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The effect of referral to an open-group behavioural weight-management programme on the relative risk of normoglycaemia, non-diabetic hyperglycaemia and type 2 diabetes: Secondary analysis of the WRAP trial

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Abstract

Aim: To examine the impact of open-group behavioural weight-management programmes on the risk of diabetes among those with a body mass index (BMI) of ≥28 kg/m^2 and those with non-diabetic hyperglycaemia (NDH).

Methods: This was a secondary analysis of data from the WRAP trial, in which participants (N = 1267; aged ≥18 years, BMI ≥ 28 kg/m^2) were randomized to brief intervention (BI; self-help booklet), a weight-management programme (WW; formerly Weight Watchers) for 12 weeks, or WW for 52 weeks. We used multinomial logistic regression to examine the effect of intervention group on the risk of hyperglycaemia and diabetes at 12 months in all participants with glycaemic status at both time points (N = 480; 38%) and those with NDH at baseline (N = 387; 31%). We used mixed effects models and linear fixed effects models to examine the effect of intervention group on body weight and HbA1c at 12 months in people with NDH.

Results: There was a 61% relative reduction in the risk of NDH at the 12-month follow-up (12 weeks vs. BI: relative risk ratio [RRR] = 0.39 [95% CI 0.18, 0.87], P = .021; 52 weeks vs. BI: RRR = 0.38 [95% CI 0.17, 0.86], P = .020). For intervention effects on the risk of diabetes, confidence intervals were wide and overlapped 1 [12 weeks vs. BI: RRR = 0.49 [95% CI 0.12, 1.96], P = .312; 52 weeks vs. BI: RRR = 0.40 [95% CI 0.10, 1.63], P = .199). Participants with hyperglycaemia at baseline in the weight-management programme were more probable to have normoglycaemia at the 12-month follow-up [12-week programme vs. BI: RRR = 3.57 [95% CI 1.24, 10.29], P = .019; 52-week programme vs. BI: RRR = 4.14 [95% CI 1.42, 12.12], P = .009).

Conclusions: Open-group behavioural weight-management programmes can help to prevent the development of NDH in people with overweight and obesity and to normalize glycaemia in people with NDH.

KEYWORDS

diabetes, non-diabetic hyperglycaemia, obesity, prevention, weight loss

1 | INTRODUCTION

Large randomized controlled trials (RCTs) have shown that intensive behavioural programmes can reduce or delay the incidence of type 2 diabetes (T2D) by 30%-60% in people with non-diabetic hyperglycaemia (NDH) identified by screening using repeated oral glucose tolerance tests (OGTTs).[1] However, population screening using OGTTs would represent a significant burden to patients and health service staff and put pressure on existing resources.[2] More pragmatic screening tests, such as HbA1c, have been recommended,[2,3] but these would still be expensive if conducted with sufficient frequency to identify the large numbers of people developing hyperglycaemia each year. Excess weight is a strong predictor of T2D[4] and identifying individuals at risk of T2D on the basis of body mass index (BMI) may be a less expensive and simpler approach.[5] Diabetes prevention programmes that only include people with BMI ≥25 kg/m^2 show a 50% greater reduction in the risk of T2D than those programmes that also enrol people with a lower BMI.[6] However, to date, no studies of diabetes prevention programmes have used excess weight as the sole inclusion criterion.

Intensive behavioural programmes evaluated in diabetes prevention trials can only be offered to a fraction of those with hyperglycaemia because they are expensive to run and the necessary specialized workforce is scarce. A recent systematic review found that less intensive behavioural programmes in routine healthcare or community settings achieved a 26% reduction in T2D risk, and a lower average weight loss of 2.6 kg (compared with a 58% risk reduction and 6 kg weight loss in the US Diabetes Prevention Programme).[7] However, this review only included programmes with the specified aim of reducing diabetes incidence and excluded most behavioural programmes that focus on weight loss, despite both types of programme encouraging very similar changes in diet and physical activity using similar behavioural strategies. Commercial open-group behavioural weight-management programmes, such as WW (formerly Weight Watchers) and Slimming World, are some of the most commonly commissioned weight-management treatments in the UK, have evidence of effectiveness from RCTs and are less expensive than most diabetes prevention programmes.[8-11] However, there is little direct evidence of the impact of these generic weight loss programmes on the risk of developing hyperglycaemia or diabetes, or on the reversion of people with diabetes or NDH to NDH or normoglycaemia.

Two recent studies have evaluated the effectiveness of referral to WW combined with a specific diabetes prevention education session among people with NDH. In a US RCT, this combined intervention achieved greater weight loss (5.5% vs. 0.2%, $P < .001$) and greater reductions in HbA1c (−0.22% vs. −0.14%; $P = .032$) at 12 months compared with a diabetes education counselling session and self-help materials developed by the US Diabetes Education Program.[12] In an uncontrolled study of a similar combined intervention in the UK National Health Service (NHS), a reduction in mean weight of 10 kg and in HbA1c of 2.8 mmol/mol was observed at 12 months using an intention to treat analysis.[13] However, no studies have examined the impact of the standard WW programme among people with NDH, or the effect of such programmes on the risk of T2D in individuals recruited on the basis of BMI alone.

In the WRAP trial (Weight loss Referrals for Adults in Primary care), 1267 adults identified by their primary care physician as having a BMI of ≥28 kg/m^2 were randomized to one of three weight loss interventions: brief intervention, a 12-week referral to a commercial open-group weight-management programme (WW) or a 52-week referral to the same programme.[9] Participants referred to the programmes lost more weight than those in the brief intervention. The 52-week programme was associated with greater reductions in weight, HbA1c and fasting blood glucose than the 12-week programme and the brief intervention. Here, we use data from the WRAP trial to examine the effect that referral to an open-group behavioural programme has on the probability of hyperglycaemia and T2D after 1 year among adults. We also quantify the effects on glycaemia in the subsample of participants with hyperglycaemia at baseline.

2 | METHODS

2.1 | Study design

The full protocol (including measures and assays) and primary analyses from the WRAP trial have been published elsewhere.[9,14] In brief, this was a multicentre, non-blinded, parallel groups trial with uneven randomization. Participants were adults aged ≥18 years, with BMI ≥28 kg/m^2, identified via a search of electronic primary care records and invited to participate by mail. We randomized 1267 eligible participants to one of three weight-management interventions in a 2:5:5 ratio: brief intervention, 12 weeks of an open-group behavioural programme (WW) or 52 weeks of the same behavioural programme.

Participants attended measurement appointments at the research centre or their local GP practice at baseline and at 12 months. The trial is registered at Current Controlled Trials (ISRCTN82857232). Given the focus of this trial on the impact of programme duration on

weight loss, we did not originally declare the incidence of hyperglycaemia or diabetes as outcomes.

2.2 | Interventions

Participants in the brief intervention group received a printed booklet of self-help weight-management strategies from the British Heart Foundation. Participants in the behavioural programmes were given vouchers to attend weekly WW meetings and to use WW web-based tools for the duration of the intervention (12 or 52 weeks). The WW intervention provides advice, support and encouragement to lose weight and then maintain any loss, and uses a range of evidence-based behavioural change techniques to support changes to a lower energy diet and increases in physical activity.

2.3 | Outcomes

The primary outcome of the WRAP trial was body weight and this was measured at each time point. Participants were also asked to report medication use in the previous 3 months. Other cardiovascular risk factors, including plasma glucose, HbA1c and lipid profile, were measured via a fasting blood sample at baseline and 12 months, which was optional for participants. For participants who provided a blood sample, we categorized participants as having normoglycaemia, NDH or T2D at baseline and 12 months using American Diabetes Association criteria for HbA1c (39-47 mmol/mol = NDH; ≥48 mmol/mol = diabetes) and fasting glucose (5.6-6.9 mmol/mol = NDH; ≥7 mmol/mol = diabetes), and the use of diabetes medication.[15]

2.4 | Statistical analysis

To examine whether the intervention group was associated with the risk of diabetes or hyperglycaemia (relative to normoglycaemia) at 12 months (primary analysis), we used multinomial logistic regression and adjusted for baseline glycaemic category, baseline weight, age, research centre and sex. Effect sizes were reported as relative risk ratios (RRRs), for example, the risk ratio of diabetes (relative to normoglycaemia) comparing 12 weeks versus brief intervention. We conducted two sensitivity analyses. The first sensitivity analysis excluded participants for whom use of metformin was the only criteria for diabetes categorization, because metformin has indications other than diabetes. The second sensitivity analysis used World Health Organization (WHO) criteria to categorize glycaemic status (for HbA1c: 42-47 mmol/mol = NDH, ≥48 mmol/mol = diabetes; for fasting glucose: 6.1-6.9 mmol/mol = NDH, ≥7 mmol/mol = diabetes).[16]

To evaluate the effect of the three interventions among participants who had NDH at baseline, we examined the differences between groups in mean change from baseline to 12 months for weight, fasting glucose and HbA1c. We undertook a missing at random analysis using a variance components model; we imputed 50

datasets using a multiple imputation with chained equations (MICE) approach, as the joint distribution of target variables did not appear to come from a multivariate normal distribution. The imputation model regressed the target variable on centre and imputation was stratified by treatment group. We then calculated mean (SE) change in the target variable from the imputed datasets. For analyses of weight change, we fit a multivariate mixed effects model using generalized least squares to each imputed dataset with intervention group, time point, intervention group by time point interaction and centre as fixed effects. Random intercepts were permitted for each participant. Results were then combined across all imputed datasets using Rubin's rules.[17] For analysis of fasting glucose and HbA1c levels, data were available for baseline and 12 months. We therefore used linear regression on the imputed datasets to estimate treatment effects, with target variable at 12 months as the outcome, with adjustments made for baseline value, centre and intervention group.

To examine whether intervention group was associated with glycaemic status category at 12 months in people with NDH at baseline, we used the same multinomial logistic regression method described above in the subsample of WRAP participants who were categorized as having NDH at baseline.

Analyses were performed using Stata version 14.2.[18]

3 | RESULTS

We ascertained glycaemic status at baseline for 879 participants, and at both baseline and 12 months for 480 participants.

The primary analysis included the 480 participants with glycaemic status at both time points. Characteristics of these participants are shown in Table 1. This subset of participants had a slightly higher mean age (difference in means = 5.92; 95% CI 4.39, 7.44 years) and a larger proportion of men (38% vs. 28%) than members of the trial population who were not eligible for inclusion in this analysis, but there was no evidence of a difference in baseline weight.

Participants referred to the 12- and 52-week programmes were less probable than those in the brief intervention group to be categorized as having NDH compared with normoglycaemia at 12 months (12-week programme vs. brief intervention: RRR = 0.39 [95% CI 0.18, 0.87], P = .021; 52-week programme vs. brief intervention: RRR = 0.38 [95% CI 0.17, 0.86], P = .020) (Figure 1A). Although the point estimates of the RRR suggested that participants in the 12- and 52-week programmes are less probable to have diabetes at 12 months, the confidence intervals were wide and compatible with both a negative and positive association (12-week programme vs. brief intervention: RRR = 0.49 [95% CI 0.12, 1.96], P = .312; 52-week programme vs. brief intervention: RRR = 0.40 [95% CI 0.10, 1.63], P = .199) (Figure 1B). Table 2 shows the frequency of changes from one diabetes status category to another by intervention group.

A sensitivity analysis, which excluded participants who were taking metformin but whose HbA1c levels were within the normal range, showed similar results. Sensitivity analyses using WHO criteria for NDH showed no evidence of a difference between groups for risk of

TABLE 1 Baseline characteristics of participants

	Participants with assessment of glycaemic status at baseline and 12 months			Participants with non-diabetic hyperglycaemia at baseline		
	Brief intervention (N = 70) Mean (SD)	12-week programme (N = 210) Mean (SD)	52-week programme (N = 200) Mean (SD)	Brief intervention (N = 66) Mean (SD)	12-week programme (N = 173) Mean (SD)	52-week programme (N = 148) Mean (SD)
Age (years)	57.7 (13.2)	56.8 (12.3)	56.7 (12.6)	54.6 (11.9)	58.1 (12.0)	56.7 (12.5)
Height (cm)	167.6 (9.6)	168.2 (8.6)	166.5 (9.2)	167 (9.9)	167 (9.5)	166 (9.2)
Weight (kg)	95.3 (14.6)	95.8 (16.6)	95.2 (16.1)	97.1 (14.7)	94.7 (14.8)	93.4 (16.5)
HbA1c (mmol/mol)	42.5 (10.6)	42.0 (11.1)	42.0 (10.4)	41.0 (2.4)	40.6 (2.6)	40.7 (3.1)
Glucose (mmol/L)	5.8 (1.5)	5.8 (1.9)	5.9 (1.8)	5.4 (0.5)	5.4 (0.5)	5.4 (0.5)
Glycaemic status (n; %)[a]						
Normal glycaemia	19 (27%)	68 (32%)	73 (37%)	–	–	–
Non-diabetic hyperglycaemia	32 (46%)	99 (47%)	86 (43%)	66 (100%)	173 (100%)	148 (100%)
Diabetes	19 (27%)	43 (20%)	41 (21%)	–	–	–

[a]May not add up to 100% because of rounding to the nearest whole number.

(A)

(B)
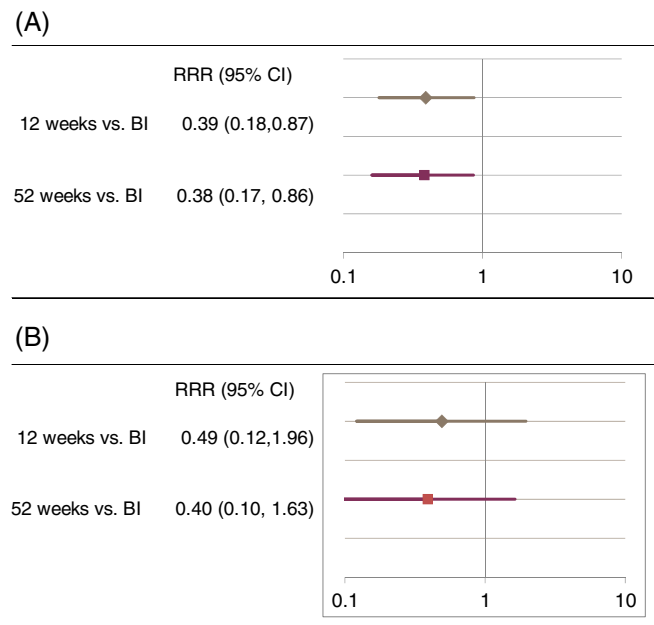
FIGURE 1 (A) Relative risk ratios (RRRs) for non-diabetic hyperglycaemia at 12 months: 12- and 52-week behavioural programmes compared with brief intervention (BI), adjusted for baseline glycaemic status, baseline age, baseline weight, sex and centre. (B) RRRs for diabetes at 12 months: 12- and 52-week behavioural programmes compared with BI, adjusted for baseline glycaemic status, baseline age, baseline weight, sex and centre

NDH (12-week programme vs. brief intervention: RRR = 0.63 [95% CI 0.25, 1.61], P = .338; 52-week programme vs. brief intervention: RRR = 0.58 [95% CI 0.23, 1.50], P = .262) and diabetes (12-week programme vs. brief intervention: RRR = 0.79 [95% CI 0.20, 3.10], P = .736; 52-week programme vs. brief intervention: RRR = 0.63 [95% CI 0.16, 2.51], P = .510) at 12 months.

At baseline, 387 participants (46%) had HbA1c levels within the NDH category (brief intervention, N = 66; 12-week programme, N = 173; 52-week programme, N = 148). Baseline characteristics of these participants are shown in Table 1. Changes in weight, fasting glucose and HbA1c between baseline and 12 months are shown by intervention group in Table 3. Participants in the 12- and 52-week programme groups lost more weight than the brief intervention group after 12 months (12-week programme vs. brief intervention: −3.00 kg [95% CI −5.05, −0.94], P = .0044; 52-week programme vs brief intervention: −4.27 kg [95% CI −6.43, −2.10], P = .0001). There was no evidence of a difference between the 52-week and the 12-week programme (−1.27 kg [95% CI −2.76, 0.22], P = .0958). There were mean reductions in HbA1c and fasting blood glucose at 12 months in all groups (Table 3), but no evidence of differences between the groups.

Using WHO criteria for HbA1c and fasting glucose to categorize glycaemic status, 156 participants had NDH at baseline. Sensitivity analysis using WHO criteria showed very similar results, but there was a larger difference in weight loss between the 12- and 52-week programmes at 12 months.

TABLE 2 Frequency table of glycaemic status at baseline and 12 months by intervention group

Glycaemic status	Baseline	Normo			NDH			Diabetes		
	12 months	Normo	NDH	Diabetes	Normo	NDH	Diabetes	Normo	NDH	Diabetes
Treatment group	Brief intervention	16 (84%)	3 (16%)	0 (0%)	5 (16%)	25 (78%)	2 (6%)	2 (11%)	2 (11%)	15 (79%)
	12-week programme	63 (93%)	5 (7%)	0 (0%)	39 (39%)	56 (57%)	4 (4%)	2 (5%)	7 (16%)	34 (79%)
	52-week programme	67 (92%)	6 (8%)	0 (0%)	37 (43%)	48 (56%)	1 (1%)	0 (0%)	9 (22%)	32 (78%)

Abbreviations: NDH, non-diabetic hyperglycaemia; normo, normoglycaemia.

(A)

(B)
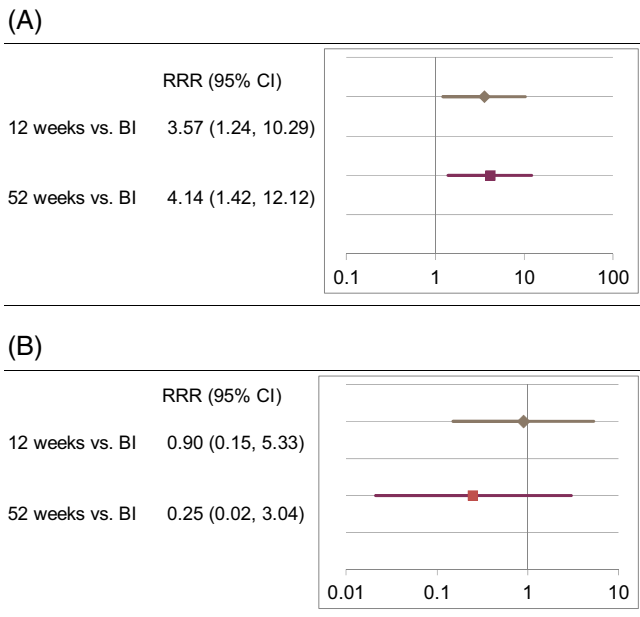
FIGURE 2 (A) Relative risk ratios (RRRs) for normoglycaemia at 12 months in participants with non-diabetic hyperglycaemia at baseline: 12- and 52-week behavioural programmes compared with brief intervention (BI), adjusted for baseline weight, age, sex and centre. (B) RRRs for diabetes at 12 months in participants with non-diabetic hyperglycaemia at baseline: 12- and 52-week behavioural programmes compared with BI, adjusted for baseline weight, age, sex and centre

Participants with NDH referred to the 12- and 52-week programmes were more probable than those in the brief intervention group to have reverted to normoglycaemia at 12 months (12-week programme vs. brief intervention: RRR = 3.57 [95% CI 1.24, 10.29], $P = .019$; 52-week programme vs. brief intervention: RRR = 4.14 [95% CI 1.42, 12.12], $P = .009$) (Figure 2A). There was little evidence to suggest that those referred to these programmes were less probable to have diabetes at 12 months as confidence intervals were wide and overlapped 1 (12-week programme vs. brief intervention: RRR = 0.90 [95% CI 0.15, 5.33], $P = .905$; 52-week programme vs. brief intervention: RRR = 0.25 [95% CI 0.02, 3.04], $P = .279$) (Figure 2B).

4 | DISCUSSION

In this secondary analysis of data from the WRAP trial, we found that participants with overweight or obesity who were randomized to an open-group behavioural weight-management programme were 61% less probable to have NDH at 12-month follow-up than participants allocated to a brief intervention. Few people were categorized as having diabetes at the 12-month follow-up (N = 7, 1%), which reduced our ability to detect differences between groups in T2D incidence, and there was no evidence of a difference between groups in diabetes status at this time point. Among participants with NDH at baseline, participants in the behavioural weight-management programmes were more probable to have normoglycaemia at 12 months than those who received brief intervention (self-help materials).

This study is limited by the comparatively small proportion of WRAP trial participants who provided blood samples at baseline and follow-up and could be included in the analyses. However, no differences were identified between these participants and the entire WRAP sample. Blood samples were only collected at baseline and 12 months. In contrast to the original explanatory diabetes prevention trials, few studies of pragmatic programmes have followed participants beyond 1 year. Nevertheless, this short follow-up meant that only a small proportion of participants developed diabetes, which reduced study power. The study is also limited by the use of a single measure of HbA1c, glucose and/or medication to classify NDH and diabetes. Given the focus of this trial on the impact of programme duration on weight loss, we did not originally declare the incidence of hyperglycaemia or diabetes as outcomes. The strengths of the study include the randomized trial design and the recruitment of a community-based sample with minimal exclusion criteria that is broadly generalizable to the UK population. While men where under-represented, there was a higher proportion (32%) of men in this trial than typically found in trials of weight-management interventions and there was no evidence that sex moderated the effect of the intervention.[9] Over half of the participating practices were in areas with a high index of multiple deprivation.[19]

Overweight and obesity is one of the strongest risk factors for T2D[4] and weight loss is the principal target of diabetes prevention programmes.[7,20] However, the dominant paradigm for diabetes prevention is identification of individuals at high risk (defined as those with NDH) via population screening, and referral to a specialist diabetes prevention programme. This study shows that delivering a behavioural weight-management programme to all people with overweight and obesity could be an effective approach to diabetes prevention, with a 60% reduction in the risk of NDH at 12-month follow-up. The reduction in the risk of diabetes was of a similar magnitude, but the width of the confidence intervals suggests that this evidence is weak.

TABLE 3 Changes in weight from baseline (mean, SE) to 12 months by intervention group in participants with non-diabetic hyperglycaemia at baseline

	N	Intervention			52-week programme vs. brief intervention		12-week programme vs. brief intervention		52-week programme vs. 12-week programme	
		Brief intervention	12-week programme	52-week programme	Adjusted difference	P-value	Adjusted difference	P-value	Adjusted difference	P-value
Weight (kg)	387	−2.66 (0.95)	−5.66 (0.62)	−6.93 (0.67)	−4.27 (−6.43, −2.10)	.0001	−3.00 (−5.05, −0.94)	.0044	−1.27 (−2.76, 0.22)	.0958
Glucose (mmol/L)	203	−0.19 (0.11)	−0.30 (0.05)	−0.32 (0.06)	−0.12 (−0.33, 0.10)	.286	−0.13 (−0.34, 0.08)	.224	0.01 (−0.13, 0.16)	.853
HbA1c (mmol/mol)	387	−1.06 (0.55)	−1.37 (0.28)	−1.94 (0.28)	−1.03 (−2.21, 0.16)	.0891	−0.45 (−1.63, 0.72)	.445	−0.57 (−1.34, 0.20)	.143
HbA1c (%)	387	−0.10 (0.05)	−0.13 (0.03)	−0.18 (0.03)	−0.09 (−0.20, 0.01)	.0891	−0.04 (−0.15, 0.07)	.445	−0.05 (−0.12, 0.02)	.143

Note: Missing at random analysis; uses 50 imputed datasets obtained from multiple imputation via chained equations (MICE). Treatment effects obtained from mixed effects models with residuals structured as a first-order auto-regressive process stratified by treatment group. Adjusted differences are shown between treatment groups. Analyses are adjusted for baseline observation and centre.

In a population-based cohort of 30 000 middle-aged people (aged 30–60 years at baseline), we showed that over a 10-year period, moderate weight loss (3%-7%), could prevent two in every five cases of T2D.[5] Using BMI to identify high-risk individuals is less expensive and more feasible than population-level testing of blood glucose and could identify people earlier in the disease trajectory, thereby preventing progression to NDH. This is important because glycaemia has an approximately linear association with cardiovascular events and mortality.[21,22] Consequently, Rose's prevention paradox may apply,[23] such that more heart attacks will be prevented by shifting the overall population distribution of BMI and glycaemia than by targeting scarce resources at the minority at highest risk. If the focus of diabetes prevention shifted to those with excess weight, commonly commissioned weight-management programmes could be readily incorporated into diabetes prevention policy. We have previously estimated that the 12-week programme, which costs ~£55 per person, is a more cost-effective intervention than the 52-week programme at ~£190 per person,[9] but these are both lower than the estimated average cost of UK NHS diabetes prevention programmes (£270 per person).[8] The large open-groups, rolling curriculum format, and variety of times and locations of meetings mean that people can start at any time, choose a time and location which suits them, and that key information is repeated if they miss any sessions. This greater flexibility than the closed-group sessions typically used in diabetes prevention programmes may increase attendance and adherence. This study also showed for the first time that a stand-alone open-group behavioural weight-management programme is a potentially effective option to reduce the risk of diabetes in people with NDH. When we restricted the eligible population to participants with NDH at baseline, we showed that the behavioural weight-management programme led to slightly greater weight loss than that reported in a meta-analysis of pragmatic diabetes prevention programmes.[6] However, our results are similar to findings from a US trial, which compared attendance at Weight Watchers meetings combined with a diabetes education session with a US National Diabetes Education Program individual counselling session and self-help materials.[12] Reductions in HbA1c were larger than the pooled mean in the meta-analysis of pragmatic interventions to prevent diabetes,[6] and similar to a US trial of a commercial programme adapted to prevent diabetes.[12] However, the confidence intervals around the estimate of this effect in our study were large and crossed zero, probably because of the comparatively small sample/group size in the current study. Taken together with evidence from a similar combined intervention in a scheme running in the UK NHS, which observed a mean reduction in weight of 10 kg and in HbA1c of 2.8 mmol/mol[13] among people with NDH in primary care, these findings suggest that this open-group behavioural weight-management programme has comparable effectiveness with dedicated diabetes prevention programmes in people with NDH, and could be incorporated into diabetes prevention pathways. It is unclear whether the education/activation session incorporated in the US trial and UK NHS models adds value, but it is clear that the weight-management programme itself is a crucial component.

The weight losses and reductions in glycaemia are smaller than those offered by bariatric surgery or formula diet meal replacements,[24,25] but are clinically meaningful and comparable with intensive, specialist-led diabetes prevention programmes.[6,7,20] Offering these programmes to all people with overweight and obesity would support people early in the disease trajectory and reduce the risk of NDH as well as diabetes. The weight loss achieved through these programmes also has other physical and mental health benefits.[26] However, where limited resources necessitate a focus on people who already have NDH, these programmes still offer an effective approach. Commercial versions of these programmes already have the existing infrastructure to enable (inter)national rollout and there is evidence that they can be incorporated into existing models of weight management and diabetes prevention.

In conclusion, among people known to have hyperglycaemia, a stand-alone open-group behavioural weight-management programme leads to successful weight loss and reductions in glycaemia which appear comparable with specialist diabetes prevention programmes. Identifying individuals at risk of diabetes on the basis of BMI alone and offering them a widely available weight-management programme might be a more pragmatic, scalable and efficient diabetes prevention strategy than screening for hyperglycaemia and referral to specialist programmes, and might facilitate intervention earlier in the disease trajectory.

CONFLICT OF INTEREST

ALA is Principal Investigator on an NIHR PGfAR-funded trial in which the intervention is delivered by WW at no cost. PA and SAJ are principal investigators on a trial funded through a grant to the University of Oxford from Cambridge Weight Plan. PA has carried out half a day's consultancy for Weight Watchers and spoken at a symposium at the Royal College of General Practitioners conference that was funded by Novo Nordisk. Neither led to payments to him personally. JCGH has a trial funded by the American Beverage Association. All the other authors declare no competing interests.

AUTHOR CONTRIBUTIONS

ALA, PA, JCGH, EJB and SAJ are Investigators on the WRAP trial and designed and conducted the trial. ALA and SJG conceived this study and ALA, SJG, GMW and SJS designed the analysis. ALA and GMW conducted the analysis. All authors were involved in data interpretation and critical revision of the manuscript and approved the final version. ALA had access to all data in the study and had the final responsibility to submit for publication.

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