ORIGINAL ARTICLE

Achieving triple treatment goals in multi-ethnic Asian patients with type 2 diabetes mellitus in primary care

Goh CC, Koh KH, Goh SCP, Koh YLE, Tan NC

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Authors:

Goh Chin Chin
(Corresponding author)
B Pharm
SingHealth Polyclinics
167, Jalan Bukit Merah, Tower 5
#15-10, Singapore 150167
Email:
goh.chin.chin@singhealth.com.sg

Kim Hwee Koh
M.Med (Fam Med), MRCS.
SingHealth Polyclinics

Soo Chye Paul Goh,
M.Med (Fam Med), FCFPS
SingHealth Polyclinics
167, Jalan Bukit Merah, Tower 5
#15-10, Singapore 150167

Yi Ling Eileen Koh
BSc
SingHealth Polyclinics
167, Jalan Bukit Merah, Tower 5
#15-10, Singapore 150167

Ngiap Chuan Tan
M.Med (Fam Med), FCFPS
SingHealth Polyclinics,
Duke NUS Medical School,
Singapore

Abstract

Introduction: Achieving optimal glycated hemoglobin (HbA1c), blood pressure (BP), and LDL-Cholesterol (LDL-C) in patients mitigates macro- and micro-vascular complications, which is the key treatment goal in managing type 2 diabetes mellitus (T2DM). This study aimed to determine the proportion of patients in an urban community with T2DM and the above modifiable conditions attaining triple vascular treatment goals based on current practice guidelines.
Methods: A questionnaire was distributed to adult Asian patients with dyslipidemia at two primary care clinics (polyclinics) in northeastern Singapore. The demographic and clinical data for this sub-population with both T2DM and dyslipidemia were collated with laboratory and treatment information retrieved from their electronic health records. The combined data was then analyzed to determine the proportion of patients who attained triple treatment goals, and logistic regression analysis was used to identify factors associated with this outcome.
Results: 665 eligible patients [60.5% female, 30.5% Chinese, 35% Malays, and 34.4% Indians] with a mean age of 60.6 years were recruited. Of these patients, 71% achieved LDL-C ≤2.6 mmol/L, 70.4% had BP <140/90 mmHg, and 40.9% attained HbA1c ≤7%. Overall, 22% achieved the triple treatment goals for glycemia, BP, and LDL-C control. The major determinants were the number of diabetic medications and intensity of statin therapy.
Conclusion: Eight in ten patients with T2DM failed to achieve concurrent glycemic, BP, and LDL-C treatment goals, subjecting them to risks of vascular complications. Primary healthcare professionals can mitigate these risks by optimizing therapeutic treatment to maximize glycemia, dyslipidemia, and BP control.

Introduction

The management of patients with type 2 diabetes mellitus (T2DM) centers on the reduction of their risks of both macro- and microvascular complications.[1] Ample and consistent evidences show that the risks of these vascular complications can be mitigated by attaining optimal control of their hyperglycemia, blood pressure and LDL-Cholesterol.[2] These vascular risks can be reduced by pharmacological intervention, lifestyle modification, and patients' adherence to therapy.

Achieving intensive glycemic control has shown to reduce the risk of microvascular endpoints by 25% and albuminuria at twelve years by 33%.[3] In addition, a 17% reduction in events of non-fatal myocardial infarction and a 15% reduction in events of coronary heart disease were recorded.[4] Oral anti-diabetic agents have emerged as valuable tools for the attenuation of atherosclerotic activity and the protection of the vasculature in patients with type 2 diabetes.[5]

Tight blood pressure control of < 130/80mm Hg in patients with hypertension and T2DM has been associated with a significantly lower risk of all-cause mortality (risk ratio (RR)=0.87; 95% CI of 0.78-0.96) For microvascular outcomes, a 10 mm Hg-lower systolic BP was associated with a lower risk of retinopathy (RR=0.87; 95% CI of 0.76-0.99) and albuminuria (RR=0.83; 95% CI of 0.79-0.87).[6] As lowering BP has been associated with improved mortality and other positive vascular outcomes, the use of medications for lowering BP among patients with T2DM should be sustained.

Reduction of Low Density Lipoprotein-Cholesterol (LDL-C) further mitigates vascular

complications. A significant 21% reduction in major vascular events occurs for every mmol/L reduction in LDL-C for people with diabetes (RR=0.79; 95% CI of 0.72–0.86; p<0.0001).[7] An increase of 0.38 mmol/L or 15 mg/dL in High Density Lipoprotein-Cholesterol (HDL-C) was associated with a 22% reduction in risk of coronary arterial disease.[2] Poor lipid profiles have been associated with poor glycemic control.[8] L. Acuña et al. found that more than half of the patients with diabetes in their study had suboptimal LDL-C levels, while 36% had low HDL-C levels of <40mg/dl (<1.0 mmol/L).[9]

However, attaining concurrent control of glycemia, blood pressure, and LDL-C in patients with T2DM is challenging. Data from the Asia and Greece study revealed that approximately 10% or less of patients achieved triple vascular disease control.[8,10,11] Data from a large Japanese working population, predominantly composed of men, reported that the younger population segment had suboptimal achievements of HbA1c, BP and LDL-C treatment goals.[8] In China, only 5.6% achieved all target goals; lower BMI (<24), higher education, and shorter duration of T2DM (< 5 years) were independent predictors of better vascular risk control.[10] In the USA, two study cohorts from the Kaiser Permanente (KP) and Denver Health (DH) health care institutions, achieved 33% and 16% simultaneous control of all three risk factors, respectively.[12] The difference was attributed to the population-based management system used by KP over a period of many years. The system identified targeted individuals who had not achieved simultaneous control in order to treat their elevated risk factors. More healthcare resources were directed towards this population-based intervention to increase the number of patients successfully achieving their treatment goals.

In order to adopt an approach similar to KP's, it is crucial to determine the proportion and baseline population characteristics of patients with T2DM who fail to attain triple treatment goals. The size of this at-risk population will determine the amount of healthcare resources needed to manage them. In Singapore, about 45% of the local multi-ethnic Asian population with T2DM is being managed in public primary healthcare due to accessibility, and the comprehensive and subsidized healthcare services provided by these polyclinics.[13] The subsidies at these polyclinics cover consultation and medications. SingHealth Polyclinics (SHP) comprises nine polyclinics, which cover half of the highly urbanized island state over the southern and eastern regions.[14] SHP has also adopted a population-based management system for patients with long-term, non-communicable diseases, such as T2DM, so that resources are allocated appropriately to cater to patients at risk of vascular complications. Hence, this study aimed to determine the proportion of patients with T2DM who failed to achieve triple treatment goals for concomitant glycemic, blood pressure, and LDL-Cholesterol (LDL-C) control. The secondary objective was to identify modifiable factors associated with triple treatment goals' achievement.

Methods

The Lipid Health study was conducted from Oct 2013 to Sep 2014 at two of SHP's polyclinics.[15] This questionnaire collected data pertaining to demographic and clinical profiles, laboratory investigations, and personal lifestyle information for patients with dyslipidemia. This paper is a sub-analysis of the data from the Lipid Health study, focusing on a segment of the study population with T2DM and dyslipidemia.

Subjects

The main study recruited patients with dyslipidemia, ranging in age from 31 to 80 years old, who visited two primary care polyclinics from Oct 2013 to Sep 2014.[15] Three major ethnic groups, namely Chinese, Malays and Indians, were equally stratified to determine their perceptions and attitudes towards lifestyle habits such as exercise, diet, and medication. Patients who fulfilled the inclusion criteria of physician-diagnosed dyslipidemia and being Singaporean or a permanent resident (at least 3 years of residence in Singapore) were interviewed by trained research assistants to complete the survey. The subjects in this paper were patients known to have T2DM, as confirmed by the diagnostic codes in their electronic health records.

Two clinical research coordinators were hired and underwent training by the principal investigator on the study and its implementation. They were further trained in the Singapore version of Good Clinical Practice (SG-GCP). Written informed consents were obtained from the patients prior to the administration of the questionnaire.

The study excluded patients who had difficulty communicating in the local major languages and dialect or were unable to provide informed consent due to cognitive, hearing, and/or visual impairments.

Definition of treatment goals

The treatment goal for T2DM is normoglycemia, defined as HbA1c ≤7.0%, according to the Ministry of Health (MOH) Clinical Practice Guidelines on Diabetes Mellitus.[16] Following the recommendations of the Eight Joint National Committee (JNC 8)[17], the blood pressure goal for patients with T2DM is defined as <140/90mmHg. The LDL-C treatment goals for the High Risk Group, including those with T2DM, is < 2.6mmol/L (<100mg/dL).[18] The intensity of statin therapy, graded as low, moderate, or high, is based on the 2013 ACC/AHA guideline on the primary and secondary prevention of cardiovascular events.[19]

Sample size calculation

The sample size was based on the aim of the main study,[15] which required a sample of at least 380 subjects for each of the three ethnic groups used in this subgroup analysis. In this paper, only those with T2DM were included in the analysis (n=665).

Questionnaire

The questionnaire was administered in English, the local common language of communication for the multi-ethnic Asian population. The trained clinical research coordinators, conversant in English, Mandarin, Malay, and local dialects, provided language assistance, as required, to patients filling in the questionnaire.

Clinical information, including laboratory investigations, such as lipid profiles (total cholesterol, HDL-C, Triglycerides (TG), and LDL-C), BP, HbA1c readings, and electronic medication prescriptions were retrieved from their electronic medical records. The questionnaire, targeted at patients with dyslipidemia, covered self-reported adherence to their prescribed medications and perceptions related to their understanding of and attitudes towards lifestyle modifications and pharmacological treatments. This paper focuses on the impact of modifiable factors, largely pharmacological treatments, in attaining triple treatment goals among the subset of patients with T2DM and dyslipidemia.

Statistical analysis

The analysis was done using the attainment of concurrent triple treatment goals of defined levels of glycated hemoglobin (HbA1c), LDL-C, and BP as the primary outcome. To assess the difference between those who have well-controlled glycated hemoglobin and those who do not, a Chi-square test or Fisher's Exact test was used to test independence for categorical responses. Continuous variables were tested using independent t-tests and the Mann Whitney U test.

Adjusted odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) were calculated using logistic regression in which all potentially significant factors were entered. Data were coded and analyzed using IBM SPSS Statistical Software 22.0. For all of the test performed, a p-value of less than 0.05 was considered statistically significant.

In terms of the measurements used for BP, HbA1c, and LDL-C, current readings of BP were carried out twice, with an interval of 15 minutes between the two measurements, and the average of the two readings was used as the BP parameter. The most recent laboratory results (HbA1c and lipid profiles), as well as details of medications prescribed, were retrieved from the medical records.

Results

The study population comprised a total of 665 patients (402 females and 263 males) with a mean age of 60.6 years old. Table 1 summarizes the demographic characteristics of the patients included in the analysis. A total of 78.2% of the patients with T2DM and dyslipidemia failed to achieve concurrent treatment goals for HbA1c, BP, and LDL-C.

Demographic variables, such as gender, educational level, and employment status were not associated with triple goal achievement. A significant proportion of patients aged 60 years and older (26.2%) and of Chinese ethnicity (28.6%) attained better simultaneous control of the three treatment goals than those from younger age groups and other ethnic groups (**Table 1**). As many as 88% of the study population had a body mass index of 23 and above, yet the levels of triple-goal control were similar for the overweight and non-overweight groups . A greater proportion of patients with T2DM and other comorbidities failed to attain

concurrent treatment goals, and the association was significant among patients with renal disease (91.4%) (**Table 1**).

The patients in this study were taking an average of 2 diabetes-related medications, while the mean duration of T2DM was 6 years. Those who failed to achieve their triple control were likely to consume a higher number of diabetic medications and had a longer duration of T2DM. The highest percentage (46%) of simultaneous control was observed among patients who were not prescribed any diabetic medications. Those who were on either oral hypoglycemic agents or insulin were more likely to achieve concurrent treatment goals compared to those on combination treatments (p<0.01) (**Table 1**).

Table 1: Demographic profiles of patients with T2DM in association with their glycemia, blood pressure, and LDL-Cholesterol controls

	Total	Glycated hemoglobin[1], BP[2] and LDL[3] goals not achieved	Glycated hemoglobin[1], BP[2] and LDL[3] goals achieved	p-value
Demographic profile	665 (100.0)	520 (78.2)	145 (21.8)	
Gender				0.30
Female	402 (60.5)	309 (76.9)	93 (23.1)	
Male	263 (39.5)	211 (80.2)	52 (19.8)	
Ethnic Group				0.01
Chinese	203 (30.5)	145 (71.4)	58 (28.6)	
Malay	233 (35)	193 (82.8)	40 (17.2)	
Indian	229 (34.4)	182 (79.5)	47 (20.5)	
Age (years)				<0.01
<60	287 (43.2)	241 (84)	46 (16)	
>=60	378 (56.8)	279 (73.8)	99 (26.2)	
Education				0.99
Secondary or below	573 (86.2)	448 (78.2)	125 (21.8)	
Diploma/ Tertiary	92 (13.8)	72 (78.3)	20 (21.7)	
Employment Status				0.65
Employed	300 (45.1)	237 (79)	63 (21)	
Unemployed	365 (54.9)	283 (77.5)	82 (22.5)	
BMI[4]				0.62
Below 23	79 (11.9)	60 (75.9)	19 (24.1)	
23 and above	584 (88.1)	458 (78.4)	126 (21.6)	
Lifestyle habits				
Current Smoker				0.70
Yes	37 (5.6)	28 (75.7)	9 (24.3)	
No	628 (94.4)	492 (78.3)	136 (21.7)	
Alcohol				0.43
Yes	9 (1.4)	8 (88.9)	1 (11.1)	
No	656 (98.6)	512 (78)	144 (22)	
Comorbidities				
Hypertension				0.92
Yes	604 (90.8)	472 (78.1)	132 (21.9)	
No	61 (9.2)	48 (78.7)	13 (21.3)	
Ischemic Heart Disease/ Coronary Artery Disease				0.94
Yes	153 (23)	120 (78.4)	33 (21.6)	
No	512 (77)	400 (78.1)	112 (21.9)	
Cerebral Vascular Disease/ Stroke/ TIA				0.49
Yes	30 (4.5)	25 (83.3)	5 (16.7)	
No	635 (95.5)	495 (78)	140 (22)	

	Total	Glycated hemoglobin[1], BP[2] and LDL[3] goals not achieved	Glycated hemoglobin[1], BP[2] and LDL[3] goals achieved	p-value
Renal Disease				<0.01
Yes	70 (10.5)	64 (91.4)	6 (8.6)	
No	595 (89.5)	456 (76.6)	139 (23.4)	
Peripheral Vascular Disease				0.76
Yes	6 (0.9)	5 (83.3)	1 (16.7)	
No	659 (99.1)	515 (78.1)	144 (21.9)	
Duration of comorbidities				
Duration of Type II Diabetes, median (IQR)	6 (3-11)	6 (3-11)	4.5 (2-9)	<0.01
Duration of Hypertension, median (IQR)	7 (3-11)	7.5 (3.3-11)	7 (3-11)	0.84
Duration of Dyslipidemia, median (IQR)	7 (3.5-11)	7 (3-11)	7 (4-10)	0.59
Medication				
Number of diabetic medications, median (IQR)	2 (1-2)	2 (1-3)	1 (1-2)	<0.01
Number of anti-hypertensive medications, median (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	0.35
Number of lipid-lowering medications, median (IQR)	1 (1-1)	1 (1-1)	1 (1-1)	0.72
Diabetic medication type				<0.01
Not on diabetic medication	76 (11.4)	41 (53.9)	35 (46.1)	
Oral	481 (72.3)	377 (78.4)	104 (21.6)	
Insulin	11 (1.7)	9 (81.8)	2 (18.2)	
Combination (Oral and insulin)	97 (14.6)	93 (95.9)	4 (4.1)	
Statin Intensity[5]				<0.01
Low	153 (25.3)	104 (68)	49 (32)	
Moderate	377 (62.4)	305 (80.9)	72 (19.1)	
High	74 (12.3)	62 (83.8)	12 (16.2)	
Fasting Lipid Profiles (mg/dL)				
HDL-C[6]				0.70
Goals not achieved	103 (15.5)	82 (79.6)	21 (20.4)	
Goals achieved	562 (84.5)	438 (77.9)	124 (22.1)	
Triglyceride Levels[7]				0.046
Goals not achieved	77 (11.6)	67 (87)	10 (13)	
Goals achieved	587 (88.4)	452 (77)	135 (23)	

[1] Glycated hemoglobin: Goals not achieved: HbA1c>7; Goals achieved: HbA1c ≤ 7

[2] Blood pressure: aged 60 years or older < 150/90mmHg; aged below 60 years < 140/90mmHg; Patients with diabetes <140/90mmHg

[3] LDL-C: For high risk group, goals achieved refers to LDL≤ 2.6mmol/L (100 mg/dL), Goals not achieved refers to LDL>2.6mmol/L (100 mg/dL).

[4] BMI value of 23 and above indicates unhealthy weight range

[5] Statin Intensity: Adopted from the 2013 American College of Cardiology and American Heart Association (ACC/AHA) Blood Cholesterol Guideline

[6] HDL-C: Goals not achieved: < 1.0 mmol/L (40 mg/dL); Goals achieved: ≥ 1.0 mmol/L (40 mg/dL)

[7] Triglyceride: Goals not achieved: ≥2.3 mmol/L (200 mg/dL); Goals achieved: < 2.3 mmol/L (200 mg/dL)

The triple-treatment goal attainments of the 665 patients in this study is presented in Figure 1. In this sample, 71.0% and 70.4% of patients achieved LDL-C and BP treatment goals, respectively. Among the three goals, glycemic control was least satisfactory, at 40.9%. Dual achievement of the Hba1c and BP goals was reported for 28%, 30% achieved both the HbA1c and LDL-C goals , while the combined BP and LDL-C goals had 52% compliance (**Figure 1**). Simultaneous control of blood glucose, blood pressure, and blood lipids was reported for 21.8% of patients.

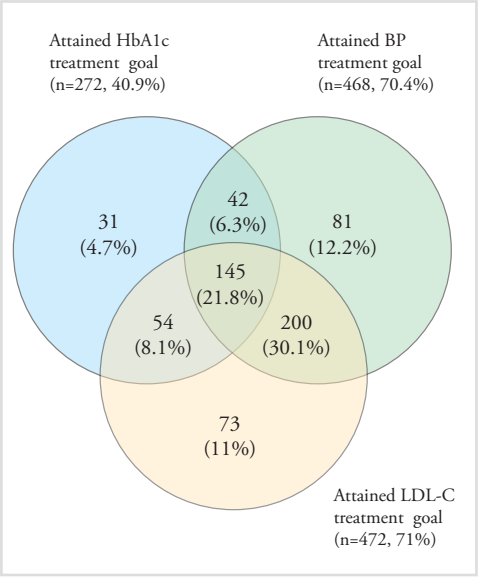

Figure 1: Venn diagram showing proportion of patients with T2DM attaining their glycemia, blood pressure, and LDL-Cholesterol treatment goals (n=665)

Table 2 shows the results of the logistic regression analysis of factors associated with attainment of the triple treatment goals. Patients who received moderate (OR=0.56, 95% CI of 0.35-0.91, p=0.02) to high intensity (OR =0.45, 95% CI of 0.21-0.97, p= 0.04) statin treatments were less likely to achieve concurrent treatment goals compared to the low intensity.

Table 2: Factors influencing glycated hemoglobin, blood pressure, and LDL-C goal achievement using logistic regression in patients with T2DM and dyslipidemia

	OR (95% CI)	p-value
Ethnic Group		
Chinese	1	-
Malay	0.72 (0.42, 1.23)	0.23
Indian	0.89 (0.53, 1.5)	0.66
Age (years)		
<60	1	-
>=60	1.53 (0.96, 2.42)	0.07
Renal Disease		
No	1	-
Yes	0.42 (0.15, 1.15)	0.09
Duration of T2DM	0.98 (0.93, 1.04)	0.56
Number of diabetic medications	0.50 (0.35, 0.73)	<0.01
Diabetic medication type		
Combination (Oral and insulin)	1	-
Not on diabetic medication	2.69 (0.63, 11.51)	0.18
Oral hypoglycemic agent only	2.33 (0.77, 7.02)	0.13
Insulin (of any type) only	2.63 (0.36, 19.14)	0.34
Triglyceride Levels		
Goals not achieved	1	-
Goals achieved	1.63 (0.74, 3.59)	0.23
Statin Intensity		
Low	1	-
Moderate	0.56 (0.35, 0.91)	0.02
High	0.45 (0.21, 0.97)	0.04

Discussion

Younger patients were less likely to attain triple treatment goals than those who were 60 years and above. This finding is compatible with that of an earlier study, which postulated that younger adult patients might be less motivated to manage their diabetic conditions, as they could be busy with their jobs and, therefore, have less time to comply with healthy lifestyle

and treatment requirements.[20] Based on their life span, they would be more susceptible to vascular complications due to earlier onset of the disease and a longer period of time in which to develop these adverse events. Sally et al. reported that young people with T2DM felt current diabetes education programs did not cater specifically to their age group in several domains.[21] They would appreciate clear and concise information in view of their time constraints. They desired family and peer support, as community acceptance was associated with a positive impact on their life experience with the medical condition.[20]

One out of five patients (21.8%) in this study attained triple treatment goals, which is lower than the 33% of such patients managed by KP. Achievement of the triple goals by patients was significantly associated with their therapeutics, including the number of anti-diabetic medications and intensity of their statin regime. This requires that physicians regularly review and adjust the dosages of these medications, which can be time and resource intensive. Instead of being heavily dependent on physicians and the primary healthcare team, the population-based management (PBM) model used by KP can be used as an alternative approach. Featured in the WHO European integrated care models,[22] the PBM leverages the stratification of the population and design of healthcare services to cater to the needs of the patient population. The majority of their patients with chronic diseases receive support for self-management of their illnesses, and high-risk patients are empowered by a combination of self-management and professional care.

PBM was adopted by and adapted to SHP in early 2013 and continues to evolve to cater to the growing population of patients with T2DM in Singapore. The institution collates monthly clinical data and laboratory reports of patients with specific disease codes (such as T2DM, hypertension, and dyslipidemia) in their electronic health records and stratifies their risk status according to their diseases based on clinical practice guidelines and indicators of their disease control. Nonetheless, the current IT system only permits the reporting of single indicators of disease control. This study presented the first ever accounting of patients who attained the triple treatment goals, setting the stage for further research and quality improvement projects to better the current benchmark.

Fewer medications and a shorter duration of T2DM were significant factors in triple control. This finding was comparable to a multinational survey in which predictors of glycemic control included short disease duration and the use of fewer anti-diabetic medications.[23] Increasing the number of medications may be required to optimize control as the disease progresses, but doing so may adversely increase the risks of poor medication adherence and side effects. Disease progression is thus associated with an increasing challenge in terms of attaining the triple goals. A longer-term strategy to curb this seemingly inevitable rise in disease burden from T2DM will be to move upstream to manage the an institutional approach, a multi-faceted national healthcare program has been launched in Singapore to fight a "war against diabetes."[24] Interventions can be designed to target the disease at the micro- (individual), meso- (healthcare system), and macro- (national) levels to enable more patients to achieve these simultaneous goals.

Strengths and limitations

Unlike most studies which reported results relating to solo glycemic control, this paper provides an examination of triple quality indicators for a highly urbanized Asian population with T2DM. The concurrent triple goal attainment is a more comprehensive mitigating measure to reduce risks of both macro- and micro-vascular complications. The results of this paper provide baseline data to trigger qualitative improvement initiatives to raise the proportion of patients with T2DM attaining this target.

However, the study population was recruited from two typical polyclinics in northeastern Singapore. Caution should be used in extrapolating the results to the entire local population. A prospective study of these patients would allow the quantification of the risk factors and identification of key measures which would optimize success in attaining triple treatment goals.

The study did not include other potential factors which may hamper the achievement of the triple treatment goals, such as patients' physical activities; social habits, such as alcoholic intake; thyroid status and possible renal impairment; genetics and local gut hormonal responses to diet and medications; and interference from gut microbiomes.

Conclusion

Simultaneous control of glycemia, hypertension and dyslipidemia was achieved by 21.8% of the study population with T2DM. Younger patients of less than 60 years of age were less likely to attain triple treatment goals. The number of diabetic medications and the intensity of statin treatment were significant factors associated with successful triple treatment goal achievement.

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Declaration of Conflicting Interests

The authors declare no conflict of interest as they are not members of the Singapore Heart Foundation, which is the independent sponsor of the study.

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