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The association between patterns of weight change, diabetes status and glycaemia among adults with overweight and obesity

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ABSTRACT

Aims: To investigate the associations between weight change patterns and 5-year incident non-diabetic hyperglycaemia (NDH), and glycated haemoglobin (HbA_{1c}) levels among individuals who had overweight or obesity.
Methods: This longitudinal cohort study (N = 435) pooled data from a weight management trial. Participants were adults with a body mass index of $\geq$28 kg/m^2. They were categorised as "no weight loss", "maintainers", and "regainers" based on their weight at 3 months and 12 months after baseline. Multivariable logistic regression models and linear regressions were conducted to examine the associations.
Results: Between 1-year and 5-year follow-ups, 77 participants developed NDH. We found no statistically significant association between weight change patterns and incident NDH at 5 years. Among weight loss maintainers, mean HbA_{1c} was −0.15% (95% confidence intervals (CI): −0.22, −0.10) lower after 1 year and −0.15% (95% CI: −0.23, −0.06) lower after 5 years compared to the no weight loss group. There was no difference between weight loss regainers and no weight loss group in HbA_{1c} levels.
Conclusions: Compared to those who did not lose weight, participants who maintained their weight loss had lower HbA_{1c} levels after 1 year and 5 years, which highlights the importance of providing long-term support to prevent weight regain.

1. Introduction

Type 2 diabetes has become a major public health challenge, affecting 5.9% of the population worldwide in 2021 [1]. One of the leading risk factors for type 2 diabetes is obesity [2]. In 2019, 14.0% of adults aged 18 years and over had obesity worldwide [3] while the prevalence of obesity in England was much higher, with 28% of adults having obesity [4]. Studies have shown higher risks of diabetes in adults who are overweight or obese. Therefore, reducing obesity was a key strategy to prevent diabetes in the population at high risk.

Randomised controlled trials (RCTs) have shown the association between 5% weight loss of baseline weight and reduced glycemia levels and incidence of type 2 diabetes in participants who had overweight or obesity [5,6]. Findings from the "Weight Loss Referrals for Adults in Primary Care" (WRAP) study showed the preventive effects of a weight loss intervention on the development of non-diabetic hyperglycaemia (NDH), the intermediate state between normoglycaemia and diabetes, in people with obesity or who are overweight and the beneficial effect of normalizing glycaemia after one year in participants with NDH at baseline [7]. Although weight loss is rarely maintained following an intervention [8], most studies reported lower diabetes incidence or improvements in metabolism related to diabetes in participants who maintained the weight loss [9,10]. However, there is a lack of research considering the potentially different impact of maintaining weight loss and regaining weight on the risk of diabetes.

Unlike the consistency in the effect of weight loss maintenance, there is limited evidence on the long-term effect of weight regain on the risk of diabetes incidence and findings are inconsistent. Some studies observed no statistically significant associations [11,12]. One study using data from the Look AHEAD (Action for Health in Diabetes) trial showed that

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when comparing to those who did not lose weight, regain of weight loss was not associated with HbA_{1c} levels after four years [11]. Another study found similar fasting plasma glucose, insulin, and insulin resistance levels between participants with stable weight and those who lost two kilograms of weight or more after six months and had regained weight by the 24th month [4,12]. Some studies demonstrated negative associations between weight loss regain and health outcomes. In one trial of 80 postmenopausal women, weight and body fat regain were found to be significantly associated with increased glucose levels and insulin resistance 12 months after the end of the 5-month weight loss intervention [13]. Another trial found that insulin sensitivity in those who regained weight was 24% worse than that of participants with stable weight [14].

Therefore, the current study aims to compare the 5-year incident NDH and glycated haemoglobin (HbA_{1c}) levels in adults who lost and regained weight, and those who lost weight and maintained the weight loss, to those who did not lose weight.

2. Methods

2.1. Study population

This observational cohort study pooled data from baseline and follow-ups from the three arms of a multi-centre RCT of behavioural

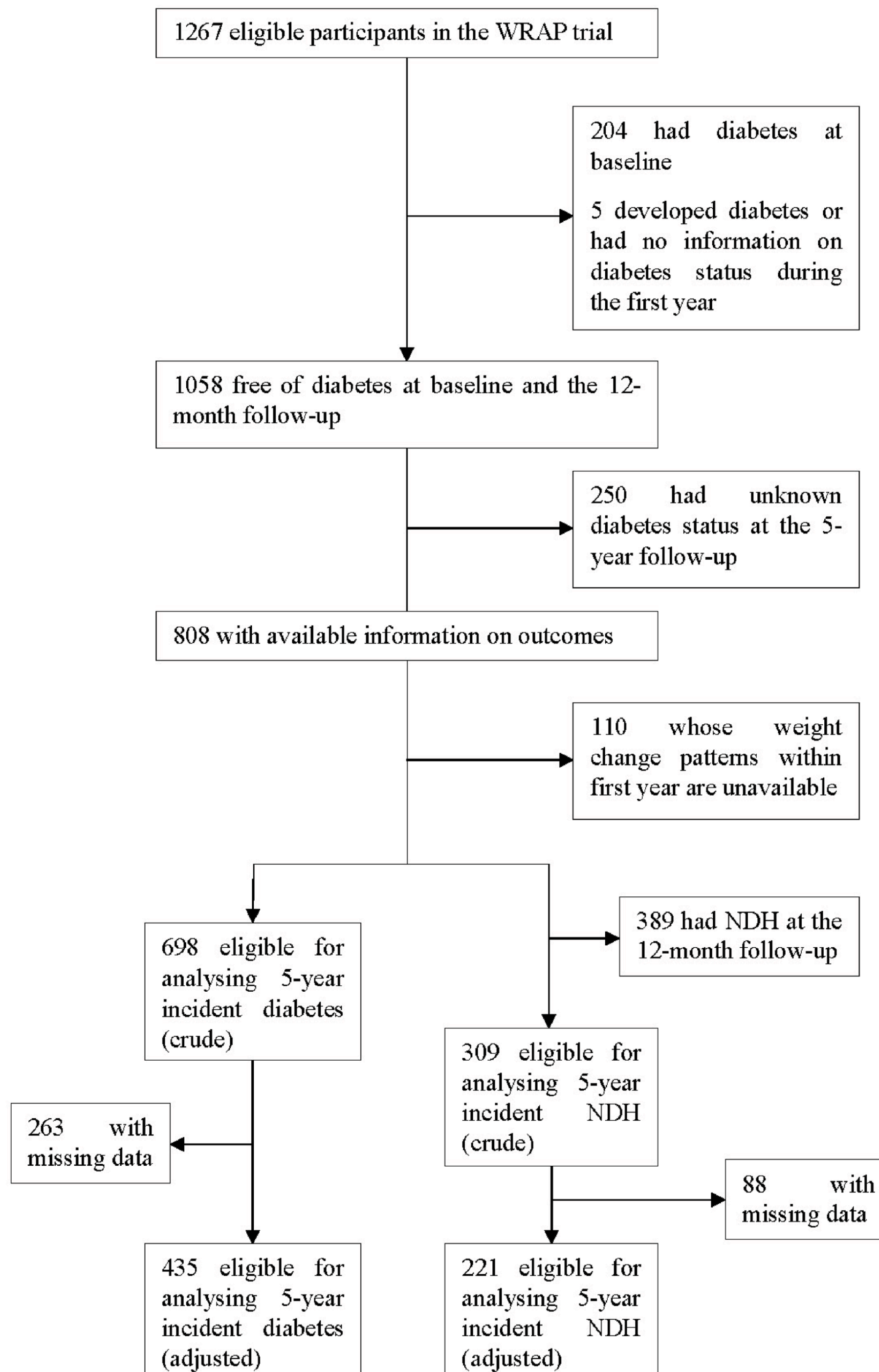


Fig. 1. Diagram of the study sample.

weight management programmes – the WRAP trial. The WRAP trial design and primary findings have been described in detail elsewhere [15,16]. Participants were 1267 English-speaking people aged 18 years and older with a body mass index (BMI) $\geq$28 kg/m^2 recruited via mailout from 23 primary care practices in England. People who planned on becoming pregnant or were currently pregnant, or had severe illnesses were excluded. After being stratified by gender and centre, eligible participants were block-randomised in blocks of 12 into three groups: a brief intervention group, a commercial behavioural weight management programme (WW, formerly Weight Watchers) for 12 weeks and the same programme for 52 weeks in a 2:5:5 ratio. Stata 12.1 was used to create the randomisation sequence, which was then coded into the trial database. Following enrolment and data entry of participants' details, the group allocation was revealed. Follow-up visits were scheduled at 3 months, and 1, 2, and 5 years after baseline. The drop-out rates at follow-ups using the number of participants at baseline as the denominator were 21% at the 3-month follow-up (n=263), 35% at the 1-year follow-up (n=444), 32% at the 2-year follow-up (n=411), and 49% at the 5-year follow-up (n=624). The mean follow-up time was 5.1 years [17]. At each follow-up, physical measurements, including weight, height, blood pressure, and HbA_{1c}, were taken by trained staff. Participants' medical records were also retrieved and those who did not attend the appointment were asked to report their weight.

2.1.1. Ethical approval

This original trial was approved by NRES Committee East of England Cambridge East, NRES Committee North West Liverpool Central and NRES Committee South Central Oxford. The 5-year follow-up was approved by West Midlands-Coventry and Warwickshire Research Ethics Committee. The registration numbers with Current Controlled Trials are ISRCTN82857232 and ISRCTN64986150. Written informed consent was obtained from all participants before randomisation.

2.1.2. Study sample

Fig. 1 presents the process of generating the study sample. As this study aims to examine 5-year incidence of diabetes, we excluded participants who had diabetes at baseline (n=204) or who developed diabetes within one year or had no information on diabetes status at baseline or during the first year (n=5) based on the American Diabetes Association (ADA) criteria (HbA_{1c} values $\geq$48mmol/mol) [18]. Participants with unknown diabetes status at the 5-year follow-up (n=250), unavailable information on weight change patterns (n=110) or on any covariates (n=263) were excluded. When analysing 5-year incident NDH, participants who had NDH at baseline or after 1 year were further excluded from the sample, resulting in 221 participants.

2.2. Data

2.2.1. Exposure

The exposure is patterns of weight change within the first year of follow-up, according to participants' measured or self-reported weight at baseline, 3 months, and 12 months after baseline. Participants who did not lose weight are defined as those whose weight loss at the 3-month follow-up was less than 5% of their weight at baseline or whose weight was higher than their baseline weight [6]. The 5% cut-off is the most widely used definition of successful weight loss given its association with health benefits [6,19–23]. There is larger disagreement regarding the definition of weight loss maintenance. We adopted a relative approach recommended by the Look AHEAD and Diabetes Prevention Program trials, which was "regaining $\leq$25% of initial weight loss during maintenance", because it might be unrealistic to require the participants not to regain any of the weight loss and this approach could account for the variations of the weight loss [24]. Therefore, among participants who lost 5% or more of their baseline weight at the 3-month follow-up, those who regained less than 25% of the weight loss at the 12-month follow-up were categorised as "Maintainers" [24]. "Regainers" were those who lost 5% or more of their weight at the 3-month follow-up and regained 25% or more of the weight loss at the 12-month follow-up.

2.2.2. Outcomes

The primary outcome is incident NDH occurring between the 1-year and 5-year follow-up. Participants with an HbA_{1c} value of $\geq$39 and <48mmol/mol were considered as having NDH according to the ADA criteria [18]. Those with HbA_{1c} levels lower than 39 mmol/mol were considered as having normoglycemia. The secondary outcome is HbA_{1c} values measured at the 1-year and 5-year follow-ups.

As a low incidence and a small sample size may increase the probability of type II error and affect the statistical power [25], incident diabetes at the 5-year follow-up and its association with weight change patterns among participants without diabetes at baseline or 1-year follow-up are presented in supplementary files. Participants who fulfilled one of the following criteria were defined as having diabetes: 1) those with an HbA_{1c} level $\geq$48 mmol/mol measured at the 5-year follow-up visit; 2) those who had diabetes according to GP records; 3) those who self-reported taking diabetes medication at the 5-year follow-up.

2.2.3. Covariates

Participants' socio-demographic characteristics at baseline were collected via questionnaires. These characteristics include age at baseline, sex (female/male), ethnicity, income, and education. Age at baseline in years was a continuous variable. Ethnicity was categorised into white or white British, and other. Annual household income was classified as <£20,000, £20,000–39 999, $\geq$£40,000, and missing or prefer not to say. Education attainment was categorised into general certificate of secondary education (GCSE) or lower, A-level or post-secondary study, university or higher, and missing. We reported participants' baseline height, blood pressure, and fasting blood glucose that were measured in the assessments. Participants were classified as having hypertension at baseline if their systolic blood pressure was $\geq$ 140 mmHg, or their diastolic blood pressure was $\geq$ 90 mmHg, or they were taking medications for high blood pressure. At the 2-year follow-up, participants were asked to report their smoking status.

2.3. Statistical analyses

2.3.1. Main analyses

Descriptive statistics for baseline characteristics by weight change patterns and for the total sample are reported, including demographics, socioeconomic factors, and biological measurements. Descriptive statistics for participants' glycaemia status at the 12-month follow-up (NDH / normoglycaemia) and smoking status at the 2-year follow-up are also reported. The means and standard deviation (SD) were calculated and shown for continuous variables; frequency distribution (n, %) was presented for categorical variables.

We calculated participants' mean weight and HbA_{1c} values by weight change patterns during follow-ups. The differences in weight across the three groups at each follow-up using one-way ANOVA and Tukey tests for pairwise comparison.

We conducted multivariable logistic regression to examine associations of 1-year weight change patterns with diabetes status at the 5-year follow-up. The potential confounders were selected based on the adjustment used in previous studies [12,13]. The adjusted confounders were study group allocation, age at baseline, gender, income, ethnicity, education, BMI at baseline, hypertension status at baseline, and smoking status at the 2-year follow-up.

We used logistic regression to estimate odds ratios (ORs) of the association between the category of weight change pattern and a binary categorisation of NDH at the 5-year follow-up. This analysis was restricted to participants who had normoglycaemia at baseline and at 1 year. ORs and 95% confidence intervals (95% CI) were reported.

We used linear regression models to estimate the association

Table 1
Participants' baseline* characteristics by patterns of weight change.

Characteristics	No weight loss group[1] N = 243	Maintainers[2] N = 132	Regainers[3] N = 60	Total N = 435
Age (years, SD)	52.0 (12.6)	55.5 (12.7)	49.5 (11.9)	52.7 (12.7)
Sex (n, %)				
Female	171 (70.4 %)	88 (66.7 %)	38 (63.3 %)	297 (68.3 %)
Male	72 (29.6 %)	44 (33.3 %)	22 (36.7 %)	138 (31.7 %)
Ethnicity (n, %)				
White or white British	225 (92.6 %)	123 (93.2 %)	57 (95.0 %)	405 (93.1 %)
Other	18 (7.4 %)	9 (6.8 %)	3 (5.0 %)	30 (6.9 %)
Annual household income (n, %)				
<£20 000	85 (35.0 %)	33 (25.0 %)	18 (30.0 %)	136 (31.3 %)
£20 000–39 999	81 (33.3 %)	48 (36.4 %)	21 (35.0 %)	150 (34.5 %)
≥£40 000	77 (31.7 %)	51 (38.6 %)	21 (35.0 %)	149 (34.3 %)
Education (n, %)				
GCSE or lower	75 (30.9 %)	47 (35.6 %)	22 (36.7 %)	144 (33.1 %)
A-level or post-secondary study	75 (30.9 %)	28 (21.2 %)	12 (20.0 %)	115 (26.4 %)
University or higher	93 (38.3 %)	57 (43.2 %)	26 (43.3 %)	176 (40.5 %)
Weight (kg), mean (SD)	94.0 (14.6)	94.4 (16.0)	96.1 (15.4)	94.4 (15.1)
BMI (kg/m^2), mean (SD)	33.6 (4.1)	33.7 (4.7)	33.9 (4.9)	33.7 (4.4)
Hypertension status (n, %)				
Yes	109 (44.9 %)	76 (57.6 %)	29 (48.3 %)	214 (49.2 %)
No	134 (55.1 %)	56 (42.4 %)	31 (51.7 %)	221 (50.8 %)
Fasting glucose (mmol/L), mean (SD)	5.2 (0.5)	5.3 (0.5)	5.2 (0.4)	5.2 (0.5)
n	154	90	41	285
Missing (n, %)	147 (37.4 %)	71 (32.0 %)	30 (36.1 %)	248 (35.5 %)
HbA_{1c} (mmol/mol), mean (SD)	37.9 (3.8)	39.0 (3.4)	37.2 (3.5)	38.1 (3.7)
n	164	93	40	297
Missing (n, %)	136 (34.6 %)	47 (21.2 %)	31 (37.3 %)	214 (30.7 %)
HbA_{1c} (%), mean (SD)	5.6 (0.3)	5.7 (0.3)	5.6 (0.3)	5.6 (0.3)
n	164	93	40	297
Missing (n, %)	136 (34.6 %)	47 (21.2 %)	31 (37.3 %)	214 (30.7 %)
Glycaemia status at the 12-month follow-up (%)				
Non-diabetic hyperglycaemia	55 (22.6 %)	24 (18.2 %)	11 (18.3 %)	90 (20.7 %)
Normoglycaemia	188 (77.4 %)	108 (81.8 %)	49 (81.7 %)	345 (79.3 %)
Smoking status at the 2-year follow-up				
Current smokers	19 (7.8 %)	6 (4.5 %)	4 (6.7 %)	29 (6.7 %)
Ex-smokers	84 (34.6 %)	37 (28.0 %)	22 (36.7 %)	143 (32.9 %)
Never-smokers	140 (57.6 %)	89 (67.4 %)	34 (56.7 %)	263 (60.5 %)

Abbreviations: BMI: body mass index, GCSE: the general certificate of secondary education, SD: standard deviation.
[1] Participants in the no weight loss group are those who lost < 5 % of their weight at the 3-month follow-up compared to their weight at baseline.
[2] Maintainers were those who lost ≥ 5 % of their weight at the 3-month follow-up and regained < 25 % of the weight loss at the 12-month follow-up.
[3] Regainers were those who lost ≥ 5 % of their weight at the 3-month follow-up and regained ≥ 25 % of the weight loss at the 12-month follow-up.
* Unless otherwise noted.

between the category of weight change pattern and HbA_{1c} values at the 1-year and 5-year follow-ups, respectively. The adjustments in the multivariable linear regression models are the same as those in the logistic regression models with an additional adjustment for baseline HbA_{1c} values. The residuals were plotted against quantiles of normal distribution to assess the normality of HbA_{1c} values. The quantile–quantile (Q-Q) plots suggested a normal distribution of HbA_{1c} residuals at the 1-year follow-up but not at the 5-year follow-up (Supplementary Figs. 1 and 2). The associations between weight change patterns and HbA_{1c} values were further examined in male and female subgroups.

All statistical analyses were performed using Stata 16 software [26]. Two-sided p-values <0.05 were considered statistically significant.

2.3.2. Sensitivity analyses

Baseline characteristics of participants with any missing data on participants' weight during the first year, or any covariates (n=485) were compared to those with complete information (n=323), using ANOVA for continuous variables, and Pearson's chi-squared test for categorical variables.

Missing values for any variables with missing data were imputed via multiple imputation using chained equations (MICE) under the missing at random assumption. All covariates in the main analyses and variables that predicted missingness were included in the imputation model. Twenty imputed datasets were created using logistic regression models. Separate results from the regression models in the 20 imputed datasets were pooled according to Rubin's rules [27]. Convergence of the imputation model was assessed by plotting the mean and variance of the estimated parameters against iteration numbers.

We have also considered an alternative categorisation of weight change patterns: 1) weight loss of < 5% of the baseline weight at both 3-month and 1-year follow-ups; 2) maintainers; 3) regainers; and 4) < 5% weight loss at the 3-month follow-up and ≥ 5% loss of baseline weight at the 1-year follow-up. The association analyses between weight change patterns, diabetes status and glycaemia were repeated.

3. Results

3.1. Socio-demographic characteristics of participants

Table 1 shows the baseline characteristics of participants in total and by patterns of weight change. The mean age of the 435 participants was 52.7 years (SD=12.7), with a range of 20–83 years. The majority were female (68.3%), and white/white British (93.1%). The mean weight and HbA_{1c} levels at baseline were 94.4 kg (SD=15.1) and 38.1 mmol/mol (SD=3.7), respectively.

The majority (n=243) of participants did not lose at least 5% of baseline weight at the 3-month follow-up (no weight loss group). In the 192 participants who achieved ≥5% weight loss, 132 regained <25% of the initial weight loss after 1 year (maintainers) and 60 regained ≥25%

of the initial weight loss (regainers). There was little difference in the mean age, sex, education levels, household income, and BMI values across the three groups. The overall mean BMI was 33.7 kg/m^2, with a range of 28.1–53.5 kg/m^2. A slightly higher proportion of the maintainer group reported a history of hypertension at baseline (57.6%), compared to 44.9% in the no weight loss group, and 48.3% in the regainers. The baseline fasting glucose was similar in the three groups. The overall proportion of NDH was 20.7% at the 12-month follow-up, with the highest proportion in the no weight loss group (22.6%). At the 24-month follow-up, over half (60.5%) of the participants reported to never smoke.

We compared the characteristics of participants with missing information to those with complete information (Supplementary Table 1) and found that participants with missing information were more likely to have lower education levels or income, and to have NDH at the 12-month follow-up.

3.2. Weight and HbA$_{1c}$ levels over the 5-year follow-up

Fig. 2**a and 2b** show participants' weight and HbA$_{1c}$ levels over the 5-year follow-up among those with no weight loss, maintainers and regainers. In Fig. 2**a**, the average weight at baseline was similar across the three groups. At 3-month follow-up, maintainers had the largest weight loss compared to baseline weight, followed by regainers and the no weight loss group. A persistent reduction between 3 months and 12 months was observed in weight in maintainers and the no weight loss group, but not regainers. Between 12-month and 5-year follow-ups, mean weights increased in those who did not lose weight and maintainers.

Supplementary Table 2 shows the p values of ANOVA tests and pairwise comparisons of participants' weight over the follow-ups by weight change patterns. At 3-month follow-up, maintainers had statistically significantly lower weight than the no weight loss group. Maintainers were likewise lighter than the other two groups at the 1-year and 2-year follow-ups. At the 5-year follow-up, the weight was similar across the three groups.

In Fig. 2**b**, maintainers had the highest HbA$_{1c}$ levels at baseline, followed by the no weight loss group and regainers. The largest reduction in HbA$_{1c}$ levels between baseline and the 12-month follow-up was observed in maintainers (Supplementary Table 3). Compared to the 12-month follow-up, the HbA$_{1c}$ levels increased similarly in all three groups at 5 years.

3.3. Weight change patterns, diabetes and NDH

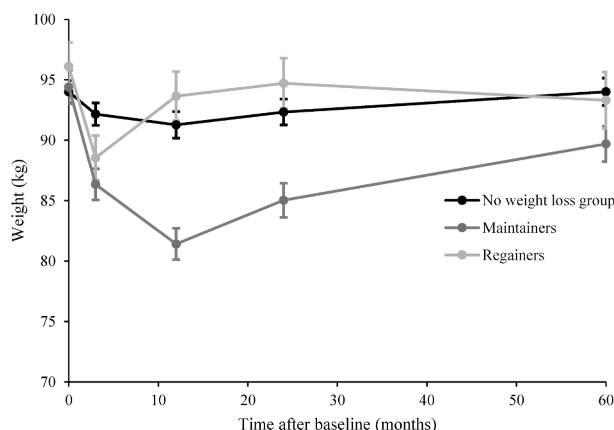
Table 2 shows the associations between patterns of weight change and 5-year incident NDH. Among 221 participants without NDH at baseline and 1-year follow-up, 77 had NDH after 5 years. Compared to the no weight loss group, the odds of developing NDH after 5 years in maintainers were close to 1 with wide CIs. The magnitude of association between regainers and NDH showed suggestive lower odds of NDH. However, the CIs were wide, and both estimates overall showed no statistically significant associations. Similar results were observed in males and females, respectively (Supplementary Table 4). We also investigated the association between patterns of weight change and 5-year incident diabetes in both sexes (Supplementary Table 5) and in females (Supplementary Table 6). The analyses were unavailable in males due to the limited number of diabetes cases in males. In a total of 435 participants without diabetes at baseline and 1-year follow-up, 17 participants developed diabetes during the 5-year follow-up. However, the few diabetes cases and the wide CIs on the estimates prevented us from drawing conclusions on the association.

Table 2
Associations of patterns of weight change with 5-year incident NDH.

	N	Number of cases	Adjusted Odds Ratios (95 % CI)[4]
5-year incident NDH			
No weight loss group[1]	111	39	Ref
Maintainers[2]	79	29	0.93 (0.47–1.84)
Regainers[3]	31	9	0.74 (0.28–1.93)

Abbreviations: NDH: Non-Diabetic Hyperglycaemia.
[1] Participants in the no weight loss group are those who lost less than 5% of their weight at the 3-month follow-up compared to their weight at baseline.
[2] Maintainers were those who lost 5% or more of their weight at the 3-month follow-up and regained less than 25% of the weight loss at the 12-month follow-up.
[3] Regainers were those who lost 5% or more of their weight at the 3-month follow-up and regained 25% or more of the weight loss at the 12-month follow-up.
[4] Adjustment: study group allocation, age at baseline, BMI at baseline, gender, income, ethnicity, education, hypertension status, and smoking status at the 2-year follow-up.

a. Participants' mean weight at baseline, 3 months, 12 months, 24 months, and 5-years, by patterns of weight change



b. Participants' HbA$_{1c}$ values at baseline, 12 months, and 5-years, by patterns of weight change

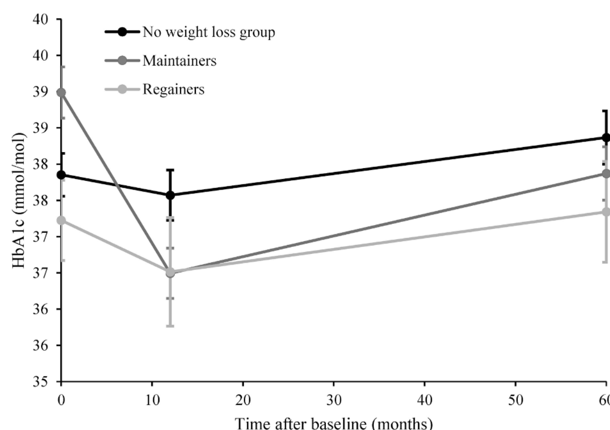


Fig. 2. Participants' mean weight and HbA$_{1c}$ values over the 5-year follow-up by patterns of weight change Mean values of measured or self-reported weights and HbA$_{1c}$ values at each timepoint are shown with standard errors as the error bars.

3.4. Weight change patterns and HbA_{1c}

Table 3 shows the associations between weight change patterns, and 1-year and 5-year HbA_{1c} levels. The adjusted difference in mean HbA_{1c} levels after 1 year in maintainers relative to the no weight loss group was −0.15% (95% CI: −0.22, −0.10) and −1.71 mmol/mol (95% CI: −2.39, −1.05). After adjusting for confounders, there were statistically significant reductions in mean HbA_{1c} levels after 5 years in maintainers of −0.15% (95% CI: −0.23, −0.06) and −1.59 mmol/mol (95% CI: −2.49, −0.68), compared to the no weight loss group. The HbA_{1c} levels between no weight loss group and regainers did not differ significantly. The associations were consistent in both male and female subgroups (Supplementary Table 7).

3.5. Sensitivity analyses

The results from the regression analyses after multiple imputation (Supplementary Tables 8 and 9) were similar to the results from the complete case analyses. Compared to the no weight loss group, non-statistically significant associations were found between weight change patterns and 5-year incident diabetes and NDH. Similar reductions were found in HbA_{1c} levels of maintainers but not in regainers, compared to the no weight loss group at the 1-year and 5-year follow-ups. The healthy convergence in the trace plots demonstrates the accuracy in the imputed values.

Supplementary Tables 10–12 present additional sensitivity analyses to examine an alternative categorisation of weight change patterns. When compared to participants with no weight loss at the 3-month and 1-year follow-ups, maintainers and those who lost weight at the 1-year follow-up had consistently lower HbA_{1c} levels. Similarly, we found no evidence for an association of weight loss maintenance or weight loss regain with 5-year incident diabetes and NDH.

4. Discussion

Using cohort data from a randomised controlled trial of three weight management programmes, we investigated the relationship between weight change patterns and diabetes, NDH and HbA_{1c} levels. There was no association between 1-year weight change patterns and incidence of NDH after 5 years. Those who maintained weight loss had lower 1-year and 5-year HbA_{1c} levels compared to those who did not lose weight. However, those who lost and regained had similar HbA_{1c} levels to the no weight loss group, indicating the necessity of maintaining weigh loss.

This study shows no associations between weight loss regain and glycaemia outcomes in regainers compared to participants who did not lose weight at the 3-month follow-up. Other research has shown a higher risk of cardiometabolic diseases including diabetes, and intermediate factors such as insulin levels, and insulin resistance, among participants who lost weight and regained, compared to participants who maintained the weight loss [13] or those who remained non-obese [14,28]. In addition to these factors directly linked with glucose regulation, weight cycling (the repetitive process of weight loss and regain) has been found to be associated with increased blood pressure, and a higher risk of dyslipidaemia [29,30]. Nonetheless, similar to the findings of the current study, some studies report no associations between weight loss regain and incident diabetes [31] and HbA_{1c} levels [11] in people with obesity. Other studies demonstrate health benefits in participants who had successful weight loss despite weight regain, including a lower risk of coronary heart disease and improved insulin resistance in people with obesity [32,33]. In the current study, the mean values of weight were similar among regainers and no weight loss group at the 2-year and 5-year follow-ups, which might partially explain the non-significant association. Another potential cause might be related to the cut-off of weight loss. In the current study, 65% of the regainers had less than 8% weight loss at the 3-month follow-up, which corresponded with moderate weight loss defined by a study based on the Look AHEAD trial [34] that reported similar non-significant association between weight loss regain and HbA_{1c} levels. The initial weight loss might not be sufficient to significantly mitigate increased glycaemia associated with the weight loss regain.

Findings of the current research add to the limited evidence on the lower HbA_{1c} levels in participants who maintained weight loss, with those who did not lose weight as the reference group. The Look AHEAD trial reported a reduction in HbA1c level (%) at the 4-year follow-up compared to baseline in participants who had $\geq$ 8% initial weight loss and maintained a weight loss between 3% and 8% of their baseline weight at the 4-year follow-up [34]. Another study using the Diabetes Prevention Program trial also observed improvements in fasting blood glucose among participants who achieved successful weight loss at the 2-year follow-up [35]. Our finding provides implication for lowering HbA_{1c} levels in diabetes prevention and management, as HbA_{1c} level is an important indicator of diabetes progression and control.

This study used longitudinal data from an RCT of a weight management programme with a 5-year follow-up [17]. The trial was one of the few weight management RCTs with a long-term follow-up [36,37] - most trials had a shorter follow-up of 1 or 2 years [4,12,13,36]. The long follow-up allowed diabetes and NDH to develop. Participants' weight was objectively measured when participants attended the follow-up visits at their local GPs or self-reported at multiple time points. This allowed us to assess longitudinal changes in weight and distinguish weight loss regain and weight loss maintenance. The outcomes of HbA_{1c}

Table 3
Associations of patterns of weight change with 1-year and 5-year HbA_{1c} values.

	N	Adjusted regression coefficient [4]	
		Mean HbA_{1c} (mmol/mol)	Mean HbA_{1c} (%)
Outcome: 1-year HbA_{1c} values	228		
No weight loss group[1]		Ref	Ref
Maintainers[2]		−1.71 (-2.39, −1.05) **	−0.15 (-0.22, −0.10) **
Regainers[3]		−0.29 (-1.19, 0.61)	−0.03 (-0.11, 0.06)
Outcome: 5-year HbA_{1c} values	221		
No weight loss group[1]		Ref	Ref
Maintainers[2]		−1.59 (-2.49, −0.68) *	−0.15 (-0.23, −0.06) *
Regainers[3]		−0.59 (-1.74, 0.56)	−0.05 (-0.16, 0.05)

[1] Participants in the no weight loss group are those who lost less than 5% of their weight at the 3-month follow-up compared to their weight at baseline.
[2] Maintainers were those who lost 5% or more of their weight at the 3-month follow-up and regained less than 25% of the weight loss at the 12-month follow-up.
[3] Regainers were those who lost 5% or more of their weight at the 3-month follow-up and regained 25% or more of the weight loss at the 12-month follow-up.
[4] Adjustment: study group allocation, age at baseline, BMI at baseline, sex, HbA_{1c} levels at baseline, income, ethnicity, education, hypertension status, and smoking status at the 2-year follow-up.
** $p < 0.01$.
* $p < 0.05$.

levels were also objectively measured using standardised methods at multiple time points throughout the study. This study is based on a weight loss trial with inclusive inclusion criteria of people who had overweight or obesity in England. Therefore, findings might be generalisable to individuals at high risk for type 2 diabetes aiming to lose weight than would be the case in a more selective trial cohort.

One limitation of the current study was the categorisation of weight loss patterns based on three specific time points when there could be additional weight loss and regain between the intervals [38], which may lead to bias towards the null in the associations. Additionally, although the statistical models have adjusted for a wide range of potential confounders, there are still several confounders that we were unable to control, such as smoking status at baseline, physical activity, and change in medications. Third, the current study is subject to missing data due to loss to follow-up and incomplete questionnaire data. However, the sensitivity analyses applying multiple imputation showed similar results to the complete case analysis on the associations between weight change patterns and glycaemia outcomes, suggesting that the results of this study are robust to the presence of missing data assuming data are missing at random with respect to the covariates included in the imputation model. Fourth, the participants' ages ranged from 20 to 83 years, and their BMI ranged from 28.1 to 53.5 kg/m^2. Therefore, the results may not be generalisable to people beyond this age and BMI range. Fifth, the Q-Q plot for residuals of HbA_{1c} at the 5-year follow-up suggested a non-normal distribution. Using the Shapiro Wilcoxon tests, we found this could be attributable to the HbA_{1c} values of the no weight loss group ($p < 0.001$). As a large sample size would mitigate the impact of non-normal outcomes in ordinary least squares linear regression [39], the small sample size in the current study may lead to bias in the estimated differences.

The findings of the current study have implications for both practice and future research. As the intervention in the WRAP trial is one of the commercial weight loss programmes in the National Health Service referral scheme for people with obesity, the finding of lower HbA_{1c} levels in maintainers highlights the importance of maintaining weight loss after completing the programme. For example, training could be provided to primary care practitioners and people who are referred to the programmes, to enhance their understanding of how to maximise the long-term benefits from the programmes. Scalable and inexpensive interventions to which people can be referred after completing a commercial weight loss programme are needed to help them consolidate what they learned and implement this over the long-term. As this study was conducted in a relatively small sample with white people in the UK as the majority, it remains uncertain whether the findings could be generalised to populations in other geographical areas or from other cultural and ethnic backgrounds. Future research with a larger sample size and higher representativeness of population subgroups is needed to address the issue of imprecision, and provide additional support to them.

5. Conclusions

Individuals at high risk for type 2 diabetes who achieved at least 5% weight loss after 3 months and maintained their weight loss for 1 year had lower HbA_{1c} levels over 5 years compared to participants who did not lose weight. In contrast, participants who lost weight and then regained weight by 1 year did not have lower HbA_{1c} levels relative to those with no weight loss. The different associations observed in maintainers and regainers suggest that maintaining weight loss is necessary to reduce glycaemic levels, as weight loss alone is not sufficient to provide these benefits. The findings highlight the importance of providing long-term weight management support to prevent weight regain among participants in weight loss intervention programmes.

CRediT authorship contribution statement

Ruoyu Yin: Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization. **Amy L. Ahern:** Writing – review & editing, Resources, Funding acquisition. **Louise Lafortune:** Writing – review & editing, Supervision. **Simon J. Griffin:** Writing – review & editing. **Jean M. Strelitz:** Writing – review & editing, Supervision, Conceptualization. **Julia Mueller:** Writing – review & editing, Supervision, Conceptualization.

Rights retention statement

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: ALA is the principal investigator on a randomised controlled trial funded by NIHR Programme Grants for Applied Research where the intervention is delivered by Weight Watchers at no cost. JM is a former Trustee of the Association for the Study of Obesity. The other authors declare no conflicts of interest.

Data availability

The dataset analysed during the current study is not publicly available. Participant consent allows for data to be shared in future analyses with appropriate ethical approval, and the host institution has an access policy (https://www.mrc-epid.cam.ac.uk/wp-content/uploads/2019/02/Data-Access-Sharing-Policy-v1-0_FINAL.pdf) so that interested parties can obtain the data for replication or other research purposes that are ethically approved. Data access is available upon reasonable request (datasharing@mrc-epid.cam.ac.uk).

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Contribution statement

RY, JM, and JMS conceived of the research idea and designed the study. RY analysed the data and wrote the first draft of the manuscript. RY, JM, and JMS contributed to the interpretation of the results. RY, JM, JMS, ALA, LL, and SJG contributed to revision of the manuscript. All authors have reviewed and approved the final manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2024.111607.

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