

INTRODUCTION

Long-term studies show that type 2 diabetes is associated with a progressive deterioration of glucose tolerance. After a median time of approx. 9 years most people with type 2 diabetes require the addition of insulin to anti-diabetic oral agents to achieve optimal glycaemic control. Currently there is no strong evidence for a specific insulin regimen for initiating insulin treatment in type 2 diabetes. Therefore, different regimens for the initiation of insulin treatment are coexisting in clinical care: (1) Basal insulin supported Oral Therapy (BOT), (2) Supplementary Insulin Treatment with prandial insulin (SIT), and (3) Conventional Insulin Treatment with biphasic insulin (CT). These different insulin regimens are requiring new skills and knowledge in people with type 2 diabetes, previously treated with lifestyle modification and oral anti-diabetic agents. Amongst these new skills are the correct injection and dosing of insulin, blood glucose self-control and the timing of insulin injection with carbohydrate intake in prandial or biphasic insulin regimens. MEDIAS 2 BOT+SIT+CT (More Diabetes Selfmanagement for People with type 2 diabetes on a BOT, SIT or CT) is a newly developed diabetes education and treatment programme for people with type 2 diabetes (PWD-T2) on a non-intensive insulin treatment regimen. The development of MEDIAS 2 BOT+SIT+CT (MEDIAS 2 BSC) was based on the self-management and empowerment theory. The efficacy of the newly developed intervention MEDIAS 2 BSC was evaluated in a randomized trial with a 6-month follow-up period. The control group (CG) participated in an established education programme (treatment- and education programme for type 2 diabetic patients with injection of prandial and/or basal insulin). The primary outcome of this study was the reduction of HbA1c.

METHODS

Both interventions consisted of 6 lessons (see table 1 with the key topics of the lessons). At baseline and follow-up, HbA1c was measured in a central laboratory. Participants also completed questionnaires to measure diabetes distress, empowerment, diabetes knowledge and hypoglycaemia awareness.

RESULTS

- 182 PWD-T2 participated in the study (see table 2 for baseline characteristics). There were no significant differences at baseline between MEDIAS 2 BSC and CG. At the 6-month follow-up, data of 160 participants could be analysed.
- 17 participants were lost to follow-up and 5 participants terminated insulin treatment (see figure 1). Patients who were lost to follow-up or terminated insulin treatment were significantly younger than participants of the per protocol population.
- HbA1c was significantly more reduced in MEDIAS 2 BSC compared to CG (-0.7 ± 0.1 vs. -0.3 ± 0.1%; p=.02 (see figure 2). Figure 3 shows the effect of MEDIAS 2 BSC in the per-protocol- and intention-to-treat-population (baseline HbA1c carried forward for participants who were lost to follow-up). All analyses showed a significant benefit of MEDIAS 2 BSC with regard to glycaemic control.
- There was no severe hypoglycaemic event reported (medical assistance required) in neither treatment group. Hypoglycaemia unawareness measured by questionnaire did not change significantly in the two groups. Thus, reductions in HbA1c was not associated with an increased risk of severe hypoglycaemia (see figure 4).
- In both intervention groups there was an improvement of Diabetes Self Care, Knowledge, Diabetes Distress, Depression and Health Related Quality of Life. However, the differences between MEDIAS 2

BSC and CG were not significant (see table 3).

- Number of insulin injections or blood glucose self-tests as well as insulin doses were only slightly changed during the intervention and follow-up period in both groups. There was a moderate increase of weight in both groups. Between groups differences did not reach significance (see table 4).
- A sensitivity analysis evaluated whether treatment differences like insulin doses, number of insulin injections or change of insulin regimen had an impact on the observed HbA1c difference in both groups. The results of these sensitivity analyses are shown in figure 5.

CONCLUSION

Participation in the newly developed MEDIAS 2 BOT+SIT+CT treatment and education programme led to a significant improvement of glycaemic control without a measurable increase in risk for hypoglycaemia. An important component of the newly developed MEDIAS 2 BOT+SIT+CT was self-titration of insulin doses; this might have contributed to the positive impact of this programme on glycaemic control. There was a positive impact of diabetes education delivered either in the control group or in the MEDIAS 2 BSC group on Diabetes Self-Care activities, Diabetes Knowledge, Diabetes Distress, Depressive Symptoms and Health-Related Quality of Life. However, the impact of the different education programmes on these psychosocial outcomes was too small to reach significance with regard to between group differences. Participants in the study had a rather high age and long diabetes duration and were highly affected by diabetes complications. This might have limited beneficial effects of diabetes education on depressive symptoms, diabetes distress and health-related quality of life. Treatment factors did not differ substantially between MEDIAS 2 BSC and the control group. The sensitivity analysis controlling for mode of insulin treatment or insulin dose suggests that the beneficial impact of MEDIAS 2 BSC on glycaemic control was not explained by treatment intensification or mode of insulin treatment.

In summary, MEDIAS 2 BOT+SIT+CT has been proven as an effective treatment and education tool.

Table 1: Content of education programmes in CG and MEDIAS 2 BOT+SIT+CT

Lessons	Control Group	MEDIAS 2 BSC
1	<ul style="list-style-type: none"> Insulin, Insulin action Insulin injection technique (Pens Syringe) Why is insulin needed Log book for results of SMBG 	<ul style="list-style-type: none"> Impact of insulin treatment on diabetes, Different insulin regimens, Rational of BOT, SIT or CT, Individual goals of diabetes treatment, Perception and experiences with insulin treatment
2	<ul style="list-style-type: none"> Technique of blood glucose self monitoring Identifying food which elevates blood glucose Characteristics of food (high fat, high protein content, high water content) Testing blood glucose before meals 	<ul style="list-style-type: none"> Blood glucose self monitoring, Basal and prandial insulin, Insulin templates for individual insulin regimen. Experiences and attitudes regarding blood glucose monitoring, Titration of insulin doses, Insulin injections
3	<ul style="list-style-type: none"> Detection of carbohydrate and carbohydrate counting Nutrition game Distribution of carbohydrates over the day Symptoms of hypoglycaemia 	<ul style="list-style-type: none"> Carbohydrates, Identifying food and drinks with carbohydrates, Avoiding fast acting carbohydrates, Carbohydrate counting (carbohydrate units) Nutrition game to check ability to identify food with carbohydrates, Exchange of carbohydrates for people with CT and SIT with fixed insulin doses
4	<ul style="list-style-type: none"> Urine glucose testing Physical exercise and insulin treatment Reducing insulin doses Check ups to detect complications 	<ul style="list-style-type: none"> Weight gain and insulin therapy, Strategies for avoiding/minimizing weight gain, Hypoglycaemia; Symptoms, causes, treatment and prevention of hypoglycaemia; Individual symptoms of low blood glucose
5	<ul style="list-style-type: none"> Increasing insulin doses Adjusting insulin doses Foot care, Prevention of foot problems Foot gymnastics 	<ul style="list-style-type: none"> Insulin injection sites, Physical exercise and blood glucose, Complications and check ups, Social support in diabetes, Prevention of diabetic foot problems
6	<ul style="list-style-type: none"> Basal insulin in the evening Blood pressure and salt Measurement of blood pressure Regulation of blood pressure Antihypertensive agents 	<ul style="list-style-type: none"> Metabolic risk factors and high blood pressure in diabetes, Insulin and driving, Social aspects of diabetes and insulin treatment, Insulin and travel, Feedback of the education programme

Table 2: Sample characteristics

Characteristics	Control group (n=90)	MEDIAS 2 BSC (n=92)	p
Mean age (± SD) yrs	63.1 (±7.9)	62.8 (±8.5)	.821
% female	47.8	41.8	.418
Mean BMI (± SD) kg/m ²	30.8 (±5.1)	32.1 (±5.4)	.116
Mean diabetes duration (± SD) yrs	11.6 (±7.4)	11.5 (±6.2)	.959
Mean number of insulin injection per day (±SD)	2.0 (±1.3)	1.9 (±1.3)	.417
Mean IU/kg (± SD)	0.40 (±0.31)	0.37 (±0.27)	.462
Mean number of SMBG per day (± SD)	2.3 (±1.3)	2.4 (±1.6)	.671
% with oral antidiabetic medication	74.4%	85.7%	.058
% without insulin	1.1	1.1	
% with bi-phasic insulin (CT)	17.6	18.8	
% with basal oral treatment (BOT)	59.3	55.8	
% with bolus insulin treatment (SIT)	3.3	2.8	
% with basal & bolus insulin (BOT+)	18.7	21.6	.838
Mean HbA1c (± SD) %	7.9 (±1.2)	8.0 (±1.3)	
Mean HbA1c (± SD) mmol/L	62.8 (±12.7)	63.7 (±14.0)	.635
% with Previous education about insulin	24.4	16.3	.175
% with complications ²	70	63	.323
Mean Unawareness Score (± SD)	2.0 (±0.8)	2.0 (±1.0)	.562
Mean Diabetes Self Care Activity Score (± SD)	3.8 (±1.2)	3.7 (±1.1)	.607
Mean Diabetes Knowledge Score (± SD)	4.2 (±1.6)	4.4 (±2.2)	.368
Mean Problem Areas in Diabetes Score (± SD)	26.8 (±18.0)	27.9 (±20.4)	.701
Mean CES-D Score (± SD)	14.9 (±8.7)	14.9 (±8.9)	.971
Mean EQ 5 D utility Score (± SD)	0.86 (±0.16)	0.86 (±0.16)	.795

¹ BOT +: Insulin treatment regimen with one or 2 injects of basal insulin and one fixed dose of prandial insulin

² One of the following complications: retinopathy, neuropathy, nephropathy, stroke, cardiovascular disease, diabetic foot syndrome, peripheral vascular disease.

Table 3: Impact of MEDIAS 2 BSC and CG von Diabetes Self Care, Knowledge, Diabetes Distress, Depression and Health-Related Quality of Life (adjusted for study centre)

Characteristics	Control group (n=78)	MEDIAS 2 BOT+SIT+CT (n=80)	Difference (95% Confidence Interval)	p
Mean Diabetes Self Care Activity Score (± SD)	+0.27 (0.05 to 0.48)	+0.31 (0.11 to 0.52)	-0.05 (-0.34 to 0.25)	.753
Mean Diabetes Knowledge Score (± SD)	+0.72 (0.30 to 1.14)	+0.34 (-0.07 to 0.75)	+0.38 (-0.21 to 0.97)	.206
Mean Problem Areas in Diabetes Score (± SD)	-2.2 (-5.44 to 1.0)	-2.45 (-5.61 to 0.71)	-0.23 (-4.76 to 4.28)	.919
Mean Depression Score (CES-D) (± SD)	-0.78 (-1.08 to 2.65)	-1.11 (-0.72 to 2.94)	-0.33 (-2.95 to 2.29)	.804
Mean EQ 5 D utility Score (± SD)	-0.00 (-0.03 to 0.03)	-0.02 (0.00 to 0.05)	-0.02 (-0.06 to 0.02)	.303

Table 4: Impact of MEDIAS 2 BOT+SIT+CT and CG on treatment factors (adjusted for study centre)

Characteristics	Control group (n=78)	MEDIAS 2 BSC (n=82)	Difference (95% Confidence Interval)	p
Mean change of number of insulin injection per day (± 95% CI)	+0.21 (-0.03 to 0.45)	+0.38 (0.14 to 0.62)	0.17 (-0.16 to -0.51)	.310
Mean change of IU/kg (± 95% CI)	+0.03 (-0.02 to 0.08)	+0.07 (0.02 to 0.12)	0.04 (-0.02 to 0.12)	.204
Mean change of number of BGSM per day (± 95% CI)	-0.30 (-0.02 to -0.58)	-0.05 (0.21 to -0.31)	-0.25 (-0.13 to -0.64)	.194
Mean change of BMI kg/m ² (± 95% CI)	+0.26 (-0.27 to 0.79)	+0.86 (0.30 to 1.41)	-0.60 (-0.18 to 1.37)	.132

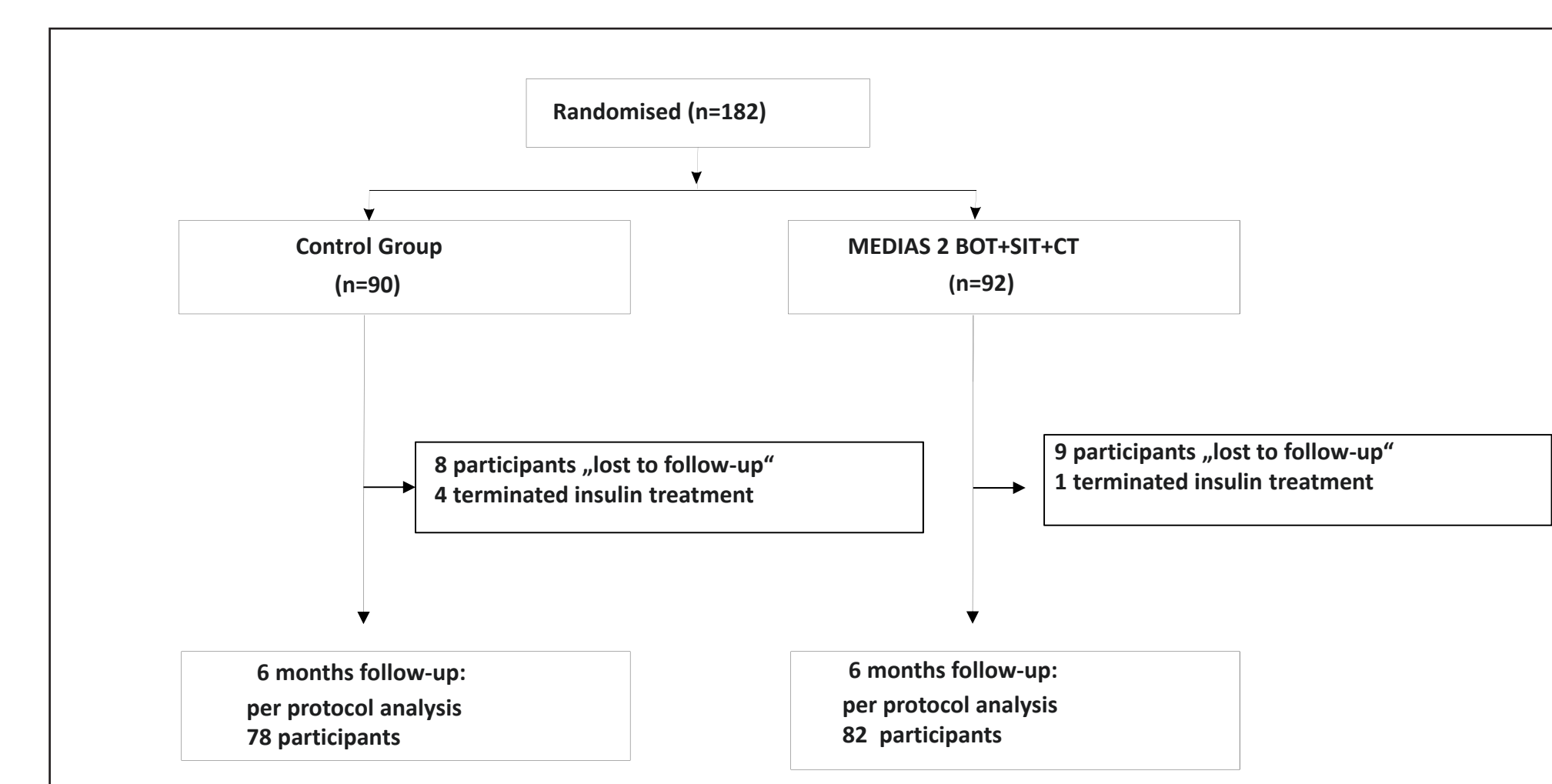


Figure 1: Consort statement: study flow

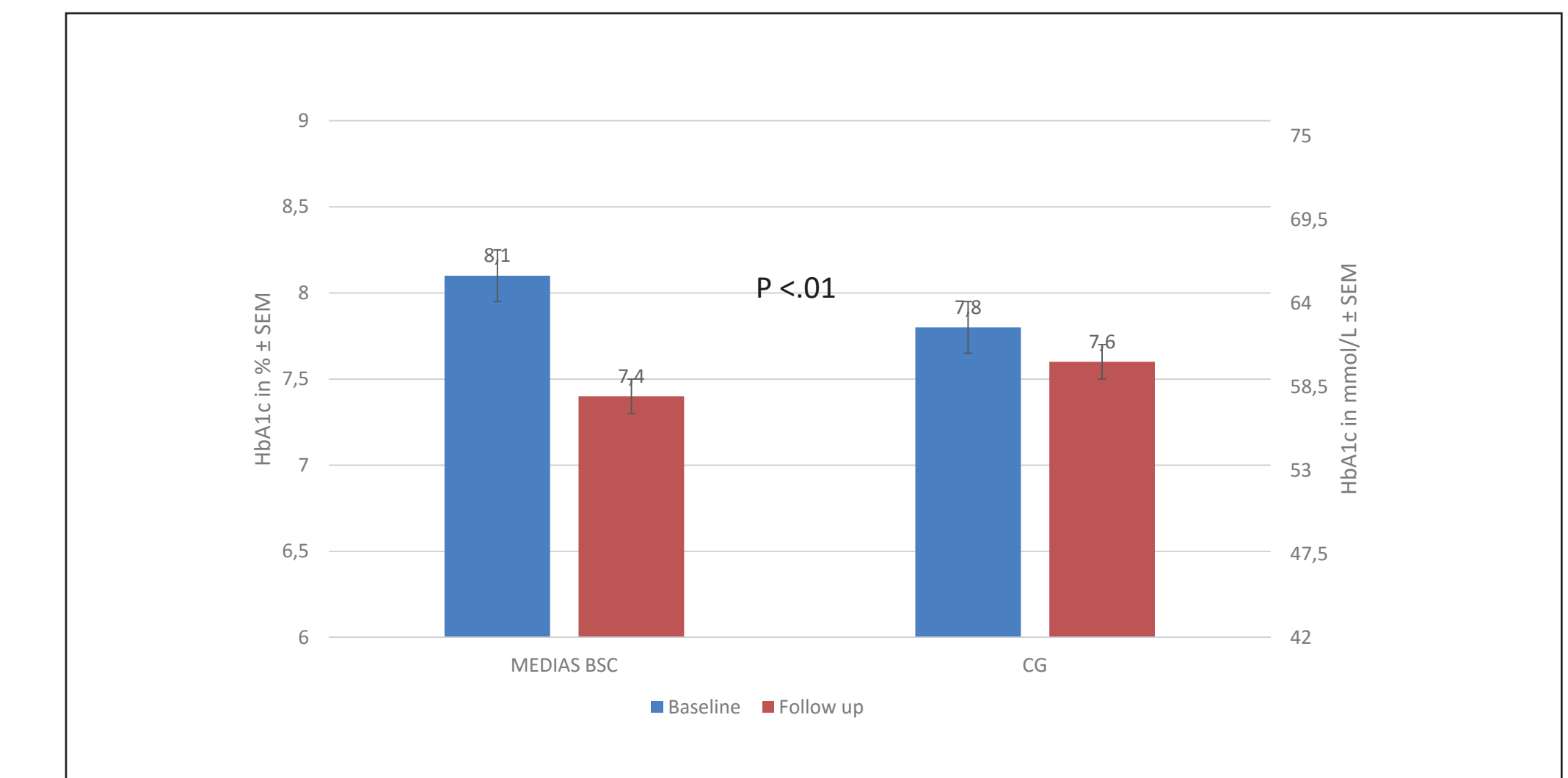


Figure 2: Effects of MEDIAS 2 BOT+SIT+CT and CG on HbA1c (adjusted for study centre)

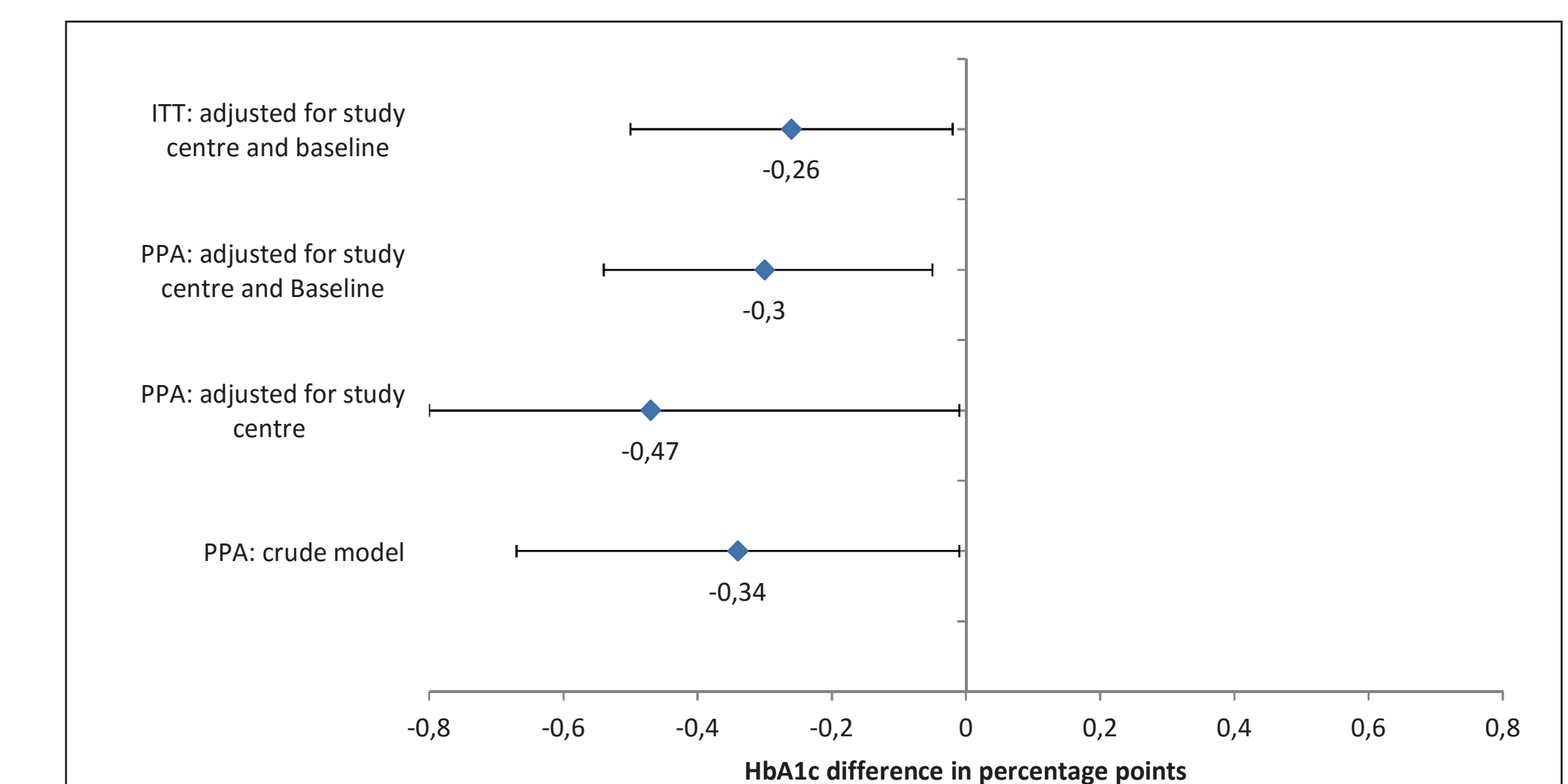


Figure 3: Effects of MEDIAS 2 BOT+SIT+CT and CG on HbA1c in per protocol and intention to treat population

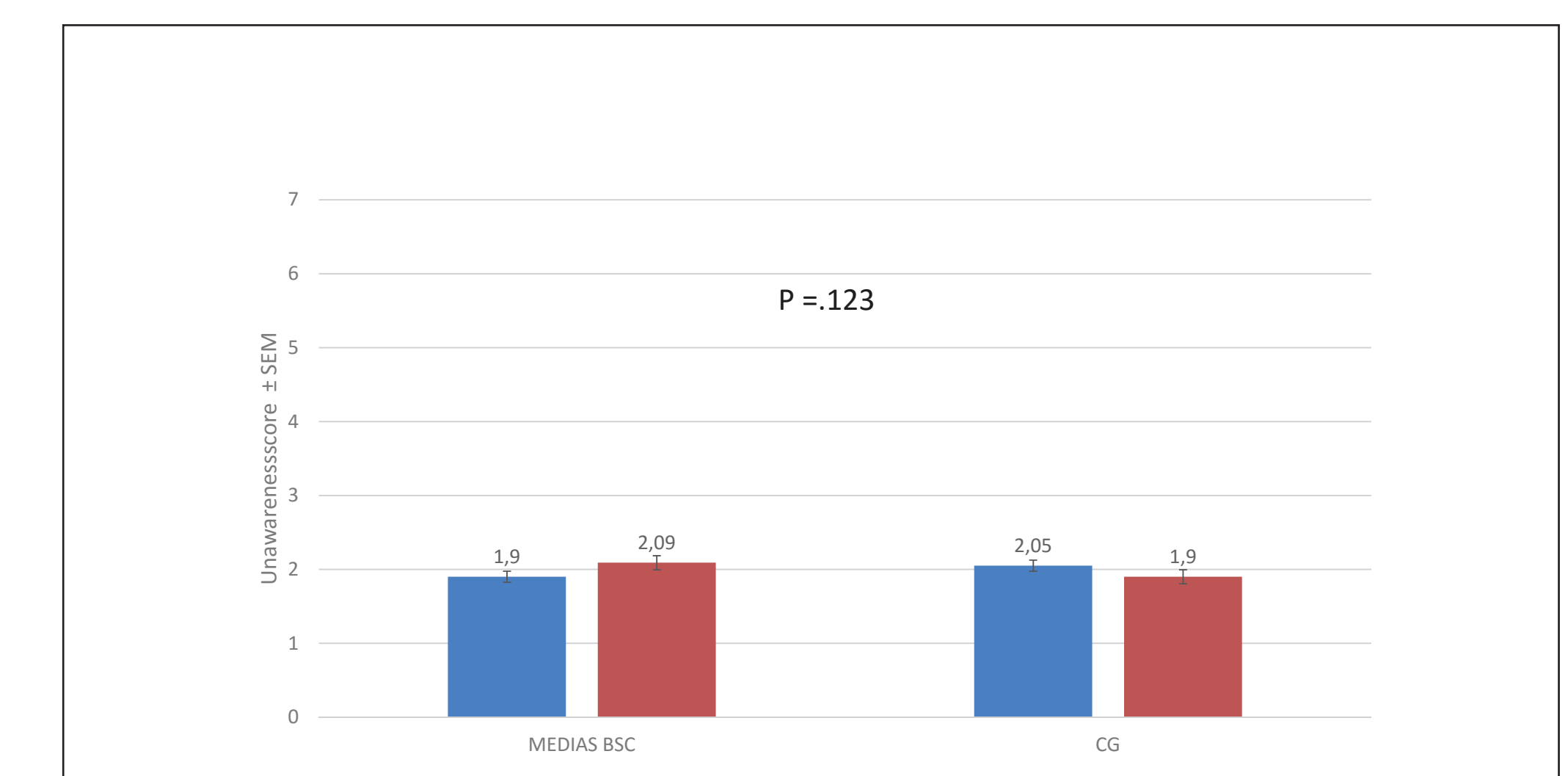


Figure 4: Effects of MEDIAS 2 BOT+SIT+CT and CG on Hypoglycaemia Unawareness

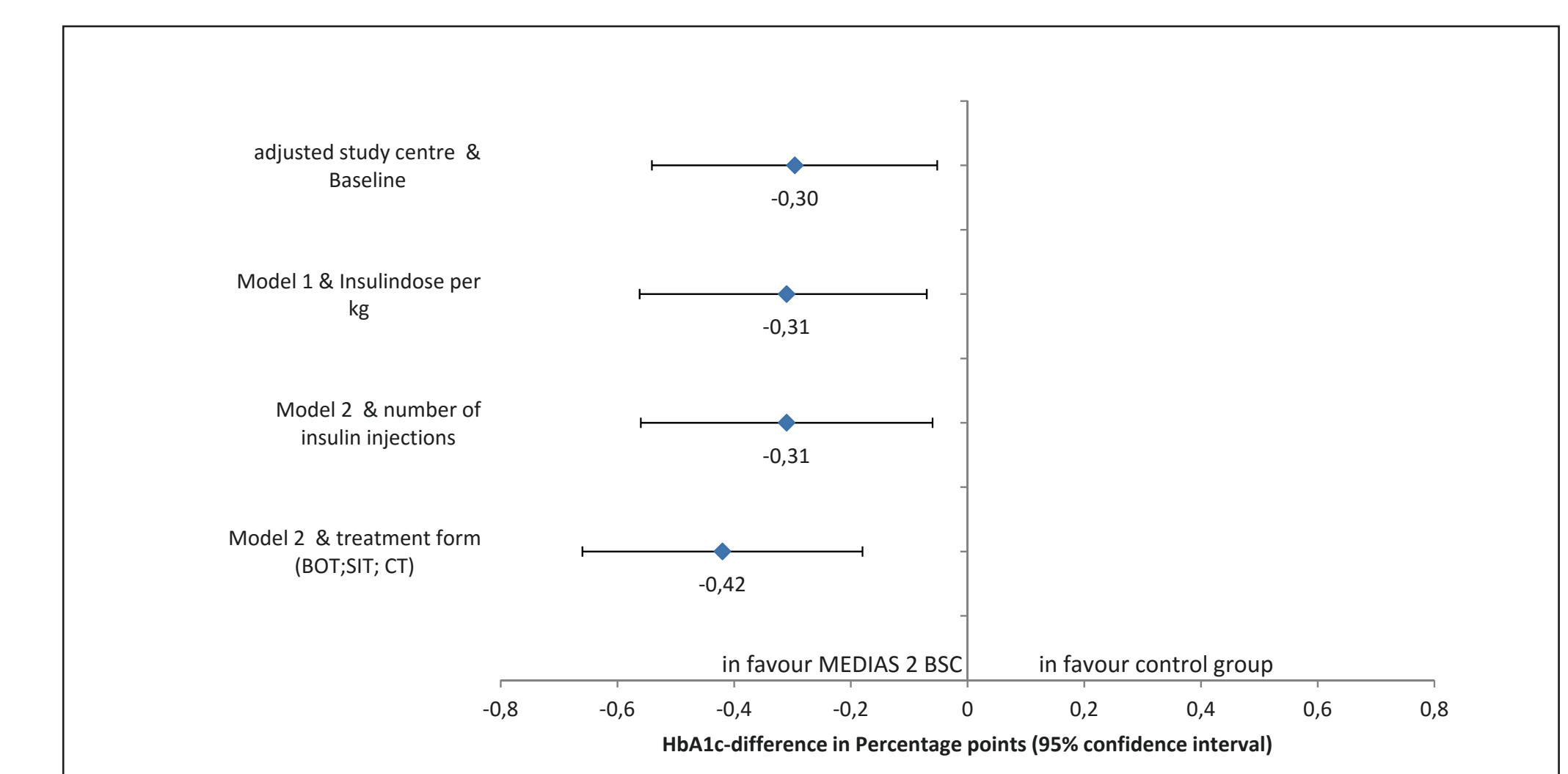


Figure 5: Sensitivity analysis of the impact of treatment factors on HbA1c differences between both groups