START (STrAtegies for RelaTives) study: a pragmatic randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of a manual-based coping strategy programme in promoting the mental health of carers of people with dementia

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Scientific summary

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Scientific summary

Background

The frequency of dementia is rising. Two-thirds of people with dementia live at home, with family providing most of their care. About 40% of family carers of people with dementia have clinical depression or anxiety; others have significant psychological symptoms. This impacts on patients, families and society as carer psychological morbidity predicts care breakdown and, therefore, institutionalisation, as well as elder abuse.

Systematic reviews report successful interventions to reduce carer depression have been individual rather than group; required active participation; and offered multicomponent strategies to be tailored to carers' individual needs. Preliminary evidence suggested that interventions for anxiety might be effective if they include relaxation techniques and strategies to manage caring demands rather than reducing contact. There are no manual-based therapies currently available for dementia carers in the NHS and no evidence regarding whether or not standardised psychological interventions can be realistically, effectively and economically delivered to family carers within NHS services. The National Institute for Health and Care Excellence (NICE) recognises that quality dementia care should include psychological therapy for family carers, but recommends further research regarding cost-effectiveness.

Objectives

To test the STrAtegies for RelaTives (START) study's clinical effectiveness and cost-effectiveness over the short term (4 and 8 months) and long term (1 and 2 years) post randomisation. The START intervention is a manual-based individual therapy for dementia carers, delivered by psychology graduates.

Methods

This is a parallel-group, superiority, randomised controlled trial recruiting participants 2 : 1 to intervention : treatment as usual (TAU) to allow for therapist clustering.

Participants

We included self-identified family carers giving informed consent and providing support at least weekly to people with dementia, living in their own homes and referred in the previous year.

Settings

We recruited through three mental health trusts and a neurology clinic, encompassing urban, suburban and rural areas, and ethnic and social diversity.

Intervention

The START manual intervention was based on the US 'Coping with Caregiving' intervention.

The eight sessions covered:

1. Learning about dementia, carer stress and understanding behaviours.

2–5. Discussion of behaviours or situations the carer finds difficult, incorporating behavioural management, identifying and changing unhelpful thoughts, assertive communication, increasing communication, acceptance, accessing emotional support and positive reframing.

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6. Future planning.

7. Pleasant activities.

8. Maintaining skills learnt.

We predefined adherence clinically, as participating in five or more therapy sessions.

Training

We trained and supervised non-clinically trained psychology graduates to deliver the intervention. Therapists recorded one randomly selected therapy session per participant. An independent rater used a checklist to score fidelity from 1, 'not at all', to 5, 'very' focused.

Treatment as usual

We expected TAU from the several teaching trusts to be based on NICE guidelines, i.e. good 'TAU'.

Randomisation

We used an online computer-generated randomisation system, stratified by trust using random permuted blocks.

Blinding

The researchers worked in two teams, each assessing outcomes blinded to randomisation status in some participants and providing therapy to the remaining participants.

Assessments

We interviewed carers at baseline and after 4, 8, 12 and 24 months. At baseline, we collected sociodemographic details. We collected clinical status and resource use at every interview.

Instruments

- The Hospital Anxiety and Depression Scale (HADS) comprises two components, the HADS-depression (HADS-D) and HADS-anxiety (HADS-A), with scores from 0 to 21. The HADS-total score (HADS-T) ranges from 0 to 42 (higher scores indicating more symptoms). We also dichotomised anxiety and depression scores into 'case' and 'non-case,' with a cut-off point of 8 or 9.
- The Zarit Burden Interview is a 22-item questionnaire. Higher scores indicate higher burden (range 0–88).
- The Neuropsychiatric Inventory (NPI) measures psychopathology in dementia patients and higher scores indicate worse symptoms (range 0–144).
- The Modified Conflict Tactics Scale (MCTS) measures potentially abusive behaviour by carers towards care recipients. Ten behaviours, ranging from shouting to slapping, over the previous 3 months are scored as occurring never (0) to all of the time (4). A score ≥ 2 on any item is classified as abusive.
- The Health Status Questionnaire (HSQ) mental health domain measures health-related quality of life (QoL). Higher scores indicate better outcome (range 0–100).
- The Client Service Receipt Inventory (CSRI) covers services used.
- Quality of life-Alzheimer's disease (QoL-AD) is family carer rating of the patient's QoL. Higher scores indicate better outcome (range 13–52).
- European Quality of Life-5 Dimensions (EQ-5D) is a health status measure used to generate quality-adjusted life-years (QALYs).

Primary outcomes (short and long term)

1. HADS-T score.
2. Cost-effectiveness: CSRI and EQ-5D.

Secondary outcomes (short and long term)

1. Depression and anxiety scores and caseness scores on the HADS.
2. Carer mental health (HSQ score) and care recipient QoL (QoL-AD).
3. MCTS.
4. Cost-effectiveness: CSRI and HADS-T.

Long-term secondary outcome

Time to care home admission.

Sample size

This was calculated to test our main hypothesis: short-term HADS-T score will be significantly lower in the intervention than in the TAU group.

We originally powered for a primary outcome of HADS-A score to detect (with 90% power, 5% significance) a 2-point difference in mean score and a 0.5 change in standard deviation (SD) (assumed SD 4). To account for therapist clustering, we used a design effect of 1.87 for the intervention group, assuming an average of 30 carers per therapist and an intracluster correlation coefficient (ICC) of 0.03. Inflating for 20% attrition, we planned to recruit 90 for TAU and 168 in the intervention group.

Following recruitment, the research team (with funding body approval) changed the primary outcome to HADS-T score. We calculated that the available sample size (87 TAU, 173 intervention group) would be sufficient to detect a 2.4-point difference in HADS-T score (with 80% power, 5% significance). This calculation assumed a SD for HADS-T score of 7.4 (from pilot data), and allowed for analysis of covariance (assumed correlation 0.5) and repeated follow-up measurements at 4 and 8 months (correlation 0.7). We factored attrition in at 10% (based on that observed), and applied a revised design effect of 1.4 for the intervention arm (ICC of 0.03 and observed average cluster size of 15 carers per therapist).

Statistical methods

Clinical outcomes

We carried out separate analyses to investigate the short- and long-term effects of the intervention. We used multilevel mixed models to estimate group differences in HADS-T score, taking into account the partially clustered design, repeated measurements and adjustment for baseline factors. We adjusted for baseline HADS-T score and centre (each trust was a centre), and for previously reported factors influencing affective symptoms (carer age, sex, burden and care recipient neuropsychiatric symptoms). Analyses were carried out on an intention-to-treat basis, but excluded carers for whom data were missing at both 4 and 8 months (short-term follow-up) or long term (12 and 24 months). We took similar approaches for secondary outcomes. We used parametric shared frailty models for time to 24-month care home admission and random-effects logistic regression for binary outcomes.

Cost-effectiveness

We examined health and social care costs over periods of 8 months and 2 years post randomisation alongside QALYs (calculated from EQ-5D by applying societal weights) and HADS-T scores. We analysed those with complete EQ-5D data at each point, as required to estimate QALYs. We calculated incremental cost-effectiveness ratios (ICERs) as the difference in the cost of START and TAU divided by the outcome difference (QALYs/HADS-T score). We plotted confidence intervals (CIs) for cost-effectiveness acceptability curves (CEACs) and net monetary benefit (NMB) to estimate the impact of uncertainty. We applied a discount rate of 3.5% to costs and outcome.

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Sensitivity analyses

We used sensitivity analyses to assess our conclusions' robustness by adjusting for baseline characteristics, imbalances between randomised groups and differential effects of treatment over time (treatment by time interaction). We investigated variation of missing outcome by baseline characteristics using logistic regression, then repeated the main analyses adjusting for factors associated with missingness.

All statistical analyses followed a predefined analysis plan, using Stata version 11 (StataCorp LP, College Station, TX, USA) for clinical outcomes and Stata version 12 for cost-effectiveness.

Results

We randomised 260 (55%) of 472 carers referred. The others declined participation ($n = 181$; 38%), did not meet inclusion criteria ($n = 22$; 5%) or were uncontactable ($n = 9$; 2%). Over the 8-month follow-up period, 12 carers from the control group and 21 from the intervention group withdrew or were lost to follow-up. The known demographics of those who did or did not consent indicate the study sample had good external validity. We randomised 173 (67%) participants to the intervention and 87 to TAU. Randomisation generally achieved good between-group balance of patient and carer demographic and clinical characteristics.

Intervention

One hundred and thirty (75%) carers in the intervention group attended five or more therapy sessions. Eight (5%) withdrew before participating in any sessions. Adherence was better in those of white ethnicity than in other ethnic groups [110 (78%) vs. 19 (61%)], in male carers than in female carers [46 (81%) vs. 84 (72%)] and in those with at least A-level education than in those with a lower level of education [56 (80%) vs. 74 (72%)]. Adherence did not differ by age [aged < 60 years, 75 (77%) vs. 55 (73%)] or work situation [paid work 49 (78%) vs. other 81 (74%)].

We scored fidelity rating for 128 out of 166 (77%) intervention participants. The mean score was 4.70 (SD 0.66). Ten therapists (seven female) delivered the intervention to between 11 and 32 carers each.

Short-term outcomes

Clinical

Analysis of HADS-T scores, adjusting for trust and baseline score, showed a significant difference in the intervention's favour with an average decrease of –1.46 (95% CI –2.89 to –0.03; $p = 0.05$). Further adjustment for factors related to outcome (carer age and sex, NPI and Zarit scores) gave similar results (mean difference –1.80 points, 95% CI –3.29 to –0.31 points; $p = 0.02$).

Sensitivity analyses adjusting for missingness predictors gave similar results (mean difference –1.53, 95% CI –2.96 to –0.10), as did adjusting for baseline imbalances (mean difference –1.78, 95% CI –3.30 to –0.27).

We found HADS-D cases in the intervention group compared with TAU was significantly reduced [adjusted odds ratio (OR) 0.24, 95% CI 0.07 to 0.76] and some evidence for a reduction in HADS-A caseness (OR 0.30, 95% CI 0.08 to 1.05).

Adjusted models for the HADS-A and HADS-D scales indicated significant beneficial intervention effects, with average decreases in scores of –0.91 (95% CI –1.76 to –0.07; $p = 0.03$) and –0.91 (95% CI –1.71 to –0.10; $p = 0.03$), respectively. The carer's HSQ mental health was significantly higher (mean difference 4.09, 95% CI 0.34 to 7.83). There was no significant difference between groups in the person with dementia's QoL-AD (mean increase 0.59, 95% CI –0.72 to 1.89) or in abusive behaviour (OR 0.48, 95% CI 0.18 to 1.27).

Cost-effectiveness

Carers who received the intervention had non-significantly higher health and social care costs (£252, 95% CI –£28 to £565 with QALY outcome and £247, 95% CI £0 to £569 with HADS-T outcome), after adjustment for baseline variables. The cost per QALY was £6000. The CEAC showed a > 99% chance of cost-effectiveness at a willingness-to-pay threshold of £30,000 per QALY gained and a high probability of cost-effectiveness on the HADS-T.

Sensitivity analyses adjusting for predictors of missingness gave similar results. The mean ICER values were now £5452 per additional QALY and £107 per 1-point difference in HADS-T score. The intervention had an approximately 95% likelihood of being seen as cost-effective, rising to 98% at the £30,000 threshold. The second sensitivity analysis results, adjusting for baseline characteristics imbalances, were again similar. The mean ICER values were £5756 per additional QALY and £112 per 1-point difference in HADS-T score. At the lower-bound NICE threshold of £20,000, the intervention has a 93% likelihood of being seen as cost-effective, rising to 98% at the £30,000 threshold. The CIs around NMB for these sensitivity analyses, taking into account uncertainty in the estimation, suggest that these findings are robust, although possibly less strong at the £30,000 threshold.

Long-term outcome analysis

Clinical

Long-term mean HADS-T scores were lower in the intervention group than in the TAU group [mean difference adjusted for trust, baseline score, carer age, sex, NPI and Zarit score –2.58 (95% CI –4.26 to –0.90)]. If the model did not include factors relating to outcome then the results were similar [–1.84 (95% CI –3.50 to –0.17; $p = 0.03$)].

Carers in the intervention group were less likely to have case-level depression (adjusted OR 0.14, 95% CI 0.04 to 0.53) and there was a trend towards reduced case-level anxiety (OR 0.57, 95% CI 0.26 to 1.24). The HADS-A and HADS-D indicated significant beneficial intervention effects, with average score decrease of –1.16 (95% CI –2.15 to –0.18) and –1.45 (95% CI –2.32 to –0.57), respectively. Intervention carers had a significantly higher HSQ mental health scale score (mean difference 7.47, 95% CI 2.87 to 12.08). There was no significant difference between groups in the person with dementia's QoL (mean QoL-AD score 0.17, 95% CI –1.37 to 1.70) or in abusive behaviour (OR 0.83, 95% CI 0.36 to 1.94).

There was no interaction of time with outcome.

There was an indication of a decrease risk of admission to 24-hour care in the intervention group. Seventeen participants (20.2%) in the TAU group and 32 (18.7%) in the intervention group were admitted to a care home (hazard ratio 0.83, 95% CI 0.44 to 1.56; $p = 0.56$).

Cost-effectiveness

In the 24-month cost-effectiveness analysis, carers included in this analysis in the intervention group had non-significantly higher costs [£336 (95% CI –£223 to £895) for QALYs; ($n = 144$); £303 (95% CI –£206 to £812) for HADS-T ($n = 156$)], after adjustment for baseline covariates. The cost per QALY was £11,200 and the CEAC showed a 75% chance of cost-effectiveness at a willingness-to-pay threshold of £30,000 per QALY gained. The probability of cost-effectiveness on the HADS-T was 78% at a willingness-to-pay threshold of £50 per 1-point HADS-T improvement.

In the sensitivity analysis adjusting for missingness predictors, the mean ICER values were £9767 per additional QALY and £125 per 1-point difference in HADS-T score. The intervention had an approximately 67% likelihood of being seen as cost-effective, rising to 75% at the £30,000 threshold. In the analysis adjusting for baseline imbalances, the mean ICER values were £8567 per additional QALY, and £209 per 1-point difference in HADS-T score. At the lower NICE threshold of £20,000, the START intervention had a 70% likelihood of being seen as cost-effective, rising to 80% at the £30,000 threshold. The CIs around

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NMB for these two sensitivity analyses taking into account uncertainty in the estimation suggest a degree of caution should be exercised when considering the finding.

Discussion

The START intervention was clinically effective and cost-effective over 8 months and 2 years. Although differences were small, they were clinically significant and sustained post intervention, as reflected in QoL improvements and possibly delayed care home admission. This was a pragmatic trial; participants were from NHS services and their diverse backgrounds suggest generalisability.

Conclusion

Future quantitative analysis is needed to consider mechanism of action and the effects on people with dementia in clinical terms (cognition, neuropsychiatric symptoms, longer-term care home admission) and on health and social care costs. In addition, we will explore the effects of carer abusive behaviour on the care recipient's care home admission and if abusive behaviour declines following admission to a care home. We plan qualitative process investigation of whether or not all of the intervention components were valued and how it could be improved.

Trial registration

This trial is registered as ISCTRN70017938.

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