

A randomised controlled trial of three psychological treatments for anorexia nervosa

S. Byrne^{1,2*}, T. Wade³, P. Hay⁴, S. Touyz⁵, C. G. Fairburn⁶, J. Treasure⁷, U. Schmidt⁷, V. McIntosh⁸, K. Allen^{1,7,9}, A. Fursland^{2,10} and R. D. Crosby^{11,12}

¹School of Psychology, The University of Western Australia, Perth, Australia; ²Centre for Clinical Interventions, Perth, Australia; ³School of Psychology, Flinders University, Adelaide, Australia; ⁴School of Medicine & Centre for Health Research, Western Sydney University, Sydney, Australia; ⁵School of Psychology, Sydney University, Sydney, Australia; ⁶Department of Psychiatry, Oxford University, Oxford, UK; ⁷Department of Psychological Medicine, Kings College London, London, UK; ⁸Department of Psychological Medicine, University of Otago, Christchurch, New Zealand; ⁹Eating Disorders Service, Maudsley Hospital, South London and Maudsley NHS Foundation Trust, London, UK; ¹⁰School of Psychology and Speech Pathology, Curtin University, Perth, Western Australia; ¹¹Department of Psychiatry and Behavioral Sciences, University of North Dakota School of Medicine and Health Sciences, Fargo, ND, USA; ¹²Department of Biostatistics, Neuropsychiatric Research Institute, Fargo, ND, USA

Background. There is a lack of evidence pointing to the efficacy of any specific psychotherapy for adults with anorexia nervosa (AN). The aim of this study was to compare three psychological treatments for AN: Specialist Supportive Clinical Management, Maudsley Model Anorexia Nervosa Treatment for Adults and Enhanced Cognitive Behavioural Therapy.

Method. A multi-centre randomised controlled trial was conducted with outcomes assessed at pre-, mid- and post-treatment, and 6- and 12-month follow-up by researchers blind to treatment allocation. All analyses were intention-to-treat. One hundred and twenty individuals meeting diagnostic criteria for AN were recruited from outpatient treatment settings in three Australian cities and offered 25–40 sessions over a 10-month period. Primary outcomes were body mass index (BMI) and eating disorder psychopathology. Secondary outcomes included depression, anxiety, stress and psychosocial impairment.

Results. Treatment was completed by 60% of participants and 52.5% of the total sample completed 12-month follow-up. Completion rates did not differ between treatments. There were no significant differences between treatments on continuous outcomes; all resulted in clinically significant improvements in BMI, eating disorder psychopathology, general psychopathology and psychosocial impairment that were maintained over follow-up. There were no significant differences between treatments with regard to the achievement of a healthy weight (mean = 50%) or remission (mean = 28.3%) at 12-month follow-up.

Conclusion. The findings add to the evidence base for these three psychological treatments for adults with AN, but the results underscore the need for continued efforts to improve outpatient treatments for this disorder.

Trial Registration. Australian New Zealand Clinical Trials Registry (ACTRN 12611000725965) <http://www.anzctr.org.au/>

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Introduction

Anorexia nervosa (AN) is a serious mental disorder that has a substantial effect on psychological, physical, social and vocational functioning (Treasure *et al.* 2001; Steinhausen, 2002; Arcelus *et al.* 2011; Paxton *et al.* 2012; Mitchison *et al.* 2013; Stice *et al.* 2013). It is notoriously difficult to treat and tends to run a chronic course (Steinhausen, 2002; Stice *et al.* 2013). Progress has been made in treating younger patients using family-based

approaches (le Grange & Eisler, 2009), but there is little convincing evidence to suggest that any psychological or pharmacological treatment consistently produces good outcomes for adults with AN. Nor is there evidence pointing to the superiority of any one treatment above another (National Collaborating Centre for Mental Health, 2004; Watson & Bulik, 2013; Hay *et al.* 2015; Zipfel *et al.* 2015).

In the past decade, two new psychological treatments have been developed for, and evaluated with, AN; the Maudsley Model Anorexia Nervosa Treatment for Adults (MANTRA) (Schmidt and Treasure, 2006) and Enhanced Cognitive Behavioural Therapy (CBT-E) (Fairburn, 2008). MANTRA targets factors specific to the cognitive–interpersonal theory

* Address for correspondence: Susan Byrne, University of Western Australia, School of Psychology, 35 Stirling Highway, CRAWLEY, Perth, Western Australia 6009, Australia.
(Email: sue.byrne@uwa.edu.au)

of the maintenance of AN. CBT-E is based on a cognitive-behavioural theory of the processes maintaining eating disorder psychopathology, and is a transdiagnostic treatment designed for all eating disorders (Fairburn *et al.* 2003; Fairburn, 2008).

MANTRA has been the focus of two randomised controlled trials (RCTs) (Schmidt *et al.* 2012, 2015) involving 72 and 142 participants, respectively, both of which involved a comparison with Specialist Supportive Clinical Management (SSCM) (McIntosh *et al.* 2005, 2006, 2010). SSCM is derived from the typical supportive approach of specialists to the management of AN. Both studies showed sustained improvements in eating disorder features and weight and no significant differences between MANTRA and SSCM (McIntosh *et al.* 2005; Schmidt *et al.* 2012; Touyz *et al.* 2013). In the first of these RCTs (Schmidt *et al.* 2012), mean body mass index (BMI) increased significantly from baseline to 12 months post-randomisation (end of treatment) for both MANTRA and SSCM (1.37 and 1.22 kg/m², respectively). In the later multi-centre RCT (the MOSAIC study; Schmidt *et al.* 2015), there was also a significant mean BMI increase at the same time point (1.75 kg/m² for MANTRA and 1.36 kg/m² for SSCM). These improvements in BMI increased to 2.25 and 2.16 kg/m² at 24 months post-randomisation (Schmidt *et al.* 2016).

The use of outpatient CBT-E in AN has been the focus of a three-centre cohort study involving adults (Fairburn *et al.* 2013; *N*=99) and a further cohort study involving adolescents (Dalle Grave *et al.* 2013; *N*=46). These studies have reported positive and equivalent findings across the treatment centres. In the Fairburn cohort study, mean BMI increased significantly by 1.8 kg/m² from baseline to end of treatment (a period of 10 months), and this increase was maintained (1.7 kg/m²) over a 60-week period of follow-up (i.e. 24 months post-randomisation). A variant of CBT-E has been compared with focal psychodynamic therapy (FPT) and 'optimised treatment as usual' (TAU) in a multi-centre RCT involving 242 adults (Zipfel *et al.* 2014). The improvements in mean BMI obtained with the three treatments were statistically significant, and there were no significant differences among them. The mean BMI increase by end of 10 months of treatment was 0.73 kg/m² for FPT, 0.93 kg/m² for CBT-E and 0.69 kg/m² for TAU; and at 12 months follow-up (22 months post-randomisation), this was 1.64 kg/m² for FPT, 1.30 kg/m² for CBT-E and 1.22 kg/m² for TAU. It therefore appears that, regardless of the type of outpatient therapy, a weight gain between 0.69 and 1.80 kg/m² over a 12-month period can be expected, rising to between 1.22 and 2.25 kg/m² at 24 months. CBT-E has not previously been compared with MANTRA or SSCM.

The aim of the current trial was to compare the efficacy of these three psychotherapies for AN. The primary outcomes were BMI and global eating disorder psychopathology, and secondary outcomes were measures of depression, anxiety, stress and psychosocial impairment. It was hypothesised that CBT-E and MANTRA would be superior to SSCM in terms of weight gain and eating disorder psychopathology as they both focus on specific maintaining processes.

Method

Study overview

The Strong Without Anorexia Nervosa (SWAN) study was a multi-centre RCT involving five treatment centres from three Australian States. Across all three treatments, participants were offered 25–40 50-min sessions over a 10-month period. The number of sessions allocated was titrated according to the participant's initial BMI (<16 = 40 sessions, 16 ≥ 17.5 = 30 sessions, 17.5 ≥ 18.5 = 25 sessions) to allow for the amount of time required to achieve weight regain. Up to four additional sessions with a close other/parent/partner were permitted. Participants were also able to have up to six booster sessions in the 12 months post-treatment. Monitoring of physical risk was conducted by participants' general practitioners. If BMI fell below 14 or medical instability emerged, treatment was suspended for up to 21 days for inpatient treatment. If a participant was unable to rejoin the trial after 21 days, he/she was withdrawn from the study and the last data points were included in the intention-to-treat analyses. Outcomes were assessed at baseline, mid-treatment, end of treatment, and at 6 and 12 months post-treatment by researchers blind to treatment allocation. Ethical approval was obtained from Human Research Ethics Committees at each site.

Recruitment

Participants were recruited directly from the community (in response to media advertisements) and from treatment centres in Perth (University of Western Australia; Centre for Clinical Interventions); Adelaide (Flinders University Services for Eating Disorders) and Sydney (Sydney University; Western Sydney University). Appropriate self-referrals and consecutive referred outpatients were assessed and offered participation if they met the following inclusion criteria: BMI ≥ 14.0 and <18.5; 17 years or over; meeting diagnostic criteria B and C for AN in the Diagnostic and Statistical Manual of Mental Disorders, Fourth edition Revised (DSM-IV-TR) [American Psychiatric Association (APA), 2000]. These criteria correspond to the current DSM-5 diagnostic criteria for AN (APA, 2013).

Exclusion criteria were: severe physical or mental illness such that outpatient treatment was inappropriate (e.g. BMI < 14.0), current severe substance dependence, current use of atypical antipsychotics because of the weight gain properties of these drugs, not being available to complete the full course of treatment, other active psychotherapy focusing on AN.

Interventions

MANTRA is a formulation-based treatment accompanied by a patient workbook. Treatment is individually tailored to match the clinical symptoms, personality traits and the neuropsychological profile of patients (Schmidt *et al.* 2013, 2014). It effects change through targeting four putative maintaining factors (the person's thinking and emotional/relational style, close others' responses to the illness, and beliefs about the utility of AN in the person's life; Treasure & Schmidt, 2013).

CBT-E for underweight patients has three phases (Fairburn, 2008) and is based on the trans-diagnostic maintenance model of eating disorders (Fairburn, 2003). In the first, the emphasis is on increasing patients' motivation to change. Then patients are helped to regain weight, while at the same time tackle their eating disorder psychopathology, including their extreme concerns about shape and weight. In the final phase, the emphasis is on helping them maintain the changes obtained while developing strategies for correcting any setbacks. The most up-to-date focused version of CBT-E (which includes the Mood Intolerance module) was used unless lack of progress indicated the use of the broad version.

SSCM combines clinical management and supportive psychotherapy within sessions emphasising normalisation of eating and restoration of weight, specialist psychoeducation and focus on other key symptoms, such as vomiting or overexercising. The remainder of the sessions focus on content dictated by the patient (McIntosh *et al.* 2005, 2006, 2010; Schmidt *et al.* 2015).

Therapists

Therapists ($N=8$) were clinical psychologists. Two of the therapists (one in Adelaide and one in Perth) had over 20 years' experience using specialised psychological treatments for eating disorders, whereas the remaining six had between 2 and 4 years clinical experience in the field. They delivered all three treatments and received training in them in a series of 2-day workshops from the treatment developers [VM (SSCM); US, JT (MANTRA) and CGF (CBT-E)]. Therapists received twice-weekly supervision provided by the Australian chief investigators (SB, TW,

PH). One supervision session was site-specific and the other was treatment-specific involving all therapists, using teleconferencing facilities. Treatment developers were consulted when necessary. All treatment sessions were audio-recorded, and therapist adherence was found to be excellent (Andony *et al.* 2015). The treatments were highly distinguishable and no inter-site differences in therapist adherence were observed (Andony *et al.* 2015).

Assessment and outcome measures

Assessment incorporated semi-structured clinical interviews and self-report questionnaires. The Mini International Neuropsychiatric Interview (Sheehan *et al.* 1998) was used to assess other current Axis 1 disorders. Outcomes included BMI, eating disorder features, general psychopathology, associated functioning and a range of additional measures to assess the goodness of fit of the theories associated with the different therapies.

Eating disorder psychopathology was measured using the Global subscale of the Eating Disorder Examination (EDE; Fairburn & Wilson, 1993), an investigator-based structured interview. Other self-reported outcomes included the short form of the Depression, Anxiety and Stress Scale (DASS; Lovibond & Lovibond, 1995) and the Clinical Impairment Questionnaire (CIA; Fairburn *et al.* 2009), a measure of the severity of psychosocial impairment due to eating disorder features. Participants' ratings of treatment credibility and the likely effectiveness of treatment were assessed at mid-treatment using a four-item Credibility and Expectations Questionnaire (CEQ; Borkovec & Nau, 1972; Devilly & Borkovec, 2000) adapted for this study (Carter *et al.* 2012). Items were rated using a nine-point Likert scale and scores were summed and divided by 4. Treatment credibility, acceptability and perceived effectiveness were also assessed at post-treatment using the CEQ (worded in the past tense).

Randomisation

The generation and implementation of the randomisation sequence was conducted, independently, by the study coordinator (KA). Participant randomisation followed CONSORT guidelines (Boutron *et al.* 2008) and made use of stratification with blocking, to ensure that treatment groups were generated with approximately equal numbers. Randomisation was stratified by site and BMI (BMI < 17.5; BMI \geq 17.5). Randomisation codes were generated electronically and then placed in sequentially numbered, sealed, opaque envelopes, to be opened at the point of randomisation (following initial assessment).

Data analyses

Sample size calculations were performed for the primary outcome hypotheses on an intention-to-treat basis. Power calculations were based upon determining power for longitudinal designs with attrition (Hedeker *et al.* 1999) with a two-tailed α of 0.05, five assessment points (with baseline serving as a covariate), attrition rates of 40% and a fixed autoregressive coefficient of 0.40. An enrolled sample size of 40 per group would provide 80% power at two-sided $p < 0.05$ to detect a clinically significant change in Global EDE (0.45 points), assuming a s.d. of Global EDE change scores of one and also to detect a difference in mean weight gain of one BMI point which, based on previous research, would be clinically important to detect (Agras *et al.* 2000).

Statistical analyses were based on the intention-to-treat principle and were carried out by a biostatistician blind to treatment allocation (RDC). To account for missing data due to attrition, withdrawal from the trial or failure to complete measures, maximum likelihood imputation was implemented using the multiple imputation procedure in SPSS statistical software. The Little's Missing Completely at Random tests obtained for our data resulted in non-significant χ^2 statistics indicating that the data were missing completely at random and we used 25 imputations. Completer only analyses were also conducted for the purpose of comparison.

Continuous outcome data were analysed using linear mixed-effects modelling, with restricted maximum likelihood estimation, adjusted for baseline values of the variable under investigation. Effect sizes were calculated using Cohen's *d*.

The χ^2 analyses were used for dichotomous categorical variables: (1) achievement of healthy weight (BMI > 18.5); (2) having a Global EDE within 1 s.d. of Australian community norms (i.e. <1.81; Mond *et al.* 2004) and (3) remission (BMI > 18.5, Global EDE < 1.8 and absence of binge eating/purging behaviours; Fairburn *et al.* 2009, 2013). For baseline data compared at one time point, χ^2 tests (categorical data) and one-way analysis of variance or independent samples median tests (continuous data) were used.

Site differences were examined for all primary and secondary outcomes.

Results

Participant flow

There were 557 enquiries regarding participation. The majority of these enquiries came from parents/partners/carers of individuals who either did not go on to make contact or who were ineligible due to age or

BMI status. One hundred and seventy one individuals were assessed for eligibility and 120 participants (97.5% female) were randomised between May 2010 and December 2013 (see Fig. 1). Seventy two participants (60%) completed treatment (progressed through all stages of treatment). Completion rates were 57.5% (23/40) for SSCM; 56.1% (23/41) for MANTRA and 66.7% (26/39) for CBT-E, $\chi^2(2) = 1.09$, $p = 0.58$. Thirty-four (28.3%) dropped out [defined as non-mutual premature termination of treatment; 13 (32.5%) in SSCM, 10 (24.4%) in MANTRA, 11 (28.2%) in CBT-E, $\chi^2(2) = 0.66$, $p = .72$]. Reasons for discontinuing included not wanting to continue with treatment ($N = 22$), inability to attend ($N = 5$), moving elsewhere ($N = 3$) and increased work commitments ($N = 4$). Fourteen participants (11.67%) were withdrawn [13 due to BMI dropping below 14 and being unable to recommence after 21 days (3 (7.5%) in SSCM, 8 (19.5%) in MANTRA, 2 (5.1%) in CBT-E); one due to recommencing olanzapine (SSCM), $\chi^2(2) = 0.42$, $p = .12$]. Eight participants [4 (10%) in SSCM, 2 (4.9%) in MANTRA, 2 (5.1%) in CBT-E] had inpatient admissions of <21 days during treatment and then re-joined the trial. Seventy-five per cent of drop outs or withdrawals ($N = 35$) occurred during the first half of treatment. There were no deaths. The median number of sessions attended was 24.5 (1–40) for SSCM, 25 (0–40) for MANTRA and 25 (0–40) for CBT-E [independent samples median test (2) = 0.5, $p = 0.78$]. Eighteen participants attended post-treatment booster sessions [2 (9.5%) in Adelaide; 12 (15%) in Perth; 4 (21%) in Sydney]. The total number of booster sessions attended at each site was 7 for Adelaide, 35 for Perth and 17 for Sydney. Of those participants who completed the end of treatment assessment ($N = 73$), 63 (86.3%) completed the 12-month follow-up. There were no site differences with regard to treatment completion, $\chi^2(2) = 0.82$, $p = 0.66$.

Participant characteristics

Baseline demographic and clinical characteristics are presented in Table 1. The mean age of the sample was 26.19 (s.d. = 9.47), median duration of illness was 4 years (IQR = 1–8) and over half (52.5%) of the sample had had at least one inpatient admission for AN. Mean pre-treatment BMI was 16.70 (s.d. = 1.22). The majority (82.5%) were Australian born and single (67.1%). Approximately half (44.2%) met diagnosis for AN-restricting subtype with the remainder being AN-binge-purge subtype. Over one-third met criteria for a depressive (38.3%) or anxiety disorder (35.8%), and 46.67% were currently taking psychotropic medication. There were no significant differences between the three treatment conditions on any of these characteristics

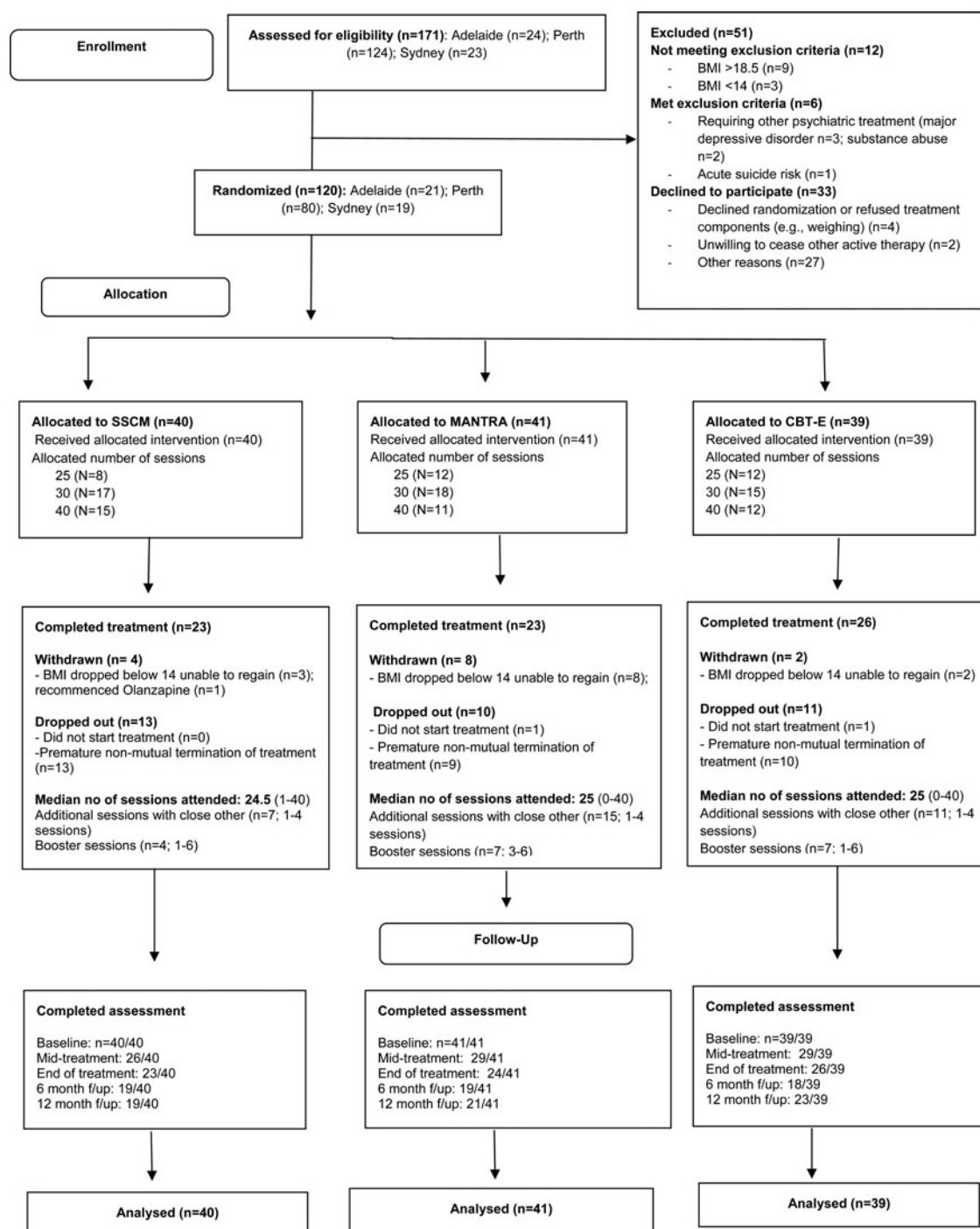


Fig. 1. CONSORT flow diagram showing participant flow through the study.

($p > 0.05$) except that a significantly smaller proportion of patients in SSCM [22.5% (9/40)] were currently depressed compared with CBT-E [51.3% (20/39)] and MANTRA [41.5% (17/41)], $\chi^2(2) = 6.75, p < 0.05$.

Participant expectations and treatment credibility

All treatments were rated highly on the CEQ at both mid-treatment and post-treatment with no significant

differences in ratings among the three treatments (mid-treatment, $F(2, 69) = 1.64, p = 0.20$; post-treatment, $F(2, 64) = 2.43, p = 0.10$) (see Table 1).

Primary outcomes

Figure 2 shows mean estimated BMI at each assessment point for the three treatment arms (using imputed values). BMI increased significantly over

Table 1. Baseline characteristics of the sample

| Demographics | Entire sample (N = 120) | SSCM (N = 40) | MANTRA (N = 41) | CBT-E (N = 39) |
|--|----------------------------|---------------|--------------------|----------------|
| Age, years [mean (SD)] | 26.19 (9.47) | 28.44 (10.94) | 25.95 (9.00) | 24.18 (8.00) |
| Males: females (<i>n</i>) | 5:115 | 3:37 | 1:40 | 1:38 |
| Country of birth [<i>n</i> (%)] | | | | |
| Australia | 99 (82.50) | 33 (82.50) | 33 (80.49) | 33 (84.61) |
| UK | 9 (7.50) | 2 (5.00) | 4 (9.75) | 3 (7.69) |
| South Africa | 5 (4.17) | 1 (2.50) | 2 (4.88) | 2 (5.13) |
| Other | 7 (5.83) | 4 (7.50) | 2 (4.88) | 1 (2.56) |
| Qualifications (<i>n</i> [%]) | | | | |
| High school | 48 (40.00) | 16 (40.00) | 19 (46.34) | 14 (35.90) |
| Trade/technical | 17 (14.17) | 2 (5.00) | 6 (14.63) | 8 (20.51) |
| Tertiary | 55 (45.83) | 22 (55.00) | 16 (39.02) | 17 (43.59) |
| Relationship status [<i>n</i> (%)] | | | | |
| Single (never married) | 80 (66.67) | 26 (65.00) | 25 (60.98) | 29 (74.36) |
| Married/ <i>de facto</i> | 36 (30.00) | 14 (35.00) | 14 (34.15) | 8 (20.51) |
| Separated/divorced/widowed | 4 (3.33) | 0 (0) | 2 (4.8) | 2 (5.13) |
| Clinical characteristics | | | | |
| AN-restricting subtype | 53 (44.17) | 21 (52.5) | 20 (48.78) | 12 (30.77) |
| AN-binge/purge subtype | 67 (55.8) | 19 (47.5) | 21 (51.2) | 27 (69.2) |
| BMI, kg/m ² [mean (SD)] | 16.70 (1.22) | 16.58 (1.18) | 16.91 (1.11) | 16.59 (1.35) |
| BMI range [<i>n</i> (%)] | | | | |
| 14 > 16 | 32 (26.7) | 8 (20) | 12 (29.3) | 12 (30.8) |
| 16 ≥ 17.5 | 50 (41.7) | 17 (42.5) | 18 (43.9) | 15 (38.5) |
| 17.5 > 18.5 | 38 (31.7) | 15 (37.5) | 11 (26.8) | 12 (30.8) |
| Duration of illness, years [median (IQR)] ^a | 4 (1–8) | 2 (1–8) | 5 (1–9) | 4 (1–7.5) |
| Previous inpatient eating disorder treatment [<i>n</i> (%)] | 63 (52.5) | 22 (55.00) | 19 (46.34) | 22 (56.41) |
| Global EDE [mean (SD)] | 3.32 (1.40) | 3.07 (1.30) | 3.38 (1.49) | 3.52 (1.40) |
| Current major depression [<i>n</i> (%)] ^b | 46 (38.33) | 9 (22.50) | 17 (41.46) | 20 (51.28) |
| Current suicidal ideation | 49 (40.83) | 11 (27.50) | 17 (41.46) | 21 (53.85) |
| Current Anxiety Disorder [<i>n</i> (%)] | | | | |
| GAD | 43 (35.8) | 14 (35.9) | 15 (36.6) | 14 (35.9) |
| Social phobia | 29 (24.17) | 7 (17.50) | 8 (19.51) | 14 (35.90) |
| OCD | 22 (18.33) | 5 (12.50) | 7 (17.07) | 10 (25.64) |
| Panic disorder | 18 (15.00) | 4 (10.00) | 7 (17.07) | 7 (17.95) |
| Alcohol dependence | 11 (9.17) | 1 (2.50) | 4 (9.76) | 6 (18) |
| Substance abuse | 5 (4.17) | 2 (5.00) | 2 (4.88) | 1 (2.56) |
| Current psychiatric medication [<i>n</i> (%)] | 56 (46.67) | 19 (48.70) | 21 (51.22) | 16 (41.02) |
| Treatment credibility and participant expectations | | | | |
| Mid-treatment CEQ [mean (SD)] | 6.64 (1.76) | 7.22 (1.66) | 6.27 (1.95) | 6.53 (1.59) |
| Post-treatment CEQ [mean (SD)] | 6.84 (1.76) | 7.58 (1.44) | 6.41 (2.00) | 6.69 (1.64) |

BMI, body mass index; IQR, interquartile range; EDE, Eating Disorder Examination; GAD, generalised anxiety disorder; OCD, obsessive compulsive disorder; CEQ, Credibility/Expectations Questionnaire.

Note: all $p > 0.05$.

^aIndependent samples median test (2) = 2.99, $p = 0.22$; ^b $\chi^2 = 6.75$, $df = 2$, $p < 0.05$.

time across all treatments, $F(3, 353.36) = 25.31$, $p < 0.001$, and the treatment by time interaction was not significant, $F(6, 353.36) = 1.66$, $p = 0.129$. CBT-E produced an estimated mean BMI increase of 2.10 [95% CI (1.65–2.79)] from baseline to post-treatment, 2.16 [95% CI (1.71–2.85)] from baseline to 6-month follow-up and 2.35 [95% CI (1.90–3.04)] from baseline

to 12-month follow-up. The equivalent figures in SSCM were 1.58 [95% CI (1.14–2.25)], 1.71 [95% CI (1.28–2.38)] and 1.90 [95% CI (1.47–2.58)]; and in MANTRA 1.37 [95% CI (0.62–1.71)], 1.35 [95% CI (0.59–1.69)] and 1.50 [95% CI (0.74–1.84)]. At 12-month follow-up, effect sizes for the differences in mean BMI were $d = 0.29$ for CBT-E v. MANTRA; $d =$

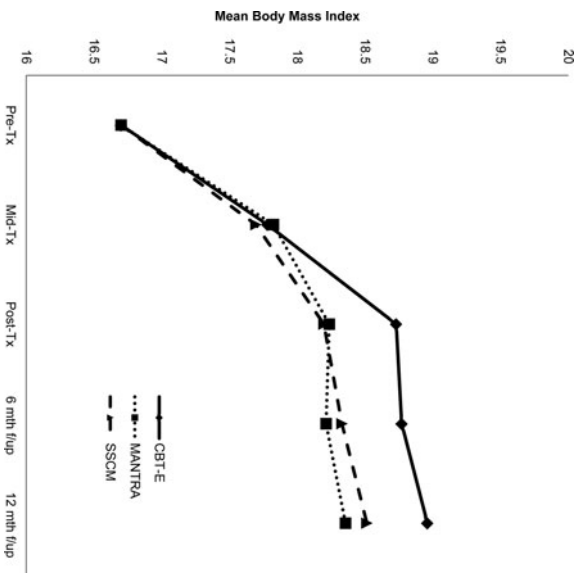


Fig. 2. Estimated mean BMI at each time point for SSCM, MANTRA and CBT-E showing 95% CIs (using the full data set with imputed values).

0.21 for CBT-E v. SSCM and $d=0.08$ for SSCM v. MANTRA. The site by treatment by time interaction was non-significant, $F(16, 434.60) = 1.61, p = 0.07$.

Table 2 presents mean Global EDE score at each assessment point for the treatment arms. Global EDE decreased significantly over time across all treatments, $F(3, 190.11) = 23.38, p < 0.001$, with no significant treatment by time interaction, $F(6, 190.11) = 0.75, p = 0.61$. Once again, the site by treatment by time interaction was non-significant, $F(16, 424.72) = 0.87, p = 0.60$.

Remission rates

The percentage of participants who achieved a BMI > 18.5 at each time point is shown in Fig. 3. At 12-month follow-up, a healthy weight had been achieved by 47.5% (19/40) in SSCM; 43.9% (18/41) in MANTRA and 59.0% (23/39) in CBT-E, with no differences among the treatments, $\chi^2 = 1.97, df = 2, p = 0.37$. The proportion of participants achieving a 'normal' Global EDE score (i.e. <1.81) at 12-month follow-up did not differ across the treatments, $\chi^2 = 1.73, df = 2, p = 0.42$ [SSCM = 25/40 (62.5%); MANTRA = 21/41 (51.2%); CBT-E = 19/39 (48.7%)] nor did the proportion of participants in remission (BMI > 18.5, Global EDE < 1.81 and absence of binge eating/purging behaviours); SSCM [32.5% (13/40)], MANTRA [22% (9/41)], CBT-E [30.8% (12/39)], $\chi^2 = 1.28, df = 4, p = 0.53$ (see Table 2). There were no significant site differences in the achievement of a healthy weight ($\chi^2 = 3.65, df = 2, p = 0.16$), normal Global EDE score ($\chi^2 = 0.27, df = 2, p = 0.87$) or remission ($\chi^2 = 0.47, df = 2, p = 0.66$). Of those

Table 2. Estimated mean Global EDE, DASS and CIA scores at each time point for the three treatment arms (using full data set with imputed values)

| | Total sample | | | | | SSCM | | | | | MANTRA | | | | | CBT-E | | | | |
|---------------------------------------|--------------|-----------|-----------|-----------|-----------|---------|-----------|-----------|-----------|-----------|----------|-----------|-----------|-----------|-----------|----------|----------|-----------|-----------|-----------|
| | Pre | Mid | EOT | 6 mth | 12 mth | Pre | Mid | EOT | 6 mth | 12 mth | Pre | Mid | EOT | 6 mth | 12 mth | Pre | Mid | EOT | 6 mth | 12 mth |
| Global EDE | 3.32 | 2.43 | 1.93 | 1.94 | 1.77 | 3.32 | 2.28 | 1.79 | 1.92 | 1.59 | 3.32 | 2.32 | 1.87 | 1.85 | 1.78 | 3.32 | 2.70 | 2.13 | 2.06 | 1.93 |
| [mean (SD)] | (1.40) | (1.13) | (1.13) | (1.12) | (1.13) | (1.40) | (1.10) | (1.16) | (1.17) | (1.10) | (1.40) | (1.24) | (1.19) | (1.07) | (1.19) | (1.40) | (1.13) | (1.09) | (1.14) | (1.16) |
| Normal global EDE score (<1.81) n (%) | 22 (18.3) | 39 (32.5) | 51 (42.5) | 49 (40.8) | 55 (45.8) | 8 (20) | 15 (37.5) | 19 (47.5) | 17 (42.5) | 22 (55.0) | 8 (19.5) | 16 (39.0) | 18 (43.9) | 17 (41.5) | 18 (43.9) | 6 (15.4) | 8 (11.6) | 14 (35.9) | 15 (38.5) | 15 (38.5) |
| DASS-depression | 9.65 | 7.17 | 6.81 | 7.75 | 5.81 | 9.65 | 7.28 | 5.91 | 8.40 | 6.00 | 9.65 | 6.22 | 6.90 | 7.43 | 5.69 | 9.65 | 8.01 | 7.62 | 7.42 | 5.73 |
| [mean (SD)] | (6.57) | (4.87) | (4.80) | (4.73) | (4.82) | (6.57) | (5.01) | (5.04) | (5.01) | (5.00) | (6.57) | (4.79) | (4.69) | (4.56) | (4.71) | (6.57) | (4.78) | (4.67) | (4.79) | (4.72) |
| DASS-anxiety | 5.85 | 4.05 | 4.25 | 3.50 | 3.31 | 5.85 | 4.05 | 3.96 | 3.72 | 3.48 | 5.85 | 3.45 | 3.90 | 3.04 | 3.12 | 5.85 | 4.63 | 4.88 | 3.73 | 3.33 |
| [mean (SD)] | (4.73) | (3.77) | (3.88) | (3.62) | (3.02) | (4.73) | (3.81) | (3.73) | (3.94) | (3.78) | (4.73) | (3.26) | (3.21) | (2.72) | (3.15) | (4.73) | (3.80) | (3.14) | (3.39) | (3.31) |
| DASS-stress | 11.58 | 9.02 | 7.85 | 7.76 | 7.54 | 11.58 | 8.95 | 7.52 | 7.89 | 7.62 | 11.58 | 8.45 | 7.98 | 7.49 | 7.56 | 11.58 | 9.66 | 8.04 | 7.88 | 7.43 |
| [mean (SD)] | (5.15) | (4.77) | (4.66) | (4.53) | (4.73) | (5.15) | (4.76) | (4.72) | (4.75) | (4.80) | (5.15) | (4.69) | (4.54) | (4.30) | (4.51) | (5.15) | (4.87) | (4.78) | (4.58) | (4.85) |
| CIA [mean (SD)] | 32.82 | 25.03 | 21.34 | 20.04 | 20.81 | 32.82 | 24.47 | 20.72 | 20.30 | 19.19 | 32.82 | 23.76 | 20.94 | 18.83 | 21.22 | 32.82 | 26.87 | 22.36 | 20.99 | 22.01 |
| | (10.76) | (13.89) | (13.53) | (12.99) | (14.17) | (10.76) | (13.89) | (13.98) | (14.06) | (14.41) | (10.76) | (14.29) | (13.48) | (12.22) | (15.70) | (10.76) | (13.66) | (13.44) | (12.95) | (13.52) |

EDE, Eating Disorder Examination; DASS, Depression, Anxiety and Stress Scale; CIA, Clinical Impairment Questionnaire; Pre, pre-treatment (baseline); Mid, mid-treatment; EOT, end of treatment; 6 mth, 6 months post-treatment; 12 mth, 12 months post-treatment.

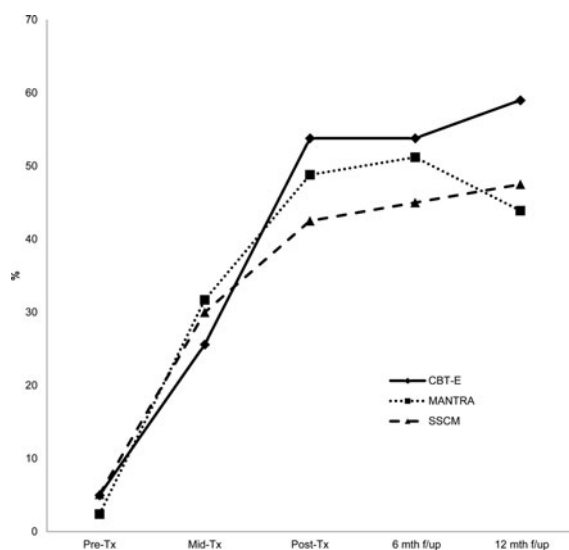


Fig. 3. Percentage of participants achieving a healthy weight [body mass index (BMI) > 18.5] at each time point (using the full data set with imputed values).

participants who were in remission at end of treatment [31/120 (25.8%)], 25 (80.6%) were still in remission at 1-year follow-up (SSCM = 11/11, MANTRA = 7/11, CBT-E = 7/9) and the remaining six were in partial remission. Another six participants (SSCM = 1, MANTRA = 1, CBT-E = 4), who had not achieved full remission by end of treatment, continued to improve over time and did so by 12-month follow-up. Of those participants who completed the 12-month follow-up ($N = 63$), 23 (36.5%) reported attending additional treatment for their eating disorder since the end of treatment (SSCM = 6, MANTRA = 9, CBT-E = 8). This treatment most commonly took the form of less than monthly appointments with a psychiatrist and/or psychologist ($N = 14$). Three participants received inpatient treatment during the follow-up period (SSCM = 1, MANTRA = 1, CBT-E = 1).

Depression, anxiety, stress and clinical impairment

On the DASS Depression subscale, there was a significant decrease in scores from baseline to 12-month follow-up across all treatment groups, $F(3, 250.72) = 10.21$, $p < 0.001$. The treatment by time interaction was also significant, $F(6, 250.72) = 2.40$, $p < 0.003$, due to differences in the trajectories of change. As can be seen from Table 2, in CBT-E there appears to be a steady improvement in depressive symptoms from baseline to 12-month follow-up; in MANTRA, the rate of improvement was most rapid up to the mid-treatment point; and in SSCM, there was a resurgence in symptoms following the end of treatment, perhaps

as a result of the loss of the supportive therapeutic relationship that is a key component of SSCM.

On both the Anxiety and Stress subscales of the DASS, there was a significant decrease in scores over time in all treatments [Anxiety: $F(3, 218.13) = 6.37$, $p < 0.001$; Stress: $F(3, 226.70) = 8.66$, $p < 0.001$]; and no treatment by time interaction [Anxiety: $F(6, 218.13) = 0.99$, $p = 0.43$; Stress: $F(6, 226.70) = 0.90$, $p = 0.50$]. CIA scores also decreased significantly over time across all treatments, $F(3, 348.35) = 16.91$, $p < 0.001$, with no treatment by time interaction, $F(6, 348.35) = 1.48$, $p = 0.18$. The site by treatment by time interaction was non-significant for all of these secondary outcomes. Estimated means for the DASS and CIA at each time point are shown in Table 2.

Completer only analyses revealed no significant differences between the treatments on any of the outcome variables.

Conclusion

We compared three outpatient treatments for adults with established AN, a notoriously treatment-resistant disorder. All three treatments were acceptable to patients and all resulted in improvements in weight and eating disorder psychopathology that were well maintained over a 12-month follow-up, although remission rates (when strictly defined) were low. There were no significant differences among the treatments with regard to BMI change over time or the achievement of a healthy BMI at 12-month follow-up. There was no difference between the treatments in the rate of improvement in eating disorder psychopathology, nor in the proportion of participants scoring in the normal range on the Global EDE at 12-month follow-up. All treatments were associated with a significant reduction in general psychopathology and psychosocial impairment.

It is of interest that, despite their focus on different mechanisms of change, the three treatments did not differ significantly in terms of outcome. This suggests that these treatments may all be considered as valuable first-line interventions for adults with AN – an important finding given the inadequate evidence base for treatments for AN in adults. It may also suggest that factors common to all three treatments, such as weekly in-session weighing, are the main drivers of change. It should also be noted that, while there were no significant differences between the treatments with regard to BMI change, and the three treatments were equivalent in their effects on psychopathology and impairment, CBT-E was superior in its ability to help patients achieve a physically healthy weight (59% at 12-month follow-up compared with 47.5% in SSCM and 44% in MANTRA), a fundamental requirement for recovery. One notable

difference between CBT-E and the other two treatments was the use of daily self-monitoring of food intake and related cognitions and behaviours. It may be that this aspect of CBT-E is particularly useful.

Comparison of outcomes with previous clinical trials

Direct comparisons of our findings with those from previous trials need to be made with caution given the differences between the samples studied; differences in the way that the treatments have been implemented; and the different ways the findings have been analysed. Weight regain is one variable that is consistently reported and, as it is a central goal of treatment, it can be compared across the studies. For CBT-E, the percentage of participants achieving a healthy weight at post-treatment and 12-month follow-up (22 months post-randomisation) in the current study (53.8% and 59%, respectively) is higher than the rates reported in the three-centre UK–Italy study (48% and 44%; Fairburn *et al.* 2013), and the mean BMI gain from baseline to end of treatment (2.1 kg/m²) is slightly greater (1.8 kg/m²). The mean BMI increase for CBT-E in this study is also greater than that reported for CBT-E in the ANTOP study (0.93 kg/m²). For SSCM, the mean BMI gain from baseline to end of treatment in the current study (1.58 kg/m²) is similar to that reported in the first SSCM trial (1.5 kg/m²; McIntosh *et al.* 2005) and in the MOSAIC study (1.36 kg/m²; Schmidt *et al.* 2015). For MANTRA, however, mean post-treatment and follow-up BMI gains were less in the current study (1.37 and 1.5 kg/m², respectively) than in the MOSAIC study (1.75 and 2.25 kg/m², respectively) (Schmidt *et al.* 2015). Thus, in the current trial, in regard to weight regain, CBT-E performed better than in previous studies, SSCM performed similarly and MANTRA performed less well.

Strengths and limitations

The study had several strengths, a major one being that the treatments were delivered in ‘real-world’ outpatient settings by therapists with varying degrees of experience. The assessments were conducted by assessors blind to treatment condition, statistical analyses were conducted by an independent biostatistician and attention was paid to measuring and ensuring therapist adherence (Andony *et al.* 2015).

The study also had limitations. The non-completion rate was high, although not unusually so for clinical trials in the field of eating disorders. The distribution of participants across sites was uneven, with more recruited to the Perth site than to Adelaide or Sydney. In addition, although therapist adherence to treatment protocols was measured, therapist competence was not assessed (Fairburn & Cooper, 2011),

which may have been valuable given the fact that the majority of the therapists involved in this RCT had been primarily trained in cognitive-behavioural therapy. Finally, the study was underpowered to detect large increases in BMI (e.g. >2 BMI points), but was powered to detect a clinically significant change in Global EDE score.

Final comments

The findings of this study add to the evidence base for these three outpatient psychological treatments in the management of adults with AN. The treatments did not differ in their effectiveness. While significant improvements in weight and eating disorder symptoms were observed in all treatments, only half of the participants were in the healthy weight range at the 12-month follow-up and less than one-third were in remission. The results of this study highlight just how difficult it is to achieve good outcomes with currently available treatments for adults with AN and underscore the need for continued efforts to improve outpatient treatments for this disorder.

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