Investigating the feasibility of a mobile mindfulness-based digital intervention for patients with asthma (MOMA)

PROTOCOL

Version 1.5: 5 June 2017

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Sponsor: University of Southampton

Ethics Reference No: South Central- Hampshire B REC: 17/SC/0088

ERGO Reference No: 24515

IRAS Reference No: 214477

Funder: National Institute for Health Research, School for Primary Care Research (NIHR SPCR)

Reference: Grant 373

Amount: £15, 500

Dates: 01/04/2017 – 31/03/2018

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Outline

- Existing research shows strong link between asthma patient-relevant outcomes and anxiety Mindfulness has been shown to be effective but 'classic' mindfulness courses are challenging to deliver.
- We have secured support from 'Headspace' to deliver a stress-reduction digital mindfulness course to 80 patients with asthma (vs. 40 control patients), with access to usage data. Headspace will supply access to their product to all participants for the duration of the study free of charge.
- Our feasibility study will quantitatively examine recruitment, retention and response rate to the Headspace intervention and the degrees to which these differ from the in-person mindfulness intervention delivered in the MIDAS study (SPCR ref: 273) as well as exploring measures of quality of life, mood (anxiety/depression) and asthma control.
- Qualitative outcomes will include the extent to which a stress-reduction based intervention is appropriate for a chronic health condition.
- Dr Ben Ainsworth has secured NIHR SPCR Translational Fellowship to cover salary and NIHR SPCR grant to cover research costs. NIHR CRN: Wessex will provide service support costs as appropriate.

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Aim

To determine the feasibility and estimate effectiveness of Headspace, a digital mindfulness-based stress-reduction app, in patients with sub-optimally controlled asthma.

Lay Summary

Mindfulness is a type of meditation-based therapy that has been used to treat a range of health conditions, most commonly mood-disorders such as anxiety and depression. To date, few studies have explored how mindfulness can help chronic health conditions such as asthma. In a previous study we looked at how acceptable a traditional 'short-course' of mindfulness could help patients with difficult asthma. Patients liked the mindfulness and felt it helped how they felt about their asthma, but attendance was low (perhaps because of the commitment of attending a weekly group meeting). We want to see if 'Headspace', a mindfulness-based 'online' programme that can be accessed by app or website, can help. The Headspace programme takes 30 days of 10-minute practices that can be done whenever it is convenient for the user. Because this is a feasibility study, we will mainly be looking at how many people want to take part in the study, how many go on to take part and how many complete the whole study.

The study will take questionnaire measures of mood and asthma-related quality of life in patients with asthma, before and after using Headspace. Change in these 80 patients will be compared to a control group of 40 patients who will receive their usual care from their GP team. Headspace have allowed free access to their intervention to all participants in the study (although the control group will only be given access after they have given their follow-up measures). Should they wish, participants in both groups will be able to request an additional 6-months of free access to Headspace at the end of the study .We will also call some of the participants and ask them questions about their experience of the study and of using Headspace, and how they think Headspace (and mindfulness more broadly) could help their asthma. This study will help us to design an online programme specifically for people with asthma, to improve their quality of life beyond what can be offered by 'pharmacological' treatments such as new medication types.

Summary

We are examining the use of 'mindfulness' training for people with poorly controlled asthma (PCA) and anxiety. Mindfulness focuses on managing bodily sensations in a calm and accepting way. Participants pay particular attention to breathing patterns. Mindfulness interventions have shown to help in anxiety, depression and chronic pain, but have had little attention in asthma. Recent research has suggested that mindfulness training can offer benefits to patients with asthma[1] Significant anxiety is six times as common in people with asthma, particularly when control is poor [2] . Having attacks of breathlessness can be frightening, increases anxiety levels even in stable and well-adjusted people with asthma, and some may become clinically anxious or depressed with evidence that the presence of psychiatric co-morbidity accounted for 29% of variation in asthma control[3].

Mindfulness practice involves purposeful, non-judgemental attention to and acceptance of experiences. This differs from interventions such as cognitive behaviour therapies, which seek to identify and correct maladaptive thoughts/behaviours [4,5,]. A recent comprehensive meta-analysis of 209 studies has shown that mindfulness-based therapy is an effective treatment for a variety of psychological problems and is especially effective for reducing anxiety, depression and stress[6]. Recent cognitive-affective models have suggested that such maladaptive thoughts may underly symptom perception and contribute to the etiology and maintenance of asthma [7, 1]. Recently, a single small (N=83) US study investigated 8 weeks of mindfulness training in PCA in a group of patients with asthma, with patients showing clinically significant improvements in QoL and perceived stress (vs. educational control program, *ps* < .001) [8]. Mindfulness is often delivered in 'mindfulness-based stress reduction' (MBSR) courses that require attendance to 8-weekly sessions, with daily homework practice and a full-day retreat. This study did however report great difficulty in both recruiting and retaining patients,

indicating that alternative and more convenient ways of delivering mindfulness training may be more acceptable and useful for the majority of asthma sufferers.

The full traditional mindfulness training programme is often challenging for patients to complete - previous research (SPCR FR9: 273) has examined the feasibility of mindfulness training to patients attending the 'difficult asthma' clinic in Southampton. In focus groups patients reported (improvements in subjective anxiety, increased relaxation, improved breathing control). However, there were a number of methodological challenges presented even by the reduced 4-week (one session/week of approx. 1 hr) group mindfulness training, including difficulty recruiting patients due to lack of time to and willingness to attend practice sessions.

Digital interventions can reach populations with long-term conditions without requiring face-to-face contact, with positive effects reported across a range of guided practices (i.e. pre-recorded), allowing convenience to patients in terms of timing and situation. Such interventions, if clinically effective, are likely to be cost-effective due to the low associated delivery costs. Headspace is the highest-rated mindfulness-based app [9] and has shown benefits in reducing anxiety and stress [10]. However, it has yet to be evaluated in patients with long-term respiratory conditions. Our group has recently received funding to explore and develop personalised 'disease specific' psychological interventions for people with asthma (BA: SPCR Postdoctoral Fellowship Award) and the matched-funding opportunity provided by Headspace will allow an assessment of recruitment response rate, intervention retention, outcome measure feasibility (see below) and variability within outcomes in order to support a definitive trial.

120 consenting volunteers will complete validated and widely used measures of control and disease-specific quality of life (including the Asthma Control Questionnaire and Asthma Quality of Life Questionnaire) as well as questionnaire measures of mindfulness using validated questionnaire tools before and after taking part in the Headspace course (or before and after treatment as usual in the control group: 80vs.40). The course consists of 8 'sessions' lasting 10 minutes, in which users listen to a guided meditation practice. The course is available on computer and on mobile devices; users are able to listen to each session as many times as they want, with a new session being unlocked each day.

Alongside the primary quantitative analysis (recruitment, retention & response rate) participants will also be invited to take part in telephone-based qualitative interviews that will discuss their experiences of taking part (for example, were there any barriers that hindered intervention usage) and the acceptability of the intervention (can the intervention be improved for use in a specific asthma population). Further investigation will also examine the extent to which Headspace usage analysis is associated with symptom improvement – particularly measures of intervention engagement and adherence, and whether they could be improved and exploration of barriers and facilitators for a subsequent fully powered randomised controlled trial.

Additional exploratory hypotheses

1. Patients in the intervention group will show improvements in measures of anxiety and asthma-specific quality of life (vs. control group).
2. Improvements in anxiety and asthma-specific quality of life will be associated with changes in self-reported mindfulness.

Design

This will be a randomised between-groups feasibility trial, using pre-post testing to assess recruitment response rate as well as exploratory analysis of within-subject impact of the intervention vs control (usual treatment).

Sample population and recruitment

120 eligible patients will be identified by their GP practices using specified inclusion and exclusion criteria to search the GP electronic patient database. If deemed eligible by the GP they will be invited to take part in the study via a letter from the GP (sample size enables detection of 20% response rate with confidence interval of

±7%, to accurately inform a randomized controlled trial for an intervention with a similar target population). GP practices will also have the option to use Docmail to help with the mail out if they prefer. There may also be opportunistic recruitment by GPs and community pharmacists with leaflets and posters about the study being on display. There will also be the opportunity to put information about the study on the GPs website, electronic visual displays at the surgery or on the surgery website or their social media page if they wish (using the electronic version of the poster).

Recruitment will take place with the help of Wessex CRN (estimate of costings attached). We will contact approximately 6-10 GP services who are interested in taking part in the study. We will aim to recruit a spread of GP practices across both urban and rural locations with different socio-economic qualities and deprivation scores.

Given the nature of this research as a well-powered feasibility study, we will not aim to balance study recruitment across age, gender, and ethnicity but will explore this in post-hoc analysis. We will, however, purposively sample across age, gender, asthma severity and ethnicity in the qualitative process analysis.

Patients will be selected as meeting the eligibility criteria below by their GP, and will be posted a copy of the participant information sheet and details of how to sign up to the study online, along with email contact details of the study team should they have any further queries.

Participants will also be sent an optional freepost reply-form to send back to the study team should they not wish to take part with the option to provide some demographic details and a reason for declining to take part in the study. It will be made clear that this is optional and it is up to the participant whether they wish to send this information back to the research team.

***Inclusion criteria*:** Patients will be: adult (18 years or over), with a confirmed diagnosis of asthma, between steps 2 and 4 of BTS Asthma Guidelines for symptom severity (mild to moderate) .They will also need access to the Internet which can be either a computer or a mobile device.
Exclusion criteria: Patients will be excluded from the study if they are under 18 years of age, have previously diagnosed major and unstable comorbid psychological disorders other than anxiety / depression, have current participation in another asthma intervention study or have had acute exacerbation of asthma (needing a course of oral steroid of increased dose of maintenance steroids) within the previous 28 days.

Participants who sign up online will enter the study website, created in the University of Southampton Lifeguide platform. Consent will be taken online and patients will then complete brief demographic information (age, gender, education, ethnicity, and work & health status) and confirm inclusion and exclusion criteria. The Lifeguide platform will automatically confirm eligibility. Non-eligible participants (based on inclusion/exclusion criteria) will be informed that they are not eligible to take part in the study and that they can contact the study team if they would like their data to be removed.

Eligible patients will complete the baseline questionnaire measures before being randomised to intervention or control using the automatic randomisation function within the LifeGuide platform. Most questionnaire measures are envisaged to be administered online but there may also be the option to complete postal paper versions if the situation arises that might require this option. Participants in the intervention group will be enrolled on to the online mindfulness course.

This sample size is well within a feasible recruitment estimate according to patient characterization (estimates of anxiety/depression comorbidity between 16 and 52 %[2]) and our study teams' experience of recruiting patients with asthma through local GP services.

Intervention

Headspace is a commercially available application which runs on all major smartphones, tablets and web-browsers. Headspace meditation scripts are designed by Andy Puddicombe, who has Buddhist monastic training and is a registered meditation consultant with the UK Health Commission. Headspace uses audio and visual media to guide users through mindfulness meditation practices and discussions of mindfulness-related content. Headspace offers simple, short mindfulness practices, described as 'bite size' that are not affiliated with any religion and can be accessed at any time of day, convenient to the user. The stress-reduction intervention consists

of 30 ten-minute guided sessions which can be accessed through the Headspace app (or on the website). Each session begins with focusing on the breath, before gradually introducing mindfulness-relevant content and ways to apply such 'attention control' to user's day-to-day life.

Users will be given a unique ID that they can use to access the intervention once they have consented to take part in the study. Usage data will be generated for each participant, including time spent practising and sessions looked at. Any necessary agreements and contracts will be dealt with by the University of Southampton and the suitable agreement between Headspace and the University will be mutually agreed. More information about Headspace can be found here: https://www.headspace.com/how-it-works

Blinding: The trial co-ordinator will be un-blinded in order to complete the intervention registration procedure to grant participants free access to Headspace but all researchers involved in quantitative analysis will remind blinded to participant group.

Assessment and follow up

Baseline: Consent, and validated questionnaires (see details below) will be administered online (in line with previous protocols of online consent conducted at the University of Southampton), at the end of which patients will be granted access to the Headspace intervention. There will also be the option to complete paper versions if the situation arises that might need this option.

Post-test: Approximately 6 weeks after completing the baseline measures participants will complete a second battery of self-report questionnaires delivered online (the intervention can be completed in 30 days and as such most users are expected to have completed the intervention 6 weeks after baseline). If patients take longer than 6 weeks to complete the intervention they will be asked to complete questionnaires regardless.

Follow-up: 3 months after the intervention participants will complete a third battery of self-report questionnaires. For post-test and follow-up, participants will be sent an email asking them to complete the questionnaires.

If participants have not completed questionnaires after approximately 2 weeks, they will receive additional email reminders and may be contacted as appropriate by a member of the research team as a gentle reminder. If completing paper versions of the questionnaires, a repeat questionnaire will also be sent out to non-responders within this time frame and followed up by the research team as appropriate.

Telephone interviews will be conducted for approximately 20-25 patients (depending on data saturation) between 1 week and approximately 6 weeks after the intervention to elicit in depth discussion on the experiences of taking part and the acceptability of the intervention. A purposive sample of participants (as detailed below) will be contacted by email to invite them to take part. A draft interview guide has been created (Appendix C). Participants will consent at the beginning of the study to be contacted by the research team regarding the option of taking part in a telephone interview. Those that agree to take part in the telephone interview will then be contacted by the researcher by phone who will take verbal consent for the telephone interview before commencing the interview. This will include taking consent for the interview to be audio recorded. They will go through the verbal consent points as detailed in the draft interview schedule.

Data collection

Quantitative: Validated questionnaires will be administered at baseline, end of treatment and at 3 months post training will assess asthma-related quality of life (Asthma Quality of Life Questionnaire, AQLQ), asthma control (The Asthma Control Questionnaire, ACQ), anxiety and depression (The Hospital Anxiety and Depression Scale, HADS), enablement (The Patient Enablement Instrument, PEI), illness perceptions (Brief Illness Perception Questionnaire, B-IPQ), mindfulness (in line with recent 'two-pronged' acceptance/awareness conceptualisations of mindfulness we will use the Philadelphia Mindfulness Scale; PMS), as well as a measure of medication adherence (Medication Adherence Report Scale for Asthma (MARS-A) and 'acceptance and action' (AAQ-II)_. Data access granted to us by Headspace also allows us to monitor intervention usage. Questionnaires will primarily be delivered online using the LifeGuide software.

Qualitative: Qualitative evaluation will involve telephone interview. A purposive sample of approximately 20 participants will be invited to take part, based on demographic data obtained at baseline. Maximum variation

sampling will be used to ensure a range of age, gender, ethnic background and those that completed the course and those that dropped out. Interviews will take place approximately between 1 week and 6 weeks after the end of the intervention to elicit in depth discussion on the experiences of taking part, the acceptability of the intervention and views on the study outcomes in order to inform future RCT. The interviews will be audio recorded with participant consent. The interview will be anonymised when transcribed. Any direct quotes used will not include any identifiable information. Participants will be reminded that they can change their mind about taking part in the study, can stop the interview at any time or decline to answer a question.

Data analysis

Quantitative: We will monitor recruitment procedures, recruitment rates/uptake, adherence and attrition using descriptive statistics in order to determine the feasibility of using Headspace.

In line with previous research, it is predicted that there will be the improvement from baseline scores in quality of life (measured by AQLQ) in the intervention group compared to control, controlling for age and gender, although this will be guided by data analysis to inform future RCTs.

If appropriate, we will also undertake exploratory statistical analysis to examine differences between baseline and follow-up questionnaires within (and between) intervention and control groups. These will be analysed with repeated-measures mixed-model ANCOVA. Bivariate correlations and linear regression modelling will be used to determine if changes in self-report measures are related to changes in quality of life, changes in disease control, mindfulness dosage/practice habits, and to control for baseline traits.

Qualitative: A preliminary qualitative topic guide has been drafted (Appendix C) which will explore participant views on the acceptability/feasibility of the intervention, barriers and facilitators to taking part in the intervention and the study, and required level of additional support. A thematic analysis of interview data will be conducted to ensure an inductive approach. Repeated readings of transcripts and listening of recordings will assist familiarisation with the data and identification of initial codes, these will then be defined and guide analysis of the full data set. Using constant comparison, a technique derived from grounded theory transcripts [12] will be compared within and between each other aiding the iterative search for themes, which will then be reviewed, defined and named.

Timeline

A Gantt Chart is attached (Appendix B).

Patient and Public Involvement

The research team has an excellent relationship with patient and public involvement representatives and Daniel Russell (PPI Representative: Asthma UK, Southampton Respiratory Biomedical Research Unit) has been consulted with during protocol development. Using resources made available by the UHS Research Design Service we have been able to meet with Daniel and discuss our research protocol and the wider research program. Specific points that have been raised and examined (and the protocol has been subsequently amended accordingly if required) were:

- Whether people with asthma will find the 'psychologically-based' Headspace intervention acceptable as a treatment for asthma.
- Whether the quantitative and qualitative research measures are acceptable and necessary to answer research questions without causing undue patient burden.
- Whether patients in the intervention and control group will receive sufficient benefit from taking part in the study.
- Whether our PPI representative (as a current member of the Asthma UK review panel) would recommend the research for funding.

In addition to this, the research team has a history of close collaboration with PPI representatives including Mark Stafford-Watson (PPI Rep: Asthma UK) and Alan Dodge (PPI Rep: Asthma UK) as well as Colette Harris from Asthma UK. MSW has been particularly helpful in the past regarding the aims and interests of the wider

'respiratory-psycho-neuro-immunology' research group, a group within which this study is conducted, We plan to involve PPI representatives at several stages of the project, including:

- Development of study materials, including Participant Information Sheet and Consent form.
- Further development of qualitative research plan, including iteration of interview topic guide.
- Interpretation of qualitative and quantitative findings for future publication.
- Research dissemination including development of poster and verbal presentations for academics, clinicians and public interest.

We have costed for time and expenses of future PPI work in line with INVOLVE guidelines.

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