

Association between weight change and remission of type 2 diabetes: a retrospective cohort study in primary care

Short title: type 2 diabetes and remission

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Abstract:

Purpose: To quantify the association between weight change and the likelihood of remission of type 2 diabetes in a population-based cohort without intensive interventions.

Methods: A retrospective analysis of adults with type 2 diabetes registered across 150 primary care practices in Southern England, United Kingdom, within the Electronic Care and Health Information Analytics (CHIA) database between 2013 and 2020. Stepwise mixed logistic models were constructed to examine the association between percentage weight change over five-years, and the likelihood of remission in the subsequent two years using four categories: weight gain $\geq 2.5\%$; weight loss $\leq 2.5-5\%$ or $\leq 5-10\%$ or $\geq 10\%$.

Results: The study cohort included 56,120 people with type 2 diabetes with a mean (SD) disease duration of 8.0 (6.7) years. 17,035 (30.4%) had microvascular complications and 10,661 (19.0%) had macrovascular complications. A total of 19.4% (10,896) lost $\geq 10\%$ of their baseline weight with 1646 (15.1%) of these achieving remission. Overall, those who lost $\geq 10\%$ in weight had a significantly higher likelihood of remission in both unadjusted and adjusted models; RR: 1.53 (95% CI: 1.40-1.68); and RR:1.51 (95% CI: 1.37-1.66), respectively. Remission was still achievable but less likely amongst younger men with a longer diabetes duration (< 5 years), higher baseline HbA_{1c} level, or pre-existing microvascular or macrovascular complications.

Conclusion: Weight loss of $>10\%$ is associated with remission of type 2 diabetes even amongst those with advanced disease and established microvascular or macrovascular complications. Our findings could motivate people with diabetes to lose weight in order to increase likelihood of remission.

Word count: 2842

Key words: primary care, type 2 diabetes, weight loss, remission

Key points

- Remission of type 2 diabetes has been shown to be associated with weight loss.
- Previous studies have assessed this in trial participants or cohort with newly diagnosed diabetes.
- We found that weight loss of >10% was associated with remission of type 2 diabetes, even in those with advanced disease with established microvascular or macrovascular complications.
- These findings were observed in a population-based cohort with previously diagnosed diabetes.
- Our findings inform clinical care by providing evidence to motivate people with diabetes to lose weight in order to increase likelihood of remission.

Abbreviations

CHIA - The Electronic Care and Health Information Analytics database

IMD- Index of Multiple Deprivation

QOF – Quality and Outcome Framework

UK – United Kingdom

US – United States

Introduction

Type 2 diabetes is a chronic progressive disease that has reached epidemic proportions affecting an estimated 400 million people globally, and predicted to reach 628 million by 2045.[1] The disease is associated with high rates of morbidity including microvascular complications, macrovascular complications and excess risk of premature death. [1] Biochemical remission of the disease has been shown to be

achievable, and is defined as a level of glycaemia below a diagnostic threshold ($\text{HbA}_{1c} < 6.5\%$ or 48 mmol/mol) in the absence of pharmacological or surgical intervention.[2–4] Previous trial evidence has demonstrated that remission can be achieved through intensive diet and physical activity programmes including a low-calorie intake of $624\text{--}700 \text{ kcal/day}$ over 8 weeks [3]; group and individual counselling sessions with a calorie goal of $1200\text{--}1800 \text{ kcal/day}$ with the use of meal-replacement products and at least 175 minutes of moderate-intensity physical activity per week [5]; and in the DIRECT trial a dietary replacement of $825\text{--}853 \text{ kcal/day}$ through a formula diet for 3–5 months, stepped food reintroduction (2–8 weeks), and structured support for long-term weight loss maintenance. [6] Studies outside of trial cohorts that are more representative of the wider diabetes population, and in the absence of intensive and expensive interventions have been limited. Moreover, these studies have examined short-term weight loss, rather than the impact or achievability of sustained weight loss. This has led to uncertainty about whether remission is a feasible clinical target and is important as glycaemia levels may increase if weight loss is not maintained.

We previously reported that remission can be achieved through weight loss as part of routine clinical care in 867 people within the follow-up phase of the ADDITION-Cambridge trial cohort which evaluated the effectiveness of a stepwise screening programme and intensive multifactorial treatment for people with newly diagnosed type 2 diabetes in primary care.[7,8] However, this was still a trial cohort and only examined those early in the course of diabetes with the sample including limited socioeconomic and ethnic diversity. Evidence from larger and more heterogenous population-based cohorts which long-term follow-up to assess the impact of sustained weight loss is necessary. This will allow understanding on whether remission is an achievable clinical target in the wider population. Moreover, examining the potential to achieve remission later on in the disease trajectory amongst those with advanced complications might offer motivation for people who have had diabetes for many years to lose weight. In this study, we quantified the association between weight change and the likelihood of achieving remission in a large population-based cohort with established type 2 diabetes receiving routine primary care, in the absence of intensive intervention.

Methods

Data source and population

The Electronic Care and Health Information Analytics (CHIA) database is a pseudo-anonymised live electronic database with routinely collected primary care records from approximately 1.5 million people who are registered across 150 primary care (GP) practices in Southern England, United Kingdom. The data includes linked records from primary care and surrounding local hospitals with anthropometric data (e.g; weight, height), biochemical measurements (e.g. HbA_{1c} , electrolytes, cholesterol), clinical diagnoses, outcomes and investigations (e.g. stroke, heart attack, hospital admissions, death) which is available for extraction at 6-monthly intervals with longitudinal follow-up. We identified a cohort of 60 715 adults (aged between 18–84 years) who had a clinical code for type 2 diabetes based on the UK's Quality and Outcomes

Framework (QOF) register and who also had continuously recorded electronic records over seven years from the 1st January 2013 to 1st April 2020 (or until death).[9]

Study exposure: weight change

We examined total percentage weight change between baseline and five-year follow-up in categories as follows: no weight change as a reference category ($\pm 2.5\%$), and then weight gain ($\geq 2.5\%$); or weight loss ($\leq 2.5-5\%$), ($\leq 5-10\%$) and ($\geq 10\%$) We used these weight change categories in line with previous studies on remission (to allow comparison), and also because a recent study shows that weight change categories are a more robust measure than average continuous weight measures in epidemiology modelling.[10]

Study outcome: remission

Remission was the outcome of interest within the last two years of follow-up (i.e. year five to year seven) and had to be achieved for at least 6 months. Although there are varying definitions of remission in the literature, we used the UK and US national guidance which is an HbA_{1c} level < 48 mmol/mol (6.5%) in the absence of diabetes medication or bariatric surgery. [2] Remission status was assessed for those alive at the end of the follow-up period (i.e. end of year seven).

Covariates

Baseline measurements were extracted at the start of the study between 1st January 2013 - 1st April 2013. Sociodemographic data included age, sex, ethnicity (White, Black, Asian, Mixed and other) and socioeconomic status. This was defined with the 2019 Index of Multiple Deprivation (IMD) quintiles. IMD 1 represents the most deprived and IMD 5 represents the least deprived groups. Baseline comorbidities were defined from the diagnostic codes of existing QOF conditions and included coronary heart disease, chronic kidney disease, chronic obstructive pulmonary disease (COPD), asthma, cancer, dementia, atrial fibrillation, epilepsy, heart failure, stroke, peripheral vascular disease, hypertension, osteoporosis, osteoarthritis, and depression. We used QOF conditions as these codes are used for National Health Service administration and payment purposes which have high levels of completeness and accuracy.[11] We also included frailty which refers to a state of increased vulnerability due to age-related decline in reserve and function, and the ability to cope with daily or acute stressors. This was using the Electronic Frailty Index score.[12] The score runs from 0 to 0.36, and a higher score indicates increasing frailty. The last recorded smoking status code was categorised as non-smoker, ex-smoker or current smoker. Measurements of weight, body mass index (BMI), systolic blood pressure, diastolic blood pressure, glycated haemoglobin (HbA_{1c}), total cholesterol, HDL-cholesterol and eGFR recordings were also extracted. For medications, we looked at repeat prescriptions in the first six months of the study as a baseline measurement, and then at every 6-month interval for the duration of the study period.

Statistical Analysis

We used descriptive statistics to summarise baseline sociodemographic characteristics. Where data were missing for HbA_{1c}, baseline weight, and IMD (which is common for routinely collected primary care records); we assumed missing at random and imputed these in a model that included age, sex, diabetes duration, total number of comorbidities at baseline, practice ID, and outcome variables. Data were multiply imputed using chained equations using STATA SE 16.0 (Stata Corp, College Station, TX, USA). We used 10 cycles of imputation. We then fitted logistic regression models in the imputed dataset to quantify the association between percentage weight change from baseline and five-year follow-up, and the likelihood of achieving remission in the subsequent two years of the study (year five to year seven) using four categories: no weight change (reference category as $\pm 2.5\%$); weight gain ($\geq 2.5\%$); ≤ 2.5 –5% weight loss; ≤ 5 –10% weight loss; and $\geq 10\%$ weight loss. We ran unadjusted and adjusted models based on *a priori* reasoning. Model 1 included baseline weight and sociodemographic variables (age, sex, ethnicity and IMD). Model 2 additionally included diabetes duration, number of co-morbidities. Model 3 additionally included clustering within practices. We then carried out subgroup analyses for weight loss and remission stratified by diabetes duration, level of HbA_{1c} and the presence of pre-existing microvascular or macrovascular complications. This was to explore the possibility that remission might be more likely if i) starting at a lower HbA_{1c} level at baseline, ii) shorter diabetes duration or iii) fewer pre-existing complications. We also explore associations using weight change as a continuous variable. Findings are reported as per STROBE and RECORD guidelines for observational studies of routinely collected data.

Results

Cohort characteristics

The study cohort included 56,120 people with type 2 diabetes with a mean (SD) disease duration of 8.0 (6.7) years. The mean duration of follow-up was 6.8 (1.3) years. The mean age of the cohort was 63.9 (11.9) years, most were male 31,980 (57.0%) and white 54,006 (96.2%). Many had previously diagnosed diabetes with 10,661 (19.0%) having macrovascular complications including stroke, MI or amputation, and 17,035 (30.4%) having microvascular complications including peripheral neuropathy, retinopathy, and nephropathy. Baseline characteristics are summarised in Table 1, stratified by remission status. Remission was achieved by 6,561 (11.7%) in the last two years of follow-up. Those who achieved remission were slightly older, had a shorter duration of diabetes, a higher proportion were female and more likely to be living in the least deprived area.

Weight change and remission of type 2 diabetes

Between baseline and five years, 22.4% (n=12,559) of those alive showed no change in weight, 8.3% (4,631) gained $\geq 10\%$ and 19.4% (10,896) lost $\geq 10\%$ of their baseline weight. 15.1% (1646) of those who lost $\geq 10\%$ of their baseline weight achieved remission (Table 2). People who lost $\geq 10\%$ weight had a significantly higher likelihood of achieving remission. This was observed in the unadjusted and adjusted models (unadjusted RR: 1.53 (95% CI: 1.40-1.68); maximally adjusted RR: 1.51 (95% CI: 1.37-1.66).

These results are summarised in Table 2 and Figure 1 below. A 1kg increase in weight (using weight change as a continuous measure) was also associated with lower risk remission (unadjusted RR: 0.99 (0.98-0.99); adjusted RR: 0.99 (0.98-0.99)).

Other sociodemographic and clinical variables associated with remission

Within our models, we also observed that older age, female sex, lower baseline weight and fewer number of co-morbidities were significantly associated with the likelihood of achieving remission. These results are shown in Table 2. We additionally carried out *a priori* subgroup analysis by Hb_{A1c} levels which showed that those with higher Hb_{A1c} (>6.5%) at baseline had a lower likelihood of remission (maximally adjusted RR: 0.93 (95% CI: 0.53-1.61) for HbA1 > 6.5% compared to Hba1c <6.5%), although this was not statistically significant. People with a shorter diabetes duration (>5 years) were more likely to achieve remission than those with less than 5 years duration (RR: 1.15 (95% CI: 1.04-1.28). People with microvascular complications or macrovascular complications were less likely to achieve remission than those with no complications (RR: 0.78 (95% CI: 0.72-0.85)) and RR: 0.81 (95% CI: 0.73-0.91), respectively).

Discussion

Principal findings

In this population-based cohort of 56,120 people with type 2 diabetes, weight loss of more than 10% over five-years significantly increased the likelihood of achieving remission. These findings were observed in a cohort of people with type 2 diabetes in the community without intensive intervention who were followed up through routine primary care. Many were able to achieve remission even amongst those with diabetes for many years (average duration of 8.0 years), with co-morbidities and microvascular/macrovascular complications. After taking into account weight loss, remission was still achievable but less likely amongst younger males with a shorter duration of diabetes (<5 years), who had a higher baseline Hb_{A1c} and more diabetes complications. Our findings suggest that remission is a realistic clinical target at a population level and could offer motivation for people with diabetes to lose weight and increase likelihood of remission of the disease.

Strengths and limitations

A key strength of the study is the sample size of over 56,000 people with type 2 diabetes from a large geographical area across 150 GP practices in England. It includes longitudinal follow-up in which we examined five-year weight changes followed by two years to assess the outcome of interest. The patient data used was drawn from an established database (CHIA) with routine primary care records having previously been validated for quality and accuracy in coding of diagnosis and clinical measurements.[13] We additionally included Quality Outcome Framework measures which are used for financial and administrative reason thus further increasing the accuracy of our variables. As our sample is taken from routine clinical care outside of clinical trials, it is more representative and generalisable to the wider type 2

diabetes population. The cohort includes heterogeneity in sociodemographic and clinical characteristics including the severity of diabetes. However, we had limited ethnic diversity which reflects the local population. Further validation work will be needed to examine more ethnically diverse populations. Other limitations of our study include the possibility of residual confounding and we did carry out several hypothesis tests, so chance remains a plausible explanation for our findings. However, our findings were consistent across all models that we ran suggesting that chance is a less likely explanation. We looked at weight change over five years, and then remission in the subsequent two years for at least a six-month period. This allowed us to examine the impact of sustained weight loss rather than short-term fluctuating weight changes which most previous studies have assessed. It is possible that some people may have achieved remission before or after this two-year outcome period, and perhaps for a shorter duration which would not have been captured in our study. A possible limitation is that we were not able to control for any unobserved characteristics of people in the remission group that may have made them more able to achieve weight loss. Our data does not tell us why weight loss was achieved or what lifestyle measures (dietary changes or physical activity), if any, were undertaken. It is possible the related co-morbidities or worsening health in some individuals could have unintentionally lead to both weight change and remission.[14] This is likely to account for a small number of individuals rather than the 11.7% (n=6561) people who achieved remission. Our results may not be applicable to other forms of diabetes (such as monogenic or autoimmune diabetes) that are very infrequent or inadequately captured in primary care data. Finally, we included within the cohort only those within the database who had a continuous seven-year follow-up in the electronic records. People who are disengaged or non-attenders who may have worse clinical parameters and are less likely to achieve remission will not have been captured in this study.

Comparison to existing literature

Our findings are consistent with previous work in which we showed that weight loss is associated with an increased likelihood of remission. [7] However, rather than examining a cohort with newly diagnosed type 2 diabetes, we now show that remission is achievable in those who have previously-diagnosed disease including people with co-morbidities, microvascular complications (19.0%) and macrovascular complications (30.4%). We provide longitudinal follow-up over seven years in a large sample. This extended follow-up is important as a recent (2019) position statement from the joint Association of British Clinical Diabetologists and the Primary Care Diabetes Society supporting remission as a target in diabetes through weight loss emphasised the need for more studies with long-term follow-up.[15] This is because previous works have been limited in duration which may not take into account weight that could be regained over longer periods. We were able to look at sustained weight change. We also show that weight loss of 10% is associated with remission which is a more modest target than has been shown in clinical trials of remission previously.[4,16] We report these findings from a population-based cohort who were followed up in routine primary care without intensive or expensive weight-loss interventions. Previous studies examining weight change and remission have included interventions with restrictive calorie intake and intensive physical activity programmes over short follow-up periods that may not be sustainable or scalable to wider

populations. [3,5,6] These trial cohorts have additionally included limited heterogeneity in terms of age and disease severity. We report that certain sociodemographic and clinical characteristics are significantly associated with the likelihood of achieving remission which might explain the range of weight change levels and remission results that have been reported in the previous literature. [3,5] Our findings suggest after taking into account weight change, age, sex, diabetes duration, co-morbidities and pre-existing diabetes complications alongside weight loss could determine the likelihood of remission. In our cohort, females were more likely than men to achieve remission. This finding is consistent with previous studies and may be due to greater motivation in females to lose weight as a result of greater dissatisfaction with weight, stronger preference for lower fat diet, and societal pressure for them to be slim. [17,18] Older people and those with fewer comorbidities were also more likely to achieve remission. It is possible some weight loss in older people (particularly those aged >65 years) was unintentional. Another explanation may be greater adherence to weight loss plans, which may be motivated by additional benefits of weight loss for comorbidities. [18,19,20] This is consistent with the positive association of number of comorbidities and remission observed in our cohort. This finding suggests the need for targeted interventions that are sensitised to preferences, attitudes, behaviours and needs of males and females as well as younger and older age groups. This might be useful in allowing greater personalisation and realistic goal setting for increasing likelihood of remission. It could inform the need for more intensive clinical and resource input amongst those who might find it harder to achieve remission.

Conclusions and implications

Remission is a realistic clinical target for people with type 2 diabetes who have achieved weight loss of >10%, even amongst those who have lived with the disease for many years and have established complications. This is achievable in the absence of intensive intervention but will be influenced by sociodemographic and clinical factors.

Data availability

We do not have governance permissions to share individual-level data on which these analyses were conducted since they derive from clinical record data. However, direct data requests can be made to the database (CHIA).

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Author contribution:

HDM designed the study, wrote the first draft of the paper, edited and contributed to subsequent versions. HH led the data analysis and revised the paper. AF contributed to the design the of study and revised the paper. BS contributed to the study design, provided advice on statistical methods and revised the paper.

Competing Interests:

None to declare.

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Ethical approval: CHIA is an anonymous National Health Service database and all individuals have consented for collection of their medical records for inclusion in the database. Ethical and governance approval for this study was obtained from the University of Southampton (ERGO 56127), and Care and Health Information Exchange Information Governance Group (CHIE IGG).

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362 **Table 1. Baseline characteristics of the type 2 diabetes CHIA cohort stratified by remission**
363 **status****

		All (n=56120)		Remission (n=6561)		Non- remission (n=49559)
	<i>n</i>		<i>n</i>		<i>n</i>	
Sociodemographic						
Age, years*	56120	63.9 (11.9)	6561	6.5 (11.4) ‡	49559	63.6 (11.9) ‡
Male gender, n(%)	56120	31980 (57.0)		3471 (52.9)	49559	28508 (57.5)
Ethnicity, n(%)	56120		6561		49559	
White		54006 (96.2)		6385 (97.3)		47621 (96.1)
Black		215 (0.4)		22 (0.3)		193 (0.4)
Asian		1494 (2.7)		119 (1.8)		1375 (2.8)
Mixed/Other		405 (0.7)		35 (0.5)		370 (0.7)
Index of Multiple Deprivation, n(%) ‡	56120		6561		49559	
quintile 1 (most deprived)		6886 (12.3)		708 (10.8)		6179 (12.5)
quintile 2		11285 (20.1)		1296 (19.7)		9989 (20.2)
quintile 3		10600 (18.9)		1202 (18.3)		9398 (19.0)
quintile 4		12216 (21.8)		1463 (22.3)		10734 (21.7)
quintile 5 (least deprived)		15133 (27.0)		1893 (28.8)		13240 (26.7)
Clinical						
Diabetes duration, years	56003	8.0 (6.7)	6480	6.5 (5.7)	49366	8.2 (6.8)
Frailty Index	56077	0.2 (0.1)	6478	0.2 (0.1)	49438	0.2 (0.1)
Total number baseline comorbidities n(%)	56120	1.4 (1.2)	6561	1.6 (1.3)	49559	1.3 (1.2)
Hypertension, n (%)	56120	30868 (55.0)	6561	4105 (62.6)	49559	26763 (54.0)
Stroke n(%)	56120	2584 (4.6)	6561	400 (6.1)	49559	2184 (4.4)
Myocardial Infarction n (%)	56120	3632 (6.5)	6561	387 (5.9)	49559	3245 (6.5)
Amputation n(%)	56120	517 (0.9)	6561	46 (0.7)	49559	471 (0.9)
Microvascular complications	56120	17035 (30.4)	6561	1539 (23.5)	49559	15496 (31.3)
Macrovascular complications	56120	10661 (19.0)	6561	1341 (20.4)	49559	9320 (18.8)
Current smoker, n(%)	56120	6028 (10.7)	6561	691 (10.5)	49559	5337 (10.8)
Weight, kg**	56120	90.5 (19.6)	6561	89.0 (19.9)	49559	90.6 (19.6)
BMI, kg/m2*	56120	31.6 (6.3)	6561	31.4 (6.5)	49559	31.6 (6.3)
Systolic blood pressure, mmHg*	56120	136.2 (15.3)	6561	136.2 (15.4)	49559	136.2 (15.3)

Diastolic blood pressure, mmHg*	56120	77.4 (9.4)	6561	76.9 (9.3)	49559	77.5 (9.4)
Total cholesterol, mmol/l*	56120	4.6 (1.2)	6561	4.6 (1.2)	49559	4.6 (1.2)
HDL cholesterol, mmol/l*	56120	1.2 (0.4)	6561	1.3 (0.4)	49559	1.2 (0.4)
HbA1c level, mmol/mol**	56120	60.0 (20.4)	6561	59.5 (20.0)	49559	60.0 (20.4)
eGFR	56120	73.8 (16.5)	6561	72.6 (16.6)	49559	74.0 (16.5)
Total number of medications prescribed#	56120	3.9 (2.4)	6561	3.8 (2.4)	49559	3.9 (2.4)
Anti-hypertensive medication, n(%)	56120	29840 (53.2)	6561	3845 (58.6)	49559	25995 (52.5)
Lipid-lowering medication n(%)	56120	38266 (68.2)	6561	4375 (66.7)	49559	33891 (68.4)
Hypoglycaemic medication, n(%)	56120	38602 (68.8)	6561	3457 (52.7)	49559	35145 (70.9)

*Mean (SD). Remission was defined as having two HbA1c < 6.5% (48mmol/mol) over a minimum period of 6 months with no oral hypoglycaemics, and no history of bariatric surgery. *Estimation sample varies across imputations; estimations based on minimum number of observations.

#Medication was defined as being prescribed during the first 6 months of the follow-up year (i.e. Jan-Jul 2013). **Remission estimated for those alive in the last two years of the study period i.e. year 5-7(n=56,120)

##Unimputed data at baseline for weight and HbA1c were 22033 and 22581 , respectively.

Microvascular complications included a composite of peripheral neuropathy, retinopathy, and nephropathy.

Macrovascular complications include a composite of stroke, MI, coronary heart disease, peripheral arterial disease (PAD) and amputation.

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372 **Table 2. Weight change categories and remission group[‡]**

	Remission	No remission
	n (%)	n (%)
% Weight change category		
No change ($\pm 2.5\%$ from baseline)	1305 (10.4)	11254 (89.6)
Weight gain ($\geq 2.5\%$ to $< 5\%$)	483 (10.8)	3987 (89.2)
Weight gain (≥ 5 to $< 10\%$)	592 (10.7)	4924 (89.2)
Weight gain ($\geq 10\%$)	538 (11.6)	4093 (88.4)
Weight loss ($\geq 2.5\%$ to $< 5\%$)	726 (10.6)	6151 (89.4)
Weight loss (≥ 5 to $< 10\%$)	1271 (11.4)	9900 (88.6)
Weight loss ($\geq 10\%$)	1646 (15.1)	9250 (84.9)

373 ***row percentages reported.** [‡]Estimation sample varies across imputations; estimations based on
374 minimum number of observations.

Table 3. Association between percentage weight change category and likelihood of remission**

	Unadjusted (n=56119)				Model 1 (n=56119)				Model 2 (n=56002)				Model 3 (n=56002)			
	Risk ratio	95% CI		p-value	Risk ratio	95% CI		p-value	Risk ratio	95% CI		p-value	Risk ratio	95% CI		p-value
% Weight change category																
No change ($\pm 2.5\%$ from baseline)	1.00				1.00				1.00				1.00			
Weight gain ($\geq 2.5\%$ to $< 5\%$)	1.04	0.91	1.20	0.539	1.05	0.91	1.20	0.514	1.05	0.91	1.20	0.500	1.05	0.91	1.20	0.510
Weight gain (≥ 5 to $< 10\%$)	1.04	0.90	1.19	0.610	1.05	0.91	1.21	0.486	1.05	0.91	1.21	0.508	1.05	0.91	1.21	0.511
Weight gain ($\geq 10\%$)	1.13	0.97	1.33	0.122	1.16	0.98	1.36	0.078	1.16	0.98	1.36	0.079	1.16	0.98	1.36	0.086
Weight loss ($\geq 2.5\%$ to $< 5\%$)	1.02	0.88	1.18	0.809	1.01	0.86	1.18	0.915	1.01	0.86	1.17	0.922	1.01	0.87	1.17	0.920
Weight loss (≥ 5 to $< 10\%$)	1.11	0.97	1.26	0.118	1.09	0.95	1.24	0.205	1.09	0.96	1.24	0.192	1.09	0.96	1.24	0.189
Weight loss ($\geq 10\%$)	1.53	1.40	1.68	< 0.001	1.46	1.33	1.60	< 0.001	1.51	1.38	1.65	< 0.001	1.51	1.37	1.66	< 0.001
Baseline weight					1.00	1.00	1.00	0.513	1.00	1.00	1.00	0.013	1.00	1.00	1.00	0.016
Diabetes duration									0.94	0.93	0.95	< 0.001	0.94	0.93	0.95	< 0.001
Total number comorbidities									1.15	1.12	1.18	< 0.001	1.15	1.12	1.18	< 0.001
Age					1.02	1.02	1.02	< 0.001	1.02	1.02	1.02	< 0.001	1.02	1.02	1.02	< 0.001
Sex					0.87	0.81	0.94	< 0.001	0.90	0.84	0.96	0.003	0.90	0.84	0.97	0.004
Ethnicity																
White																
Black					0.95	0.56	1.62	0.850	0.97	0.56	1.66	0.901	0.97	0.58	1.62	0.896
Asian					0.73	0.59	0.90	0.004	0.74	0.60	0.91	0.005	0.74	0.57	0.95	0.021
Mixed/ Other					0.78	0.51	1.17	0.225	0.82	0.54	1.24	0.346	0.82	0.54	1.24	0.345
IMD																
Q1 (Most deprived)																
Q2					1.10	0.98	1.22	0.103	1.10	0.99	1.23	0.086	1.10	0.98	1.24	0.117
Q3					1.05	0.94	1.18	0.388	1.08	0.96	1.21	0.221	1.08	0.94	1.23	0.284
Q4					1.11	0.98	1.24	0.095	1.12	1.00	1.27	0.056	1.12	0.98	1.29	0.090
Q5 (Least deprived)					1.15	1.03	1.28	0.010	1.18	1.06	1.31	0.003	1.18	1.03	1.34	0.016

*Model 1 adjusted for baseline weight and sociodemographic variables (age, sex, ethnicity and IMD).

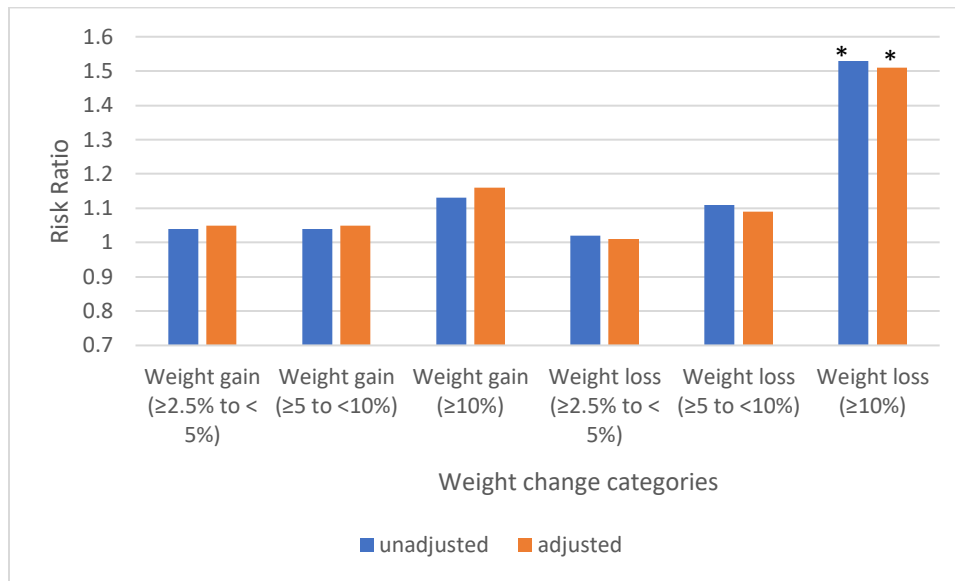
*Model 2 adjusted for baseline weight, sociodemographic variables, diabetes duration, number of co-morbidities.

#Model 3 adjusted for baseline weight, sociodemographic variables, diabetes duration, number of co-morbidities and clustering within practices.

**Weight change estimated between baseline and 5-year follow-up. Remission estimated for those alive in the last two years of the study period from year 5 to year 7 (n=56,120)

*Estimation sample varies across imputations; estimations based on minimum number of observations.

Figure 1. Relative Risks of resmission by weight change category



***statistically significant**

****Reference weight change category= No change ($\pm 2.5\%$ from baseline)**