The effect of non-surgical weight management on weight and glycaemic control in people with type 2 diabetes: a comparison of interventional and non-interventional outcomes at three years

Shani Botha, PhD, Faculty of Health Sciences, North-West University, Potchefstroom, South Africa

Lorna Forde, BSc, NHS Greater Glasgow and Clyde, Glasgow, UK

Sheila MacNaughton, BSc, NHS Greater Glasgow and Clyde, Glasgow, UK

Ross Shearer, DClinPsy NHS Greater Glasgow and Clyde, Glasgow, UK

Robert Lindsay, PhD, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK

Naveed Sattar, PhD, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK

David Morrison, PhD, Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

Paul Welsh*, PhD, Institute of Cardiovascular and Medical Sciences, University of Glasgow, UK

Jennifer Logue*, MD, Institute of Cardiovascular and Medical Sciences, University of Glasgow, UK

*Joint Senior Authors

Corresponding Author

Dr Jennifer Logue

Institute of Cardiovascular and Medical Sciences

University of Glasgow, 126 University Place, Glasgow, UK, G12 0QH

jennifer.logue@glasgow.ac.uk

Abstract

Background

Lifestyle weight management interventions are recommended in clinical guidelines for patients with type 2 diabetes and obesity, but lack evidence regarding their long term effectiveness.

Materials and Methods

Electronic health records were used to follow 23,208 patients with type 2 diabetes and obesity in Glasgow, Scotland, for up to 3 years between 2005 and 2014. Patients were stratified by referral to and attendance at a lifestyle weight management intervention, and by attainment of a target weight loss of ≥5kg over 7-9 sessions ("successful completers"). Outcomes were change in weight, HbA1c, and diabetes medications.

Results

3471 potentially eligible patients were referred to the service, and less than half of those attended (n=1537). Of those who attended 7-9 sessions, >40% successfully completed with a 5kg weight loss (334/808). Successful completers maintained greater weight loss (change at 3 years -8.03kg; 95%CI -9.44;-6.62) than the non-completers (-3.26kg; 95%CI; -4.01;-2.51; $p<0.001$) and those not referred to the service (-1.00kg; 95%CI -1.15;-0.85; $p<0.001$). Successful completers were the only patient group who did not increase their use of diabetes medication and insulin over 3 years. In adjusted models, successful completers had a clinically significant reduction in HbA1c ((-3.7mmol/mol; 95%CI -5.82;-1.51) after 3 years; $p\leq0.001$) compared to non-completers and unsuccessful completers.

Conclusions

A real-life structured weight management intervention in patients with diabetes can reduce weight in the medium term, result in improved glycaemic control with fewer medications, and may be more effective than pharmacological alternatives. Challenges include getting a higher proportion of patients referred to and engaged with interventions.

250 words

Introduction

Obesity is a major risk factor for type 2 diabetes[1] and consequently the majority of adults with type 2 diabetes (T2DM) in Scotland have a body mass index (BMI) greater than 30kg/m^2[2]. The risk of mortality in patients with type 2 diabetes increases with increasing BMI above 30kg/m^2[3–5]. International diabetes guidelines recommend that weight loss interventions should be prescribed to patients with coexisting type 2 diabetes and obesity, aiming for an initial 5-10% (typically a 5-10kg) weight loss[6–8]. However there are barriers to implementing this guidance in practice , including a lack of funded services[9–11].

A lack of an evidence base for the longer term clinical outcomes of non-surgical weight management in type 2 diabetes is a major barrier to both the public and insurance-based funding of suitable services[11,12]. The LookAHEAD[13] randomised controlled trial included 5145 participants with type 2 diabetes, who were assigned to an intensive lifestyle intervention or to three sessions of diabetes support and education. The intervention was far more intensive than support generally available to patients with type 2 diabetes in the community, and included near weekly individual or group sessions for a year, monthly sessions for the subsequent four years, along with optional meal replacements and a focus on high levels of supported physical activity. The results were impressive with an 8.5% weight loss and 7mmol/mol reduction in HbA1c after one year, attenuating to 4.7% and 2mmol/mol after four years[13]. However, selection bias is a potential issue for such an intensive trial with an entry criterion that included the ability to perform an exercise test; this may have resulted in a healthier and more adherent cohort than is seen in routine clinical care.

There is therefore an urgent need to improve the evidence base for the longer term clinical outcomes of real-life non-surgical lifestyle weight management interventions in patients with type 2 diabetes. Evaluations of existing services[14–18] have shown modest results with a minority of patients achieving clinically significant short term weight loss. However, these interventions are low cost and low risk, with negligible ongoing costs if non-responding patients discontinue. It follows that if these interventions are effective in improving clinical outcomes in type 2 diabetes for those that do

successfully lose weight, then they should become a much greater part of usual care with investment in research to improve uptake and success.

This study will answer the questions 1) whether a sustainable non-surgical weight management intervention helps patients achieve a long term 5-10% weight loss and 2) whether such weight loss improves glycaemic control and 3) whether such weight loss reduces anti-glycaemic medication use. The clinical outcomes from non-surgical weight management in the general diabetes patient population will be established by utilising data from a large multi-disciplinary weight management programme and routine diabetes care records. The use of routine data allows efficacy for longer term clinical outcomes to be established beyond the length of the weight management intervention, including the effect on glycaemic control and medication usage, while highlighting the important issues of uptake and adherence.

Methods

The National Health Service Greater Glasgow and Clyde (NHS GGC) health board area, Scotland, covers a population of almost 1.15 million people. A cohort of all patients who resided in NHS GGC and had type 2 diabetes was created from routine diabetes patient care records (Scottish Care Information Diabetes Collaboration [SCI-Diabetes]). SCI-Diabetes is a Scottish population-based clinical information system, containing demographic and clinical data from patients that have been diagnosed with diabetes. This register includes data from all but five of over 1000 general practices in Scotland and was shown to detect 99.4% of patients with diabetes in Scotland.

These diabetes data were then combined with patients' records from NHS GGC Weight Management Service (GCWMS), using the Community Health Index (CHI) number. The CHI number is unique to each individual patient and used for every healthcare interaction, allowing record linkage. As a result, clinical data for weight management in patients with type 2 diabetes were generated alongside a cohort of all patients with type 2 diabetes who lived within the GCWMS catchment area but had not been referred to the service. Data were accessed via the NHS Greater Glasgow and Clyde Safe Haven which allowed access to data, with patient identifiers removed, via a virtual private network. NHS

GGC Safe Haven acts as the Local Privacy Advisory and ethical review committee for this research and granted ethical approval and data access for this study.

The GCWMS intervention, which was developed in 2004, is a time-limited structured educational lifestyle programme employing cognitive behavioural therapy techniques alongside a 600 kcal deficit diet and physical activity advice for patients with complex obesity that are 18 years or older[19]. It is delivered as part of the National Health Service and is free of charge to all patients with type 2 diabetes, a BMI $\geq$30kg/m^2 and who reside in the health board area. Referrals to GCWMS are made by general practitioners or hospital doctors, providing patients with the choice to opt-in (by telephoning the service) to be assessed and thereafter to attend the first session. Records of each assessment and visit are kept electronically, linked by the patient's CHI number, thereby minimising missing data. Phase 1 of the intervention includes nine 90 min sessions delivered fortnightly over a 16-week period in groups of up to 16 participants. It is delivered in a range of hospital and community venues. Upon completion of phase 1, patients can choose to enter phase 2, which consists of four 1-h group sessions delivered at monthly intervals and includes a range of treatment options including further lifestyle advice or a prescribed structured low-calorie diet or pharmacotherapy (orlistat). At the end of phase 2, or directly from the end of phase 1, dependent on patient choice, patients enter a weight maintenance programme (phase 3) comprising 12 1-h group sessions delivered at monthly intervals. Patients who fail to achieve the target weight loss of 5kg can choose to repeat phase 2 once more and then enter the maintenance programme. If patients fail to lose 5kg, and have a BMI $\geq$40kg/m^2 or a BMI $\geq$35kg/m^2 with comorbidities, they can opt to be considered for bariatric surgery. Overall the complete programme represents 43 hours of contact time with a dietician, delivered in groups of 12. Participants are regrouped each phase to account for drop-outs and the programme therefore totals 3.6h of dietician contact time per participant.

Data handling

Data handling and exclusions are summarised in figure 1. All biochemical data were measured by routine NHS clinical laboratories. Where multiple values were recorded within a specific time window, the chronologically earliest was used. For those who were referred, if no weight data were

recorded for a specific session, it was regarded as "not attended" for that session. Specific details on data handling for patients referred to, and those not referred to GCWMS can be found in supplementary material.

Group definitions in the patients referred to GCWMS

Those who attended at least one session were labelled "attenders" (Fig 1). Attenders were further divided into "non-completers" (those who attended 1-6 sessions within phase 1) and "completers" (those who attended at least 7/9 [80%] of the sessions within phase 1). We classified "unsuccessful completers" as those who attended at least 80% of sessions, but did not lose 5kg (this was the definition used within the service and therefore affected the subsequent intervention), while "successful completers" attended at least 80% of sessions and achieved at least 5kg weight loss by the end of Phase 1.

Statistical analyses

We compared reported means and standard deviations (for Gaussian variables), medians and inter-quartile ranges (for non-Gaussian continuous variables), and proportions where appropriate. We conducted tests of the null hypothesis between groups with independent t-tests, ranks sum tests, and $\chi 2$ tests, respectively. Differences in continuous variables across time were assessed by taking the difference in individual measurements and conducting a one sample t-test. Difference in insulin use was defined as the net change in the proportion using insulin at different time-points. Weight loss targets are often set at 5% (instead of 5kg in GCWMS). Thus, for the sake of comparability, we additionally used a cut point of 5% of initial weight and reported three-year change in HbA1c in these groups, thereby exploring the independent effect of the intention to treat in the GCWMS programme on glycaemic control.

To assess the effectiveness of successful completion of the GCWMS programme on clinical outcomes, we further performed a multivariable linear regression analysis with successful completion (non- and unsuccessful completers vs successful completers) as the predictor variable and either weight, HbA1c or unique diabetes medications used at each time point, as the outcome variable, with

adjustment for potential confounding variables. Similarly, logistic regression was conducted with insulin use as the outcome.

A value of $p \leq 0.05$ was considered statistically significant. The method of analysis and reporting is specified in the footnote of each table. All data handling and analyses were performed using Stata®SE v12.1 (Stata Corporation) and IBM® SPSS® Statistics v22 (IBM Corporation) statistical software packages.

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Data sharing: the data used for this study are available to bona fide researchers via NHS Greater Glasgow and Clyde Safe Haven (http://www.nhsggc.org.uk/about-us/professional-support-sites/nhsggc-safe-haven/)

Results

Baseline characteristics by GCWMS status

We identified 23,208 patients with type 2 diabetes and co-existent obesity, with the required routine data for inclusion, residing in the Greater Glasgow and Clyde Health Board area of Scotland, and all potentially eligible to attend GCWMS. In total, 3471 were referred to the service, and of these 1537 attended at least one session (44.3%), with 808 (23.3%) attending ≥7 sessions ("completers"). Of these, 336 patients ("successful completers") went on to lose 5kg in phase one of the programme (9.7% of all those referred) (Fig 1).

The baseline characteristics of 19,737 patients who were not referred to GCWMS, and 3471 who were referred and attended the service are shown in table 1. Those referred and attending were generally slightly younger and were more likely to be female, white, and were less likely to be socioeconomically deprived (with 14.8% being in the least deprived quintile (Q5) of SIMD compared to 12.1% of those not referred). The BMI of those who were referred and attended was higher than those not referred (medians 38.5 vs 33.9kg/m2) with 56.8% of those referred and attaining having a BMI ≥40kg/m^2. Among those referred, glycaemic control was poorer than among those not referred

(HbA1c median 57 vs 56 mmol/mol), reflecting a greater duration of diabetes, and a higher number of unique diabetes medications (mean and standard deviation 1.5 ± 1.1 vs 1.3 ± 1.0), although insulin use was similar.

Those attending the service were categorised as completers if they completed ≥80% of lifestyle sessions and success is defined as 5kg weight loss by the end of the lifestyle phase. Of those referred and attending, 808/1537 (56.6%) completed the lifestyle phase, with 334/808 (41.3%) of completers (21.7% of those referred and attending) being defined as successful (table 2). The only significant difference between those individuals successfully completing compared to those that were unsuccessful completers, was a higher initial weight in those who were successful (116.6kg ±24.8 vs 113.2kg ±23.1; p=0.045).

Changes in clinical variables over follow-up by GCWMS status

All comparator groups lost weight within the first year but successful completers had the greatest weight loss after one year (-8.66 kg, 95% CI -9.59 to -7.74) and maintained this weight loss with weight change at year three, relative to baseline, of -8.03kg (95% CI -9.44 to -6.62) (Table 3, Fig 2).

Successful completers improved their glycaemic control in comparison to the other groups over the 3 years (Table 3, Fig 2). HbA1c decreased the most compared to baseline after one year in the successful completers (-7.19mmol/mol, 95% CI -8.83 to -5.55). Non-completers had an increased HbA1c after 3 years when compared to baseline (2.02mmol/mol [95% CI 0.40 to 3.63]), and those not referred to GCWMS also had a slight increase in HbA1c (0.35mmol/mol [95% CI 0.10 to 0.59]). By contrast, HbA1c in successful and unsuccessful completers was comparable to baseline at 3 years.

The number of unique diabetes medications used increased gradually over three years in every group except successful completers (Table 3, Supp fig 1). For example, at year 3 those not referred had an increased mean number of unique diabetes medications (0.33 [95% CI 0.32 to 0.34]), as did unsuccessful completers (0.39 [95% CI 0.29 to 0.48]), yet successful completers had no change in the number of unique diabetes medications (0.04 [95% CI -0.07 to 0.14]). In general, the trend was

towards an increasing use of insulin over time in most groups, but insulin use did not change over 3 years of follow-up in the successful completers (Table 3; Fig 3).

The effect of attending the GCWMS programme and successfully losing 5kg, compared to non-completers and unsuccessful completers, adjusted for age, sex, ethnicity, SIMD, time since type 2 diabetes diagnosis, baseline HbA1c, weight, BMI, diabetes medication use and insulin use, is shown in table 4. Successful attenders in GCWMS had a number of metabolic and clinical benefits over 3 years, including greater sustained weight loss, a greater improvement in glycaemic control, and use of fewer diabetes medications compared to non-completers and unsuccessful completers. Those who lost 5kg in GCWMS were >50% less likely to have been prescribed insulin at 1 and 2 years, although the effect was not significant at 3 years. Similar results were seen for the prescription of dipeptidyl peptidase-4 inhibitors and glucagon-like peptide-1 receptor agonists, with successful completers around 50% less likely to have been prescribed these medications at 3 years compared to unsuccessful and non-completers (supplement table 1).

In order to explore the GCWMS-specific effect of weight loss on HbA1c, the effect of 5% weight loss on change in HbA1c over 2 years, compared to baseline, was assessed within each of the GCWMS groups (not referred, non-completers and completers), adjusted for potential confounding variables (Table 5). The effect of 5% weight loss on change in HbA1c over 2 years was significant within each group but was largest in those who completed the programme (-2.49, 95%CI -3.53; -1.46; $p<0.001$). The test for interaction comparing the effect of weight loss on HbA1c across groups was highly significant ($p<0.001$).

Time spent in the weight management programme and changes in weight in both phase 1 and the whole programme, by completion status is shown in Table 6. Those who successfully completed phase 1 eventually spend 11.9 months (IQR 7.1-17.3) in the programme and lost an average of 9.9kg ±8.24kg by their final visit.

Discussion

In this large study of patients with type 2 diabetes and obesity, using a real world data from a sustainable structured weight management intervention, we show those who attend and lose at least 5kg in the first 16 weeks maintain that weight loss over 3 years. Patients who successfully lose 5kg in the programme also have an independent, clinically significant, reduction in HbA1c (6.6, 5.7, and 3.7mmol/mol at year 1, year 2, and year 3, respectively) compared to non-attenders and unsuccessful attenders. Successful completers of the weight management programme have a reduction in number of diabetes medications and less of them progress to requiring insulin. However, only a small number of potentially eligible patients were referred, and less than half of those referred actually attended the service. Of those who attended ≥7 sessions, >40% achieved a 5kg weight loss. This research shows that a structured weight management programme can be clinically effective for at least some patients with type 2 diabetes; the main challenge is getting a higher number of patients referred to and engaging with intervention programmes.

Those patients who successfully lost 5kg in the first 16 weeks of the programme went on to attend for an average of 11.9 months. This is likely related to the large weight loss and successful weight maintenance in that group and is supportive of current guidelines that recommend that patients receive monthly counselling for at least 1 year in order to better maintain weight loss[20]. The effects of weight loss on glycaemic control that we have found are very similar to those found by the NIH funded LookAHEAD study[13]. There are large differences between our study and LookAHEAD: the lookAHEAD intervention was far more intensive, it included supervised exercise and meal replacements, and the population included volunteer participants in a clinical trial. This is in contrast with real world data from a completely free of charge weight management programme which may be a better representation of the general diabetes population. For those reasons LookAHEAD achieved weight loss in a far higher proportion of their participants, yet their results of weight loss on HbA1c were very similar with a change of -7mmol/mol at year 1, attenuating to -2.8mmol/mol by year 3[13] compared to our -7.19mmol/mol at year 1 and -1.86mmol/mol by year 3. A recent small study based on real-life clinic data from Boston, USA, also showed similar results of attenuation of HbA1c reduction over time despite maintenance of weight loss[22]. The mechanisms of this attenuation in

HbA1c are unknown and possible explanations include improved medication adherence during the intervention period that decreases with time, or a difference in the metabolic response to acute weight loss as opposed to the maintenance of lower weight in the longer term. What also remains unknown is the effect of this albeit temporary reduction in HbA1c on glucose-related diabetes end-points such as retinopathy, nephropathy and neuropathy, and also on the future trajectory of glycaemic control compared to those who did not lose weight. If improved glycaemic control can be achieved against a background of less prescribed medication in those who lose weight, then that alone suggests that weight management interventions may be very cost-effective in patients with type 2 diabetes.

. The obesity paradox is a phenomenon seen in observational studies whereby people with higher BMI experience better health outcomes compared to those with a BMI within the normal range (20-25kg/m^2). The obesity paradox has been described in a range of disease states including type 2 diabetes[23]. Non-intentional weight loss is often cited as a potential source of bias in such analyses; that is, body mass being lower due to weight loss associated with a life-limiting illness or, as in the case of diabetes, weight loss due to poor glycaemic control. Our dataset allowed us to explore assumed intentionality of weight loss and its effect on HbA1c and we found that 5% weight loss in those who attended weight management (and therefore assumed to be intentional weight loss) results in a greater reduction in HbA1c than 5% weight loss in the general population with type 2 diabetes and co-existing obesity. This may be due to non-intentional weight loss as a result of a disease-state or poor glycaemic control in the general population, or a wider behavioural effect of the weight management programme on medication adherence.

While the patients who successfully lost 5kg in the first 16 weeks of the weight management programme had weight loss maintenance and improvements in glycaemic control, they represent 41.3% of those completing the first part of the programme and 21.7% of those attending. 11.9% of the eligible population (5855 out of 49137) were referred to the weight management programme, with many of those referred not opting in for an appointment. Clearly there are major unsolved issues surrounding access to weight management programmes and having access to integrated health records from primary care, referral systems, and weight management programmes, which allows the full

details of these patterns to be seen; it should be remembered that those not attending are no longer an expense to the service. Given GCWMS is a NHS funded programme, free at the point of use and widely advertised to primary and secondary care clinicians, there is not the same level of commitment to the programme from all who are referred or start attending than would be the case in a more selective programme that required a specialist referral route or would cost the participant money. One advantage of this system is that our population is close to representative of the population of the local health board area which has high levels of socio-economic deprivation. However, even then there is an underrepresentation of men in the referred population and a higher non-completion rate from those who live in areas of higher socio-economic deprivation. This may be related to the structure of the programme, location and access; this is an issue across all weight management programmes and an area for the focus of future research. There is little published research with which to compare our research for attendance and completion as the majority of published literature is from either research-based interventions with selected volunteers, or real-world programmes that have little or no information on their eligible population or those who refused referral. Other UK based interventions make the best comparators due to the unique set-up of the National Health Service (NHS). Ahern et al[24] studied 29376 patients who were referred by NHS primary care in the UK to a 12 week programme of Weight Watchers, of whom 22519 were first-time referrals. 11851 (57%) completed the programme and 6755 (29.9%) lost ≥5% body weight. The diabetes status of these patients was not reported but it can be assumed to be far less than half with T2DM; patients with T2DM generally lose less weight with weight management interventions than those without[25,26]. There are many reasons why patients may not attend or complete weight management programmes which can include competing priorities like caring commitments and other health issues, or issues related to the programme such as venues that cannot be reached easily by public transport, or timings that exclude hours regularly accessible by those that work. Staff in primary care report a lack of confidence in raising the issue of obesity and weight management with their patients; the use of effective behaviour change techniques in this initial conversation may help improve attendance and completion rates[27,28]. Our own programme is undergoing review to ensure equality of access, educating clinicians about discussing obesity and making referrals, and greater use of local rather than central venues where

possible. We feel strongly that the fact that those who did lose weight maintained that weight loss and had clinically meaningful improvements in glycaemic control, shows the potential of weight management interventions in type 2 diabetes to improve clinical outcomes. Given this clinical potential, there is an urgent need for more research in this area to develop and deliver interventions that are accessible for all our patients.

Limitations

This study is based on data from electronic health records and therefore the major limiting issue is missing data. We applied strict criteria about the availability of key variables which would have been obtained through annual diabetes review, plus weight and age criteria to reduce the bias of misclassification of diabetes, and excluded 61.1% of those not referred to GCWMS and 40.7% of those who were referred. Given that missing data often is due to a missed annual diabetes review, and therefore adverse health behaviour, it may be that we biased the cohort towards a population with better overall diabetes management. It could be argued that this could affect the result in either direction due to better adherence to the intervention or a smaller potential for improvement in glycaemic control.

We have shown that patients with type 2 diabetes who attended a weight management programme and lost weight in a real-world setting have a subsequent improvement in glycaemic control over 3 years of follow-up. These results are from observation of a weight management intervention and the link between the intervention and the resultant clinical effect cannot be deemed to be causal. However the results are very close to those seen in a large randomised control trial of efficacy[13] and produce corresponding effectiveness data. While there are still remaining issues about access, attendance and adherence, weight management interventions have the potential to improve clinical outcomes for patients with type 2 diabetes and co-existent obesity, and we need to invest in interventions, evaluation and improvement to maximise this potential.

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Figures:

Figure 1. Data handling and classification of patients who were referred to the GCWMS.
GC&C, Greater Glasgow and Clyde area; GCWMS, Glasgow and Clyde Weight Management Service; BMI, body mass index; HbA1c, glycated haemoglobin.

Figure 2. Difference in a) mean weight, b) mean HbA1c, c) mean change in weight and d) mean change in HbA1c over time in patients diagnosed with type 2 diabetes and co-existent obesity in NHS Greater Glasgow and Clyde by referral and completion status in the Glasgow and Clyde Weight Management Service. HbA1c, glycated haemoglobin.

Figure 3. Absolute change in insulin use over time in patients diagnosed with type 2 diabetes and co-existent obesity in NHS Greater Glasgow and Clyde by referral and completion status in the Glasgow and Clyde Weight Management Service.

Supplemental figure 1. Mean number of unique diabetes medications prescribed to patients diagnosed with type 2 diabetes and co-existent obesity in NHS Greater Glasgow and Clyde by referral and completion status in the Glasgow and Clyde Weight Management Service.

Table 1 Characteristics of patients diagnosed with type 2 diabetes and co-existent obesity in NHS Greater Glasgow and Clyde by referral status in GCWMS

	Not referred to WMS (n=19737)	*Referred to and attended WMS (n=1537)*	*p-value*
Age, years	58.9 ± 9.8	57.4 ± 9.2	<0.001
Male sex	11,062 (56.1%)	638 (41.5%)	<0.001
Ethnicity, n(%)			<0.001
White (Scottish and other)	17,337 (88.9%)	1422 (94.7%)	
Other	2375 (12.1%)	80 (5.3%)	
SIMD score quintiles, *n* (%)			<0.001
Q1 Most deprived	8975 (45.6%)	617 (40.3%)	
Q2	3709 (18.9%)	263 (17.2%)	
Q3	2441 (12.4%)	241 (15.7%)	
Q4	2158 (11.0%)	184 (12.0%)	
Q5 Least deprived	2384 (12.1%)	227 (14.8%)	
Diabetes duration, years	3.7 (0.7-8.3)	5.3 (2.1-9.6)	<0.001
Initial weight, kg*	99.1 ± 15.3	113.5 ± 23.2	<0.001
Initial BMI, kg/m^2	33.9 (31.7-37.4)	40.2 (36.1-44.8)	<0.001
Initial BMI categories, *n* (%)			<0.001
30-34 kg/m^2	9991 (50.6%)	198 (12.9%)	
35-39 kg/m^2	6236 (31.6%)	465 (30.3%)	
40-49 kg/m^2	3166 (16.0%)	680 (44.2%)	
≥50 kg/m^2	344 (1.7%)	194 (12.6%)	
Systolic blood pressure, mmHg	136 ± 15	137 ± 14	0.62
HbA1c, mmol/mol	56 (48-68)	57 (49-73)	<0.001
Total cholesterol, mmol/L	4.58 ± 1.11	4.48 ± 1.04	<0.001
Triglycerides, mmol/L	2.0 (1.5-2.9)	2.0 (1.5-2.8)	0.038
HDL cholesterol, mmol/L	1.11 ± 0.29	1.12 ± 0.28	0.06
LDL cholesterol, mmol/L	2.47 ± 0.93	2.37 ± 0.88	0.002
Any insulin, *n* (%)	1744 (8.8%)	132 (8.6%)	0.74
Number of unique diabetes medications **	1 (0-2)	1 (1-2)	<0.001

GCWMS, Glasgow and Clyde Weight Management Service; SIMD, Scottish Index of Multiple Deprivation; BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
Values are n(%), mean (standard deviation), or median (interquartile range)
*Back calculated from BMI by using a constant height value.
**Number of unique diabetic medications taken from nine possible categories.

Table 2 Baseline characteristics of patients diagnosed with type 2 diabetes and co-existent obesity attending GCWMS by eventual completion status

	Non-completers (n=729)	*Completers (n=808)*		*p-value comparing unsuccessful and successful completers*
		Unsuccessful (n=474)	*Successful (n=334)*	
Age, years	56.8 ± 9.4	57.9 ± 9.1	58.2 ± 8.8	0.64
Male sex	283 (38.8%)	199 (42.0%)	156 (46.7%)	0.18
Ethnicity, n(%)				0.99
White (Scottish and other)	656 (92.3%)	452 (96.8%)	314 (96.9%)	
Other	55 (7.7%)	15 (3.2%)	10 (3.1%)	
SIMD score quintiles, *n* (%)				0.61
Q1 Most deprived	314 (43.3%)	180 (38.1%)	123 (36.8%)	
Q2	130 (17.9%)	78 (16.5%)	55 (16.5%)	
Q3	117 (16.1%)	75 (15.9%)	49 (14.7%)	
Q4	75 (10.3%)	67 (14.2%)	42 (12.6%)	
Q5 Least deprived	90 (12.4%)	72 (15.3%)	65 (19.5%)	
Diabetes duration, years	5.4 (2.2-9.7)	5.1 (2.2-9.5)	5.3 (2.1-9.6)	0.87
Initial weight, kg	112.3 ± 22.5*	113.2 ± 23.1	116.6 ± 24.8	0.045
Initial BMI, kg/m^2	40.1 (36.1-44.8)	39.9 (35.8-44.6)	40.7 (36.1-44.9)	0.099
Initial BMI categories, *n* (%)				0.13
30-34 kg/m^2	94 (12.9%)	71 (15.0%)	33 (9.9%)	
35-39 kg/m^2	222 (30.5%)	145 (30.6%)	98 (29.3%)	
40-49 kg/m^2	333 (45.7%)	196 (41.4%)	151 (45.2%)	
≥50 kg/m^2	80 (11.0%)	62 (13.1%)	52 (15.6%)	
Systolic blood pressure, mmHg	136 ± 13	137 ± 14	137 ± 15	0.94
HbA1c, mmol/mol	58 (48-75)	57 (50-73)	56 (49-68)	0.06
Total cholesterol, mmol/L	4.52 ± 1.06	4.47 ± 1.01	4.40 ± 1.03	0.39
Triglycerides, mmol/L	2.0 (1.5-2.8)	2.0 (1.5-2.8)	1.9 (1.4-2.5)	0.12
HDL cholesterol, mmol/L	1.11 ± 0.28	1.14 ± 0.29	1.12 ± 0.28	0.45
LDL cholesterol, mmol/L	2.38 ± 0.87	2.36 ± 0.91	2.36 ± 0.86	0.99
Any insulin, *n* (%)	66 (9.1%)	42 (8.9%)	24 (7.2%)	0.39

Number of unique diabetes medications **	1 (1-2)	1 (1-2)	1 (0-2)	0.11

GCWMS, Glasgow and Clyde Weight Management Service; SIMD, Scottish Index of Multiple Deprivation; BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Values are n(%), mean (standard deviation), or median (interquartile range)

*Back calculated from BMI by using a constant height value.

**Number of unique diabetic medications taken from nine possible categories.

Table 3 Changes in key variables (95% CI) over time in patients diagnosed with type 2 diabetes and co-existent obesity in NHS Greater Glasgow and Clyde by referral and completion status in GCWMS

	Not referred to GCWMS (n=19737)	*Referred to and attended GCWMS (n=1537)*			
		Total (n=*1537)*	*Non-completers* (n=*729)*	*Completers* (n=*808)*	
				Unsuccessful (n=*474)*	*Successful* (n=*334)*
Weight, kg					
1 year change	-0.57 (-0.68;-0.47)	-4.23 (-4.63;-3.83)	-2.74 (-3.26;-2.23)	-3.33 (-4.00;-2.67)	-8.66 (-9.59;-7.74)
n	*15310*	*1384*	*649*	*430*	*305*
2 year change	-0.70 (-0.83;-0.57)	-4.55 (-5.06;-4.03)	-3.03 (-3.83;-2.23)	-3.78 (-4.55;-3.01)	-8.78 (-9.87;-7.68)
n	*14390*	*1309*	*595*	*424*	*290*
3 year change	-1.00 (-1.15;-0.85)	-4.64 (-5.23;-4.05)	-3.26 (-4.01;-2.51)	-4.26 (-5.36;-3.16)	-8.03 (-9.44;-6.62)
n	*13083*	*1127*	*504*	*376*	*247*
HbA1c mmol/mol					
1 year change	-2.13 (-2.32;-1.94)	-2.50 (-3.30;-1.71)	-0.86 (-2.07;0.35)	-1.68 (-2.99;-0.38)	-7.19 (-8.83;-5.55)
n	*17852*	*1466*	*690*	*455*	*321*
2 year change	-0.90 (-1.12; -0.68)	-0.64 (-1.54;0.26)	0.77 (-0.59;2.13)	0.12 (-1.46;1.70)	-4.73 (-6.50;-2.96)
n	*17067*	*1381*	*636*	*445*	*300*
3 year change	0.35 (0.10;0.59)	1.03 (-0.02;2.07)	2.02 (0.40;3.63)	1.44 (-0.34;3.21)	-1.68 (-3.83;0.47)
n	*15539*	*1170*	*531*	*386*	*253*
Change in number of unique diabetes medications					
1 year change	0.22 (0.21;0.23)	0.16 (0.12;0.20)	0.19 (0.13;0.24)	0.19 (0.13; 0.25)	0.06 (-0.14; 0.13)
n	19737	1537	729	474	334
2 year change	0.32 (0.31;0.33)	0.22 (0.18;0.26)	0.26 (0.19; 0.32)	0.31 (0.24; 0.39)	0.00 (-0.84; 0.84)
n	19737	1491	690	470	331
3 year change	0.33 (0.32;0.34)	0.30 (0.25;0.36)	0.38 (0.29; 0.46)	0.39 (0.29; 0.48)	0.04 (-0.07;0.14)
n	19737	1281	589	410	282
Change in insulin use					
1 year net change compared to baseline	1.2% (1.0%; 1.4%)	1.7% (0.01; 2.6%)	2.5% (1.0%; 4.0%)	1.7% (0.0%; 3.3%)	0.0% (-1.1; 1.1%)
N on insulin/n at risk (absolute %)	*1975/19737 (10.0%)*	*158/1537 (10.3%)*	*84/729 (11.5%)*	*50/474 (10.6%)*	*24/334 (7.2%)*

2 year net change compared to baseline	1.9% (1.7%; 2.2%)	3.3% (2.2%; 4.4%)	4.5% (2.7%; 6.3%)	3.4% (1.2% 5.6%)	0.6% (-1.1%; 2.4%)
N on insulin/n at risk (absolute %)	*2127/19737 (10.8%)*	*174/1491 (11.7%)*	*90/690 (13.0%)*	*58/470 (12.3%)*	*26/331 (7.9%)*
3 year net change compared to baseline	2.7% (2.4%; 3.0%)	5.0% (3.6%; 6.4%)	7.0% (4.6% 9.3%)	4.4% (1.9% 6.8%)	1.8% (-1.1% 4.6%)
N on insulin/n at risk (absolute %)	*2280/19737 (11.6%)*	*178/1281 (13.9%)*	*95/589 (16.1%)*	*55/410 (13.4%)*	*28/282 (9.9%)*

GCWMS, Glasgow and Clyde Weight Management Service; HbA1c, glycated haemoglobin. Data are expressed as arithmetic mean ± SD, 95% confidence intervals or *n*.

Table 4 Adjusted effect of attending GCWMS programme and successfully losing 5kg compared to non-completers and unsuccessful completers

	Effect estimate	*95% CI*	p-*value*
HbA1c, mmol/mol			
1 year change (*n*=1432)	-6.62	-8.19;-5.04	<0.001
2 year change (*n*=1351)	-5.70	-7.49;-3.92	<0.001
3 year change (*n*=1146)	-3.67	-5.82;-1.51	0.001
Weight, kg			
1 year change (*n*=1352)	-5.43	-6.39;-4.47	<0.001
2 year change (*n*=1280)	-4.85	-5.99;-3.71	<0.001
3 year change (*n*=1106)	-3.61	-5.00;-2.20	<0.001
Unique diabetes medications use[*]			
1 year change (*n*=1497)	-0.13	-0.20;-0.05	0.001
2 year change (*n*=1453)	-0.28	-0.36;-0.19	<0.001
3 year change (*n*=1254)	-0.34	-0.45;-0.23	<0.001
Insulin use (Odds ratio)			
1 year use (n=1497)	0.42	0.18; 0.97	0.042
2 year use (n=1453)	0.40	0.20; 0.83	0.014
3 year use (n=1254)	0.54	0.25; 1.17	0.12

HbA1c, glycated haemoglobin.

NB HbA1c, weight & diabetes medication are absolute values; Insulin use is odds ratio.

[*]Number of unique diabetic medications from nine possible categories.

Model adjusted for age, sex, ethnicity, SIMD, time since T2DM diagnosis, baseline HbA1c, weight, BMI, diabetes medication and insulin use.

Table 5 Adjusted effect of 5% weight loss on difference in HbA1C after 2 years stratified by GCWMS status

	Effect estimate	*95% CI*	p-*value*
Change in HbA1c, mmol/mol			
Not referred (n=15,000)	-0.50	-0.69;-0.31	<0.001
Non-completer (n=566)	-1.32	-2.24;-0.41	<0.001
Completer (n=677)	-2.49	-3.53;-1.46	<0.001

Model adjusted for age, sex, ethnicity, SIMD, time since T2DM diagnosis, baseline HbA1c, weight, BMI, diabetes medication and insulin use. p for interaction <0.001.

Table 6 Attendance and weight outcomes of patients diagnosed with type 2 diabetes and co-existent obesity in NHS Greater Glasgow and Clyde by completion status in GCWMS

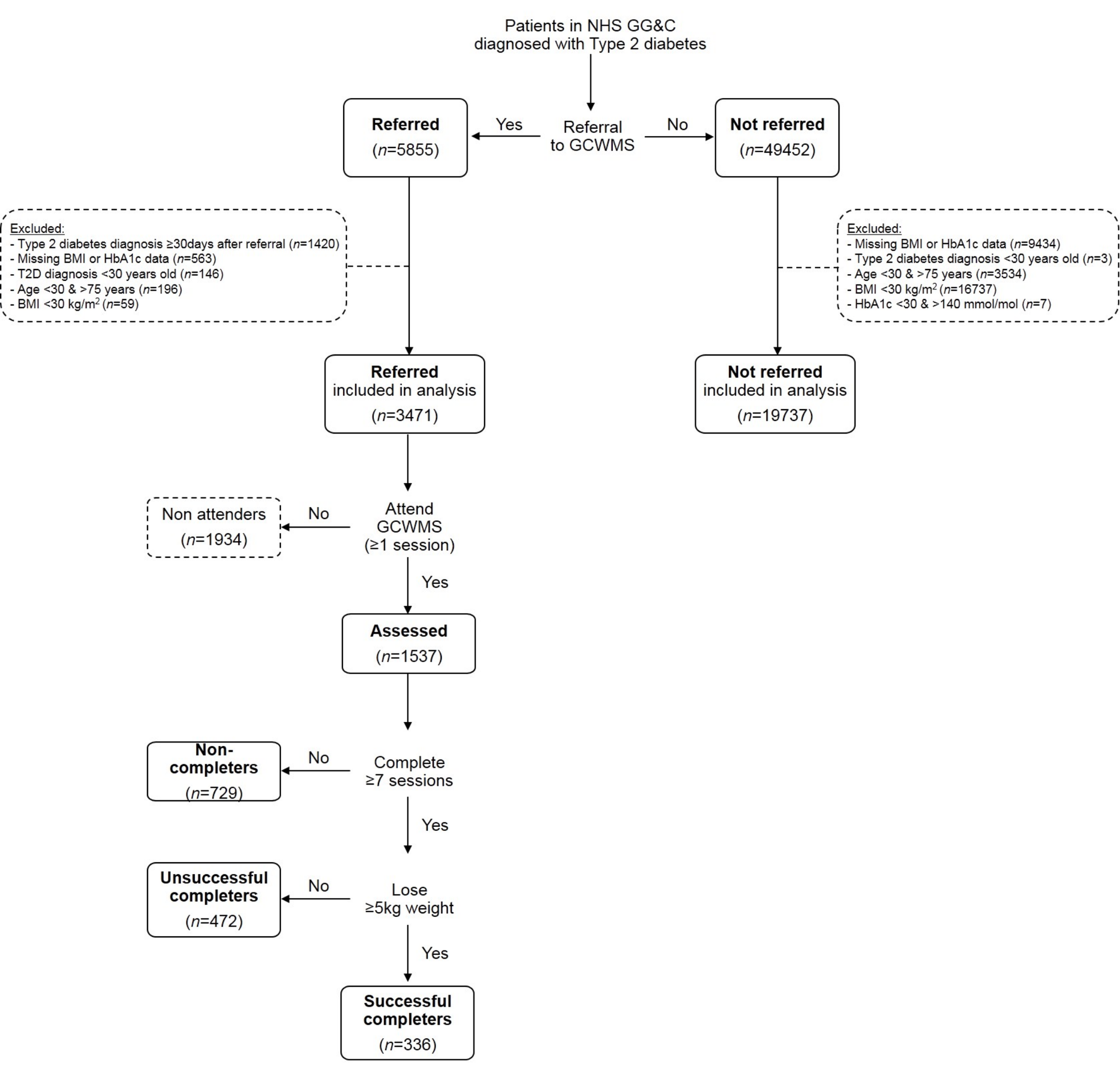
	Total attenders (n=*1537*)	*Non-completers* (n=*729*)	*Completers* (n=*808*)	
			Unsuccessful (n=*474*)	*Successful* (n=*334*)
Phase I:				
Time attended, months*	3.7 (2.3-3.7)	1.8 (0.9-3.2)	3.7 (3.7-4.1)	3.7 (3.7-3.7)
n	*1387*	*582*	*471*	*334*
Last weight recorded, kg	110.5 ± 23.0	110.9 ± 22.7	111.3 ± 23.3	108.2 ± 23.3
n	*1537*	*729*	*474*	*334*
Change in weight, kg*	-3.27 ± 4.08	-1.55 ± 2.89	-1.74 ± 2.30	-8.44 ± 3.45
n	*1392*	*584*	*474*	*334*
Total programme:				
Time attended, months*	5.5 (2.3-12.4)	1.8 (0.9-3.7)	7.4 (4.6-14.9)	11.9 (7.1-17.3)
n	*1387*	*582*	*471*	*334*
Last weight recorded, kg	109.8 ± 22.9	110.8 ± 22.7	110 ± 23.2	106.7 ± 22.8
n	*1537*	*729*	*474*	*334*
Change in weight, kg*	-4.01 ± 6.29	-1.72 ± 3.32	-2.69 ± 4.71	-9.90 ± 8.24
n	*1391*	*584*	*473*	*334*

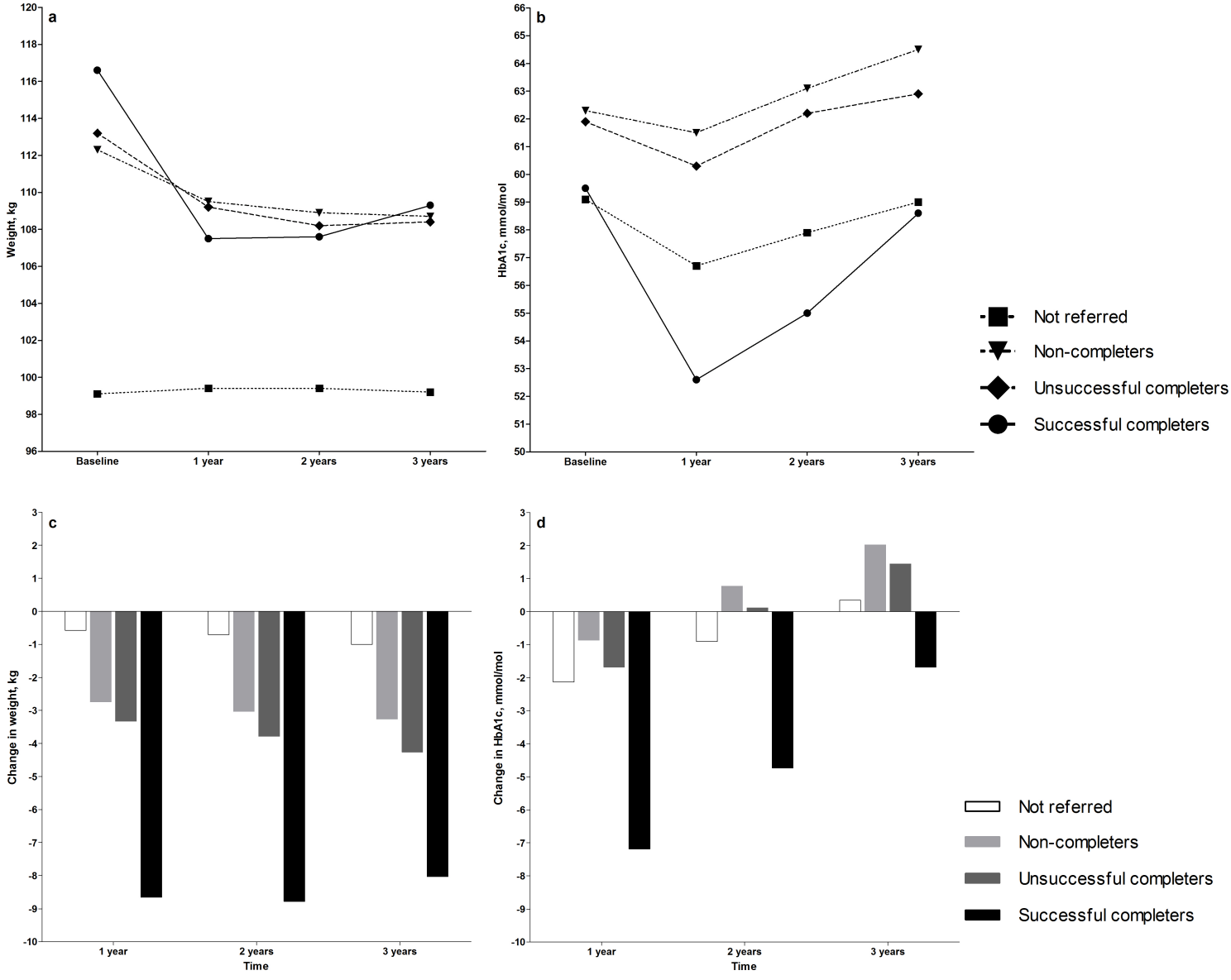
Data are expressed as arithmetic mean ± standard deviation. $P \leq 0.05$ regarded as statistically significant.
*Only for those who attended >1 session.

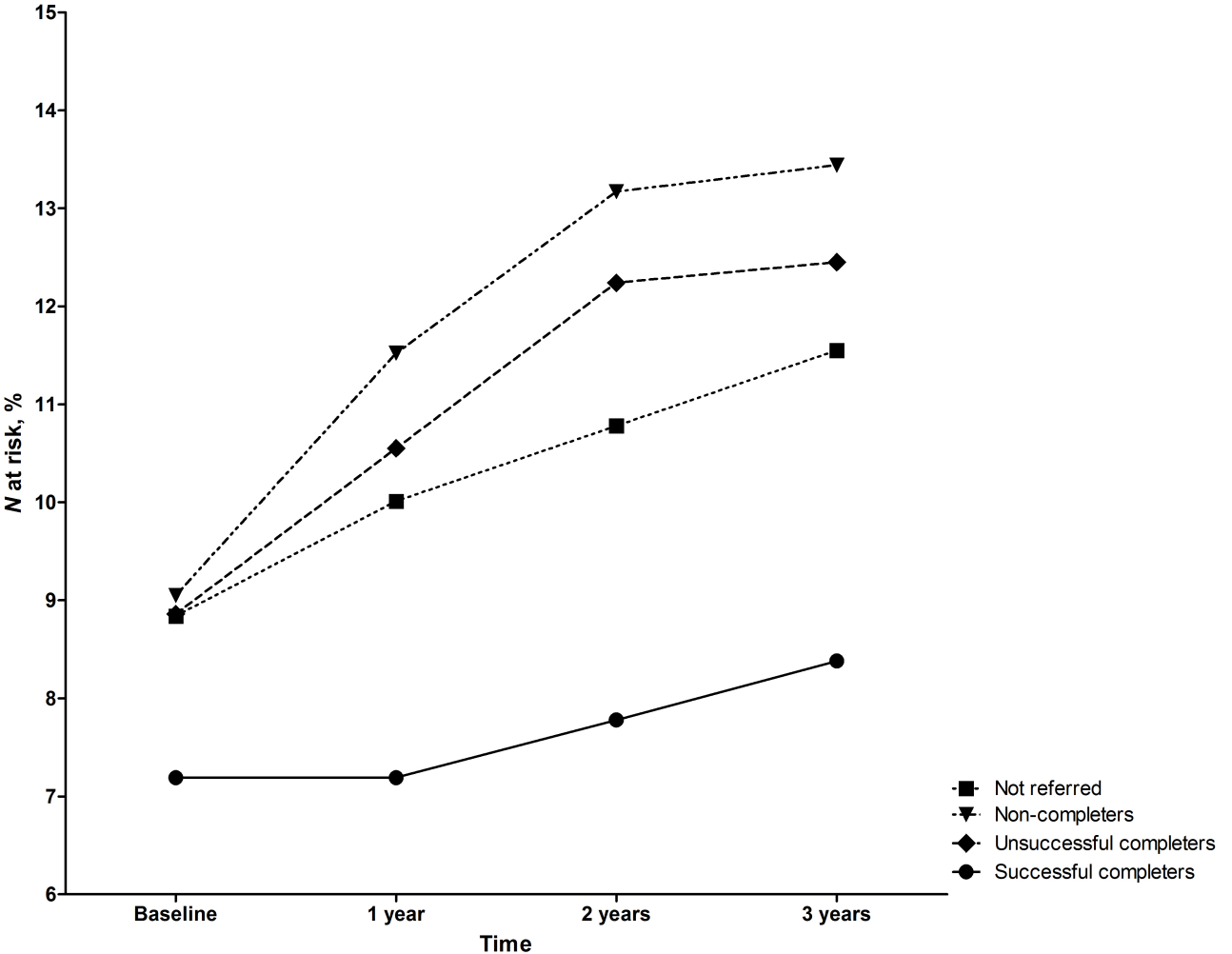
Supplement table 1 Adjusted effect of attending GCWMS programme and successfully losing 5kg compared to non-completers and unsuccessful completers

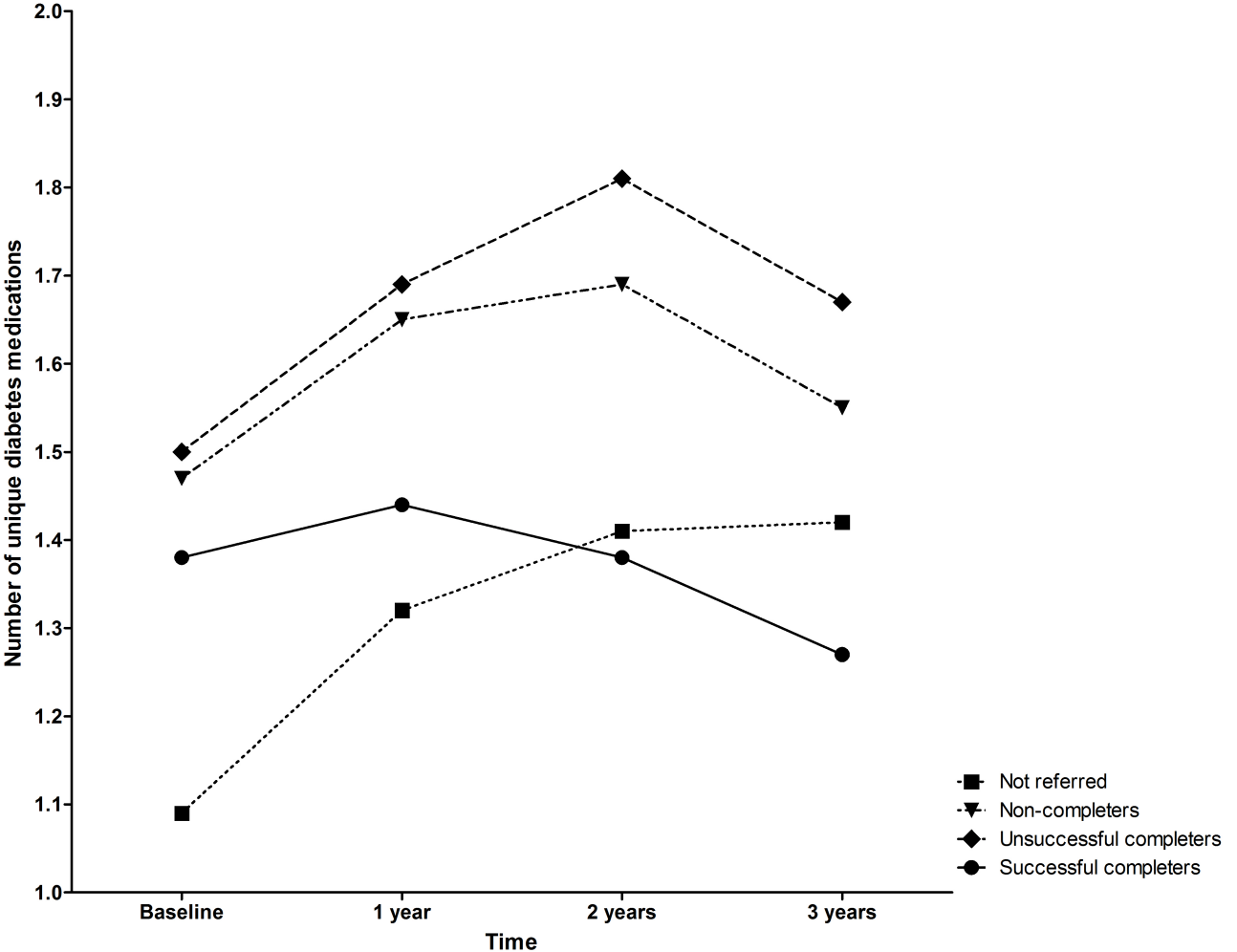
	Odds ratio	*95% CI*	p-*value*
GLP-1 agonist use			
1 year use (n=1497)	0·60	0·35; 1.03	0·063
2 year use (n=1453)	0·70	0·45; 1.09	0·12
3 year use (n=1254)	0·50	0·32; 0.80	0·003
DPP-4 inhibitor use			
1 year use (n=1497)	0·83	0·54; 1.26	0·38
2 year use (n=1453)	0·54	0·36; 0.83	0.004
3 year use (n=1254)	0·48	0·31; 0.75	0·001

Model adjusted for age, sex, ethnicity, SIMD, time since T2DM diagnosis, baseline HbA1c, weight, BMI, diabetes medication number, baseline insulin, sodium/glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) agonists, and dipeptidyl peptidase 4 (DPP-4) inhibitor use.
Note: SGLT2 inhibitor use was too rare to model over the timeframe of this study


Patients in NHS GG&C diagnosed with Type 2 diabetes
Referral to GCWMS
Yes
No
Referred (n=5855)
Not referred (n=49452)
Excluded:
- Type 2 diabetes diagnosis ≥30days after referral (n=1420)
- Missing BMI or HbA1c data (n=563)
- T2D diagnosis <30 years old (n=146)
- Age <30 & >75 years (n=196)
- BMI <30 kg/m2 (n=59)
Excluded:
- Missing BMI or HbA1c data (n=9434)
- Type 2 diabetes diagnosis <30 years old (n=3)
- Age <30 & >75 years (n=3534)
- BMI <30 kg/m2 (n=16737)
- HbA1c <30 & >140 mmol/mol (n=7)
Referred included in analysis (n=3471)
Not referred included in analysis (n=19737)
Attend GCWMS (≥1 session)
No
Non attenders (n=1934)
Yes
Assessed (n=1537)
Complete ≥7 sessions
No
Non-completers (n=729)
Yes
Lose ≥5kg weight
No
Unsuccessful completers (n=472)
Yes
Successful completers (n=336)


a
Weight, kg
120
118
116
114
112
110
108
106
104
102
100
98
96
Baseline
1 year
2 years
3 years
b
HbA1c, mmol/mol
66
65
64
63
62
61
60
59
58
57
56
55
54
53
52
51
50
Baseline
1 year
2 years
3 years
Not referred
Non-completers
Unsuccessful completers
Successful completers
c
Change in weight, kg
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
1 year
2 years
3 years
Time
d
Change in HbA1c, mmol/mol
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
1 year
2 years
3 years
Time
Not referred
Non-completers
Unsuccessful completers
Successful completers


15
14
13
12
11
10
9
8
7
6
N at risk, %
Baseline
1 year
2 years
3 years
Time
Not referred
Non-completers
Unsuccessful completers
Successful completers


2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
Number of unique diabetes medications
Baseline
1 year
2 years
3 years
Time
Not referred
Non-completers
Unsuccessful completers
Successful completers