

## Review article

## Solving a weighty problem: systematic review and meta-analysis of nutrition interventions in severe mental illness†

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**Background**

Nutrition interventions would appear fundamental for weight management and cardiometabolic risk reduction in people experiencing severe mental illness (SMI). Comprehensive evaluation of nutrition interventions is lacking.

**Aims**

To subject randomised controlled trials of nutrition interventions in people with SMI to systematic review and meta-analysis, and to measure anthropometric and biochemical parameters and nutritional intake.

**Method**

An electronic database search identified trials with nutrition intervention components. Trials were pooled for meta-analysis. Meta-regression analyses were performed on anthropometric moderators.

**Results**

Interventions led to significant weight loss (19 studies), reduced body mass index (17 studies), decreased waist circumference (10 studies) and lower blood glucose levels (5 studies). Dietitian-led interventions (6 studies) and studies delivered at antipsychotic initiation (4 studies) had larger effect sizes.

**Conclusions**

Evidence supports nutrition interventions as standard care in preventing and treating weight gain among people experiencing SMI.

**Declaration of interest**

None.

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People with severe mental illness (SMI) consume diets that are more energy-dense, highly processed, higher in salt and contain less fruit and vegetables, compared with the general population.<sup>1</sup> People with SMI also engage in lower levels of physical activity,<sup>2</sup> and have higher rates of smoking and substance use.<sup>3,4</sup> Antipsychotic medications induce greatly increased hunger, decreased satiety and increased cravings for sweet foods and drinks.<sup>5,6</sup> Additionally, a number of adverse eating styles have been observed, including fast-eating syndrome, disordered eating habits (e.g. only eating one main meal daily), increased consumption of junk food and low food literacy.<sup>5–7</sup> Although the poor physical health of people with SMI is well established, consensus on the appropriate prevention and/or treatment interventions is in evolution, with calls for increased emphasis on lifestyle interventions aimed at reducing overweight/obesity and consequent metabolic abnormalities in established SMI,<sup>8</sup> and preventing these adverse health trajectories in the early stages of psychosis.<sup>9,10</sup> The mandate for improved physical healthcare and physical health protection in severe mental illness has led to an international working group and declaration, Healthy Active Lives (HeAL), that has established goals for the prevention of cardiometabolic decline in first-episode psychosis ([www.iphsys.org.au](http://www.iphsys.org.au)).<sup>11</sup> Strong evidence now exists for holistic lifestyle interventions,<sup>8</sup> and as part of this the inclusion of physical activity interventions for people living with severe mental illness.<sup>12</sup>

Poor physical health in people experiencing SMI stems from both modifiable and non-modifiable risk factors linked to the illness itself, compounded by significant medication effects. Antipsychotic medications induce rapid weight gain with associated metabolic abnormalities.<sup>13,14</sup> This weight gain contributes to the high rates of overweight and obesity and metabolic complications in people with established SMI, with diabetes and hypercholesterolaemia rates respectively two and five

times higher than those observed in the general population.<sup>15–18</sup> To date, the efficacy of specific components, including modes of delivery, of nutrition interventions has not been systematically evaluated. With irrefutable evidence demonstrating the crucial role of nutrition in weight management,<sup>19</sup> and the prevention and treatment of metabolic disease in the general population,<sup>20,21</sup> a comprehensive assessment of various nutrition intervention strategies employed to assist a highly vulnerable and challenging populations is a priority. The specific questions to be answered by this review and meta-analysis of randomised controlled trials (RCTs) were the following.

- Do nutrition interventions improve anthropometric measures (weight, body mass index and waist circumference) and biochemical profiles (lipids, glucose and insulin) of people living with SMI?
- Do nutrition interventions improve the nutritional intake of people living with SMI?

**Method**

The aims and method of this systematic review and meta-analysis were registered with the PROSPERO database prior to conducting the review (CRD42014014017). Reporting was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>22</sup>

**Search strategy**

An electronic database search was completed from earliest record to February 2015 using Medline, EMBASE, the Cochrane Central Register of Clinical Trials, PsycINFO and CINAHL, using key nutritional, anthropometric and psychiatric terminology. Google Scholar and relevant published systematic reviews were manually searched for additional titles. Study eligibility was assessed according to inclusion criteria by two investigators. If agreement

†See editorial, pp. 94–95, this issue.

was not established, a third investigator acted as arbitrator. Data were extracted by the two investigators and pooled for meta-analysis.

### Quality assessment

Trial quality was assessed using a modified version of the Critical Appraisal Skills Programme (CASP) Randomised Controlled Trial Checklist.<sup>23</sup> Trial characteristics were assessed across four criteria: concealed allocation, assessor masking, treatment equality between groups (excluding intervention) and accounting for all participants randomised. One point was allocated for each criterion, giving a maximum score of four.

### Participants

Randomised controlled trials recruiting participants 18 years old or over meeting DSM or ICD criteria for SMI (schizophrenia spectrum disorder, bipolar affective disorder, depression with psychotic features) were eligible for inclusion. There was no restriction on medication use.

### Interventions

Studies of stand-alone nutrition interventions or nutrition interventions delivered as part of a multidisciplinary intervention were included. Interventions comprising individualised nutrition counselling, group nutrition education, shopping or cooking classes were eligible. No restriction was placed on intervention setting: interventions in in-patient services, out-patient programmes and community volunteer services or otherwise were included. The process of referral to the study, location where the intervention was delivered, and the professional background of those who delivered the intervention were recorded. No restriction was placed on intervention intensity or duration.

### Outcome measures

All trials that met inclusion criteria were included in a qualitative analysis. Trials were included in the meta-analysis if they provided adequate data on anthropometric (primary outcomes: weight, body mass index and waist circumference) and biochemical and/or nutritional parameters (secondary outcomes: total cholesterol, low-density lipoprotein, high-density lipoprotein, triglycerides, blood glucose, insulin and dietary intake). Data collection time points included pre- and post-intervention and follow-up. Where necessary, corresponding authors of included trials were contacted to provide additional data for inclusion in the meta-analysis. A follow-up and final email was sent 3 weeks later if corresponding authors did not reply to the initial request.

### Statistical analysis

Because of the anticipated heterogeneity we used a random effects meta-analysis and calculated Hedges' *g* and 95% confidence intervals as the effect size measure. The meta-analysis was conducted in the following stages. First, we calculated Hedges' *g* and the 95% CI for the primary outcome measures: weight, body mass index (BMI) and waist circumference. Second, we conducted subgroup analyses to investigate differences in the primary outcomes for the main analysis according to whether interventions were delivered by a dietitian or not, and whether they were delivered at initiation of antipsychotic therapy ( $\leq 3$  months exposure to second-generation antipsychotic medication) or subsequent to antipsychotic use. For each subgroup analysis we investigated the between-subgroup difference in effect size and report the corresponding *P* value. Third, we conducted meta-regression analyses investigating potential moderators of the

primary outcome results including the percentage of men and mean age in both control and intervention groups, percentage receiving antipsychotics, duration of intervention, the profession delivering the intervention and exercise intensity. In order to test whether the profession of the person who delivered the intervention (dietitian *v.* other healthcare professional) was an independent predictor of our primary outcomes from other variables (in particular, exercise participation in multimodal programmes), we conducted multivariate meta-regressions. In order to correct for multiple testing of covariates in our meta-regression, a Bonferroni correction was made and a new *P* value to indicate significance was set at 0.006 (0.05 divided by 8). In the next stage, we calculated Hedges' *g* and 95% CI for the secondary outcomes including systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, blood glucose and insulin. We investigated heterogeneity with the  $I^2$  statistic. Publication bias was assessed with a visual inspection of funnel plots and with the Begg–Mazumdar Kendall's tau and Egger bias test.<sup>24,25</sup> If we encountered publication bias, we adjusted for this by conducting a trim and fill adjusted analysis to remove the most extreme small studies from the positive side of the funnel plot,<sup>26</sup> and recalculated the effect size at each iteration until the funnel plot was symmetrical about the (new) effect size. All analyses were conducted with Comprehensive Meta-Analysis software version 3.

## Results

After accounting for duplicates, 7045 unique records were screened from the database searches. Full-text articles were accessed for 176 records; 150 did not meet the inclusion criteria and were subsequently excluded (Fig. 1). Twenty-six studies met the inclusion criteria,<sup>27–52</sup> but 6 studies reported incomplete data and could not be pooled for meta-analysis.<sup>31,32,36,41,46,48</sup> For the primary outcomes measures, 19 studies were pooled for weight,<sup>27–30,33–35,37,38,40,42–45,47,49–52</sup> 17 studies for BMI,<sup>27–29,33–35,37,39,40,42–45,47,50–52</sup> and 11 studies for waist circumference.<sup>28,33–35,37,39,40,44,47,50,52</sup> For secondary outcomes 8 studies were pooled reporting the impact of nutrition interventions on biochemical outcomes (blood pressure, lipids, glucose, insulin).<sup>28,29,34,37,39,42,45,47</sup> Measures of nutritional intake were reported in 6 studies.<sup>28,31,32,38,44,46</sup> These measures could not be pooled for quantitative analysis, but were included in qualitative analysis. Longer-term follow-up of 2 included studies was reported in separate publications.<sup>53,54</sup> Comprehensive datasets were obtained directly from corresponding authors for 2 studies.<sup>37,42</sup>

### Characteristics of included trials

The sample size within studies ranged from  $n=15$  to  $n=291$ . Mean participant age ranged from 26 years (s.d.=15.5) to 54.8 years (s.d.=8.2). Diagnoses within included studies were schizophrenia (18 studies), schizoaffective disorder (12 studies), schizophreniform disorder (3 studies), bipolar affective disorder (7 studies), delusional disorder (2 studies), brief reactive psychosis (2 studies), psychosis not otherwise specified (2 studies), personality disorder (2 studies), anxiety (2 studies) and depression (2 studies). First-episode psychosis, major affective illness, major depressive disorder, psychotic depression and post-traumatic stress disorder were identified in one study each. More general diagnostic descriptors were also employed in a minority of studies: SMI (4 studies), psychosis (2 studies), schizophrenia spectrum (1 study) and autism spectrum (1 study). Participants were recruited from out-patient settings (21 studies), in-patient

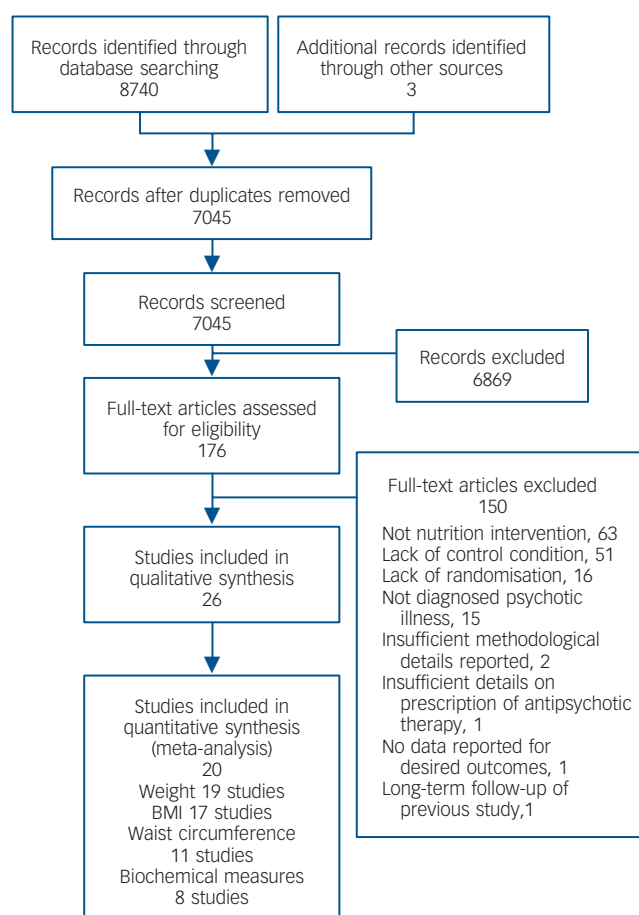


Fig. 1 Flowchart of study search. BMI, body mass index.

settings (3 studies) or included a mix of out-patients and in-patients (2 studies). Characteristics of included trials are summarised in online Table DS1.

## Interventions

Nutrition intervention delivery methods included individualised counselling (12 studies), group education (12 studies) and a mixture of group and individual components (2 studies). Seven studies primarily used dietitians to deliver interventions,<sup>33,35,42,45,48,49,52</sup> with an additional 5 studies including a nutrition professional as a smaller part of the intervention primarily delivered by other clinicians.<sup>28,30,37,41,47</sup> Fourteen studies did not report input from a nutrition professional.<sup>27,29,31,32,34,36,38–40,43,44,46,50,51</sup> Seven studies adopted a manual-based lifestyle intervention,<sup>27–29,31,32,43,50</sup> predominantly delivered by mental health clinicians. Studies delivered predominantly by dietitians involved individualised assessment and intervention approaches. Other interventions included general nutrition education aimed at improving food literacy (not individualised counselling), weight management guidance and healthy-eating education. Cooking classes were reported in 4 studies.<sup>33,36,37,41</sup> One study incorporated two meal replacements per day,<sup>30</sup> and another solely assessed the impact of providing free fruit and vegetables to participant households.<sup>46</sup>

All studies described strategies to alter participant behaviour, such as cue elimination, food diary/record-keeping and food sampling, although the specific behaviour change models used were more difficult to identify and interpret. Psychoeducation was described in 7 studies.<sup>27,28,33,43–45,49</sup> Cognitive-behavioural

therapy was identified in 3 studies,<sup>29,42,51</sup> and social cognitive therapy in 1 study.<sup>34</sup> Within the cognitive framework, motivational interviewing and more generally motivational counselling/support were commonly used.<sup>27,28,31,32,36,37,39,44,50</sup> In addition, the 'stages of change' model was described in 2 studies where motivational interviewing was used.<sup>39,50</sup> Finally, 1 study described the use of behaviour self-management therapy.<sup>34</sup> Psychoeducation was combined with motivational counselling/support in 3 studies.<sup>27,28,44</sup> Control groups received treatment as usual with or without written physical health information.

## Outcome measures

Twenty-five studies assessed anthropometric measures, predominantly weight and BMI.<sup>27–45,47–52</sup> Additional measures included waist circumference, waist-to-hip ratio and body fat percentage. Eleven studies (42%) included biochemical outcome measures, predominantly lipids (cholesterol studies and triglycerides), glucose and insulin.<sup>28,33,34,37,39,41,42,45,47,51,52</sup> Studies including measures of nutritional intake were limited to 6 studies (25%), which recorded energy intake (kilojoules/calories), servings of food groups (such as fruit and vegetables), macronutrients (including fat and subgroups unsaturated and saturated fat), fibre and portion size.<sup>28,31,32,38,44,46</sup> In addition, one study used a 'ten good food score'.<sup>44</sup>

## Trial quality

Seven studies (27%) scored the maximum four points,<sup>27,28,31,32,34,40,44</sup> 4 studies (15%) scored three,<sup>33,36,50,51</sup> 13 studies (50%) scored two,<sup>29,30,37–39,41–43,45–48,52</sup> and 2 studies (8%) scored one (see online Table DS2).<sup>35,49</sup> 'Group treatment equality' and 'all participants being accounted for' were reported in 25 studies (96%) and 22 studies (85%) respectively. Methodological uncertainties included 'concealed group allocation' and 'assessor blinding', described in 12 studies (46%) and 9 studies (35%) respectively.

## Meta-analysis results

All the meta-analyses results including subgroup analyses are presented in Table 1.

### Primary outcomes

Pooled analysis showed that nutrition interventions were significantly more effective in reducing weight *v.* control (19 studies:  $g = -0.39$ , 95% CI  $-0.56$  to  $-0.21$ ,  $P < 0.001$ ,  $I^2 = 55\%$ ; Fig. 2). There was evidence of publication bias (Begg  $-0.41$ ,  $P = 0.01$ ; Egger  $-1.7$ ,  $P = 0.08$ ), whereas the Duval & Tweedie trim and fill effect size adjusting for publication bias remained similar and statistically significant ( $g = -0.33$ , 95% CI  $-0.44$  to  $-0.22$ ). Nutrition interventions also reduced BMI compared with control groups (17 studies:  $g = -0.39$ , 95% CI  $-0.56$  to  $-0.22$ ,  $P < 0.001$ ,  $I^2 = 51\%$ ) (see online Fig. DS2a). The results remained statistically significant when adjusted for publication bias in the trim and fill analysis ( $g = -0.34$ , 95% CI  $-0.45$  to  $-0.23$ ). Nutrition interventions were also effective in reducing waist circumference *v.* control (11 studies:  $g = -0.27$ , 95% CI  $-0.42$  to  $-0.12$ ,  $P < 0.001$ ,  $I^2 = 17\%$ ; see online Fig. DS3a). The results remained statistically significant in the trim and fill analysis ( $g = -0.25$ , 95% CI  $-0.38$  to  $-0.12$ ).

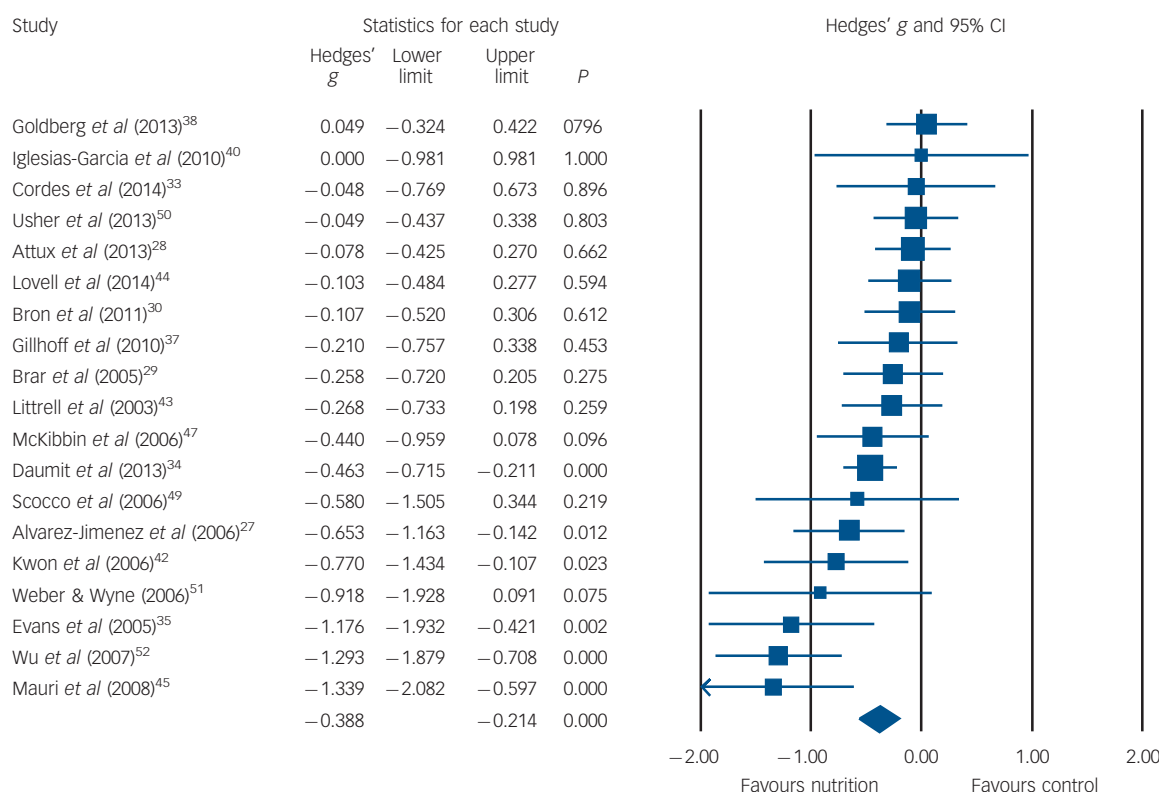
### Subgroup analysis: antipsychotic use

A larger effect size was found for studies delivered at the start of antipsychotic pharmacotherapy (4 studies:  $g = -0.61$ , 95% CI

**Table 1** Meta-analysis of primary, secondary and subgroup outcomes

Analysis	Number of RCTs	Meta-analysis of mean differences			Meta-analysis of Hedges' g			Heterogeneity $I^2$ (%)	
		Mean difference	95% CI	$P^a$	Between-group $P^a$	Hedges' g	95% CI		$P^a$
Primary outcomes									
Weight (kg)	19	-2.706	-3.347 to -2.064	<0.001		-0.388	-0.563 to -0.214	<0.001	55
Stage of antipsychotics									
At antipsychotic initiation	4	-2.948	-4.381 to -1.515	<0.001	0.70	-0.613	-1.051 to -0.175	0.006	0.27
Subsequent to antipsychotic use	15	-2.639	-3.396 to -1.883	<0.001		-0.345	-0.533 to -0.158	<0.001	34
Delivered by					0.02			<0.001	57
Dietitian/nutrition professional	6	-3.577	-4.560 to -2.594	<0.001		-0.904	-1.217 to -0.577	<0.001	48
Other healthcare professional	13	-2.060	-2.906 to -1.214	<0.001		-0.233	-0.379 to -0.088	0.002	8
BMI (kg/m <sup>2</sup> )	17	-0.870	-1.119 to -0.621	<0.001		-0.390	-0.560 to -0.221	0.001	51
Stage of antipsychotics					0.73			0.40	
At antipsychotic initiation	3	-0.953	-1.506 to -0.400	<0.001		-0.559	-0.986 to -0.132	0.01	66
Subsequent to antipsychotic use	14	-0.843	-1.136 to -0.550	<0.001		-0.359	-0.547 to -0.172	<0.001	50
Delivered by					0.02			<0.001	
Dietitian/nutrition professional	5	-1.228	-1.589 to -0.866	<0.001		-0.799	-1.106 to -0.419	<0.001	69
Other healthcare professional	12	-0.655	-0.943 to -0.368	<0.001		-0.253	-0.410 to -0.096	0.002	0
Waist circumference (cm)	11	-2.281	-3.267 to -1.296	<0.001		-0.267	-0.415 to -0.118	<0.001	17
Stage of antipsychotics					0.07			0.41	
At antipsychotic initiation	2	-4.189	-6.500 to -1.878	<0.001		-0.532	-0.940 to -0.124	0.011	82
Subsequent to antipsychotic use	9	-1.857	-2.947 to -0.768	<0.001		-0.225	-0.375 to -0.074	0.003	0
Delivered by					0.03			0.006	
Dietitian/nutrition professional	3	-4.223	-6.257 to -2.189	<0.001		-0.575	-0.939 to -0.211	0.002	68
Other healthcare professional	8	-1.685	-2.182 to -0.559	0.003		-0.206	-0.346 to 0.067	0.004	0
Secondary outcome measures									
Systolic BP (mmHg)	7	0.632	-1.857 to 3.122	0.619		0.054	-0.179 to 0.286	0.651	54
Diastolic BP (mmHg)	6	-1.686	-3.603 to 0.231	0.08		-0.232	-0.500 to -0.037	0.091	61
Glucose (mmol/L)	5	-0.473	-0.915 to -0.030	0.04		-0.372	-0.692 to -0.053	0.022	68
Total cholesterol (mmol/L)	7	-0.131	-0.288 to 0.027	0.103		-0.130	-0.286 to 0.029	0.101	0
LDL cholesterol (mmol/L)	7	-0.061	-0.168 to 0.045	0.259		-0.091	-0.248 to 0.067	0.258	0
HDL cholesterol (mmol/L)	7	-0.060	-0.158 to 0.042	0.239		-0.087	-0.243 to 0.069	0.272	0
Triglycerides (mmol/L)	7	-0.116	-0.249 to 0.018	0.089		-0.146	-0.304 to 0.011	0.069	0
Insulin (mU/ml)	3	-0.880	-2.652 to 0.892	0.330		-0.195	-0.426 to 0.035	0.097	18
BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RCT, randomised controlled trial. a. After applying the Bonferroni correction, significance was set at $P=0.006$ ; values in bold.									

BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RCT, randomised controlled trial.  
a. After applying the Bonferroni correction, significance was set at  $P=0.006$ , values in bold.



**Fig. 2** Effect of nutrition interventions on weight v. control group.

-1.02 to -0.18,  $P=0.006$ ,  $I^2=34\%$ ) compared with studies delivered subsequent to antipsychotic use (15 studies:  $g=-0.35$ , 95% CI -0.54 to -0.16,  $P<0.001$ ,  $I^2=57\%$ ; see online Fig. DS1a). Similar results were seen for BMI ( $g=-0.56$  v.  $g=-0.36$ ) and waist circumference ( $g=-0.53$  v.  $g=-0.23$ ) (see online Figs DS2b and DS3b). Between-group differences did not reach statistical significance after applying a Bonferroni correction (Table 1).

#### Subgroup analysis: profession delivering intervention

Subgroup analysis investigating the effect of who delivered the nutrition intervention revealed that dietitians delivering specialised dietary interventions (6 studies: Hedges'  $g=-0.90$ , 95% CI -1.22 to -0.58,  $P<0.001$ ,  $I^2=48\%$ ) had a significantly larger effect ( $P=0.0005$ ) compared with interventions predominantly delivered by other health professionals or mental health clinicians (13 studies: Hedges'  $g=-0.23$ , 95% CI -0.38 to -0.09,  $P=0.002$ ,  $I^2=8\%$ ) (online Figs DS1b, DS2c and DS3c).

### Meta-regression analyses

#### Weight

Single meta-regression analyses found that the profession delivering the intervention (dietitian v. other healthcare professional,  $\beta=-0.69$ , 95% CI -1.05 to -0.32,  $P<0.001$ ) was a significant predictor of weight change (Table 2). Multivariate regression analysis found that profession remained a significant predictor of weight change independent of exercise ( $\beta=-0.72$ , 95% CI -1.06 to -0.37,  $P<0.001$ ). The percentages of men in the control group ( $\beta=0.01$ , 95% CI 0.0 to 0.02,  $P=0.05$ ) and in the nutrition group ( $\beta=0.02$ , 95% CI -0.0 to 0.03,  $P=0.01$ ) were positive predictors of weight (i.e. more difficult to lose weight).

#### Body mass index

A dietitian-delivered intervention was a significant moderator of BMI results ( $\beta=-0.53$ , 95% CI -0.9 to -0.16,  $P=0.005$ ). This finding was confirmed through multivariate regression analysis and the results remained significant independent of exercise participation ( $\beta=-0.52$ , 95% CI -0.85 to -0.20,  $P=0.001$ ), with exercise not found to be a significant moderator ( $\beta=-0.21$ , 95% CI -0.44 to 0.02,  $P=0.07$ ).

#### Waist circumference

There was a non-significant trend for dietitian-delivered interventions to moderate waist circumference results ( $\beta=-0.37$ , 95% CI -0.76 to -0.02,  $P=0.06$ ). Multivariate regression analysis confirmed the trend for the profession delivering the intervention as a moderator independent of exercise intensity ( $\beta=-0.36$ , 95% CI -0.76 to -0.03,  $P=0.072$ ).

#### Secondary outcomes

The meta-analyses for the secondary outcomes are presented in Table 1. The analyses demonstrated that nutrition interventions reduced glucose ( $g=-0.37$ , 95% CI -0.69 to -0.05,  $P=0.02$ ,  $I^2=68\%$ ; online Fig. DS4); however, this was not statistically significant after applying the Bonferroni correction. Triglyceride levels ( $g=-0.15$ , 95% CI -0.30 to 0.01,  $P=0.07$ ,  $I^2=0\%$ ) were not significantly affected by nutrition interventions, although trends were evident. Other secondary outcome measures were not significant.

### Impact on nutritional intake

Results for all six studies that assessed changes in nutritional intake favoured the intervention group but could not be pooled for meta-analysis owing to the varying outcomes



**Table 2** Meta-regression of moderators of primary outcomes

Moderator	$\beta$	95% CI	P	R <sup>2</sup>
<i>Weight</i>				
Mean age control group	0.007	−0.012 to 0.027	0.456	0.06
Mean age nutrition group	0.002	−0.018 to 0.021	0.874	0.00
Percentage men control group	0.011	0.000 to 0.021	0.045*	0.41
Percentage men nutrition group	0.015	−0.003 to 0.026	0.012*	0.67
Duration of intervention	0.003	−0.006 to 0.012	0.536	0.00
Profession delivering intervention	−0.685	−1.050 to −0.320	<0.001***	0.82
Multivariate analysis				
Profession delivering intervention	−0.719	−1.064 to −0.374	<0.001***	1.00
Exercise intensity	−0.180	−0.399 to 0.040	0.108	
<i>BMI</i>				
Mean age control group	0.002	−0.017 to 0.021	0.826	0.00
Mean age nutrition group	−0.002	−0.020 to 0.017	0.868	0.09
Percentage men control group	0.010	−0.003 to 0.023	0.145	0.21
Percentage men nutrition group	0.009	−0.004 to 0.022	0.161	0.20
Duration of intervention	0.003	−0.005 to 0.011	0.403	0.00
Profession delivering intervention	−0.528	−0.896 to −0.160	0.005**	0.59
Multivariate analysis				
Profession delivering intervention	−0.526	−0.848 to −0.204	0.001***	1.00
Exercise intensity	−0.208	−0.435 to 0.019	0.072	
<i>Waist circumference</i>				
Mean age control group	−0.009	−0.027 to 0.009	0.340	0.00
Mean age nutrition group	−0.010	−0.027 to 0.008	0.448	0.00
Percentage men control	0.003	−0.014 to 0.020	0.742	0.00
Percentage men nutrition group	0.006	−0.005 to 0.018	0.291	0.00
Duration of intervention	0.001	−0.005 to 0.006	0.859	0.00
Profession delivering intervention	−0.369	−0.759 to 0.021	0.064	0.00
Multivariate analysis				
Profession delivering intervention	−0.365	−0.762 to −0.033	0.072	0.00
Exercise intensity	0.016	−0.259 to 0.291	0.907	

BMI, body mass index.  
\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

measured.<sup>28,31,32,38,44,46</sup> Three studies used the Dietary Instrument for Nutrition Education (DINE) to assess fat (unsaturated and saturated) and fibre intake.<sup>28,31,32</sup> One study providing hour-long weekly discussion groups did not find significant changes in anthropometric measures and also did not find significant changes in fat or fibre intake.<sup>28</sup> Two studies delivered by keyworkers using a lifestyle manual, individually, which found small but significant improvements in anthropometric measures, found improvements in saturated fat and fibre intake,<sup>31</sup> and improvements in saturated fat, fruit and vegetable intake.<sup>32</sup> One study used the Block Fruit, Vegetable, and Dietary Fat Screeners to assess dietary change in an intervention providing healthy eating and weight-loss advice, delivered by research staff.<sup>38</sup> This study did not find significant differences in dietary behaviours. A fifth study used a food frequency questionnaire, which appears validated in women in the general population;<sup>44</sup> this questionnaire assessed the frequency of ten foods associated with better diet and ten foods associated with poorer diet. Individual psychoeducation and goal-setting significantly improved the score of foods associated with good diet compared with the control group, but not the score of foods associated with poorer diet.<sup>44</sup> Finally, one trial involved using the Scottish Health Survey to assess whether providing free fruit and vegetables to families improved nutritional intake.<sup>46</sup> Although improvements in fruit and vegetable intake were found, these were not sustained after the trial – and subsequent access to free fruit and vegetables – had ceased.

## Discussion

To our knowledge this is the first systematic review to assess the impact of key components that comprise, and modes of delivery

of, nutrition interventions on physical health measures of people with severe mental illness. We found that nutrition interventions improved anthropometric measures by reducing weight, BMI and waist circumference. Importantly, our review provides evidence about the most effective goals and delivery methods, including preventing weight gain from the initiation of anti-psychotic therapy and the use of qualified health professionals such as dietitians to deliver individualised interventions. Our results indicated that nutrition interventions were most effective when delivered by a dietitian, with meta-regression analyses confirming this in multivariate models. These findings show a clear and important role for dietitians as part of the multi-disciplinary mental health team.

Although the overall effect size for anthropometric measures was within the small to moderate range, it provided further evidence to support implementation of lifestyle interventions. Although between-group differences did not reach statistical significance, the larger effect size ( $g = -0.61$ ) seen in a pooled analysis of studies providing intervention in the early stages of antipsychotic therapy, where weight gain is most rapid,<sup>13</sup> provides evidence for the achievability of goal 5 of the Healthy Active Lives declaration – that is, to restrict weight gain to no more than 7% of pre-illness weight in 75% of people experiencing first-episode psychosis, 2 years after commencing antipsychotic treatment.<sup>11</sup> Targeting interventions to coincide with initiation of antipsychotic therapy is also warranted given the clinical benefits of preventing significant weight gain and metabolic deterioration. Given the large effect size ( $g = -0.90$ ) found for key anthropometric outcomes, nutrition interventions delivered by dietitians, in particular individualised counselling sessions, should have a central role in addressing cardiometabolic abnormalities and premature mortality in people with SMI.<sup>18,55</sup>

It was not possible to conduct a meta-analysis on nutritional intake owing to a lack of consensus on data collection methods together with the wide variety of outcome measures used. Nutritional intake can be notoriously difficult to assess accurately because of intake variability and the wide range of nutrients to consider, particularly if the assessment method is not targeted to the specific population. To date, there is no validated nutrition assessment tool developed for use in people living with severe mental illness, a significant gap in the literature requiring urgent attention. In addition, improvements in cardiometabolic health as a result of changes in nutritional intake, independent of weight change, have not been assessed in this population. This is a significant area requiring research, given the enduring weight challenges in this population.

Our results are broadly similar to previous non-pharmacological and physical activity intervention analyses completed by Álvarez-Jiménez *et al*, Bruins *et al* and Rosenbaum *et al*.<sup>12,56,57</sup> Effect sizes (ES) from these analyses on anthropometric measures were respectively  $Z=7.85$ ,  $ES=0.63$  and standardised mean difference=0.24. However, ours is the first review to consider the impact of nutrition interventions and provides further recommendations for dietitian-led interventions incorporated from the early stages in SMI. As with the general population, nutrition interventions are most likely to be effective when combined with physical activity.

### Limitations and future research

Several factors may have influenced the results obtained by this review, largely reflecting limitations in the primary studies. First, nutrition interventions were often delivered as part of a comprehensive lifestyle programme, thus participants were potentially receiving concomitant additional lifestyle interventions such as physical activity, which may have had a synergistic effect on participant outcomes. Although it was not possible to separate the impact of the nutrition intervention from additional components, we attempted to investigate the impact of nutrition interventions through a series of adjustments for potential confounders. For instance, for the primary outcome, our multivariate meta-regression analyses consistently demonstrated that nutrition interventions were most effective when delivered by a dietitian, even when we adjusted for concomitant exercise elements. Although the results from our subgroup analyses consistently demonstrated higher effect sizes of dietitian-led nutrition interventions and interventions delivered at antipsychotic initiation, these findings did not reach statistical significance after applying the Bonferroni correction. Although Bonferroni corrections are not routinely used in meta-analyses,<sup>58</sup> we have opted for a conservative approach, and although our findings did not reach significance, they suggest more favourable outcomes and warrant further investigation. Second, the RCTs included a range of nutrition interventions including group education, individualised plans, practical shopping and cooking sessions and meal replacements. Subgroup analyses were run where possible, but were limited by the small numbers of studies and highly variable methods. Future research should seek to establish homogeneity in the use of appropriate outcome measures and nutrition interventions. Third, the potential for significant effects on relevant biochemical measures may have been affected by the short duration of interventions in many studies and the target outcomes frequently being limited to anthropometric measures. Future long-term studies encompassing specific dietary strategies to target dyslipidaemia are required, with adequate follow-up to see the impact of nutrition interventions in this population.<sup>59</sup> Fourth, we did encounter some

evidence of publication bias, but after recalculating the effect sizes using Duval & Tweedie's trim and fill method our results were broadly similar.<sup>26</sup> Fifth, we did encounter moderate heterogeneity in some of our analyses. Nonetheless, our multivariate meta-regression analyses explained all ( $R^2=1.0$ ) of the observed heterogeneity for weight and BMI meta-analyses results. We were, however, unable to explain the heterogeneity in waist circumference; high levels of variability and inaccuracies in waist circumference measuring may be a factor.<sup>60</sup> Finally, we were unable to access data from some of the identified studies, reducing the number of studies included and sample sizes included in some of the meta-analyses. In addition, some studies did not clearly identify the specific psychiatric diagnoses of participants, limiting the ability to draw further conclusions regarding the potential impact of diagnosis on the intervention outcomes obtained.

Nevertheless, allowing for these caveats, the results of this meta-analysis offer hope to clinical teams and patients alike that providing nutrition interventions as part of a wider multidisciplinary lifestyle intervention can be effective in preventing weight gain, particularly when delivered by a dietitian. University dietetic programmes will also need to evolve to increase the knowledge and understanding of SMI.

### Study implications

Nutritional intake is fundamental to weight management and future physical health. This systematic review and meta-analysis found that nutrition interventions significantly improved weight, BMI, waist circumference and glucose levels in people with SMI. Further, nutrition interventions delivered by dietitians, and those aiming to prevent weight gain at antipsychotic initiation had the largest effect sizes. The evidence supports the early inclusion of nutrition intervention in mental health service delivery to people with SMI. Further RCTs are required to determine the most effective nutrition intervention to optimise weight and cardiometabolic health in people with SMI.

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## psychiatry in history

### James Foulis Duncan (1812–1895)

Brendan D. Kelly

James Foulis Duncan was the last of the Duncan family to own Farnham House, a private asylum in Finglas, County Dublin, Ireland. He served as president of the King and Queen's College of Physicians in Ireland (1873–1875) and of the Medico-Psychological Association (MPA) in 1875.

Duncan's mother died when he was young so he grew up with his father at the asylum. They ate with the patients and Duncan's earliest lessons in Latin, mathematics and science were provided by patients whom he later described as the best and noblest persons of our race, of gifted intellect and high attainment.

Building on this unusual but effective foundation, Duncan graduated from Trinity College Dublin in 1837. Throughout his medical and psychiatric career, Duncan was acutely socially aware, especially of the effects of poverty on health. He supported the use of scientific comparisons to test treatments (in language that prefigured later ideas about clinical trials) and was highly religious in outlook, as evidenced in his 1852 publication, *God in Disease, or, The Manifestations of Design in Morbid Phenomena*.

In his presidential address to the MPA in 1875, Duncan vehemently denounced a great many features of 19th-century life, ranging from the substitution of machinery for handicraft labour to the employment of children in factories and consequent loosening of family bonds. He was not, however, a man to be easily defeated, not even by great, unstoppable forces of history. Duncan saw education as the answer to all of these problems and advocated for better medical education, broader public education, and moral education of the young, which he felt held the greatest hope for preventing mental disorder.

Duncan typified a certain model of 19th-century asylum doctor: enterprising, powerful, prolific and keen to promote asylum medicine in the eyes of other doctors and the public. He died on 2 April 1895 at the age of 83 years. Obituaries in the *British Medical Journal* and *Medical Press* noted the professional esteem in which he was held, as well as his devotion to the promotion of religion and his reputation as a man of charity.

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Data supplement to Teasdale et al. Solving a weighty problem: systematic review and meta-analysis of nutrition interventions in severe mental illness. British Journal of Psychiatry. doi: 10.1192/bjp.bp.115.177139

<b>Table DS1</b> Characteristics of included studies											
Trial	Age, years: mean (SD)		Diagnoses	Source from population	Delivered by	Delivery method	Nutrition intervention	Additional components	Control	Outcome(s)	Trial quality <sup>a</sup>
	Active	Control									
Alvarez-Jimenez et al, 2006 [27] N = 61	26 (15.5)	27.5 (8.5)	SCZ, SAD, SCZF, DD, BRP, PNOS	Outpatient	Clinical psychologist, nurse	Individual	Conducted according to set lifestyle manual	Exercise program	Usual care	Wt, BMI	4
Attux et al, 2013 [28] N = 160	36.2 (9.9)	38.3 (10.7)	SCZ spectrum	Outpatient	Nurse, occupational therapist, clinical psychologist, dietitian	Group	Conducted according to set lifestyle manual	Education: physical activity, anxiety and self-esteem management	Usual care	Wt, BMI, WC, BP Lipids, glucose DINE	4
Brar et al, 2005 [29] N = 71	40 (10.1)	40.5 (10.6)	SCZ, SAD	Mixed	Group leader	Group	Conducted according to set lifestyle manual	Education: exercise to burn calories	Usual care + encouraged to lose weight individually	Wt, BMI, WC, WHR	2
Brown & Chan, 2006 [31] N = 17	45.1	41.7	SMI	Outpatient	Key worker	Individual	Conducted according to set lifestyle manual	Education: exercise, daily activity and substance misuse	Usual care + health package post study	Wt, BMI, BP DINE	4
Brown & Smith, 2009 [32] N = 26	50.4	47	Psychosis, MAI, PD	Outpatient	Key worker	Individual	Conducted according to set lifestyle manual	Access to smoking cessation clinic and gym	Usual care + health package post study	Wt, BMI, BP DINE	4
Brown et al, 2011 [30]	44.6 (10.9)		SMI	Outpatient	Nurse,	Individual	Twice daily meal	Exercise	Usual care	Wt	2

N = 89					occupational therapist or dietitian		replacements + education + goal setting	program			
Cordes et al, 2014 [33] N = 25	43.6 (6.9)	39.9 (12.7)	SCZ, SAD	Inpatient	Dietitian	Group	Healthy isocaloric diet education, practical shopping + cooking class	Exercise education module	Usual Care	Wt, BMI, WC BP Fasting lipids, glucose	3
Daumit et al, 2013 [34] N = 291	46.6 (11.5)	44.1 (11)	SMI	Outpatient	Community health educator	Individual + group	Weight management sessions	Group exercise sessions	Usual care + standard nutrition and physical activity information	Wt, BMI, WC BP, lipids Glucose, insulin	4
Evans et al, 2005 [35] N = 34	34.6 (9.6)	33.6 (11.6)	SCZ, SAD, SCZF, BAD, DEP	Mixed	Dietitian	Individual	Best practice dietetic intervention	NA	Usual care + nutrition education booklet	Wt, BMI, WC	1
Forsberg et al, 2010 [36] N = 41	39.8	42.8	SCZ, BAD, PD, other psychotic disorders, autism spectrum	Outpatient	Not specified	Group	Theoretical diet training within practical shopping & cooking sessions	Physical activity sessions; substance use education	Usual care + art group sessions	Psychological outcome measures only	3
Gillhoff et al, 2010 [37] N = 50	48.1 (11.5)	48.9 (12)	BAD	Outpatient	Psychotherapist/psychiatrist, nutrition counsellor, fitness trainer	Group	Nutrition advice & cooking classes	Individual physical activity training; stress & symptom management	Usual care + intervention post study	Wt, BMI, WC, BP Blood lipids, HbA1c	2
Goldberg et al, 2013 [38] N = 109	50.5 (9.9)	53.5 (8.1)	SCZ, SAD, BAD, MDD, PTSD, severe	Outpatient	Research staff	Individual + group	Healthy eating & weight loss education	Exercise education	Usual care + nutrition and exercise information brochures	Wt, Diet	2

			anxiety disorder								
Hjorth et al, 2014 [39] N = 97	M: 48.0 (13.6) F: 47.8 (11.1)	M: 41.5 (12.4) F: 45.0 (17.9)	SMI	Inpatient	Project leader + research nurse	Individual + group	Stage of Change + Motivational Interviewing, focus groups (patients + staff) & education sessions (staff)	Smoking cessation, physical activity encouragement	Usual care + individual sessions post study	Wt, BMI, WC, body fat %, BP Lipids, glucose	2
Iglesias-Garcia et al, 2010 [40] N = 15	Not specified		SCZ	Outpatient	Psychiatric nurse	Group	Structured information given to participants plus group discussion	Exercise/health habits and self-esteem	Usual care with weekly anthropometric measures	Wt, BMI, WC BP	4
Jean-Baptiste et al, 2007 [41] N = 18	52.4	40.7	SCZ, SAD	Outpatient	Dietitian, psychiatrist	Group	Nutrition education sessions based on national standards, food provision, grocery store visit + cooking demonstration	Physical activity encouraged, pedometers given	Usual care followed by intervention (cross-over design)	Wt, BP Fasting lipids, glucose	2
Kwon et al, 2006 [42] N = 39	32 (9.4)	29.8 (6.1)	SCZ, SAD	Outpatient	Dietitian + exercise coordinator.	Individual	Best practice dietetic intervention	Exercise education + activity diary	Usual care + verbal recommendations for physical activity and eating behaviour	Wt, BMI Lipids, glucose	2
Littrell et al, 2003 [43] N = 70	33.7 (9.2)	34.5 (10)	SCZ, SAD	Outpatient	Master's-level clinician (nurse)	Group	Psychoeducation class using set lifestyle manual	Fitness and exercise education module	Usual care	Wt, BMI	2



Lovell et al, 2014 [44] N = 105	25.6 (5.5)	25.9 (6)	SCZ, SAD, SCZF, DD, BRP, PNOS, FEP	Outpatient	Support, time and recovery workers	Individual	Psychoeducation plus patient- centred goals + action plan	Optional sports groups	Usual care	Wt, BMI, WC FFQ	4
Mauri et al, 2008 [45] N = 33	38.9		SAD, BAD, Psychotic DEP	Outpatient	Dietitian	Individual	Psychoeducation with individualised diet and food diary	Step counter with aim of reaching 10,000 steps	Usual care followed by intervention post study (cross-over design)	Wt, BMI Lipids, glucose, insulin	2
McCreadie et al, 2005 [46] N =	45 (13)		SCZ	Outpatient	Occupational therapist, case workers	Group (house)	Free fruit + vegetables +/- associated instructions	NA	Usual care	Scottish Health Survey - fruit, vegetables, global assessment of diet + individual nutrients	2
McKibbin et al, 2006 [47] N = 57	53.1 (10.4)	54.8 (8.2)	SCZ	Outpatient	Not specified	Group	Psychoeducation on diabetes, nutrition and lifestyle education	Exercise education with pedometer	Usual care + diabetes education brochures	Wt, BMI, WC, BP Lipids, glucose	2
Milano et al, 2007 [48] N = 36	46	45	SCZ, BAD	Outpatient	Not specified	Individual	Nutrition counselling with specified diet including calorie reduction and nutritional balance	Physical activity program	Usual care with regular diet and no physical activity	Wt, BMI	2
Scocco et al, 2006 [49] N = 17	51.7 (12.4)	39.3 (9.9)	SCZ, SAD	Outpatient	Dietitian	Individual	Education, food diary, energy deficit	Non-structured exercise with tailored advice	Usual care + intervention post study	Wt, BMI	1
Usher et al, 2013 [50] N = 101	Not specified		SCZ, BAD, DEP, Anxiety	Outpatient	Nurse	Group	Nutrition education in accordance with lifestyle booklet	Exercise education plus pedometer	Usual care + healthy lifestyle booklet	Wt, BMI, WC	3

Weber & Wyne, 2006 [51] N = 15	Not specified		SCZ, SAD	Outpatient	Nurse	Group	Cognitive/behavioral lifestyle intervention	Exercise education plus activity diary	Usual care	Wt, BMI, WHR, glucose	3
Wu et al, 2007 [52] N = 53	42.2 (7.5)	39 (6.7)	SCZ	Inpatient	Dietitian	Individual	Dietary plan with caloric restriction and nutritional balance	Exercise program	Usual care	Wt, BMI, WC, WHR, body fat % Lipids, glucose, insulin	2

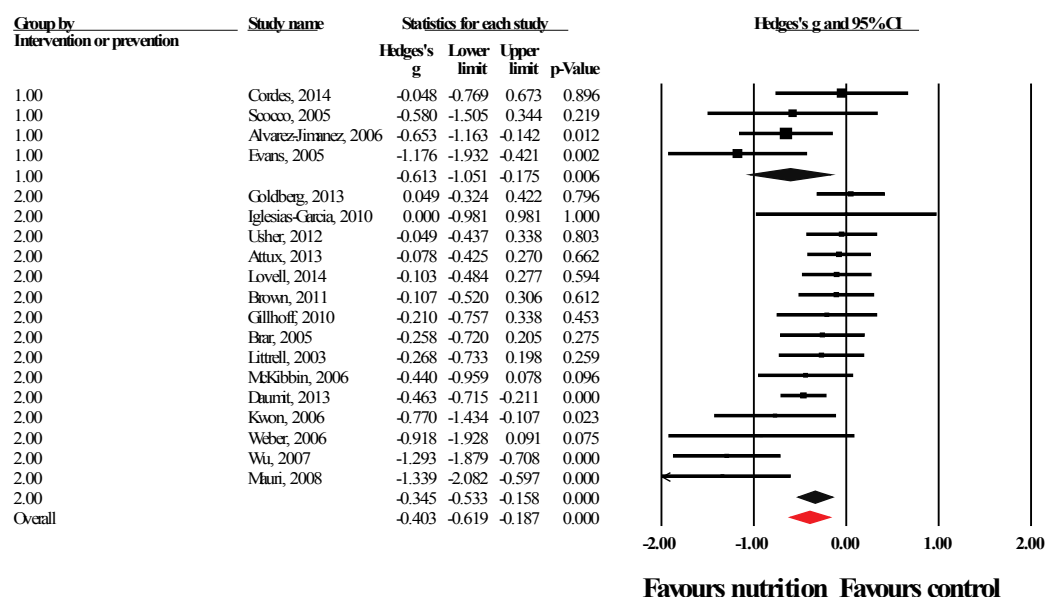
SCZ = Schizophrenia, SAD = Schizoaffective disorder, SCZF = Schizophreniform disorder, BAD = Bipolar affective disorder, DD = Delusional disorder, BRP = Brief reactive psychosis, PNOS = Psychosis not otherwise specified, MAI = Major affective illness, PD = Personality disorder, SMI = Severe mental illness, MDD = Major depression disorder, DEP = Depression, FEP = First-episode psychosis, PTSD = Post traumatic Syndrome Disorder, Wt = Weight, BMI = Body mass index, WC = Waist circumference, WHR = Waist-to-hip ratio, BP = Blood pressure, FFQ = Food Frequency Questionnaire, DINE = Dietary Instrument for Nutrition Education, HbA1c = Glycated haemoglobin.

a. Criteria used for trial quality scores included (i) concealed allocation, (ii) assessor blinding, (iii) group treatment equality, and (iv) all participants accounted for. Individual scoring for each trial is available in Table DS2.

**Table DS2** Methodological quality of included trials for primary systematic review

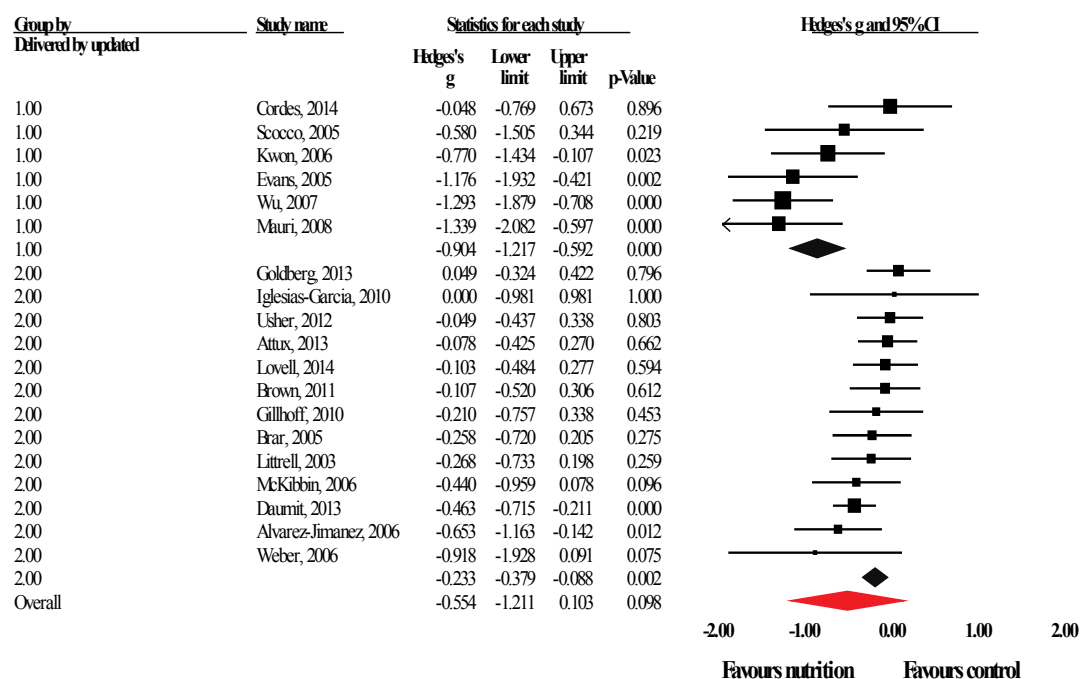
Trial	Concealed allocation	Assessor blinding	Group treatment equality	All participants accounted for	Total
Alvarez-Jimenez et al, 2006	Yes	Yes	Yes	Yes	4
Attux et al, 2013	Yes	Yes	Yes	Yes	4
Brar et al, 2005	No	Yes	No	Yes	2
Brown et al, 2006	Yes	Yes	Yes	Yes	4
Brown et al, 2009	Yes	Yes	Yes	Yes	4
Brown et al, 2011	Yes	No	Yes	No	2
Cordes et al, 2014	Yes	No	Yes	Yes	3
Daumit et al, 2013	Yes	Yes	Yes	Yes	4
Evans et al, 2005	No	No	Yes	No	1
Forsberg et al, 2010	Yes	No	Yes	Yes	3
Gillhoff et al, 2010	No	No	Yes	Yes	2
Goldberg et al, 2013	Yes	No	Yes	No	2
Iglesias-Garcia et al. 2010	Yes	Yes	Yes	Yes	4
Hjorth et al, 2014	No	No	Yes	Yes	2
Jean-Baptiste et al, 2007	No	No	Yes	Yes	2
Kwon et al, 2006	No	No	Yes	Yes	2
Littrell et al, 2003	No	No	Yes	Yes	2
Lovell et al, 2014	Yes	Yes	Yes	Yes	4
Mauri et al, 2008	No	No	Yes	Yes	2
McCreadie et al, 2005	No	No	Yes	Yes	2
McKibbin et al, 2006	No	No	Yes	Yes	2
Milano et al, 2007	No	No	Yes	Yes	2
Scocco et al, 2006	No	No	Yes	No	1
Usher et al, 2013	Yes	No	Yes	Yes	3
Weber et al, 2006	No	Yes	Yes	Yes	3
Wu et al, 2007	No	No	Yes	Yes	2
Total / 26	12	9	25	22	

**Fig. DS1a** Subgroup analysis of timing of antipsychotic medication on weight.



(1 = weight-gain prevention studies, 2 = weight-loss studies)

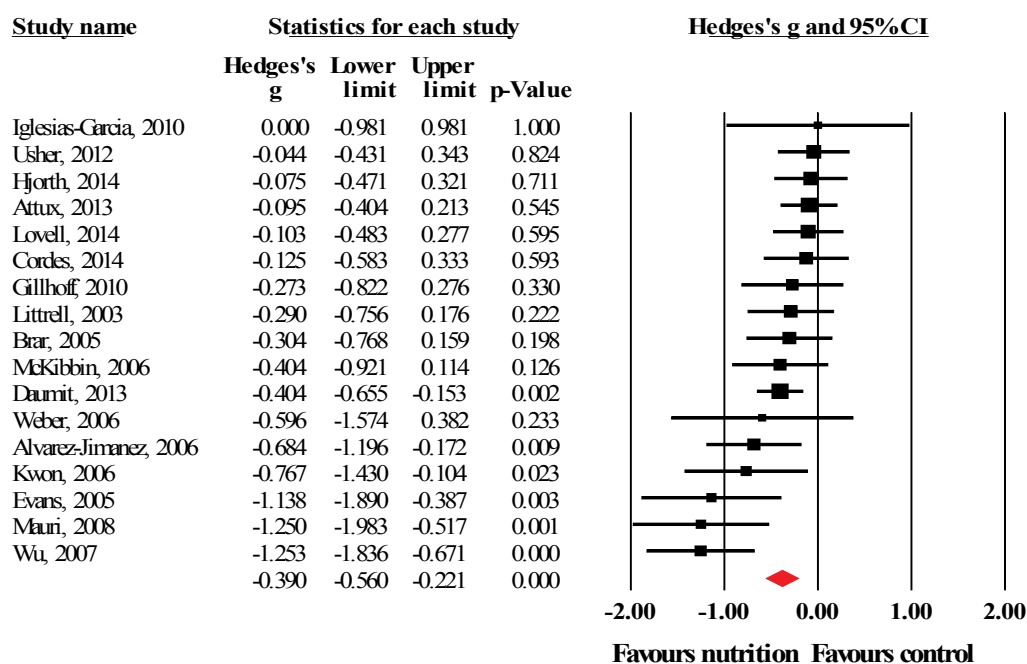
**Fig. DS1b** Subgroup analysis of those who delivered the intervention on weight.



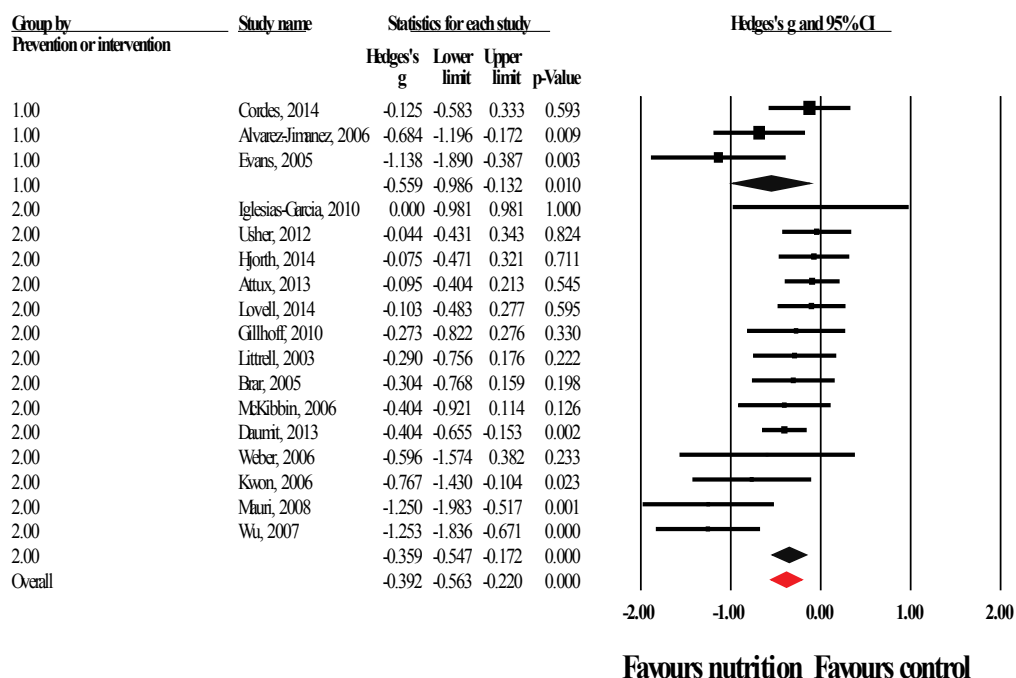
(1 = dietitian-led, 2 = predominantly delivered by other health professionals)



**Fig. DS2a** Main analysis of interventions on BMI.

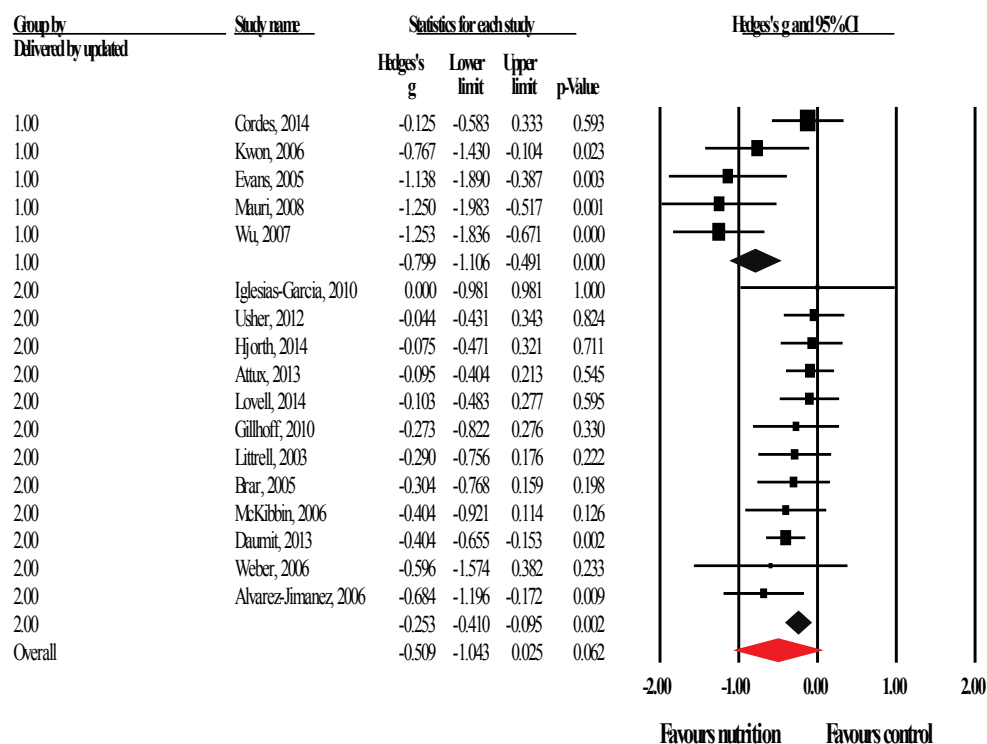


**Fig. DS2b** Subgroup analysis of timing of antipsychotic medication on BMI.



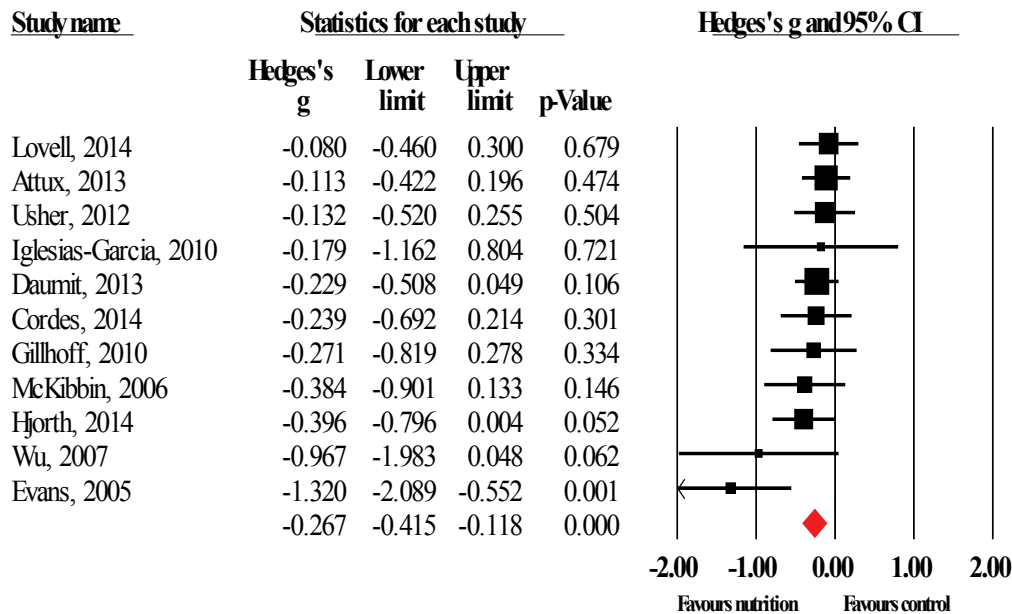
(1 = delivered at initiation of antipsychotic medication, 2 = delivered subsequent to antipsychotic use)

**Fig. DS2c** Subgroup analysis of those who delivered the intervention on BMI.

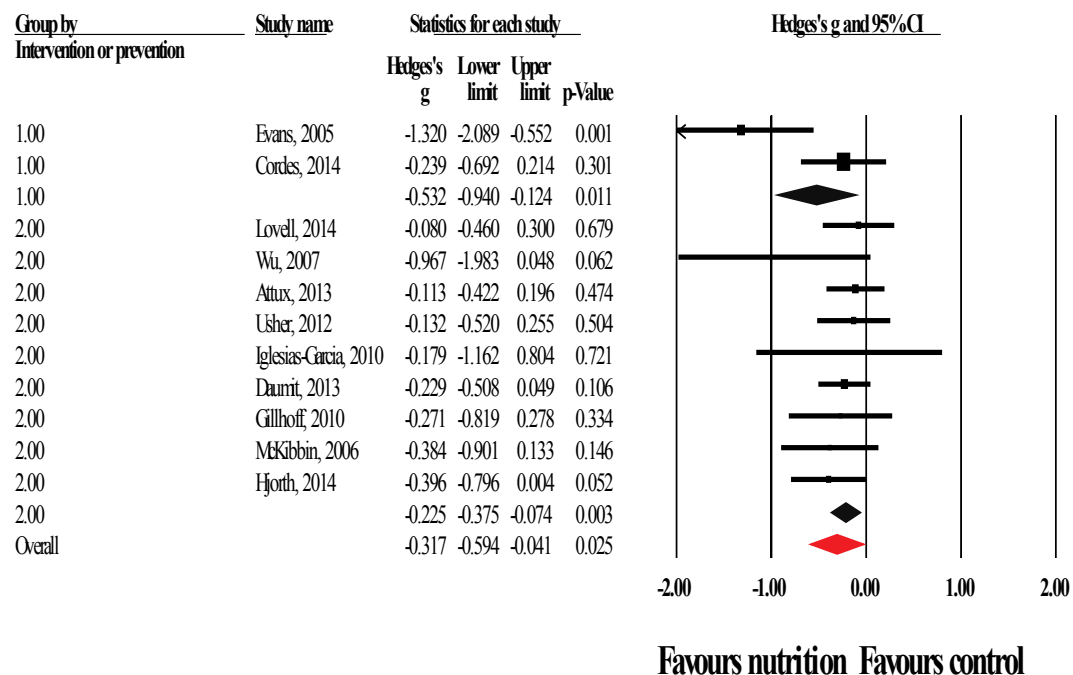


(1 = dietitian, 2 = mixed with dietitian input, 3 = no dietitian input, 4 = not reported)

**Fig. DS3a** Main analysis of interventions on waist circumference.

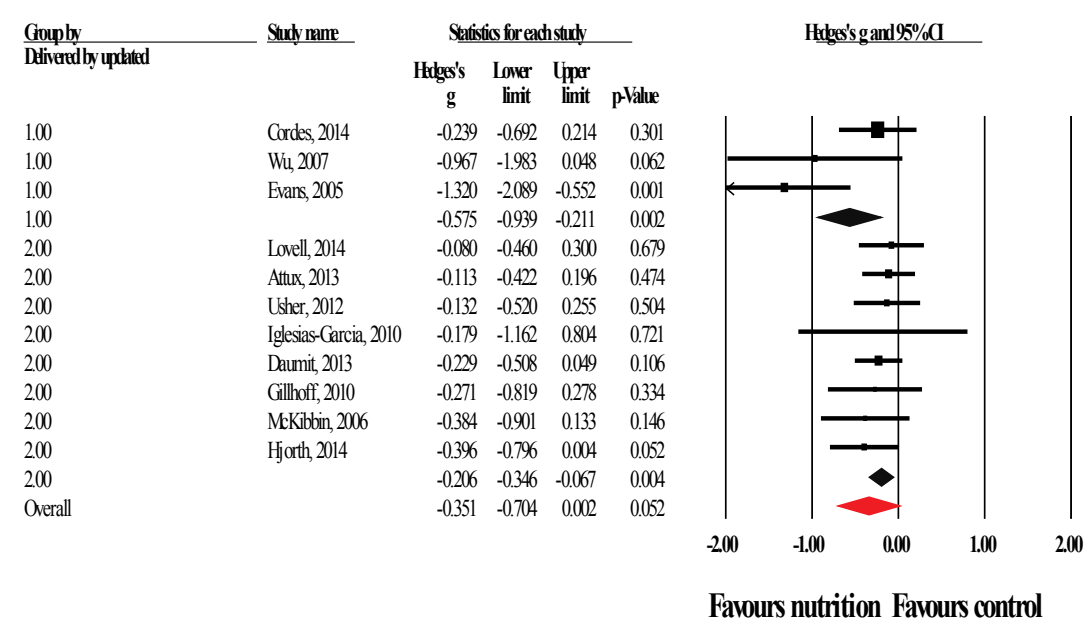


**Fig. DS3b** Subgroup analysis of timing of antipsychotic medication on waist circumference.



(1 = weight-gain prevention studies, 2 = weight-loss studies)

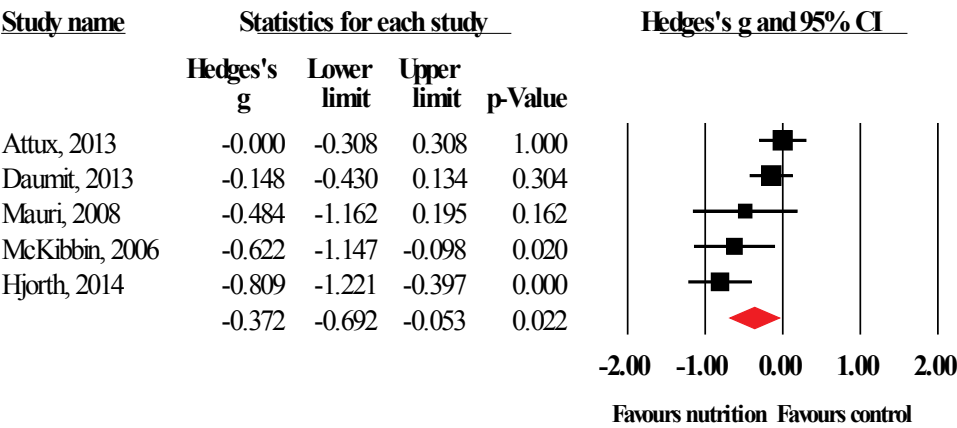
**Fig. DS3c** Subgroup analysis of those who delivered the study on waist circumference.



(1 = dietitian, 2 = mixed with dietitian input, 3 = no dietitian input, 4 = not reported)



**Fig DS4** Main analysis of nutrition interventions on glucose.



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## **Solving a weighty problem: systematic review and meta-analysis of nutrition interventions in severe mental illness**

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### **Supplementary Material**

Supplementary material can be found at:  
<http://bjp.rcpsych.org/content/suppl/2016/10/21/bjp.bp.115.177139.DC1>

### **References**

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