Improving the Effectiveness of Psychological Interventions for Depression and Anxiety in Cardiac Rehabilitation: The PATHWAY Research Programme Including 4 RCTs

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Scientific summary

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Background

Cardiac rehabilitation (CR) aims to improve heart disease patients' health and quality of life and reduce the risk of further cardiac events: 28% of cardiac patients have clinically significant anxiety and 19% have depression. Such patients are at greater risk of death, further cardiac events and poorer quality of life and use more health care, leading to higher NHS costs.

Available psychological treatments for patients with heart disease have small effects on improving anxiety, depression and quality of life. Therefore, more effective treatments for depression and anxiety need to be explored and made available in CR services.

Research in mental health contexts shows that a style of thinking dominated by rumination and worry maintains distress. A psychological intervention [metacognitive therapy (MCT)] reduces this style of thinking and alleviates depression and anxiety. The PATHWAY study evaluated two versions of MCT applied in heart disease patients attending CR: (1) a 6-week intervention delivered face to face in a group setting by CR staff (group-based MCT) and (2) a paper-based, six-module, self-directed intervention (home-based MCT).

Objectives

The primary aim is to improve access to more effective psychological interventions for the range of heart disease patients attending CR services.

The specific objectives were to:

1. conduct a pilot randomised controlled trial (RCT) of group-based MCT (Group-MCT) to evaluate the acceptability and feasibility of delivering the intervention to CR patients who have symptoms of anxiety and depression
2. establish evidence of the effectiveness and cost-effectiveness of Group-MCT in CR in a full-scale RCT
3. produce a rigorous, well-specified Group-MCT package
4. develop a home-based metacognitive intervention (Home-MCT) for CR patients with depression and/or anxiety
5. establish the feasibility and acceptability of integrating Home-MCT into the CR pathway in a pilot RCT
6. establish provisional evidence of the effectiveness and cost-effectiveness of Home-MCT
7. develop a protocol and manual for Home-MCT to inform a full-scale RCT
8. conduct a full-scale RCT evaluating the effectiveness of Home-MCT.

Methods

We conducted a randomised controlled pilot trial and a full-scale RCT comparing usual CR alone against CR plus group-based MCT [work stream (WS) 1 and WS2; *n* = 332)]. We also conducted a randomised controlled pilot trial and a full-scale RCT of home-based metacognitive therapy (WS3 and WS3+; *n* = 240). All trials included integrated qualitative (*n* = 52) and economic evaluations (*n* = 339; stated preference survey).

Participants

A total of seven NHS trusts that provided a routine CR service participated in the research, with the number of participants and specific sites varying by trial.

Work streams 1 and 2 explored the acceptability and effectiveness of Group-MCT integrated into usual CR in hospital settings, whereas WS3 and WS3+ explored the acceptability and effectiveness of Home-MCT integrated into usual CR in hospital and community settings.

Work stream 1 recruited participants from three NHS trusts in north-west England. Participant recruitment for WS2 took place in five NHS trusts across north-west England. WS3 and WS3+ patients were recruited from CR services at five NHS hospital trusts across north-west England.

Participating CR patients in all trials had to score ≥ 8 on the anxiety and/or depression subscale of the Hospital Anxiety and Depression Scale (HADS), be aged ≥ 18 years and meet the British Association for Cardiovascular Prevention and Rehabilitation criteria for attending CR. Participants were randomly allocated in a one-to-one ratio to receive either MCT plus usual CR or usual CR only using a randomisation procedure that balanced the trial arms with respect to gender, HADS scores and trial sites.

Interventions

Group-MCT: a 6-week manualised MCT intervention delivered face to face in a group setting. Therapists were CR staff who were not mental health specialists (e.g. clinical psychologists) but were trained to deliver the intervention. The intervention was developed by Adrian Wells based on the metacognitive model of psychological disorder and uses effective metacognitive therapy methods tested in mental health settings.

Home-MCT: a paper-based, self-directed MCT intervention consisting of six modules in a treatment manual following a structure and content like that of the group-based MCT intervention.

Adrian Wells provided pre-trial training for staff but was not involved in the ongoing supervision of staff delivering the intervention to maintain blinding and objectivity.

Outcome measures

The primary outcome was HADS total score at 4 months, with HADS total scores at 12 months as a secondary outcome (WS1 and WS2, i.e. group-MCT only). Other secondary outcomes were the separate HADS anxiety and depression subscales, traumatic stress symptoms, and psychological mechanisms including metacognitive beliefs and repetitive negative thinking.

For both interventions, qualitative interviews were conducted to assess patients' emotional experiences and needs following cardiac events, and their understanding and experience of MCT. In Group-MCT, practitioners were interviewed to understand their experience of delivering the intervention and their understanding of patients' responses to it and patients' emotional needs.

Statistical analysis

For the pilot studies, statistical analysis was principally descriptive. We assessed the acceptability of adding Group-MCT and Home-MCT to usual CR regarding rates of recruitment into the study, attrition by the primary end point, and numbers of MCT and CR modules/sessions completed. The feasibility of conducting a full RCT was assessed against the completion of follow-up questionnaires, adequate variability in the outcome measures, and re-estimation of the required sample size based on pilot study findings. Therapist adherence to the Group-MCT treatment protocol was also assessed.

The full-scale RCTs of Group-MCT and Home-MCT were designed to detect a standardised mean difference (SMD) between trial arms of 0.4 in HADS total score at 4-month follow-up with 90% power,

based on effect sizes reported for other psychological interventions for depression. Analysis was conducted following a prespecified plan detailing the analytic models, primary and secondary outcomes, choice of covariates, sensitivity analyses, and all other key aspects of the analysis. The primary analyses used intention-to-treat principles. To reduce bias, data from the trial were managed by a separate clinical trials unit and locked prior to analysis. The chief investigator (AW), trial statisticians and research assistants were kept unaware of patient treatment allocation throughout the programme and the analyses followed a prespecified plan.

Cost-effectiveness analysis

For Group-MCT only, a within-trial cost-effectiveness analysis with a 12-month time horizon compared the cost-effectiveness of MCT plus usual CR with that of CR alone, from a UK health and social care perspective. Key measures included health status (measured using the EuroQol-5 Dimensions, five-level) and self-reported health and social care use. Total costs and quality-adjusted life-years (QALYs) were calculated for the trial follow-up. Missing values were addressed using multiple imputation. The primary outcome was the incremental cost-effectiveness ratio. Regression analysis was used to estimate net costs and net QALYs, and 10,000 bootstrapped pairs of net costs and QALYs were generated to inform the probability of cost-effectiveness. For the home-based MCT pilot study, a simple between-group comparison of the available economic data (health status and NHS and social care costs), using summary statistics, was performed.

Two stated preference studies (using discrete choice experiment designs), one focused on Group-MCT and the other on Home-MCT, were conducted to explore patient preferences for the delivery of psychological therapy in CR. Participants were asked to choose between two hypothetical interventions, described using five attributes. The cost to the NHS was used to estimate willingness to pay for aspects of intervention delivery.

Results

Group-MCT

Fifty-two CR patients were consented to the pilot trial of Group-MCT + CR versus CR alone, of whom 23 were randomly allocated to Group-MCT + CR and 29 to CR. The trial recruited to target, and > 70% of participants completed the 4-month follow-up questionnaire. More than half of the patients in both arms attended at least six CR sessions, and 57% of Group-MCT participants completed an a priori defined minimal dose of the intervention likely to produce the benefit of at least four of the six MCT sessions. The addition of MCT to rehabilitation did not negatively impact on CR attendance, and we observed high therapist adherence to the protocol. The trial concluded that Group-MCT is an acceptable and feasible intervention to deliver in CR services. The Trial Steering Committee and NIHR as funder agreed to support the progression to a full-scale RCT of the Group-MCT intervention. No substantive changes were required to the trial procedures; therefore, the pilot and full RCT samples were pooled for final analysis.

A total of 332 patients (including 52 from the pilot trial) consented to the full-scale RCT of Group-MCT + CR versus CR alone, with 163 randomly allocated to Group-MCT + CR and 169 randomly allocated to CR alone; 81% returned data at 4-month follow-up. The adjusted group difference on the primary outcome of HADS total score at 4 months significantly favoured Group-MCT + CR [−3.24, 95% confidence interval (CI) −4.67 to −1.81, $p < 0.001$; SMD 0.52], as did the difference at the 12-month secondary outcome point (−2.19, 95% CI −3.72 to −0.66, $p < 0.01$; SMD 0.33). Patients in the Group-MCT + CR arm also had lower mean HADS anxiety and depression subscale scores at 4 months ($p < 0.001$). Differences in anxiety remained statistically significant at 12 months ($p < 0.01$), but those in depression did not ($p = 0.065$). Most of the other secondary outcomes also favoured the MCT intervention.

Attendance at CR sessions did not differ between trial arms. Over 60% of Group-MCT + CR participants attended four or more of the six MCT intervention sessions. However, Group-MCT did not appeal to some patients, with 40 (25%) of the 163 patients randomised to receive MCT attending no MCT intervention sessions.

Home-MCT

One hundred and eight CR patients consented to the pilot trial of Home-MCT, with 54 randomised to Home-MCT + CR and 54 randomised to CR alone. The trial recruited to target, with 96% of CR only and 83% of Home-MCT + CR participants completing 4-month follow-up measures. Forty-four per cent of patients in the MCT arm completed a minimally effective dose of more than four out of six modules. Exit questionnaire ratings were good. However, views about telephone support were mixed and the quality of calls was rated low.

Home-MCT appeared to be acceptable and feasible to deliver in CR services. The Trial Steering Committee and NIHR as funder agreed to support the progression to a full-scale RCT of the Home-MCT intervention. We submitted a no-additional-cost variation to contract (VTC) on 29 January 2019 to progress WS3 to a full-scale RCT (WS3+). The VTC was awarded on 12 March 2019. No substantive changes were required to the trial procedures; therefore, the pilot sample was pooled with the sample from the full RCT in final analysis.

A total of 240 patients (including 108 from the pilot trial) were consented to the full-scale RCT of Home-MCT, with 118 randomly allocated to Home-MCT + CR and 122 randomly allocated to CR alone; 89% returned 4-month follow-up data. The adjusted group difference on the primary outcome of HADS total score at 4 months significantly favoured the MCT + CR arm (−2.64, 95% CI −4.49 to −0.78, $p = 0.005$; SMD 0.38). Patients in the MCT + CR arm also reported significantly lower mean HADS anxiety and depression scores ($p < 0.05$). Most other secondary outcomes also favoured the MCT intervention.

Attendance at CR sessions did not differ between the trial arms. Over 70% of participants in the Home-MCT arm completed more than four MCT modules, but the intervention did not appeal to some patients; 21 participants (18%) withdrew or were not contactable at 4 months, compared with only one in the CR-alone arm. An investigation of the impact of differential attrition on the findings using last-observation-carried-forward resulted in no changes in statistical significance for the primary outcome and most of the secondary outcomes.

In the primary cost-effectiveness analysis, the Group-MCT intervention was dominant, that is cost saving (net cost −219, 95% CI −£1446 to £1007) and health increasing (net QALY 0.015, 95% CI −0.015 to 0.045). However, the CIs are wide and overlap zero, indicating a high level of variability in the data and uncertainty in the estimates. Stated preference research indicated a preference for the inclusion of psychological therapy as part of a programme of CR.

Conclusions

There is not currently a standardised approach for psychological interventions in CR, and interventions can vary. There is a preference for the inclusion of psychological therapy in rehabilitation. Group-based MCT and Home-MCT were associated with significantly better anxiety and depression outcomes when added to CR compared with CR alone. The implications for health care are (1) MCT could be provided as part of the menu of approaches used in CR and (2) patients could be given the option to choose between group-based or home-based treatment to increase access. The recommendations for future research are (1) implementation studies that assess barriers to and enablers of roll-out in the NHS, (2) studies of longer-term outcomes of home-based MCT and (3) an evaluation of MCT against alternative therapies.

Trial registration

Work stream 1/work stream 2: NCT02420431 and ISRCTN74643496; work stream 3: NCT03129282; work stream 3+: NCT03999359. The trial is registered with clinicaltrials.gov NCT03999359.

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