**Behaviour change, weight loss and remission of type 2 diabetes: a community based prospective cohort study**

Running title: Behaviour change, weight loss and remission of type 2 diabetes

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**Abstract**

**Aim:** To quantify the association between behaviour change and weight loss after diagnosis of type 2 diabetes, and the likelihood of remission of diabetes at five-year follow-up.

**Method:** A prospective cohort study of 867 people with newly diagnosed diabetes aged 40 and 69 years from the ADDITION-Cambridge trial. Participants were identified via stepwise screening between 2002 and 2006 and underwent assessment of weight change, physical activity (EPAQ2 questionnaire), diet (plasma vitamin C and self-report), and alcohol consumption (self-report) at baseline and one year after diagnosis. Remission was examined at five years after diabetes diagnosis via HbA1c level. We constructed log binomial regression models to quantify the association between change in behaviour and weight over i) the first year after diagnosis and ii) the subsequent one to five years, and remission at 5-year follow-up.

**Results: Diabetes remission was achieved in** 257 (30%) participants at five-year follow-up. Compared to people who maintained the same weight, those who achieved ≥ 10% weight loss in the first year after diagnosis had a significantly higher likelihood of remission (RR 1.77 (95% CI 1.32 to 2.38, p<0.01)). In the subsequent one to five years, achieving ≥10% weight loss was also associated with remission ((RR 2.43 (95% CI 1.78 to 3.31, p<0.01)).

**Conclusion:** In a population-based sample of adults with screen-detected type 2 diabetes, weight loss of 10% or more, early in the disease trajectory was associated with a doubling of the likelihood of remission at five years. This was achieved without intensive lifestyle interventions or extreme calorie restrictions. Greater attention should be paid to enabling people to achieve weight loss following diagnosis of type 2 diabetes.

Keywords; type 2 diabetes, remission, weight loss, health behaviours

**What’s new?**

* Biochemical remission of type 2 diabetes in the absence of pharmacological or surgical intervention has been shown to be achievable
* This has been previously demonstrated in short-term studies and only in selected populations through intensive weight loss programmes
* We found that weight loss of 10% or more, in the first few years after diagnosis was strongly associated with remission of type 2 diabetes at five years
* This was achieved without intensive lifestyle interventions or extreme calorie restrictions
* Our findings should inform discussions with people who have newly diagnosed type 2 diabetes as a motivation towards remission of the disease without restrictive and sometimes unachievable calorie restrictions

**Introduction**

Type 2 diabetes affects 400 million people globally and has been characterised as a lifelong progressive disease.[1,2] However, biochemical remission or ‘cure’, defined as a level of glycaemia below the diagnostic threshold (HbA1c < 6.5% or 48 mmol/mol) [3] in the absence of pharmacological or surgical interventions, is achievable through significant calorie restriction and weight loss [4,5]. Although there are varying definitions of remission in the literature, we have adhered to that based on HbA1c levels in line with UK and US national guidance. [3] Intensive low-calorie diet (total energy intake of 624-700kcal/day) for 8 weeks was associated with remission in 87% of people with recently diagnosed diabetes (<4 years) and in 50% of people with longstanding disease (>8 years)[4].Similarly, The Action for Health in Diabetes (Look AHEAD) study included an intensive 4-year program designed to increase physical activity and reduce initial weight by 7% or more [6] . Participants had a median duration of diabetes of five years and in the first year after the intervention, 11.5% achieved partial or complete remission compared to only 2.0% in the usual care group. In the DIRECT trial participants who had been diagnosed with diabetes in the previous six years underwent an intensive intervention including withdrawal of diabetes and blood pressure medication, diet replacement of 825–853 kcal/day through a formula diet for 3–5 months, stepped food reintroduction (2–8 weeks), and structured support for long-term weight loss maintenance [7]. Remission was achieved in 46% of the intervention group. Collectively, these studies support the hypothesis that healthy behaviour change and weight loss can result in remission of diabetes.

However, in all these studies selected participants were recruited to intensive weight loss interventions. Evidence is therefore required from representative population-based samples undergoing less intensive interventions that are more feasible and potentially scalable to the wider population. Furthermore, most studies have either examined remission in the short-term or amongst people who have lived with diabetes for a few years, or both [6,7]. It is unclear if behaviour change and weight loss early in the disease trajectory could lead to long-term remission. This is important as there could be a window of opportunity following diagnosis when people might be more receptive to interventions concerning weight loss. Using data from the ADDITION-Cambridge population-based study of screening for type 2 diabetes, we quantified the association between behaviour change and weight loss in the year after diagnosis and the subsequent five years, in relation to the likelihood of remission of diabetes at five-year follow-up.

**Methods**

Study design and setting

We conducted a cohort study analysis using prospectively collected data from the *ADDITION-Cambridge* trial (trial registered as ISRCTN86769081). This is a pragmatic, parallel group cluster randomised controlled trial in 49 general practices in the East of England. Individuals aged 40-69 years who were not known to have diabetes and had a Cambridge Diabetes Risk Score ≥ 0.17 (corresponding to the top 25% of participants’ risk distribution) were invited to attend a stepwise screening programme for type 2 diabetes including initial random capillary glucose and HbA1c testing followed by a fasting capillary glucose and a confirmatory oral glucose tolerance test [8–10]. Diagnosis of type 2 diabetes was based on the 1999 World Health Organization criteria [11]. Exclusion criteria were current pregnancy, lactation, psychiatric disease that prevented informed consent or an illness with a likely prognosis of less than a year at the time of diabetes diagnosis. All 867 participants identified by screening agreed to participate and were randomised at a practice level into either the intervention group (multifactorial treatment) or control group (routine care). In the routine care group, practices were advised to follow current UK national guidelines for diabetes management [12]. Intensive treatment included more frequent consultations including a 30-minute annual review in addition to three 10-minute consultations with a GP and nurse, provision of educational materials and guidelines, and practice-based academic detailing sessions encouraging earlier use of medication to improve control of risk factors with a local diabetologist and a GP opinion leader who described treatment algorithms and targets. A detailed description of the trial has been reported in previous publications [9,13]**.**

Participants gave written informed consent and the study was approved by an Ethics Committee (Eastern MREC, reference 02/5/54 and ADDITION 5 Year: Cambridgeshire 1 REC, reference 08/H0304/67).

#### Exposure and outcome measurements

All measures were taken at baseline, one and five-year follow-up**.** Physical activity was assessed by self-report using the validated EPIC Physical Activity Questionnaire (EPAQ-2) [14]. Dietary intake was assessed by self-report using a validated semi-quantitative food frequency questionnaire which enabled estimation of daily intake of total energy, fat as a percentage of energy and fibre intake [15,16]. Alcohol intake and smoking status (categorised as never smoked, ex-smoker or current smoker) were assessed by self-report via questionnaire. Clinical and biochemical measures were collected by trained staff following standardised protocols, as previously described.[18,19] Blood pressure was calculated as the mean of three measurements using an automatic sphygmomanometer. Body weight and height were measured in light clothing and without shoes using a scale (SECA) and a fixed rigid stadiometer, respectively. Venous blood samples were collected for analysis of lipid and HbA1c levels.

Remission was defined as an HbA1c level < 6.5% (48 mmol/mol) in the absence of any diabetes medication or bariatric surgery. Information on medication use and a history of bariatric surgery was self-reported and we also reviewed patient electronic GP records. At baseline, none of the participants included in this cohort were on any hypoglycaemic agents. We then followed-up this whole cohort for five years regardless of whether they were subsequently commenced on medications. Those who went into remission were by definition not on hypoglycaemic medication at the five-year follow-up.

### Statistical analysis

Data were pooled from both trial groups and presented for the whole cohort adjusted for trial group. Participant characteristics were summarised at baseline and one-year follow-up using means (SDs) or frequencies. To examine differences in characteristics between participants who achieved remission and those who did not, we used the chi-square and t-test where appropriate. We also examined differences between characteristics of participants with and without missing data; we assessed predictors of missing weight or remission information by comparing distributions of factors measured at baseline between those who were and were not missing weight or remission data. Percentage weight change over the first year after diagnosis was the main exposure variable. We also examined percentage weight change between one and five years. We constructed models using percentage weight change in four categories as follows; no weight change (reference category as ± 2.5%), weight gain (≥2.5%), ≤ 2.5-5% weight loss, between ≤5-10% weight loss, ≥10% weight loss . We also examined weight change in kilograms as a continuous variable. Change over the first year, and between one and five years in physical activity and diet as continuous variables (daily intake of total energy, fat as a percentage of energy, fibre, alcohol and plasma vitamin C) were then examined. We constructed log binomial regression models to examine the association between change in these exposures and 5-year risk of remission, generating risk ratios (RR) and 95% confidence intervals (CI). Multivariable nested models were then constructed adjusted on *a priori* reasoning. Model 1 adjusted for baseline weight and follow-up period. Model 2 additionally adjusted for age, sex, ethnicity (white or other), education level (full-time education finished at <16year or >16year, occupation (managerial and professional, intermediate and manual) trial group, date of diabetes diagnosis and clustering within practices. Given the possibility that remission might be more easily achieved amongst participants who had a lower HbA1c level at baseline, we carried out a subgroup anlaysis that included only those with an HbA1c level >6.5%. Statistical analysis was conducted in STATA version 14 (Stata, College Station, TX)

**Results**

Participant characteristics

Of the 867 participants at baseline, 730 (84%) had weight and HbA1c measures at 5-year follow-up and were included in the analysis. The mean (SD) age of included participants was 61(7) years. Most were male (61%) and white (97%). There were 49% who continued in full-time education after the age of 16 years and 43% reported unskilled or manual occupations. 55% of participants were commenced on hypoglycaemic medications at the five-year follow-up. There were few differences between those with and without data on weight change and HbA1c. Compared to included participants, those with missing data were less likely to have stayed in education over 16 years (15 and 11% respectively).

Between baseline and one-year follow-up, improvements were seen in the majority of health behaviours and CVD risk factors. Baseline participant characteristics and changes over the first year are shown in table 1 stratified according to remission status at five years. Diabetes remission was achieved in 257 (30%) participants in this cohort. Those who achieved remission were more likely to be male, smokers and to have remained in full-time education over 16 years.

Weight change and remission of diabetes at five years

In log binomial regression models, we observed that people who lost ≥ 10% body weight in the first year after diagnosis of diabetes were significantly more likely to achieve remission at five years compared to those with stable or increased weight. We observed similar trends with more modest weight loss of 5-10% or lower over the first year after diagnosis but this was not statistically significant; these results are shown in table 2. Similar associations were observed in the analysis of unit changes in weight with strong positive correlations between one-kilogram weight loss and remission, as shown in table 4. Similar trends were observed between 1- 5 year follow-up. The greater the amount of weight loss achieved, the higher the likelihood of remission in all models (table 3 and 5). In the subgroup analysis amongst participants with a baseline HbA1c >6.5%, similar trends were observed between weight change and remission. This is shown in the supplementary tables.

Behaviour change and remission of diabetes at five years

We did not observe any consistent patterns of associations between unit changes in health behaviours and remission of diabetes. A positive association with remission was noted with unit changes in alcohol levels but these varied between unadjusted and adjusted models which are shown in table 4.

**Discussion**

Principle findings

In this prospective cohort study, we investigated the association between weight loss and remission of type 2 diabetes at five-years. We found that modest weight loss of 10% or more in the first year or first five years after diagnosis is strongly associated with remission of type 2 diabetes. Our findings suggest that remission is achievable without intensive lifestyle interventions or extreme calorie restrictions.

Comparison to previous studies

Our findings support and add to previous research that has demonstrated associations between weight loss and remission of type 2 diabetes [5,7,20]. For example, The DIRECT trial, also set in UK primary care, reported varying rates of remission of diabetes depending on weight loss. The trial had aimed for a 15kg weight loss through an intensive intervention that included withdrawal of antidiabetic and antihypertensive drugs, total diet replacement (825–853 kcal/day formula diet for 3–5 months), stepped food reintroduction (2–8 weeks), and structured support for long-term weight loss maintenance. On average 10 kilograms (15%) of weight was lost in the intervention group and half of the participants achieved remission. [7][21]Other studies with similar intensive interventions in highly selected populations include the Counterbalance trial and The Look AHEAD trial. The Look AHEAD study did not report remission as a primary outcome but did include intensive support through dietary and physical activity programmes which resulted in remission. Whilst our observational findings are consistent with these trials, the specific amount of weight loss required to achieve remission varies. Most previous studies advocate significant weight loss (> 15%) with the DIRECT, Counterbalance and Look AHEAD trials reporting between 5 and 20-kilogram weight loss in order to achieve diabetes remission [5,7]. However, while baseline HbA1c values were lower in our screen-detected cohort, our results suggest that more modest weight loss of >10% is associated with a higher likelihood of remission if this occurs early in the disease trajectory. This may provide some rationale for motivating people with newly diagnosed type 2 diabetes to lose weight rather than focussing on specific and potentially unachievable weight targets. Previous studies have shown that when attempting to lose weight, people often set unrealistically high weight loss goals that could be detrimental to success, and evidence on whether weight loss counselling with specific targets is always successful is inconsistent [22]. Indeed, the DIRECT trial did not manage to achieve the weight loss targets intended for most participants with only 24% managing the 15 kg target weight loss despite the intensive support. Furthermore, these interventions are unlikely to be scalable to the wider population due to their intensity and cost and the limited availability of facilitators [7]. Our data suggest that in addition to extending availability of intensive weight loss interventions, policymakers should consider a range of accessible approaches targeting weight loss amongst people with newly diagnosed diabetes.

Finally, while we observed associations between weight change and remission, we did not observe consistent associations between behaviour change and remission. This might be due to the differential precision of the exposure measurements most of which were self-reported and therefore subject to error and bias. For example, we found that self-reported alcohol intake was associated with remission. Although there is some mixed evidence in the literature suggesting that moderate alcohol intake could be associated with positive cardiovascular outcomes, our findings were not consistent between adjusted and unadjusted models.[23] It is therefore unlikely to be a true association. It could be due to due to chance or residual confounding.

Strengths and limitations

Our study includes people with type 2 diabetes from a large population-based sample across an extensive geographical area in the East of England in routine clinical follow-up. We used measures of remission that are available in clinical practice to allow translation of our findings to practice. This cohort also includes heterogeneity amongst socio-economic groups, disease severity and health behaviours. There were also no specific dietary or physical activity restrictions for participants. This means that our study is generalisable to wider diabetes populations outside clinical trial cohorts. However, our sample does not exhibit ethnic diversity with predominantly white European participants which reflects the local population. Other strengths include the duration of follow-up which was five years, most previous remission studies are less than 12 months in duration. Also, the participant retention in this cohort was high at 95% at one-year follow-up and 83% at the five-year follow-up. Behaviours were measured using previously validated questionnaires and repeated measures with the same instruments, reducing our concerns about measurement error. We did, however, conduct a number of hypothesis tests so chance remains a plausible explanation for our findings.

Conclusions

Remission of type 2 diabetes is achievable in the longer term with modest weight loss of >10% early in the disease trajectory. This can be achieved without intensive interventions in free-living populations. Our findings should inform discussions with people who have newly diagnosed type 2 diabetes as motivation towards remission of the disease without restrictive and sometimes unachievable calorie restrictions. Further work is needed to replicate these findings in more ethnically and socially diverse populations. Further examination will need to include an assessment of the relationship between remission and longer-term clinical outcomes such as mortality.

**Ethical approval**: All participants provided written informed consent, and ethical approval was obtained (Eastern MREC, reference 02/5/54 and ADDITION 5 Year: Cambridgeshire 1 REC, reference 08/H0304/67). The ADDITION-Cambridge trial is registered as ISRCTN86769081.

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**Data availability:** Data are available on request from authors

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**Author Contribution:** HDM contributed to the design of the study, wrote the analysis plan, conducted the analysis, drafted and revised the paper. AD conducted analysis and revised the paper. GI contributed to the design of the study and revised the paper. JS revised the paper. SJG contributed to the design of the study and revised the paper. SJG is guarantor.

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**Table 1: Participant characteristics in the ADDITION-Cambridge cohort according to five-year diabetes remission status**

unless otherwise stated data are n (%), \* indicates data are mean (SD)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Remission of diabetes** | | | | **Non-remission of diabetes** | | | | | | |
| Variables | n | Baseline | n | 1-year | n | Baseline | n | | 1-year | |
| ***Sociodemographic*** |  |  |  |  |  |  |  | |  | |
| Age (years) \* | 257 | 62 (6.9) | \_ | \_ | 610 | 61 (7.3) | \_ | | \_ | |
| White ethnicity | 257 | 251 (97) | \_ | \_ | 610 | 597(96) | \_ | | \_ | |
| Male | 257 | 152 (59) | \_ | \_ | 610 | 232 (38) | \_ | | \_ | |
| Social class |  |  |  |  |  |  |  | |  | |
| Professional | 253 | 83 (33) | \_ | \_ | 594 | 194(33) | \_ | | \_ | |
| Education |  |  |  |  |  |  |  | |  | |
| full-time education  finished between  16- 18 years | 252 | 110(44) | \_ | \_ | 599 | 225(38) |  | |  | |
| ***Clinical*** |  |  |  |  |  |  |  | |  | |
| BMI (kg/m2) \* | 255 | 33 (5.7) | 228 | 31 (5.5) | 607 | 34 (5.7) | 505 | | 33 (5.6) | |
| Waist circumference (cm) \* | 257 | 111(14.5) | 228 | 107 (14.1) | 607 | 112 (12.9) | 505 | | 109 (13.1) | |
| Systolic blood pressure (mmHg)\* | 257 | 141 (19.4) | 228 | 135 (18.1) | 608 | 142 (20.5) | 504 | | 137 (18.7) | |
| Total cholesterol  (mmol.l-1)\* | 249 | 5.3 (1.1) | 229 | 4.4 (0.9) | 559 | 5.4 (1.2) | 504 | | 4.6 (1.0) | |
| HbA1c  %\*  mmol/mol\* | 250 | 6.7 (1.2)  50 (9) | 225 | 6.1 (0.7)  43 (5) | 596 | 7.8(1.8)  62 (14) | 501 | | 6.7 (0.9)  50(7) | |
| Previous stroke | 251 | 7 (2) | 224 | 11 (5) | 606 | 24(4) | 503 | | 25 (5) | |
| Previous MI | 251 | 15(6) | 225 | 15 (7) | 602 | 59(10) | 506 | | 47 (9) | |
| Antihypertensive medication | 249 | 149 (59) | 229 | 157(68) | 601 | 350(65) | 522 | | 347(59) | |
| Lipid lowering medication | 148 | 40 (27) | 131 | 84 (64) | 609 | 147 (24) | 507 | | 322(64) | |
| ***Health behaviour*** |  |  |  |  |  |  |  | |  | |
| Physical activity  (net MET h.day-1)\* | 256 | 11.4 (8.2) | 227 | 11.2(7.5) | 608 | 11.4(7.2) | 520 | | 11.9(7.6) | |
| Alcohol intake  (units.week -1)\* | 254 | 9(12) | 228 | 8(11) | 599 | 7(11) | 508 | | 6(11) | |
| Current smoker | 256 | 38(15) | 229 | 27(12) | 610 | 119(20) | 515 | | 84(16) | |
| Diet |  |  |  |  |  |  |  | |  | |
| Total energy  (kcal day-1)\* | 254 | 1941(654) | 225 | 1710(597) | 601 | 1977(739) | 518 | | 1720(607) | |
| Energy from fat  (%)\* | 254 | 32(6) | 225 | 30(7) | 601 | 33(6) | 518 | | 31(6) | |
| Fibre  (g.day-1)\* | 254 | 17(7) | 225 | 19(11) | 601 | 17(7) | 518 | | 19(11) | |
| Vitamin C intake  (mg/day)\* | 254 | 133(71) | 225 | 142(99) | 601 | 128(66) | 518 | | 139(107) | |
|  |  |  |  |  |  |  | |  | |  | |  |  |  |  |
|  |  |  |  |  |  |  | |  | |  | |  |  |  |  |

**Table 2: Association between percentage weight change category in the first year after diagnosis, and the risk of remission at five-years in the ADDITION-Cambridge study**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | % weight change category | n | | risk ratio | 95% CI | | P-value |
| unadjusted | no change (±2.5% change from baseline) | 867 | 266 | 1 |  |  |  |
| weight gain (≥2.5%) | 207 | 0.89 | 0.64 | 1.21 | 0.44 |
| weight loss >2.5-<5% | 151 | 1.01 | 0.72 | 1.40 | 0.97 |
| weight loss ≥5-<10% | 138 | 1.32 | 0.97 | 1.79 | 0.07 |
| weight loss ≥10% | 105 | 1.85 | 1.39 | 2.45 | <0.01 |
| adjusted model 1\* | no change (±2.5% change from baseline) | 670 | 226 | 1 |  |  |  |
| weight gain (≥2.5%) | 97 | 0.77 | 0.50 | 1.17 | 0.23 |
| weight loss >2.5-<5% | 140 | 1.01 | 0.72 | 1.40 | 0.95 |
| weight loss ≥5-<10% | 118 | 1.29 | 0.94 | 1.77 | 0.11 |
| weight loss ≥10% | 89 | 1.76 | 1.31 | 2.35 | <0.01 |
| adjusted model 2\*\* | no change (±2.5% change from baseline) | 648 | 221 | 1 |  |  |  |
| weight gain (≥2.5%) | 96 | 0.79 | 0.52 | 1.21 | 0.28 |
| weight loss >2.5-<5% | 135 | 1.00 | 0.71 | 1.40 | 0.99 |
| weight loss ≥5-<10% | 113 | 1.24 | 0.91 | 1.72 | 0.17 |
| weight loss ≥10% | 83 | 1.77 | 1.32 | 2.38 | <0.01 |

\* Model 1 adjusted for baseline weight and follow-up period

\*\* Model 2 adjusted for baseline weight, follow-up period, age, sex, ethnicity, socioeconomic group, education level, occupation, trial group, clustering of practices and date of diabetes diagnosis

**Table 3: Association between percentage weight change category between one to five years after diagnosis, and the risk of remission at five-years in the ADDITION-Cambridge study**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | % weight change category |  | n | | risk ratio | 95% CI | | P-value |
| unadjusted | no change (±2.5% change from baseline) |  | 867 | 242 | 1 |  |  |  |
| weight gain (≥2.5%) |  | 392 | 0.75 | 0.57 | 0.98 | 0.05 |
| weight loss >2.5-<5% |  | 93 | 1.24 | 0.90 | 1.74 | 0.19 |
| weight loss ≥5-<10% |  | 103 | 1.36 | 0.99 | 1.85 | 0.05 |
| weight loss ≥10% |  | 37 | 2.30 | 1.71 | 3.09 | <0.01 |
| adjusted model 1\* | no change (±2.5% change from baseline) |  | 670 | 227 | 1 |  |  |  |
| weight gain (≥2.5%) |  | 230 | 0.86 | 0.64 | 1.17 | 0.33 |
| weight loss >2.5-<5% |  | 88 | 1.24 | 0.89 | 1.76 | 0.22 |
| weight loss ≥5-<10% |  | 93 | 1.39 | 1.01 | 1.91 | 0.04 |
| weight loss ≥10% |  | 32 | 2.50 | 1.86 | 3.37 | <0.01 |
| adjusted model 2\*\* | no change (±2.5% change from baseline) |  | 648 | 222 | 1 |  |  |  |
| weight gain (≥2.5%) |  | 225 | 0.85 | 0.63 | 1.15 | 0.30 |
| weight loss >2.5-<5% |  | 82 | 1.35 | 0.95 | 1.91 | 0.09 |
| weight loss ≥5-<10% |  | 89 | 1.43 | 1.03 | 1.98 | 0.02 |
| weight loss ≥10% |  | 30 | 2.43 | 1.78 | 3.31 | <0.01 |

\* Model 1 adjusted for one-year weight and follow-up period

\*\* Model 2 adjusted for one-year weight, follow-up period, age, sex, ethnicity, socioeconomic group, education level, occupation, trial group, clustering of practices and date of diabetes diagnosis

**Table 4: Associations between change in weight and health behaviours in the first year after diagnosis and the risk of remission at five years**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Unadjusted | | | | | model 1 \* | | | | | model 2 \*\* | | | | |
| **Variable** | **n** | **RR** | **95% CI** | | **P-value** | **n** | **RR** | **95% CI** | | **P-value** | **n** | **RR** | **95% CI** | | **P-value** |
| Weight | 730 | 1.06 | 1.03 | 1.09 | <0.01 | 635 | 1.07 | 1.04 | 1.11 | <0.01 | 632 | 1.07 | 1.04 | 1.11 | <0.01 |
| (kg) |
| Physical activity | 747 | 0.99 | 0.96 | 1.01 | 0.37 | 702 | 0.99 | 0.96 | 1.01 | 0.45 | 702 | 0.98 | 0.96 | 1.02 | 0.50 |
| (net MET h.day-1) |
| Alcohol intake | 726 | 1.00 | 0.98 | 1.03 | 0.65 | 683 | 1.03 | 1.00 | 1.07 | 0.04 | 683 | 1.04 | 1.00 | 1.08 | 0.04 |
| (units.week -1) |
| Current smoker | 744 | 0.72 | 0.30 | 1.73 | 0.47 | 699 | 0.69 | 0.23 | 1.89 | 0.50 | 699 | 0.69 | 0.23 | 2.01 | 0.50 |
| Total energy | 736 | 1.00 | 0.99 | 1.00 | 0.44 | 692 | 1.00 | 0.99 | 1.00 | 0.38 | 692 | 1.00 | 0.99 | 1.00 | 0.38 |
| (kcal day-1) |
| Energy from fat | 736 | 1.00 | 0.98 | 1.03 | 0.47 | 692 | 1.00 | 0.97 | 1.02 | 0.91 | 692 | 0.99 | 0.97 | 1.02 | 0.91 |
| (%) |
| Fibre | 736 | 1.00 | 0.99 | 1.01 | 0.79 | 692 | 1.00 | 0.97 | 1.03 | 0.90 | 692 | 1.00 | 0.97 | 1.03 | 0.90 |
| (g.day-1) |
| Vitamin C  intake | 739 | 0.99 | 0.99 | 1.00 | 0.96 | 692 | 0.99 | 0.99 | 1.00 | 0.90 | 692 | 1.00 | 0.99 | 1.00 | 0.58 |
| (mg/day) |

\* Model 1 adjusted for baseline health behaviour and follow-up period

\*\* Model 2 adjusted for baseline health behaviour, follow-up period, age, sex, ethnicity, socioeconomic group, education level, occupation, trial group, clustering of practices and date of diabetes diagnosis

**Table 5: Associations between change in weight and health behaviours between one and five years after diagnosis and the risk of remission at five years**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Unadjusted | | | | | model 1 \* | | | | | model 2 \*\* | | | | |
| **Variable** | **n** | **RR** | **95% CI** | | **P-value** | **n** | **RR** | **95% CI** | | **P-value** | **n** | **RR** | **95% CI** | | **P-value** |
| Weight | 680 | 1.06 | 1.03 | 1.09 | <0.01 | 628 | 1.07 | 1.04 | 1.10 | <0.01 | 607 | 1.08 | 1.04 | 1.11 | <0.01 |
| (kg) |
| Physical activity | 632 | 0.98 | 0.96 | 1.01 | 0.24 | 632 | 0.99 | 0.96 | 1.01 | 0.26 | 611 | 0.99 | 0.99 | 1.01 | 0.28 |
| (net MET h.day-1) |
| Alcohol intake | 635 | 0.99 | 0.96 | 1.01 | 0.48 | 626 | 0.98 | 0.95 | 1.00 | 0.18 | 606 | 0.98 | 0.95 | 1.01 | 0.24 |
| (units.week -1) |
| Current smoker\*\*\* | 643 | 0.70 | 0.35 | 1.40 | 0.38 | 643 | 0.73 | 0.35 | 1.53 | 0.41 | 621 | 0.77 | 0.36 | 1.63 | 0.49 |
| Total energy | 623 | 1.00 | 0.99 | 1.00 | 0.73 | 619 | 1.00 | 0.99 | 1.00 | 0.72 | 599 | 1.00 | 0.99 | 1.00 | 0.59 |
| (kcal day-1) |
| Energy from fat | 623 | 1.00 | 0.97 | 1.02 | 0.84 | 619 | 1.00 | 0.97 | 1.02 | 0.86 | 599 | 0.99 | 0.99 | 1.02 | 0.92 |
| (%) |
| Fibre | 623 | 1.00 | 0.99 | 1.02 | 0.31 | 623 | 1.00 | 0.98 | 1.02 | 0.82 | 602 | 1.00 | 0.98 | 1.02 | 0.72 |
| (g.day-1) |
| Vitamin C  intake | 623 | 1.00 | 0.99 | 1.00 | 0.96 | 623 | 1.00 | 0.99 | 1.00 | 0.76 | 602 | 1.00 | 0.99 | 1.00 | 0.71 |
| (mg/day) |

\* Model 1 adjusted for baseline health behaviour and follow-up period

\*\* Model 2 adjusted for baseline health behaviour, follow-up period, age, sex, ethnicity, socioeconomic group, education level, occupation, trial group, clustering of practices and date of diabetes diagnosis

\*\*\* Refers to change in smoking status

Supplementary tables:

**Association between percentage weight change category in the first year after diagnosis, and the risk of remission at five-years in the ADDITION-Cambridge study amongst participants with HbA1c > 6.5**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | % weight change category | n | risk ratio | 95% CI | | P-value |
| unadjusted | no change (±2.5% change from baseline) | 561 | 1 |  |  |  |
| weight gain (≥2.5%) | 0.67 | 0.39 | 1.13 | 0.13 |
| weight loss >2.5-<5% | 0.93 | 0.57 | 1.53 | 0.78 |
| weight loss ≥5-<10% | 1.49 | 0.96 | 2.30 | 0.07 |
| weight loss ≥10% | 1.86 | 1.20 | 2.87 | 0.01 |
| adjusted model 1\* | no change (±2.5% change from baseline) | 429 | 1 |  |  |  |
| weight gain (≥2.5%) | 0.54 | 0.27 | 1.11 | 0.10 |
| weight loss >2.5-<5% | 0.89 | 0.53 | 1.43 | 0.60 |
| weight loss ≥5-<10% | 1.30 | 0.81 | 2.06 | 0.26 |
| weight loss ≥10% | 1.60 | 1.01 | 2.51 | 0.04 |
|  |  |  |  |  |  |  |
| adjusted model 2\*\* | no change (±2.5% change from baseline) | 413 | 1 |  |  |  |
| weight gain (≥2.5%) | 0.56 | 0.28 | 1.14 | 0.11 |
| weight loss >2.5-<5% | 0.88 | 0.53 | 1.44 | 0.59 |
| weight loss ≥5-<10% | 1.26 | 0.77 | 2.05 | 0.36 |
| weight loss ≥10% | 1.65 | 1.04 | 2.63 | 0.03 |

**Association between percentage weight change category between one to five years after diagnosis, and the risk of remission at five-years in the ADDITION-Cambridge study amongst participants with HbA1c > 6.5%**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | % weight change category | n | risk ratio | 95% CI | | P-value |
| unadjusted | no change (±2.5% change from baseline) | 561 | 1 |  |  |  |
| weight gain (≥2.5%) | 0.65 | 0.41 | 1.04 | 0.07 |
| weight loss >2.5-<5% | 1.69 | 1.04 | 2.74 | 0.03 |
| weight loss ≥5-<10% | 1.77 | 1.10 | 2.84 | 0.01 |
| weight loss ≥10% | 3.48 | 2.29 | 5.30 | <0.01 |
|  |  |  |  |  |  |  |
| adjusted model 1\* | no change (±2.5% change from baseline) | 429 |  |  |  |  |
| weight gain (≥2.5%) | 0.81 | 0.48 | 1.39 | 0.45 |
| weight loss >2.5-<5% | 1.76 | 1.06 | 2.93 | 0.03 |
| weight loss ≥5-<10% | 1.88 | 1.16 | 3.06 | 0.01 |
| weight loss ≥10% | 3.80 | 2.50 | 5.89 | <0.01 |
| adjusted model 2\*\* | no change (±2.5% change from baseline) | 413 |  |  |  |  |
| weight gain (≥2.5%) | 0.76 | 0.44 | 1.30 | 0.32 |
| weight loss >2.5-<5% | 1.91 | 1.14 | 3.22 | 0.02 |
| weight loss ≥5-<10% | 1.88 | 1.15 | 3.08 | 0.01 |
| weight loss ≥10% | 3.99 | 2.59 | 6.16 | <0.01 |