Effectiveness and cost-effectiveness of referral to a commercial open group behavioural weight management programme in adults with overweight and obesity: 5-year follow-up of the WRAP randomised controlled trial

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Summary

Background There is evidence that commercially available behavioural weight management programmes can lead to short-term weight loss and reductions in glycaemia. Here, we aimed to provide the 5-year impact and cost-effectiveness of these interventions compared with a brief intervention.

Methods WRAP was a non-blinded, parallel-group randomised controlled trial (RCT). We recruited from primary care practices in England and randomly assigned participants to one of three interventions (brief intervention, 12-week open-group behavioural programme [WW, formerly Weight Watchers], or a 52-week open-group WW behavioural programme) in an uneven (2:5:5) allocation. Participants were followed up 5 years after randomisation using data from measurement visits at primary care practices or a research centre, review of primary care electronic medical notes, and self-report questionnaires. The primary outcome was change in weight at 5 years follow-up, assessed using analysis of covariance. We also estimated cost-effectiveness of the intervention. This study is registered at Current Controlled Trials, ISRCTN64986150.

Findings Between Oct 18, 2012, and Feb 10, 2014, we recruited 1269 eligible participants (two participants were randomly assigned but not eligible and therefore excluded) and 1040 (82%) consented to be approached about additional follow-up and to have their medical notes reviewed at 5 years. The primary outcome (weight) was ascertained for 871 (69%) of 1267 eligible participants. Mean duration of follow-up was 5·1 (SD 0·3) years. Mean weight change from baseline to 5 years was –0·46 (SD 8·31) kg in the brief intervention group, –1·95 (9·55) kg in the 12-week programme group, and –2·67 (9·81) kg in the 52-week programme. The adjusted difference in weight change was –1·76 (95% CI –3·68 to 0·17) kg between the 52-week programme and the brief intervention; –0·80 (–2·13 to 0·54) kg between the 52-week and the 12-week programme; and –0·96 (–2·90 to 0·97) kg between the 12-week programme and the brief intervention. During the trial, the 12-week programme incurred the lowest cost and produced the highest quality-adjusted life-years (QALY). Simulations beyond 5 years suggested that the 52-week programme would deliver the highest QALYs at the lowest cost and would be the most cost-effective. No participants reported adverse events related to the intervention.

Interpretation Although the difference in weight change between groups was not statistically significant, some weight loss was maintained at 5 years after an open-group behavioural weight management programme. Health economic modelling suggests that this could have important implications to reduce the incidence of weight-related disease and these interventions might be cost-saving.

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Introduction

The prevalence and health consequences of overweight and obesity demand effective and scalable treatment options. There is strong evidence that referral to a commercial open-group behavioural weight management programme can help adults with overweight and obesity to lose weight and reduce glycaemia in the short term.[1–3] Modelling of longer-term outcomes suggests that this treatment could be cost-effective due to reductions in risk of chronic disease and in the associated health-care costs.[1] However, estimations of the effect of this treatment on disease incidence and long-term cost-effectiveness depend on weight regain.[4] No randomised controlled trials of this type of commonly available, non-specialist-led intervention, where new members can join at any time, have measured outcomes for longer than 2 years.

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See **Comment** page e806

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Research in context

Evidence before this study

There is good evidence that open group commercial weight management programmes can help people to lose weight and reduce glycaemia in the short term, but little evidence of their effects beyond 2 years. A US Preventive Services Task Force review identified randomised controlled trials (RCTs) and cluster RCTs of behavioural weight management interventions for adults with overweight or obesity that were, or could feasibly be, implemented in primary care settings and were published from Jan 1, 2010, to June 6, 2017. We ran an updated search of MEDLINE, Cochrane database, and PsycINFO for articles published from June 6, 2017, to March 5, 2021, using the search terms from the US Preventive Services Task Force review. We identified 91 relevant studies and screened these to identify any RCTs of primary care-relevant behavioural interventions for obesity that had followed up with participants for longer than 2 years. We found that three studies had follow up with participants for 5 years or longer. These three studies all evaluated specialist-led interventions delivered individually or in closed groups. There were no studies of open-group programmes led by trained lay people with follow-up longer than 2 years.

Added value of this study

Our study provides the first RCT evidence of the effect of commonly available commercial bodyweight management programme on weight and related outcomes at 5 years. We showed that at 5-year follow-up, participants randomly assigned to WW (formerly Weight Watchers) for 12 or 52 weeks weighed on average 2·0–2·5 kg less than they did at the start of the study, compared with an average 0·5 kg reduction in participants randomly assigned to a brief intervention group (booklet of self-help materials). Although differences between groups were not statistically significant, the differences seen counter the common belief that all weight lost is quickly regained. However, there was no evidence within the trial that cardiovascular risk factors improved or that diabetes incidence was reduced.

Within-trial economic evaluation suggested that the 12-week programme is marginally more cost-effective, but with high levels of uncertainty. When observed weight trajectories were modelled over a lifetime horizon, we found that the 52-week programme offered the best value for money and might be cost-saving because of reductions in weight-related disease that manifest beyond 5 years.

Implications of all the available evidence

Referring people with overweight and obesity to an open-group behavioural weight management programme for at least 12 weeks is a cost-effective way for policy makers to reduce weight-related disease and related health-care costs. Investment in referrals for 52-weeks achieves greater weight loss and is likely to be cost-saving over a lifetime horizon because the costs of the programme are more than offset by reductions in incidence of diabetes, cardiovascular diseases, and other comorbidities.

Consequently, there is uncertainty about the long-term effectiveness of these programmes on weight, diabetes, and other obesity-related conditions. Studies of specialist closed-group programmes (where all participants join at the same time and go through the programme together) suggest that most of the weight lost is regained, but that there are small, sustained reductions in weight for up to 5 years.[5,6]

To address this uncertainty, we followed up with participants from the WRAP trial[1] at 5 years after randomisation. In the WRAP trial, we showed that referral to a commercial open-group behavioural programme (WW, formerly Weight Watchers) for 12-weeks or 52-weeks resulted in greater weight loss during 2-year follow-up than a brief intervention (a booklet of self-help weight-management strategies); participants in the 52-week programme lost more weight than those in the 12-week programme; and, at 1 year, participants in the 52-week programme had greater reductions in glycaemia than participants in the other two groups.[7] In our previous modelling of long-term cost-effectiveness, we assumed that all participants returned to baseline weight by 5 years, and there would be no difference between groups from that point.[1] Weight loss cost-effectiveness models are highly sensitive to assumptions about the maintenance of weight loss over time.[4]

In this Article, we report the primary outcome (weight) and secondary outcomes (fat mass, glycated haemoglobin concentration, lipid profile, blood pressure, and diabetes status) at 5 years. We also assessed the cost-effectiveness of the open-group behavioural weight management programmes using data collected from the 5-year follow-up and modelled the lifetime cost-effectiveness.

Methods

Study Design

The WRAP trial was a multi-centre, non-blinded, multi-arm randomised controlled trial with imbalanced randomisation. Full details of the study design[8] and outcomes after 2 years of follow-up have been reported.[1] Between Oct 18, 2012, and Feb 10, 2014, eligible participants from 23 primary care practices in England were recruited and randomly assigned (2:5:5) to one of three interventions (brief Intervention, 12-week open-group behavioural programme [WW, formerly Weight Watchers], or a 52-week WW programme). Participants completed outcome assessments at a primary care practice or a research centre at 3 months, 1 year, and 2 years.

Between Feb 5, 2018, and Aug 3, 2019, we did a 5-year outcome assessment consisting of measurement visits at primary care practices or a research centre, review of primary care electronic medical notes, and self-report questionnaires.

Ethical approval was obtained from West Midlands-Coventry and Warwickshire Research Ethics Committee on Dec 8, 2017 (17/WM/0432). The original trial and the 5-year follow-up were both prospectively registered with Current Controlled Trials (ISRCTN82857232 and ISRCTN64986150).

Participants

WRAP participants were adults (≥18 years) with a body-mass index (BMI) ≥28 kg/m². Staff at 23 primary care practices in England searched their electronic records to identify eligible patients and sent them a letter inviting them to take part in the trial. Exclusion criteria were planned or current pregnancy, previous or planned bariatric surgery, current participation in a structured monitored weight loss programme or other research that could confound outcome measures, eating disorders, and non-English speaking or special communication needs.

We mailed invitations to these participants and followed up with three telephone or email contacts from their local GP practice or the coordinating centre (Cambridge Epidemiology and Trials Unit; CETU) to arrange a clinic visit after 5 years of enrolling in the original trial. We used the patient status and tracking service provided by UK National Health Service (NHS) Digital to recontact participants who had moved address or changed their contact telephone number.

Randomisation and masking

We randomly assigned to one of the three interventions in an uneven (2:5:5) allocation, stratified by centre and gender with a block size of 12. The randomisation sequence was generated in Stata (version 12.1) by the trial statistician (SJS) and programmed into the database; the randomisation sequence was unknown to research staff. Participants and research staff were not masked to intervention allocation after randomisation.

Procedures

Participants in the behavioural programmes were given vouchers and asked to attend local WW weekly meetings and access WW web tools at no cost for the duration of the intervention (12 weeks or 52 weeks). Participants allocated to the brief intervention were given a 32-page booklet from the British Heart Foundation that contained advice and strategies on how to lose weight. Research staff read a scripted introduction that drew attention to each section of the booklet. Participants continued to receive standard care throughout the 5-year trial period and there were no restrictions on participants in any group accessing other weight management interventions.

Clinic visits mainly took place at the primary care practices from which participants were recruited. If participants had moved house, they could attend any of the participating practices or a Cambridge Epidemiology and Trials Unit research site. Visits were done by trained clinical or research staff, in line with standard operating procedures and under written informed consent from all participants. Participants received a £30 shopping voucher for to compensate them for their time and any expenses incurred in attending the visit.

Height was measured in cm using a stadiometer and weight and fat mass were measured in kg using a calibrated Tanita body composition analyser. Blood pressure was measured three times in a rested state using the practices' own validated Omron meters. Blood samples were taken and mailed the same day to the NIHR Cambridge Biomedical Research Centre Core Biochemical Assay Laboratory at Addenbrookes Hospital for analysis of glycated haemoglobin A1c (HbA_{1c}) and lipid profiles. To remind general practitioners and nurses to weigh participants when they were attending routine visits, their primary care records were tagged. These data were used if participants were unable to attend a study visit but consented to notes review. Participants were asked to complete an online or paper questionnaire that included a health-care resource use questionnaire, a self-report measure of quality of life (EQ5D-3L),[9] and measures of psychosocial variables.

Participants were also asked to report their self-measured weight, diabetes status, and smoking status via questionnaire, or by telephone when study assistants were arranging appointments. We asked participants to weigh themselves before they reported their weight and encouraged those without weighing scales at home to measure their weight elsewhere. Participants who could not attend visits were mailed a copy of this short questionnaire with a pre-paid envelope and offered a £10 shopping voucher to complete and return it.

Notes reviews of electronic primary care records were done by nurses to obtain data on health-care resource use (visits to general practitioners and community health-care workers; outpatient appointments; accident and emergency; inpatient stays; and use of medications), diabetes status, recent measures of weight, HbA_{1c} profile, and blood pressure. We intended to calculate 10-year cardiovascular risk (Q-Risk v2) but were unable to extract sufficient reliable data from medical records.

We collected health-care resource use data from trial case record forms, health-care resource use questionnaires, and medical records. The cost of the interventions was calculated consistent with the 2-year analysis, which assumed that the NHS would be charged only if the participant attended at least one session.[1]

Outcomes

The primary outcome was weight at 5 years follow-up. Secondary clinical outcomes were fat mass, HbA_{1c} profile,

lipid profile, blood pressure, and diabetes status (normoglycaemia: HbA_{1c} <42 mmol/mol; non-diabetic hyperglycaemia: HbA_{1c} 42–47 mmol/mol; and diabetes: HbA_{1c} ≥48 mmol/mol or a clinical diagnosis or documented history of current treatment for diabetes). Weight loss as a proportion of baseline weight was included as an outcome post-hoc.

The outcome of the health economic analysis at 5 years after randomisation was NHS and social care costs, quality-adjusted life years (QALY), and weight loss. QALY was assessed using the EQ-5D-3L, which asks patients to report their current health-related quality of life (HRQOL) in relation to five domains (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) with three levels of severity (none, some, or extreme). UK population-based tariffs were applied to the EQ-5D-3L responses to convert them into utility values ranging from –0·594 (extreme problems on all five domains) to 1 (perfect health) and anchored at 0 (death).[10] The utility values reported by each patient at each timepoint were used to calculate the QALYs by calculating the area under these utility values. Additional details on methods used to calculate HRQOL and QALYs are reported in the supplementary material section on methods and health outcomes (appendix pp 6–7). The outcomes of the long-term cost-effectiveness were NHS and social care costs and QALYs. All economic analyses were discounted at 3·5% in line with the UK National Institutes for Health and Care Excellence (NICE) reference case.[11] Any adverse events reported to the study team were logged and serious adverse events were assessed for expectedness and relatedness.

See Online for appendix

Statistical analysis

Analyses were prespecified (ISRCTN64986150); all individuals were included in the group to which they were randomly assigned, regardless of whether they followed the allocated intervention. For continuous outcomes, we estimated differences and 95% CIs comparing the intervention groups (52-week programme *vs* 12-week programme, 12-week programme *vs* brief intervention, and 52-week programme *vs* brief intervention) using analysis of covariance, with adjustment for baseline value, research centre and gender (ie, the randomisation stratifiers). If measured weight was not available, we used the most recent clinical record of measured weight if this was no longer than 12 months from the 60-month visit due date; if neither measured weight nor eligible recorded weight were available, we used self-measured weights. If HbA_{1c} profile was not measured at the study visit, we used the most recent clinical record of HbA_{1c} profile if it was no longer than 12 months from the 60-month visit due date.

For continuous outcomes, we included participants with a missing baseline value of the variable in the analysis using the missing indicator method.[12] For each outcome, we used a multiple imputation model using chained equations, which included values of the outcome at previous timepoints, randomised group, research centre, and other baseline characteristics (age, sex, education, income, diabetes status, HbA_{1c} profile, weight, BMI, waist circumference, fat mass, total cholesterol, HDL and LDL cholesterol, log triglycerides, and systolic blood pressure). 20 imputation datasets were created, and parameter estimates from fitting the analysis model to each imputed dataset were combined using Rubin's rules (mi impute chained and mi estimate commands in Stata).[13] This model assumed that missing data were missing at random.

For the primary outcome, we tested potential interactions between intervention and gender, educational qualifications (as a binary variable grouping: all education categories up to and including A levels as below post-secondary and categories above A levels as post-secondary and above), and baseline diabetes status (normoglycaemia or non-diabetic hyperglycaemia *vs* diabetes) by including the relevant multiplicative parameters in the ANCOVA model.

Due to the multiplicity of outcomes and comparisons, p values are only reported for the main effects and interaction analyses of the primary outcome; we reported 95% CIs for all outcomes and comparisons.

For weight and HbA_{1c} profile, we did the following preplanned sensitivity analyses: effects estimates adjusted for the follow-up duration and completers-only analysis. For the analyses of incident diabetes, women who were defined as having diabetes solely on the basis a history of treatment with metformin (and no other treatments) were included as not having diabetes because metformin can be prescribed for other indications, particularly in women (eg, polycystic ovarian syndrome).

It is common to report the proportion of people with a follow-up weight of at least 5% below baseline, so we did this analysis post-hoc and presented these data to support comparison with other studies.

Statistical analyses of the clinical outcomes were done in Stata (version 16.1), within-trial cost-effectiveness analysis (CEA) were done in R (version 3.4.1), and the lifetime CEA were done in R (version 4.0.2).

We did a within-trial CEA to compare the costs incurred by the NHS and the health consequences of each intervention included in the study (brief intervention, 12-week, and 52-week programmes) over a 5-year time-horizon. Results are shown as incremental cost (£) per additional kg of weight loss and Net Monetary Benefits (NMB), assuming that the monetary value of one QALY was £20 000. A description of methods used is in the appendix (pp 5–8).

For long-term (lifetime) modelling methods, we used the School for Population Health Research diabetes prevention model (version 4.0), which is an individual patient microsimulation in which a representative sample of individuals eligible for the intervention was drawn from the Health Survey for England 2014. The

development of the economic model and the design of the economic evaluation were done in line with UK guidelines for economic evaluations.[11] As such, we calculated health outcomes and costs over the natural length of life of the population cohort and a NHS and Personal Social Services perspective. The health status of these individuals was updated in annual cycles and we calculated major health events, lifetime costs, and QALYs. We estimated metabolic trajectories (BMI, systolic blood pressure, total cholesterol, and HbA_{1c} profile) for each trial group (brief intervention, 12-week programme, and 52-week programme). We also simulated a natural history trajectory from the default modelling trajectories for comparison with a do-nothing scenario. We determined the simulated individual natural history trajectories for BMI using non-linear growth models, in which BMI change was conditional on baseline BMI, age, sex, and family history. The sample population mean BMI trajectory shows a pattern of increasing BMI with the growth rate diminishing to weight loss over time. We fitted statistical models of the BMI, systolic blood pressure, total cholesterol, HDL cholesterol, and HbA_{1c} profile to the WRAP trial data to describe individual metabolic trajectories and intervention differences up to 5 years. Except for BMI, all metabolic trajectories returned to the simulated natural history after 5 years. Differences in BMI between trial groups and the simulated natural history were assumed to reduce linearly to return to natural history after 10 years by extrapolating the linear trend. Metabolic risk factors were associated with major health events, which included diabetes, cardiovascular disease, microvascular disease, osteoarthritis, cancer, depression, and dementia. Death from fatal health outcomes relating to cardiovascular disease or cancer were simulated in the model, with other cause mortality simulated based on UK lifetables. We aggregated simulated EQ-5D estimates over a lifetime to estimate QALYs discounted at 3·5% annually. We identified utility decrements from published literature, which were applied to baseline EQ-5D values following major health events and ageing. Additional details of the modelling methods are detailed in the appendix (pp 26–101).

Role of the funding source

Neither the funders nor WW had any role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Results

We recruited 1269 participants (two were excluded, as described in Ahern and colleagues;[1] figure 1) and 1040 (82%) participants consented to be approached about additional follow-up and to have their medical notes reviewed at 5 years. The primary outcome (weight) was ascertained for 871 (69%) of 1267 participants; 632 (50%) participants attended a study visit at a primary

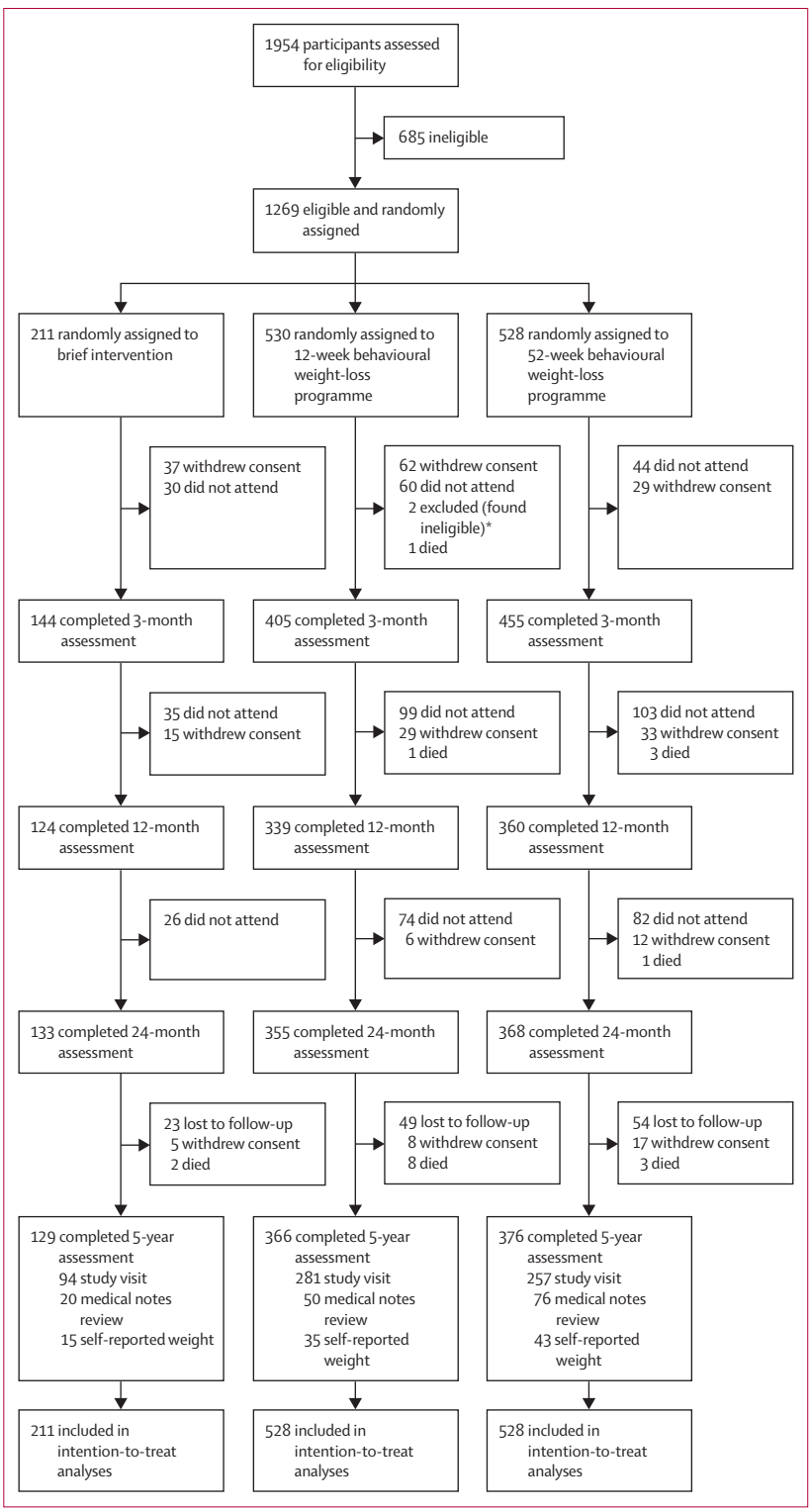

Figure 1: **Trial profile**
*Excluded from intention-to-treat analyses.

For more on the **NHS and Personal Social Services perspective** see https://www.nice.org.uk/process/pmg9/chapter/foreword

	Brief intervention (N=211)		12-week programme (N=528)		52-week programme (N=528)	
	N or n (%); N	Mean (SD)	N or n (%)	Mean (SD)	N or n (%)	Mean (SD)
Age (years)	211	51·9 (14·1)	528	53·6 (13·3)	528	53·3 (14·0)
Weight (kg)	211	96·1 (16·4)	528	96·6 (17·9)	528	95·7 (16·4)
Height (cm)	211	166·9 (9·5)	528	166·7 (8·9)	528	166·6 (9·0)
Body-mass index (kg/m²)	211	34·4 (4·6)	528	34·7 (5·4)	528	34·4 (5·0)
Fat mass (kg)	204	39·2 (9·9)	515	39·6 (11·8)	517	39·4 (11·1)
Waist circumference (cm)	210	110·3 (11·9)	528	111·1 (12·4)	528	110·4 (12·7)
Systolic blood pressure (mm Hg)	210	130·6 (15·7)	526	133·5 (17·2)	527	133·3 (18·1)
Diastolic blood pressure (mm Hg)	210	79·7 (9·2)	526	80·7 (9·7)	527	79·9 (10·0)
HbA_{1c} (mmol/mol)	143	41·9 (11·2)	354	40·9 (9·8)	338	41·7 (10·4)
HbA_{1c} (%)	143	6·0 (1·0)	354	5·9 (0·9)	338	6·0 (0·9)
Total cholesterol (mmol/L)	146	5·4 (1·2)	357	5·3 (1·1)	339	5·3 (1·1)
LDL cholesterol (mmol/L)	145	3·1 (1·2)	353	3·0 (1·0)	337	2·9 (1·0)
HDL cholesterol (mmol/L)	146	1·6 (0·6)	357	1·6 (0·6)	339	1·7 (0·6)
Sex						
Women	143 (68%); 211	..	357 (68%); 528	..	359 (68%); 528	..
Men	68 (32%); 211	..	171 (32%); 528	..	169 (32%); 528	..
Ethnicity						
White or white British	181 (91%); 200	..	480 (94%); 513	..	475 (93%); 510	..
Asian or Asian British	9 (5%); 200	..	11 (2%); 513	..	15 (3%); 510	..
Black or Black British	4 (2%); 200	..	12 (2%); 513	..	6 (1%); 510	..
Mixed or multiple ethnic group	4 (2%); 200	..	4 (1%); 513	..	7 (1%); 510	..
Other	2 (1%); 200	..	6 (1%); 513	..	7 (1%); 510	..
Education						
Higher degree or equivalent	23 (12%); 196	..	79 (17%); 474	..	68 (15%); 467	..
University degree or equivalent	48 (24%); 196	..	108 (23%); 474	..	97 (21%); 467	..
Post-secondary education	10 (5%); 196	..	14 (3%); 474	..	10 (2%); 467	..
A-Levels or equivalent	53 (27%); 196	..	95 (20%); 474	..	110 (24%); 467	..
GCSEs or equivalent	55 (28%); 196	..	153 (32%); 474	..	155 (33%); 467	..
None	7 (4%); 196	..	25 (5%); 474	..	27 (6%); 467	..
Gross household income (per annum)						
<£20 000	39 (26%); 151	..	79 (21%); 384	..	106 (27%); 396	..
£20 000–39 999	56 (37%); 151	..	132 (34%); 384	..	137 (35%); 396	..
≥£40 000	51 (34%); 151	..	132 (34%); 384	..	123 (31%); 396	..

Table 1: **Participant characteristics at baseline**

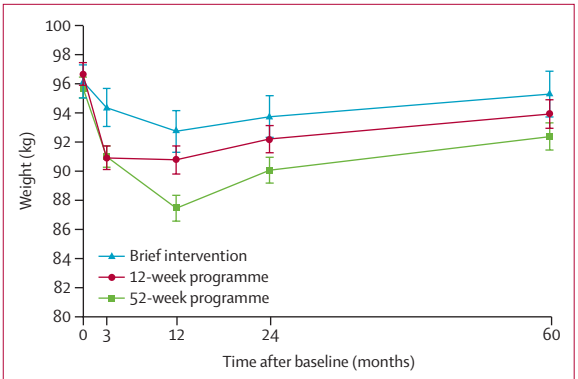

Figure 2: **Bodyweight over 5 years of follow-up**
Data are mean of all measured weights at each timepoint (SE).

care practice or a research centre, 146 (12%) had recent weight recorded in their primary care notes, and 93 (7%) provided a self-measured weight. Mean duration of follow-up was 5·1 years (SD 0·3). Table 1 shows characteristics for all participants randomly assigned. The proportion of participants with missing weight data at 5 years varied by randomised group: 39% (brief intervention), 31% (12-week programme), 29% (52-week programme). Participants with primary outcome data had a slightly higher mean age and lower mean weight at baseline than did those with missing data (appendix pp 112–114 shows baseline characteristic by missingness and by data source).

The weight trajectories of the three intervention groups at each timepoint using all measured weights are shown in figure 2. Mean weight change from baseline to 5 years was –0·46 (SD 8·31) kg in the brief intervention group,

	5-year change from baseline			Pairwise comparisons		
	Brief intervention (SD), mean	12-week programme (SD), mean	52-week programme (SD), mean	52-week programme *vs* brief intervention (95% CI)	52-week programme *vs* 12-week programme (95% CI)	12-week programme *vs* brief intervention (95% CI)
Primary outcome						
Weight (kg)	−0·46 (8·31)	−1·95 (9·55)	−2·67 (9·81)	−1·76 (−3·68 to 0·17)	−0·80 (−2·13 to 0·54)	−0·96 (−2·90 to 0·97)
Secondary outcomes						
Weight (proportion of baseline weight)	−0·58 (8·79)	−1·96 (9·36)	−2·66 (9·70)	−1·68 (−3·59 to 0·22)	−0·78 (−2·11 to 0·54)	−0·90 (−2·82 to 1·02)
HbA_{1c} (mmol/mol)	1·15 (7·38)	0·13 (11·15)	−0·23 (7·67)	−1·16 (−3·63 to 1·31)	−0·06 (−1·83 to 1·72)	−1·10 (−3·46 to 1·25)
HbA_{1c} (%)	0·10 (0·68)	0·01 (1·02)	−0·02 (0·70)	−0·11 (−0·33 to 0·12)	−0·01 (−0·17 to 0·16)	−0·10 (−0·32 to 0·11)
Fat mass (kg)	2·49 (6·35)	0·72 (7·82)	0·47 (8·14)	−1·27 (−2·93 to 0·38)	0·08 (−1·01 to 1·18)	−1·36 (−3·14 to 0·42)
Total cholesterol (mmol/L)	−0·35 (0·91)	−0·30 (0·93)	−0·29 (0·73)	0·028 (−0·23 to 0·29)	0·02 (−0·17 to 0·21)	0·01 (−0·27 to 0·29)
LDL cholesterol (mmol/L)	−0·33 (0·84)	−0·17 (0·87)	−0·12 (0·72)	0·05 (−0·14 to 0·25)	−0·03 (−0·18 to 0·13)	0·08 (−0·13 to 0·29)
HDL cholesterol (mmol/L)	−0·22 (0·49)	−0·23 (0·49)	−0·28 (0·51)	0·04 (−0·04 to 0·11)	0·06 (0·00 to 0·13)	−0·03 (−0·11 to 0·06)
Triglycerides (mmol/L)*	0·29 (0·82)	0·26 (0·86)	0·25 (0·61)	−0·07 (−0·19 to 0·05)	−0·03 (−0·11 to 0·04)	−0·04 (−0·16 to 0·09)
Systolic blood pressure (mm Hg)	−0·73 (16·13)	−2·63 (16·17)	−0·10 (16·66)	3·30 (0·01 to 6·60)	2·76 (0·45 to 5·07)	0·54 (−2·65 to 3·73)
Diastolic blood pressure (mm Hg)	−1·74 (10·02)	−2·15 (10·18)	−0·59 (9·52)	1·07 (−1·05 to 3·19)	1·08 (−0·44 to 2·61)	−0·015 (−2·05 to 2·02)

Estimated differences from ANCOVA model with multiple imputation. For the proportion of weight loss outcome (included post-hoc at the request of a reviewer), since proportion of weight lost not defined at baseline, the baseline variable included in the model was weight (kg). HbA_{1c}=glycated haemoglobin A1c. *Log-transformed.

Table 2: **5-year change from baseline and pairwise comparisons in primary and secondary outcomes**

−1·95 (9·55) kg in the 12-week programme group, and −2·67 (9·81) kg in the 52-week programme (table 2). The adjusted mean difference in weight change between the 52-week programme and the brief intervention was −1·76 (95% CI −3·68 to 0·17) kg. The difference between the 52-week programme and the 12-week programme was −0·80 (−2·13 to 0·54) kg. The difference between the 12-week programme and the brief intervention was −0·96 (−2·90 to 0·97) kg. The mean adjusted difference between the 52-week programme and the other groups combined was −1·07 (−2·32 to 0·18) kg. There was no evidence that the intervention effect on weight differed by participant gender (p=0·50), educational attainment (p=0·85), or baseline diabetes status (p=0·82). Pre-planned sensitivity analyses found that follow-up duration did not substantively influence results or the interpretation of findings.

5-year changes, and comparisons between groups, in proportion of weight loss, fat mass, HbA_{1c} profile, lipid profile, and blood pressure are shown in table 2. There was no evidence of any differences between groups in these secondary outcomes. There was no difference between groups in progression from normoglycaemia or non-diabetic hyperglycaemia at baseline to diabetes at 5 years (appendix pp 115–117).

At 5-year follow-up, 31 (21%) of 129 participants in the brief intervention group, 116 (32%) of 366 participants in the 12-week programme group, and 135 (36%) of 376 participants in the 52-week programme group were at least 5% below baseline weight. Participants in the 52-week programme had greater odds of being 5% below baseline weight than did those in the brief intervention group (OR 1·79 [95% CI 1·13–2·83]) but 95% CIs crossed 0 for the comparison between 52-weeks and 12-weeks interventions (1·22 [0·90–1·65]) and 12-weeks and brief interventions (1·47 [0·93– 2·34]).

No participants reported adverse events related to the intervention.

In the within-trial cost-effectiveness analysis, the total NHS and social care costs per person in each group were very similar, as were the QALYs since randomisation (table 3). Consequently, the expected net monetary benefits were very similar, but the point estimates suggested that the 12-week programme was the most cost-effective, with the brief intervention and 52-week programme being less effective and more expensive (ie, dominated). Uncertainty and subgroup analyses are reported in the appendix (pp 9–24).

In modelling the impact of each intervention over a lifetime, all three interventions (brief Intervention, 12-week programme, and 52-week programme) had lower expected lifetime costs and generated QALY gains compared with the do-nothing scenario. The 12-week and 52-week programmes were cost saving and generated QALY gains compared with the brief Intervention. Relative to natural history, the 52-week programme generated greater QALY gains (0·0298 [simulated 95% CI −0·002 to 0·0688]) and lower estimated lifetime costs (−£424 [simulated 95% CI −926 to −51]) than did the 12-week programme (0·0248 [−0·0024 to 0·0599] and −£336 [−792 to 141]). There was a 65% probability that the 52-week intervention was cost-effective over a lifetime, relative to brief intervention, when judged against the UK NICE threshold of £20 000 per additional

	Total discounted NHS and social care costs per person (£)	Total discounted QALYs per person	Incremental costs (£)	Incremental QALYs	Incremental cost-effectiveness ratio vs next most effective option (£)	Expected net monetary benefit (£)*	Incremental expected net monetary benefit (£)	Rank on expected net monetary benefit†
Within-trial analysis (adjusted 5-year analysis)								
Brief intervention	4118 (3654 to 4622)	3·82 (3·74 to 3·91)	..	..	Dominated	72 332 (70 410 to 74 285)	..	2
12-week programme	3987 (3661 to 4322)	3·82 (3·77 to 3·87)	−130·74 (−754·85 to 427·92)	−0·00 (−0·11 to 0·1)	Estimated as most cost-effective	72 415 (71 132 to 73 616)	83·16	1
52-week programme	4159 (3816 to 4549)	3·79 (3·73 to 3·85)	40·64 (−572·23 to 637·55)	−0·03 (−0·14 to 0·07)	Dominated	71 675 (70 268 to 72 967)	−656·51	3
Long-term modelling analysis (lifetime analysis)†								
Simulated natural history	33 880 (26 536 to 46 288)	11·3675 (10·5124 to 12·1586)	..	..	Dominated	193 470 (169 924 to 213 752)	..	4
Brief intervention	33 755 (26 418 to 45 830)	11·3694 (10·5161 to 12·1584)	−125 (−656 to 731)	0·0019 (−0·0499 to 0·0416)	Dominated	193 633 (170 446 to 213 724)	163 (−1628 to 1402)	3
12-week programme	33 544 (26 375 to 45 494)	11·3923 (10·5479 to 12·1737)	−336 (−792 to 141)	0·0248 (−0·0024 to 0·0599)	Dominated	194 302 (171 540 to 214 125)	832 (−90 to 1814)	2
52-week programme	33 456 (26 288 to 45 339)	11·3973 (10·5663 to 12·1715)	−424 (−926 to −51)	0·0298 (−0·002 to 0·0688)	Estimated as most cost-effective	194 490 (171 720 to 214 121)	1020 (90 to 2152)	1

Data are in mean (95% CI) unless specified. Dominated=intervention was associated with fewer QALYs at higher costs. ICER=incremental cost-effectiveness ratio. NHS=UK National Health Service. QALYs=quality-adjusted life-years. *£20 000 per QALY. †1 is the most cost-effective and 4 is the least cost-effective. ‡Simulated 95% CIs.

Table 3: **Short-term and long-term cost-effectiveness results with discounted costs and QALYs**

QALY. The equivalent value for the 12-week intervention was 30%. The full probabilistic sensitivity analysis and subgroup analyses are reported in the appendix (pp 101–106) and showed comparable results.

Discussion

5 years after being randomly assigned to one of three weight management interventions, participants in all groups had regained some of the weight that they had lost at the 1-year follow-up. Nevertheless, participants allocated to the behavioural programmes weighed on average 2·0–2·5 kg less than they did before the programme, compared with a 0·5 kg reduction in the brief intervention group. Pairwise comparisons suggested that participants in the 52-week programme lost more weight than those receiving the brief intervention, but wide 95% CIs mean that they were also compatible with there being no effect of the intervention. Although the consistency of differences in weight across timepoints and the apparent dose-response effect of the interventions suggest that the differences were not due to chance, we cannot rule this out. Participants in the 52-week programme also had greater odds of being 5% below baseline weight at 5 years, widely considered to represent clinically significant weight loss. There was no evidence of a difference between groups in changes in HbA_{1c} profile, fat mass, lipid profile or blood pressure at 5 years, or in the development of type 2 diabetes, but estimates were imprecise. The results of the economic evaluation were similar across all groups but the 12-week programme was the most likely to provide best value for money over the course of 5 years. However, over a lifetime, modelling suggests that the 52-week intervention would improve health and reduce costs the most.

This study is the first RCT of a commercial open-group behavioural weight management programme to measure outcomes at 5 years. By measuring outcomes following at least 4 years of post-intervention follow-up, it provides data on the medium-term weight trajectories following scalable programmes of relatively short duration (12 weeks or 52 weeks). Participants were free-living during the post-intervention follow-up and some might have chosen to use weight loss treatments during this time. However, these behaviours reflect what would happen in routine care and randomisation should mean that this tendency was evenly distributed between groups, or that any subsequent weight management might have been prompted by the allocated intervention and hence a consequence of the experience. A strength of this study was the minimal exclusion criteria, which means that the participant sample is broadly generalisable to the target population of people with excess weight. All eligible patients at participating practices were invited to take part; however, men, younger people, and those from more deprived areas were less likely to take up the invitation to participate in this trial.[14] Primary outcome data were collected on 69% of participants, which compares favourably to retention rates typically seen in trials of behavioural weight management programmes.[15] Furthermore, differences in characteristics between participants with and without data for the primary outcome were small, and intervention effects did not vary by gender, education, diabetes status, and in sensitivity and sub-group analyses. It is important to note that the sample size was originally calculated to enable detection

of moderate differences in weight at 12 months, not smaller differences in weight, cardiovascular disease risk factors, and diabetes incidence at 5 years. The large variability in these outcomes mean that effect size estimates were imprecise and do not signify definitive evidence of no difference between groups. Longer follow-up is required to reduce uncertainty about the impact of behavioural weight management programmes on clinical endpoints.

Our long-term modelling describes a natural history of an increasing mean BMI trajectory for the study population over 10 years (appendix pp 38–39). This BMI trajectory is consistent with a UK-based population cohort study of adults with a BMI of more than 25 kg/m² from UK primary care electronic health data (mean BMI increase of 1·06 kg/m² over 10 years).[16] A meta-analysis of prospective studies reported a smaller increase in those with a BMI of over 30 kg/m² during 6 years (mean BMI increase of 0·12 kg/m²).[17] Notwithstanding this uncertainty concerning natural history, the analysis from WRAP suggests that all three groups appear to have maintained some benefit from the intervention after 5 years.

Initial weight losses in WRAP were comparable to those in the US Diabetes Prevention Programme (DPP)[18] in which the behavioural intervention was led by specialist and intervention contact continued throughout the trial. In the US DPP, average weight loss in the lifestyle intervention group was around 7 kg at 1 year and around 2 kg at 5 years. In the DPP, cumulative incidence of type 2 diabetes was reduced in the lifestyle intervention group despite weight regain, suggesting a legacy effect.[6] In contrast to the 1-year follow-up,[7] the current study found no evidence of a difference between groups in transition from normoglycaemia or non-diabetic hyperglycaemia to type 2 diabetes. However, given the small number of participants with non-diabetic hyperglycaemia at baseline and diabetes at 5 years, the study is underpowered to detect potentially important differences between groups. Findings can also be compared with a systematic review of hypoenergetic dietary interventions, which had an average of 8·8 kg initial weight loss over an average of 19 weeks of treatment and an average weight loss of around 2 kg at 4·5 years follow-up, with 18% of initial weight loss maintained.[5] However, weight losses are more modest than might be expected from more invasive and expensive interventions, such as some pharmacotherapy interventions[19] or bariatric surgery.[20] These findings should be considered when treating patients with severe obesity and when managing expectations of patients.

Randomised experiments provide an unbiased estimate of the short-term effect of interventions on a narrow set of outcomes. However, within-trial analyses are rarely precise enough to quantify even short-term effects on these outcomes and so might under-estimate programme cost-effectiveness. Furthermore, excess weight is associated with increased risk of a range of non-communicable diseases such as diabetes, cardiovascular disease, and cancers. In addition, most trials have a limited time-horizon. Consequently, the cost and consequences of behavioural weight management interventions over the course of an individuals' life are likely to have been underestimated. Over a 5-year horizon, the within-trial cost-effectiveness analysis showed that, compared with the other groups, the 12-week behavioural programme generated the largest expected NMB and represents a marginally more efficient allocation of resources in the medium term. Once the lifetime costs and consequences were considered, we found that both 12-week and 52-week group behavioural weight loss programmes were cost-effective and cost saving compared with a simulated do-nothing scenario or the brief intervention. The 52-week programme offered greater cost savings and health benefits compared with the 12-week programme and, hence, the greatest estimated NMB. This was because the 52-week programme led to greater weight loss, which more than offsets the greater costs of the programme through reduced incidence of diabetes, cardiovascular diseases, and other comorbidities beyond 5 years, resulting in additional QALY gains and cost savings to the NHS and social services when compared with the short-term results.

Our findings suggest that the common assumption that all weight lost after behaviour change is regained within 5 years is incorrect. Incorporating this evidence into the long-term cost-effectiveness analysis increased the predicted QALY gains and cost savings of weight loss programmes. However, these benefits are expected to be incurred beyond 5 years of follow-up when reductions in incidence of type 2 diabetes and cardiovascular disease are realised. Modelling suggests that provision of these kind of low-cost, high-reach weight loss programmes, targeting people with overweight and obesity, is likely to represent good value for the public purse and might be cost saving in the long run. Such programmes should therefore be made more widely available and implemented alongside complementary strategies targeting the wider collective environmental and societal determinants of obesity.

Contributors

ALA is the Chief Investigator of the WRAP trial. ALA, PB, FF, SJS, AJH, CAH, RD, JW, JB, SM, and SJG designed the WRAP 5-year follow-up study and developed the protocol. ALA, JW, FW, MS, and SJG were responsible for data collection. CB was responsible for data curation. SJS analysed the effectiveness data with input from NI and GMW. FF and SM conducted the within trial cost-effectiveness analysis. PB, SB, CT, and AB conducted the long-term cost-effectiveness analysis. JB chaired the Patient and Public Involvement panel. ALA, FF, and PB wrote the first draft of the manuscript. ALA, SAJ, PA, EB, JCGH, and GMW designed and conducted the original WRAP trial. All authors contributed to the interpretation of data and critically reviewed the manuscript. SJS and CB directly accessed and verified the underlying data and ALA was responsible for the decision to submit the manuscript for publication. All authors approved the final version.

Declaration of interests

ALA reports research grants from the UK National Institute for Health and Care Research (NIHR), UK Medical Research Council (MRC) and the European Association for the Study of Obesity and membership of the Scientific Advisory Board for WW (all payments to her institution). PB reports research grants to her institution from NIHR and consultancy fees from Genomics. NI reports grants from the UK Office for National Statistics, Canadian Institutes of Health Research, Health Data Research UK, and NIHR; is an advisory board member of the WHO-UN Technical Advisory Board, *The BMJ* Research Forum and *BMJ Medicine*; and has received consultancy fees and payments from *The BMJ*. GMW reports grants from MRC and Innovate UK; has received payment from AstraZeneca and support for meeting attendance from Eli Lilly; and is a committee member of the NIHR Statistics Group Early Stage Trials Section, UK National Cancer Research Institute Teenage and Young Adult and Germ Cell Therapies subgroup, and the MRC Experimental Medicine Funding Panel. AJH reports grants to his institution from NIHR and payment for advice from Slimming World. CAH reports consultancy fees from Novo Nordisk; payments or honoraria for presentations; manuscript writing or educational events from Novo Nordisk, Ethicon, Alva Health and International Medical Press; and is an Advisory Board Member for Novo Nordisk. RD reports research grants from NIHR and the Wellcome Trust. SB reports research grants from the Wellcome Trust and NIHR; consultancy fees from the UK Office for Health Improvement and Disparities and Dark Peak Analytics; and is on the Editorial Board of the *Journal of Medical Decision Making*. SJ has received grants from NIHR and is Chair of the UK Food Standards Agency. PA reports research grants to his institution from NIHR, British Heart Foundation and Nestle Life Sciences, and materials or services from Nestle Life Sciences. EB reports grants to her institution from NIHR, Public Health England, and WHO, and consultancy fees from WHO. JCGH has received grants from Novo Nordisk and the American Beverage Association; consulting fees from Novo Nordisk, Dupont, Boheim Inhelheim, and Mars; support for meeting attendance from Novo Nordisk; and is an Advisory Board Member for Dupont (all payments to his institution). SM and AB report grant funding to their institution from NIHR. SJG reports grants to his institution from NIHR and MRC; consultancy fees to his institution from Genomics; payments for educational events from AstraZeneca; and unpaid membership of the Board of Trustees for the Novo Nordisk UK Research Foundation. FF, SJS CC, CT, JW, MS, FW, and CB report no competing interests beyond funding to their institutions for the current project.

Data sharing

WRAP data are not publicly available. Participant consent allows for data to be shared for future analyses with appropriate ethical approval. Non-identifiable data and analysis code can be made available to bona-fide researchers on submission of a reasonable request to datasharing@mrc-epid.cam.ac.uk. The principles and processes for accessing and sharing data are outlined on the UK Medical Research Council Epidemiology Unit Data Sharing Portal: epi-meta.mrc-epid.cam.ac.uk. Meta data for the WRAP study is available at https://epidata-ext.mrc-epid.cam.ac.uk/ddic/overview/WRAP/.

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