Treatment of anorexia nervosa: a multimethod investigation translating experimental neuroscience into clinical practice

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Scientific summary

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Background

Anorexia nervosa (AN) is characterised by self-starvation, weight loss, hyperactivity and, in some cases, bingeing and purging. Psychological features include morbid fear of fatness and body image disturbance. Neurocognitive and social cognitive impairments may contribute to onset and maintenance of the illness. Physical complications affect all organs. The risk of death or disability is high and quality of life is poor. The family are usually the main carers and they experience significant distress in this role. Those who become pregnant have high-risk pregnancies and have difficulties feeding and playing with their children. Many parts of the UK lack NHS provision of specialist services for AN. There is therefore a need to develop better treatments and disseminate specialist interventions.

Aims and objectives

The overall aim of this programme was to improve knowledge of optimal disease management for people with AN at all stages of illness. To achieve this, seven work packages (WPs) had the following objectives: WP1a, to develop a training programme for school staff to enable them to detect and manage eating disorders (EDs); WP1b, to develop and test a schools-based prevention programme for risk factors of EDs; WP2a, to develop an improved outpatient treatment for adults with AN and to evaluate the efficacy and cost-effectiveness of this treatment; WP2b, to test components of this treatment, designed as intensive modules for inpatients with AN; WP3, to evaluate the efficacy and cost-effectiveness of a carer skills training intervention; WP4, to produce improved understanding of the nature of a debilitating core symptom of AN (i.e. hyperactivity); WP5, to develop and test a relapse prevention programme for inpatients with AN; WP6, to obtain information on the needs of mothers with an ED and the risks for their offspring to inform the development of an intervention for mothers with an ED; WP7a, to study existing care pathways for AN, with a focus on the impact of having access to specialist eating disorder services; and WP7b, to study service utilisation and cost of illness in EDs.

Work package 1a: detection and early intervention

This WP designed and evaluated a teacher training programme to improve school staff's knowledge and attitudes about EDs and their confidence to manage EDs in school. Studies 1 and 2 explored the experiences of EDs in 511 secondary school students and 826 school staff, using online questionnaires. Only 7% of students would confide in a teacher about an ED. Seventy-four per cent of staff had received no training on EDs. In study 3, 63 members of staff from 29 UK schools participated in focus groups asking them about their training needs in relation to early detection and management of EDs. In study 4, 45 school staff participated in a 1-day ED training programme based on the earlier findings. Participants completed a questionnaire about their ED knowledge, attitudes and confidence pre-intervention, post intervention and at follow-up after 3 months. The intervention had a significant positive impact on these outcomes, with gains maintained at 3 months.

Work package 1b: prevention

This WP aimed to design and evaluate a universal prevention programme for EDs in secondary schools. The intervention consisted of six sessions, delivered by teachers targeting risk factors for EDs, and was evaluated using a cluster randomised controlled trial (RCT) comparing intervention lessons with a curriculum-as-usual control in 448 female school students. Participants completed questionnaire measures pre-intervention, post intervention and at follow-up after 3 months. There were significant between-group differences in body esteem favouring the intervention group post intervention ($d = 0.12$) and at the 3-month follow-up ($d = 0.19$). There were also significant between-group differences in thin-ideal internalisation ($d = 0.17$, maintained at follow-up, $d = 0.16$) and self-esteem ($d = 0.20$, not maintained at follow-up). There were no between-group differences in the other outcomes. Fidelity to intervention material and acceptability of the programme varied across the three schools.

Work package 2a: outpatient treatment

This WP evaluated the efficacy of a novel psychological therapy for AN (Maudsley Model of Anorexia Nervosa Treatment for Adults; MANTRA) compared with specialist supportive clinical management (SSCM) in a multicentre RCT. Participants were adult outpatients meeting *Diagnostic and Statistical Manual of Mental Disorders*-Fourth Edition criteria for AN or an AN-type eating disorder not otherwise specified, recruited from four specialist ED services in England. Participants were randomised to 20 once-weekly sessions of MANTRA or SSCM and optional additional sessions depending on severity and clinical need. Seventy-two patients were allocated to MANTRA and 70 were allocated to SSCM. Patients in both treatment groups improved significantly in terms of body mass index (BMI), ED and other outcomes, with no differences between groups. Patients rated MANTRA as more acceptable and credible than SSCM at 12 months. As such, both treatments appear to have value as first-line outpatient treatments of adults with AN.

Work package 2b: inpatient treatment

This WP aimed to evaluate Cognitive Remediation and Emotional Skills Training (CREST) for inpatients with AN. CREST is an intervention teaching cognitive, emotion regulation, recognition and processing skills. The evaluation involved a qualitative study of service users' views about CREST and a quasi-experimental comparison of CREST plus treatment as usual (TAU) versus TAU alone in two inpatient settings. The qualitative assessments demonstrated CREST to be acceptable to patients. However, the quantitative data showed no difference between CREST and TAU groups in neuropsychological or clinical outcomes. Future work will focus on revisions to the CREST manual.

Work package 3: carer interventions

This WP aimed to examine the impact of the addition of Experienced Carers Helping Others (ECHO), a skills-training programme for carers, to standard inpatient care. Patients with AN and their carers were recruited from 15 inpatient services in the UK. Patients were randomly allocated to either receive ECHO [a book, digital versatile discs (DVDs) and 10 telephone coaching sessions] added to TAU or TAU only. One hundred and seventy-eight families were recruited and patient and carer outcomes were measured at discharge and 6 and 12 months after discharge. Compared with TAU-only patients, patients in the ECHO group had significantly reduced ED psychopathology and improved quality of life at 6 months. Carers in the ECHO group spent less time caregiving and had lower carer burden and lower levels of unhelpful caregiving behaviour at 6 months than carers in the TAU-only group. Sharing skills and information with family members is therefore of benefit for patients and carers.

Work package 4: activity in anorexia nervosa

This WP aimed to explore physical activity (PA) in AN and associations between drive to exercise, ED pathology, anxiety and endocrine measures. Female participants were recruited into four groups: AN outpatients ($n = 37$), AN inpatients ($n = 18$), those with anxiety ($n = 34$) and healthy controls ($n = 30$). Actigraphy and self-report were used to measure PA, together with drive/reasons for exercise, ED and general psychopathology, BMI, body composition, salivary cortisol and serum leptin levels. Psychopathology and endocrine measures were consistent with diagnosis. Levels of (especially self-reported) PA were highly variable. Objective PA levels did not differ significantly between groups, yet AN groups reported 57–92% higher total PA than healthy controls. Drive to exercise was significantly higher in AN groups, who rated improving tone and affect regulation as important, and health and enjoyment as less important exercise motivators.

Work package 5: relapse prevention

This WP aimed to assess the feasibility of a relapse prevention programme and to acquire information to inform a future RCT. Participants ($n = 41$) were inpatients with AN who were randomly allocated at discharge from hospital to receive a manual-based e-mail-guided self-care intervention [internet-based Maudsley Model of Anorexia Nervosa Treatment for Adults (iMANTRA); see *Work package 2a: outpatient treatment*] for 12 months combined with TAU or TAU alone. Outcome assessments included BMI, ED and general psychopathology, quality of life and service utilisation. At 6 months post randomisation there was little difference between groups. At 12 months, patients receiving the experimental intervention had a higher BMI ($d = 0.41$) and lower scores on the Depression Anxiety and Stress Scales ($d = 0.64$). Readmission rates were 5 out of 22 (22.7%) in the experimental group and 5 out of 16 (31.2%) in the TAU group. These findings suggest that this low-intensity relapse prevention intervention has potential in the aftercare of inpatients with AN and that a large-scale RCT is justified.

Work package 6: mothers with an eating disorder

This WP consisted of three studies examining the effects of maternal EDs on fertility and their offspring's diet and growth. Participants were 11,088 women from the Avon Longitudinal Study of Parents and Children birth cohort and their children. The outcome measures were maternal report of fertility difficulties, maternal report of child diet (up to 103 months), and child weight and height (up to age 10 years). Women with EDs reported more fertility difficulties. There was a complex pattern of differences in diet, trajectories of height, Ponderal Index and BMI between the children of women with an ED and the children of those without an ED. These results suggest that continuity of care from pre-conception to the postnatal period is paramount for women with an ED.

Work package 7a: service utilisation

This WP aimed to explore how access to specialist outpatient eating disorders services affects rates of referrals, admissions for inpatient treatment, continuity of care and service user experiences. Mental health services in London were asked to identify adolescents who presented for treatment of an ED over a period of 2 years. Retrospective data about service use was collected from case notes. A small sample of adolescents and parents were interviewed about their experiences of services. Direct access to specialist outpatient services was associated with higher referral rates, lower admission rates and greater consistency of care. Service users identified a number of advantages of specialist service provision. This suggests that facilitating direct access to specialist services for adolescents with AN may result in better outcomes, lower costs and higher satisfaction among service users.

Work package 7b: economic evaluation

This WP aimed to identify services and treatments used by people with AN and associated costs, estimate unit costs of ED treatments, explore cost variations by patient characteristics, explore the economic consequences of AN and estimate the annual costs of AN for England. Data collected in WPs 2a, 3 and 7a and from the British Cohort Study (1970) were used. Service costs were driven by hospital admissions. Costs vary based on age, ethnicity, severity of illness and treatment history. Those treated in non-specialist outpatient services incurred higher costs than those treated in specialist services only, but there were no differences in outcome. Women with AN were more likely to be long-term sick or disabled in adulthood, to receive benefits and to have completed a degree, with no differences in weekly income or employment compared with people without AN. The annual costs of AN in England are estimated at between £45M and £230M.

Overall conclusions

This programme has focused on development of interventions for AN and related EDs. The programme's studies have a number of important implications for the management of AN (and ED) across the full course of this disorder. Future research is essential to further our understanding of optimal disease management for AN.

Recommendations for health care

- Brief training can improve school staff knowledge and attitudes towards EDs. Staff can also be trained to deliver efficacious preventative interventions. Following effectiveness testing, these interventions may improve management and prevention of ED in schools.
- In adult outpatients with AN both MANTRA and SSCM significantly improve clinical outcomes, but patients see MANTRA as more acceptable and credible. Both interventions can be considered as first-line outpatient treatments.
- In adult inpatients with AN, CREST is valued by patients, but the addition of CREST to TAU is not superior to TAU alone. Further work is needed to determine CREST's role in inpatient care.
- The addition of an intervention for carers of people with AN to inpatient treatment reduces carer time caregiving, burden and unhelpful caregiving behaviours. Patients show reduced ED psychopathology and improved quality of life. Skills sharing with family members benefits patients and carers.
- Exercise is driven and rewarding to sufferers with AN. Clinicians need to develop interventions that address the pathological drive to exercise rather than exercise per se.
- iMANTRA is a feasible and safe intervention that has promise in the aftercare of inpatients with AN.
- EDs are common in pregnancy and they are associated with unplanned pregnancies and fertility treatment. Children of mothers with EDs are at risk of growth difficulties and disordered eating patterns. Interventions for mothers with EDs may benefit them and their children.
- There are clear benefits in having specialist community-based outpatient services which are easily accessible from primary care: they provide good clinical outcomes with significantly lower rates of hospital admissions and better continuity of care than generic services can deliver.
- AN is associated with a high risk of adult disability. Effective prevention and early intervention to prevent long-term disability are therefore likely to provide patient benefit and cost savings. Although inpatient treatment is the largest contributor to treatment costs, participants with AN access a wide range of services. There may be scope to develop collaborations with community-based services to improve early identification and ensure appropriate treatment.

Recommendations for research

- To carry out a fully powered study to test the effectiveness of the school staff training programme developed in WP1a.
- To conduct a large-scale cluster RCT of the prevention programme developed in WP1b to determine effectiveness of this programme in a range of school environments.
- To gain 2-year follow-up data from the RCT in WP2a, which are essential to determine the relative efficacy of the two psychological treatments and the maintenance of treatment gains.
- To conduct a RCT to explore benefits of CREST (examined in WP2b) in comparison with other manualised treatments of similar length.
- To examine whether or not adding the carer intervention evaluated in WP3 onto standard outpatient care improves outcomes and to examine whether or not adding a more intensive family intervention (workshops) improves inpatient care.
- To replicate findings from WP4 in a larger sample and to develop and test interventions targeting drive to exercise in AN.
- To carry out a large-scale RCT of iMANTRA (piloted in WP5), with economic analyses and longer-term follow-ups.
- To follow the children and women with EDs into adolescence and develop and test a tailored intervention for pregnant women with EDs.
- To evaluate the role of specialist ED services beyond the metropolitan London context in a larger scale study.
- To conduct a longitudinal study investigating the impact of AN on education, employment and potential earnings differential and to use longer-term follow-ups of clinical trials with accompanying economic evaluation to better reflect the longer-term costs of treatment.

Trial registration

These trials are registered as ISRCTN42594993, ISRCTN67720902, ISRCTN06149665 and ISRCTN18274621.

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