrier to her use of the service*

ID no.	VAS-Distress	VAS-Breathlessness at Worst	VAS-Breathlessness at Best	Mastery CRQ	HADS anxiety	HADS depression
Level of change required for clinically significant improvement	1 cm+	1 cm+	1 cm+	0.5+	1.5+	1.5+
Achieved?	X	X	X	X	X	X
Baseline – follow up scores	9.4–8.8	9.7–9.2	1.8–5.3	1.5–1.75	19–18	18–17

Extracts from follow up interview:
P Oh, well the thing is nothing changes, you know. I can't... you know, she said, 'How do you feel?' I still feel the same as when I sort of seen her before.
I [...] So do you feel that seeing the service was any benefit, or not?
P I think it's nice to talk to someone about it, you know, but erm... I don't want to waste people's time.
I Well you're not doing that at all. But did... so speaking about it is helpful you think?
P Yeah, I think so. I don't think the hypnotism...
I No, you don't think it made any difference/
P /No.
I What is it about talking about it that's helpful? How does that help you?
P Well they seem to understand what you're going through.
I Right. I understand. And do you think they made any difference to your breathlessness?
P No.
I No. But it was useful to have someone to talk to?
P Mmm.
I Did they tell you, teach you anything that you didn't know already about breathlessness?
P [...] She gave me a fan and told me to, you know, put it on... and then blow out. I do try to do it, but I get so out of breath doing it. I give up. Yeah.
I Oh right. Does the fan help at all?
P Well if I'm really hot I've got air-conditioning in my bedroom. I go in there and put that on and it does it full.
[...]
P Well to be... I knew really [they] couldn't really help me.

the measures; Table 5 presents a case study of a patient who made no significant improvements on any of the measures.

DISCUSSION

This Phase II study shows various beneficial trends for patients with advanced COPD referred to BIS. Mean distress due to breathlessness decreased at a clinically significant level and this level of improvement was apparent for eight of the 13 patients. Mean Breathlessness at Worst scores decreased although not at a clinically significant level; however 4/11 improvers made clinically significant improvements. Mean Breathlessness at Best scores increased (deteriorated) although not at a clinically significant level; however for 5/7 patients who reduced their scores (improved) this was clinically significant. Mean mastery scores (CRQ) improved but not at a level suggesting important changes in patients' day-to-day lives; however 7/8 individual improvers had clinically significant changes.

Although mean changes (improvements) were identified, and were clinically significant for distress due to breathlessness, the small sample size prevented statistical testing. Further, a small sample size has the potential to lead to type ii errors (false-negative findings). Plotting individuals' changes enabled exploration of trends that summary statistics can hide (Matthews et al., 1990). Further, charting clinically significant changes across measures identifies patients who responded to the intervention and those who did not, e.g., four made clinically significant improvements across four or more measures whereas three made no significant improvements on any. Exploration of individual level data, together with qualitative data on the experience of using BIS, enables optimization of the intervention by examining cases in which a clinically significant change has and has not occurred, and consideration of what could have been done differently for this latter group, e.g., active screening for anxiety and depression given the high HADS scores of Case Study 013 and the known relationship between anxiety and COPD (Brenes, 2003).

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Overall the data suggests that BIS reduced the impact of intractable breathlessness for some patients. A Phase III fully-powered definitive RCT is warranted and underway for all referrals to BIS i.e. patients with malignancies as well as those with non-malignant conditions (NCT00678405; ISRCTN04119516). Phase III is based on methods piloted in Phase II, and includes an economic evaluation and an embedded analysis of those who benefit more from the service and those who do not in order to enable targeting.

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