Developing & Evaluating the Cambridge Breathlessness Intervention Service (BIS)

INSPIRED Workshop - Vancouver
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Breathlessness

- Common in advanced malignant and non-malignant conditions (e.g. COPD & heart failure)
- Difficult to treat and manage (pharmacological interventions frequently ineffective)
- Patients suffer: physical disability, loss of independence & dignity
- Families suffer: isolation, reduced activity, anxiety, role change
Breathlessness Intervention Service (BIS)

- Multi-disciplinary palliative care service: consultant, OT, physio
- Aims to help people live with breathlessness
- Any diagnosis (cancer or non-cancer)
- Works jointly with patients & carers, & advises referrers
- Hospital-based service - but functions in the community, in collaboration with primary care
- ‘Toolkit’ of pharmacological and non-pharmacological interventions

Pharmacological

- Opioids (low dose oral morphine)
- Anxiolytics (benzodiazepines)
- Antidepressants
- Oxygen
- Nebulized drugs & saline
- Optimize dose & delivery
- Symptom management pain, nausea & vomiting, psychological distress
Non Pharmacological

- Reassurance, explanation & education
- Anxiety - cycle & management
- Handheld fan
- Activity & rehabilitation
- Breathing techniques
- Modifying ADL, pacing, good rest & positioning
- Airway clearance techniques
- Relaxation, visualisation, meditation
- Nutrition & hydration
- Personal / self management plan
- Positive psychological support, wellbeing interventions
Developing & Evaluating BIS

- New interventions require independent evaluation & feedback for effective development

- BIS is a ‘complex intervention’ (series of components: multi-disciplinary professionals delivering multiple interventions)

- Complex interventions:
  - notoriously hard to evaluate
  - notoriously hard to roll-out into the real world

  “Framework for the Development & Evaluation RCTs for Complex Interventions to Improve Health”

**Theory**
- Explore relevant theory to ensure best choice of intervention and Hypothesis and to predict major confounders and strategic design issues

**Modelling**
- Identify the components of the intervention and the underlaying mechanisms by which they will influence outcomes to provide evidence that you can predict how they relate to and interact with each other

**Exploratory trial**
- Describe the constant and variable components of a replicable intervention and a feasible protocol for comparing the intervention with an appropriate alternative

**Definitive randomised controlled trial**
- Compare a fully defined intervention with an appropriate alternative using a protocol that is theoretically defendable, reproducible, and adequately controlled in a study with appropriate statistical power

**Long term implementation**
- Determine whether others can reliably replicate your intervention and results in uncontrolled settings over the long term

*Continuum of increasing evidence*
Pre-clinical Phase (theory)

- Qualitative study lung cancer & COPD patients’ experiences of breathlessness
- Clinical-academic collaboration
- Breathlessness: frightening, disabling & restricting
- Significant suffering among informal carers: severe anxiety, felt helpless & powerless
- Existing services: highly valued, but inconsistent & sporadic

Pre-clinical Phase (theory)

• Results fed into development of pilot BIS:
  • evidence base for need for / role of BIS
  • beginnings of evidence-base for the BIS model (e.g. community-functioning)

• Evidence base for the interventions BIS uses:
  • literature on theories of breathlessness e.g. role of anxiety
  • literature on interventions for breathlessness triggers e.g. anxiety management

Phase I (modelling)

- Pilot service set up (November 2003) based on:
  - pre-clinical empirical findings
  - theoretical underpinning (palliative care model)
  - (growing) evidence-base on individual pharmacological & non-pharmacological interventions for intractable breathlessness

- Qualitative study: users’ experience of the pilot service (Summer 2004)
  - patients (n=10) & carers
  - referrers & providers (BIS staff)
Phase I (modelling) – Findings of User Study

- Told us what they liked about BIS & what could be improved (patients, carers & referrers)
- Findings fed back to BIS: led directly to re-modelling of a complex intervention
- Auditable trail of service changes
- Guided choice of RCT outcomes

MRC Framework for Complex Interventions

**Theory**
- Explore relevant theory to ensure best choice of intervention and hypothesis and to predict major confounders and strategic design issues

**Preclinical**
- Identify the components of the intervention and the underlying mechanisms by which they will influence outcomes to provide evidence that you can predict how they relate to and interact with each other

**Modelling**

**Phase I**
- Describe the constant and variable components of a replicable intervention and a feasible protocol for comparing the intervention with an appropriate alternative

**Phase II**

**Exploratory trial**

**Phase III**
- Compare a fully defined intervention with an appropriate alternative using a protocol that is theoretically defensible, reproducible, and adequately controlled in a study with appropriate statistical power

**Definitive randomised controlled trial**

**Phase IV**
- Determine whether others can reliably replicate your intervention and results in uncontrolled settings over the long term

**Long term implementation**

*Continuum of increasing evidence*
RCTs in Palliative Care

• RCTs: ‘gold standard’ for evaluating services
• BIS: palliative care service
• RCTs notoriously difficult in palliative care - patient recruitment is challenging
  • patients’ ability to participate (both initially & then inevitable deterioration)
  • randomization potentially denies access to the intervention (limited life expectancy) – issue for referrers (gatekeeping) & patients
Fast-track RCT

- Fast-track RCT:
  - ‘fast-track’ group (intervention immediately)
  - ‘control’ group (intervention after waiting list)
  - everyone gets the intervention

- Strength of an RCT, but may be more acceptable to patients & referrers


- Pragmatic RCT, but…
…Single Blinded – To Reduce Bias
Phase II (exploratory trial)

- Pilot pragmatic single-blind fast-track RCT of the re-developed BIS for COPD patients -v- standard care

- Feasibility study:
  - could we do an RCT of BIS? (palliative care service)
  - and could we learn anything more about BIS?

- Mixed methods RCT:
  - integrated qualitative topic-guided interviews & quantitative outcomes
  - patients (n=13) & carers

- Qualitative interviews:
  - referrers
  - providers (BIS staff)
What Did Phase II Tell Us?  
– About BIS

- Emphasised value of non-pharmacological strategies & positive, educational approach
- Being seen at home was key (patients, carers, referrers, providers)
- Time & expertise highly valued (patients, carers & referrers)
- Need to further develop assessment of carer need & support


What Did Phase II Tell Us?
– About RCT Design

• Fast-track RCT acceptable for patients, carers, referrers & BIS
• Procedures worked (e.g. recruitment & randomisation)
• Single blinding successful – to a point
• Some outcome measures unsuitable


What Else Did Phase II Tell Us?

- Modify BIS service model:
  - shorten duration of intervention delivery… so RCT protocol could be shorter
- Important finding for a palliative care RCT using fast-track design

Phase III ("definitive" RCT)

- Pragmatic mixed method single-blind fast-track RCT of BIS -v- standard care for any diagnosis

- NIHR RfPB & Macmillan Cancer Support Post-Doctoral Fellowship

- Mixed methods RCT:
  - integrated qualitative interviews & quantitative outcome measures
  - patients (n=130: 60m & 70nm) & carers
  - qualitative interviews: referrers & providers (BIS staff)
  - economic evaluation

Different Disease Trajectories…
Differing Service Models by Disease Group

- Patients with non-malignant conditions (e.g. COPD, heart failure):
  - 2-3 visits
  - 2-3 phone calls
  - over 4-week period

- Patients with malignancies (any cancer):
  - 1 visit (ideally with primary care)
  - 2 phone calls
  - over 2-week period

- Two sub-protocols… two RCTs…
WEEK
1 2 3 4
Baseline interview (t1)
Withdrawn
Eligible patients
Agreed to recruitment visit
Baseline interview (t1)

Fast track - Receives BIS
End of intervention (t3)

Waiting list - Standard care
End of waiting (t3) – Receives BIS

Follow up interview (t5)
End of intervention (t5)

BIS PhIII (malignant conditions)

= intervention
Baseline interview (t1)

Eligible patients

Agreed to recruitment visit

Waiting list group – standard care

Fast track group – Receives BIS

Mid-intervention (t2)

End of intervention (t3)

End of waiting (t3) – receives BIS

Mid-intervention (t4)

Follow up (t5)

Mid-waiting (t2)

End of intervention (t5)

Withdrawn

BIS PhIII (non-malignant conditions)

1 = intervention
Phase III RCT: Key Patient-reported Measures

- Breathlessness (modified Borg & NRS)
- Distress due to breathlessness (POM) (NRS)
- Anxiety & depression (HADS)
- Disease-specific HRQoL (Chronic Respiratory Disease Q’aire)
- Breathlessness experience & expectations of / satisfaction with BIS (qualitative)
- Economic evaluation:
  - service use (Client Services Receipt Inventory)
  - HRQoL (EQ-5D)
Phase III RCT: Key Carer-reported Measures

- Carer assessment of patient’s breathlessness (modified Borg & NRS)
- Carer distress due to patient breathlessness (NRS)
- Carer anxiety & depression (HADS)
- Caring experience & expectations of / satisfaction with BIS (qualitative)
- Caregiver burden (Lawton Appraisal Scale & Zarit Burden Inventory)
Randomized & Completed by Disease Sub-protocol

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<th>No. of patients</th>
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<td>Feb 10</td>
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Original target:
- Randomised (nm)
- Completed RCT (nm)
- Randomised (m)
- RA in clinic (m)
- Completed RCT (m)

Diagram showing the number of patients over time with different markers for original target and randomised/completed RCT at months (m) and years (nm).
Phase III RCT: Quantitative Data

• **Malignant disease:**
  - BIS is effective & cost-effective
  - significantly reduced patient distress due to breathlessness (primary outcome: $-1.29; 95\% \text{ CI} -2.57$ to $-0.005; P = 0.049$)
  - 96% of respondents reported a positive impact

• **Non-malignant disease:**
  - trends in the right direction – no statistically significant differences
  - 92% of respondents reported a positive impact
Phase III RCT: Qualitative Analysis Data

• Purposively sampled:
  • on change in primary outcome measure (“biggest improvers”, “moderate improvers”, “limited improvers” & “worseners”)
  • transcripts from 20 patients and their carers (for each disease group)

• Framework analysis (facilitated by NVIVo) to explore:
  • nature of the impacts of BIS
  • aspects of BIS valued by patients & carers (model & interventions)
  • mechanism of impact
Phase III RCT: Impact of BIS

- **Nature of impacts:**
  - less frightened, less anxious, less worried, less panicked
  - more confident about their breathlessness
  - true for both disease groups
Phase III RCT: Helpful BIS Interventions

- Handheld fan
- Encouragement of exercise (pedometer and goal-setting)
- Breathing techniques & positioning
- Pacing
- Relaxation (BIS mindfulness-based body scan CD & visualisation techniques)
- Occupational therapy aids
- Learning “being breathless won’t kill me”
- Information (verbal, printed info sheets & hand-drawn diagrams)
- Medication changes
- Referral on to other services (such as hospice day care)
- Daily strategies or tips (“lots of little things”)

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“...She’s given me a fan, which she drew all pictures [of] and she said ‘oh, you’re brain’s telling this […], and if you try and do this that’ll help you’. When she gave me that fan I thought ‘well, I don’t know’, but that does work. I took it up to bed with me and I got puffy and I got to the top of the stairs and I put it on and that was really good. So it’s something what I would have disregarded and not given it a thought. That’s really good”

536t3pc m; Impact Categorisation Level 1 – Significant impact; Cell 2 – Low Improver on primary outcome measure
“She said to me put my lips ... like that ... and [breathe] through my mouth. I thought [...] ‘how is that going to work?’ [...] but I must be honest, it’s brilliant. Do you know it helps more than doing it through your nose? [...] well I was very interested, because I went to the bathroom and of course when I got back I couldn’t breathe [...] and I thought ‘well give it go’, you know, and ... do you know, it does help, it really does. [...] and another thing as well, when I get out of breath, is to put my hand on my tummy ... puff puff puff ... and do that, and you know, it’s amazing really. It sounds so pathetic when you say something... It’s simple. It’s not a thing you’d think of doing [putting] your hands on your tummy and do that... [...] She was really helpful”
I : “…What was the most helpful thing [she] did from your point of view?”

P : “[She told me] breathlessness is not harmful. […] because I thought getting out of breath wasn’t good for you. It’s not good for you, but it’s not going to harm you […] And that reassures you, because if you do get out of breath you think ‘I’m not going to die, this is just a blip, you’ll get over it’ […] and now I know what to do. So she was really helpful. I wouldn’t have known that if I hadn’t seen her. I would have just gone on thinking ‘oh dear’ […] And the panic, you see, makes you feel worse. If you’re panicked about something it makes your breathing worse because you breathe different when you panic. Even you would if you was in a panic - you would be breathing different. […] and I don’t get that any more. […] I know how to deal with it”.

603t3pc m; Impact Categorisation Level 1 – Significant impact; Cell 1 – Big Improver on primary outcome measure
Phase III RCT: Valued BIS Model

- Multi-disciplinary staff:
  - experts in breathlessness & strategies to manage breathlessness
  - understood life with breathlessness
- Positive staff behaviours: relaxed, easy to talk to, listening skills & reassuring (*how interventions were delivered was key*)
- Time to talk about breathlessness
- Being seen in their own homes
- Positive “can do” approach
- Unexpected attention given to carers
Phase III RCT: Mechanism of BIS Impact

- **Mechanisms of impact:**
  - *gaining knowledge* about breathlessness
  - enhanced patients’ and carers’ understanding of symptom & *confidence* in living with it
  - *legitimised* breathlessness (symptom acknowledged by experts)
  - no longer felt alone
  - suggests modulation of central perception
  - True for both disease groups

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**Continuum of increasing evidence**
What Did This Inspire? (1)

- BIS continues

- BIS roll-out:
  - BIS learning set
  - BIS manual
  - UK BIS-modelled services
    - e.g. Breathlessness Support Service (BSS) King’s College London

- INSPIRED!
What Did This Inspire? (2)

- Programme of research on breathlessness in advanced disease:
  - Living with Breathlessness study (LWB)
    - Identifying trajectories of patient & carer need in advanced COPD
  - Learning about Breathlessness study (LaB)
    - Developing an educational intervention for carers of patients with breathlessness (COPD & cancer)
  - Two studies in development:
    - Developing, validating & piloting a patient support needs assessment tool for advanced COPD
    - Developing & piloting the Carer Specialist Nurse role for advanced non-malignant disease (COPD & heart failure)
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