The Impact of Comorbid Chronic Pain on Older Adults Depression and Treatment of Behavioral Activation: A Nested Qualitative Sub-Study of Participants in the BASIL+ Trial

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This study will form part of a National Institute of Health and Care Research (NIHR) North East North Cumbria Applied Research collaboration (NENC ARC) funded doctoral research study undertaken by a collaborator of the BASIL$^+$ team (Alexandra Carne (AC)). This work will be led by AC with support from other members of the BASIL$^+$ team.

Chronic Pain, also known as persistent pain, is characterised by pain which has continued for more than 3 months (1). Chronic pain affects approximately 50-60% of UK older adults (2) and often coexists with depression (3, 4, 5). This comorbid indication affects approximately 13% of older adults (6). Pain interference in everyday life increases with age (7) and the combination of experiencing both conditions leads to poorer health outcomes and overall functioning than experiencing either condition alone (4). The literature on the impact of pain on depression outcomes has been steadily rising. Patients who suffer from depression with comorbid pain report significantly lower benefits, including less relief from depressive symptoms when taking antidepressant medication(8) and limited the effectiveness of a US collaborative care trial for older adults with depression which incorporated problem-solving therapy and antidepressant medication (9). Together, these findings suggest that pain may be a potential barrier to depression treatment. It is unknown, however, how comorbid chronic pain impacts patients' engagement in collaborative care and more specifically brief psychological therapy such as behavioural activation (BA). The BASIL$^+$ trial will provide an opportunity to explore this qualitatively. This sub-study will aim to explore if chronic pain impacts patients' depression and treatment.

In-depth, semi-structured interviews of a sub-sample of BASIL$^+$ participants will be conducted. Potentially eligible participants will include existing BASIL+ participants (those participants who have not yet completed their 12 month follow-up) and those BASIL+ participants who have completed their 12 month follow up, who were randomised to the BA intervention and who expressed experiencing pain as defined as a response of "moderate, quite a bit or extremely" on question 8 of the SF-12 at baseline ("During the past 4 weeks, how much did pain interfere with your normal work (including work outside the home and housework?)") and/or responded as having "moderate or extreme pain or discomfort" on question 4 of the EQ-5D at baseline ("Please indicate which statements best describe your own health state today: I have no pain or discomfort, I have moderate pain or discomfort, I have extreme pain or discomfort"). This will indicate that these BASIL+ participants were experiencing some level of pain at study entry. These baseline data will be provided to AC by the BASIL+ statisticians. No other member of the BASIL+ team will have access to these baseline data

Eligibility for this sub-study will be confirmed by AC. This will involve asking potentially eligible BASIL+ participants two telephone screening questions which will assess how often participants have pain and how pain limits their life/work activities in the last three months. This will confirm the presence or absence of chronic pain (10). Participants who respond as "never" or "some days" to question 1 ("In the past three months, how often did you have pain?") will be ineligible for the sub-study as chronic pain is absent. These BASIL+ participants will be thanked for their time and, where appropriate, will be reminded

that a researcher will be in contact for their 12-month follow-up. Participants who respond as “most days” or “everyday” to question 1 will be eligible and will be asked the second question (“Over the past three months how often did pain limit your life or work activities?”). Participants who respond as “never” or “some days” will be graded as having mild/bothersome chronic pain; those who respond as “most days” or everyday” will be graded as having high impact chronic pain. For those BASIL+ participants where presence of chronic pain is indicated, the BASIL$^+$ statisticians will provide AC with participants' details to inform the sampling framework (to include participant ID, age, gender, ethnicity, PHQ9 baseline scores, EQ-5D baseline scores, SF-12 baseline scores, postcode (for deprivation indices) and BA ‘treatment response’ (categorised as either a ‘favourable’ or ‘(non) favourable’ response). To define a ‘favourable’ or ‘(non) favourable’ response to the BA treatment, a reliable change index of 0.5 SD between participant’s PHQ9 scores at screening/baseline and three month post-randomisation (primary outcome measure) will provide the best opportunity to identify participants who have responded favourably and ‘(non) favourably’ to the BASIL+ BA intervention. The change index will provide a general idea of how participants responded to the BA intervention which will be discussed further in the sub-study interview. The above data will be provided to AC by the BASIL+ statisticians. No other member of the BASIL+ team will have access to these data.

Approximately 10 participants will be recruited initially. If after the initial recruitment round new themes are still arising, then further rounds of recruiting three participants at a time will be conducted until no new pertinent themes are arising, or unless no eligible participants remain to be approached. Participants will not be approached about this sub-study until completion of their BASIL$^+$ primary outcome assessment (at 3 months post-randomisation).

The existing BASIL$^+$ participant information sheet advises participants that they may be approached to provide their feedback on their experiences of taking part in the BASIL$^+$ study (see section 4.5). The BASIL+ team will provide AC with a list of BASIL+ participants who were randomised to the intervention and who have either not yet completed their 12 month follow up (existing BASIL+ participants) or who have completed their 12 month follow up. This list will include only those BASIL+ participants who provided their consent to participate in a qualitative interview as part of the BASIL$^+$ study (as outlined in section 4.5). For those participants who have completed their 12 month follow up, the eligible participant list will include only those participants who also provided their consent (as part of their consent to join BASIL+) to be contacted (by the BASIL+ team) about future related studies.

In addition, participants who took part in or have been approached for the BASIL$^+$ qualitative study (see section 4.6) or the therapeutic alliance sub-study (see section 4.15) will not be approached for this chronic pain sub-study and will be removed from the eligible participant list. Equally, any participants invited to or who participate in this sub-study will be relayed back to the BASIL$^+$ qualitative team and ER so they are not approached for their

respective qualitative studies. This will ensure no participants are contacted for more than one qualitative study and, therefore, reduce any further participant burden

AC will contact potential participants by telephone to invite them to provide their feedback on the sub-study and how their potential pain impacted their depression and experience of the 'BA Support' (BA intervention) in the BASIL+ study. If participants are interested, verbal consent to screen for confirmation of chronic pain will be received and recorded. Participants who do not wish to answer these questions will be thanked for their time and will not complete an interview. AC will ask participants in the last three months how often they have had pain and how often pain limited life or work activities(10). Participants whose responses to these questions indicate the presence of chronic pain will be asked if they would like to take part in this sub-study.

For those participants who meet the sub-study criteria and are willing to complete an interview, AC will confirm a date and time suitable for the participant to have the interview and the participant's preferred method of meeting either by telephone or via an approved virtual platform. Verbal consent for each participant will be received before the interview commences and will be audio recorded (as detailed in section 4.13). The interview should last approximately 45 minutes. Where real or potential risk is identified during the interviews AC will follow all appropriate and robust BASIL+ risk protocols (see section 6.6 for risk management).

All interviews will be digitally recorded (with participant consent) on an encrypted Dictaphone (or any other approved method), anonymised and transcribed. Transcription of the audio recordings will be completed by AC or via an approved transcription service. The transcripts will form the data for analysis. The audio recordings and any electronic transcriptions will be stored securely on password-protected secure servers at the University of York with access limited as relevant to the delivery of this sub-study. The interview topic guide has been developed in consultation with the BASIL+ team, AC's PhD supervisors (experts in chronic pain, behavioural activation, and qualitative methodology). The topic guide will be piloted with the first two participants and amended iteratively if required.

Thematic analysis (based on Braun and Clarke (11, 12) will be used to analyse the data to understand the nature of people's experiences (i.e phenomenology). Codes will be generated from the transcripts which will form themes, these themes will be reviewed, defined, and reported.

This chronic pain sub-study forms part of AC's doctoral research. A quantitative effect modification study is being undertaken simultaneously based on data from three of the largest BA trials in the UK (CASPER (13), CASPER+ (14) and SHARD (15)) in a mixed-methods design. The results of these two studies together will indicate to what extent pain impacts depression and potentially identify sub-groups of individuals in which BA is less effective. This will inform the next stage of this doctoral research which will continue under the wider MODS programme of research.

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