

ORIGINAL ARTICLE



Perception towards Insulin Therapy and Factors Related to Insulin Refusal among Insulin Naive Type 2 Diabetes Mellitus Patients in Primary Care Clinics PKD Lipis

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ABSTRACT

Introduction: Insulin is one of the suggested treatments to prevent and reduce long-term diabetes complications. However, due to many factors such as socio-demographic factors, many Type 2 diabetes mellitus patients refuse this treatment. This study aimed to determine perception towards insulin among naive Type 2 diabetes mellitus patients, to calculate the prevalence of rejecting insulin therapy, and to find out factors related to the refusal.

Materials and methods: This cross-sectional study involved 188 insulin naive Type 2 diabetes mellitus patients attending five primary health clinics in Lipis district, Pahang from October to November 2017. A five-point Likert Scale was used to determine perception towards insulin therapy and the Chi-square test was used to assess the proportion of acceptance of the therapy. Simple and multiple logistic regressions were utilised to study the associated factor(s).

Results: Mean score of 60.5 ± 8.2 pointed towards a negative appraisal of insulin therapy. Embarrassment to inject in public (69.1%) and concern of frequent hypoglycaemia (52.7%) were the most common perception. Nearly half of the respondents (46.3%) refused insulin therapy upon suggestion. After adjusting the variables using multiple logistic regressions, only gender (Adjusted OR=0.20, 95% CI=0.10-0.40, $p < 0.001$), educational level (Adjusted OR=0.17, 95% CI=0.06-0.50, $p = 0.001$), age (Adjusted OR=1.04, 95% CI=1.01-1.08, $p = 0.012$) and glycated haemoglobin level (Adjusted OR=1.33, 95% CI=1.07-1.67, $p = 0.013$) remained significant.

Conclusion: In conclusion, insulin refusal among insulin naive patients was common in Lipis with an overall negative perception towards therapy. By tailoring strategies according to the patient's factors such as gender, educational level, age, and glycated haemoglobin level, the insulin refusal rate might decrease in the future.

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Introduction

Diabetes situation in Malaysia is worrying as the trend continues to increase by year. As reported by National Health and Morbidity Survey (NHMS) in 2011, the prevalence of diabetes in Malaysia showed an increment from 11.6% in 2006 to 15.6% in 2011. By the year 2020, the prevalence of diabetes among Malaysian adults will be expected to increase up to 21.6% (Ministry of Health, 2012). Meanwhile, in Pahang, the NHMS survey 2015 concluded that 14.8% (147676) of adults 18 years and above are diagnosed with diabetes (Ministry of Health, 2015).

Throughout the year of therapy, β cell function in patients with diabetes will diminish, causing treating diabetes with oral glucose lowering-drugs (OGLDs) alone will be insufficient. Thus, insulin therapy is required for optimal control of glucose level. According to the 6th Edition of Malaysian CPG Management of Type 2 Diabetes Mellitus (T2DM), OGLDs remain the mainstay treatment of T2DM in combination with lifestyle intervention and appropriate dietary regimen. Insulin therapy can be initiated for all ages and at any stage of T2DM. The variety of treatment options and regimens available make it possible for better personalisation of the treatment to the patient (Ministry of Health, 2018).

Insulin therapy should be considered when good glycaemic control is not achieved or maintained despite optimal dose and number of OGLDs. It is also suggested as initial therapy in newly diagnosed T2DM, particularly when the level of glycated haemoglobin (HbA1c) > 10% or fasting plasma glucose (FPG) > 13.0 mmol/L (Ministry of Health, 2018). Early use of insulin has proven to have greater improvement in HbA1c and FPG with lower risk or no difference in the occurrence of hypoglycaemia (Westphal et al., 2006; Fonseca et al., 2011). Besides, many complications can be prevented with the early introduction of insulin in the management of suboptimal controlled diabetes (Gerstein et al., 2006; Vinik, 2007; Rubino et al., 2007).

The insulin refusal rate among Type 2 diabetes mellitus (T2DM) patients are high even though some eventually accept the treatment. To enhance patient quality of life and to prevent complications of uncontrolled diabetes, health care providers are responsible to help patients achieve the targeted blood glucose range. However, rejection of insulin therapy is one of the main challenges when treating diabetes patients, particularly those with poor control.

Studies done in several countries suggested that insulin naive patient refusal rate is varied. It ranged from 70.6% in Singapore, 42.5% in Bangladesh to nearly 28.2% in the United States of America region (Wong et al., 2011; Khan et al., 2008; Polonsky et al., 2004). A high refusal

rate was observed in a local study which discovered 51% of participants were reluctant to start insulin therapy (Azmiah et al., 2011).

Patient's acceptance of insulin therapy can be influenced by many factors such as socio-demographic factors, clinical factors or psychological factors. The combination of these factors makes the initiation of insulin therapy even more challenging. Older age was one of the socio-demographic factors that contributed to insulin therapy refusal (Tan et al., 2015; Ghadiri-Anari, et al., 2013; Batais et al., 2016). Gender, particularly female was more likely to refuse insulin therapy (Polonsky et al., 2004; Azmiah et al., 2011; Hassan et al., 2013; Kaur et al., 2018). Other socio-demographic factors that were observed in previous studies included educational backgrounds (Wong et al., 2011; Tan et al., 2015; Batais et al., 2016), employment status (Khalili et al., 2016; Tan et al., 2015), ethnicity (Azmiah et al., 2011; Tan et al., 2015) and marital status (Khalili et al., 2016). Meanwhile, the long duration of having diabetes and poor control of diabetes which was determined by a high level of HbA1c was known clinical factors for insulin therapy refusal that were already addressed by previous literature (Tan et al., 2015).

Despite the efficacy and benefits of insulin have been proven in many studies, these negative thoughts of patients towards insulin are a huge barrier for them to start insulin therapy. It is important to understand the patient perception of insulin and the reasons for refusal so that better service and counselling for the patient can be provided. Therefore, this study was conducted to determine perception towards insulin among insulin naive T2DM patients. This study was also done to calculate the prevalence of rejecting insulin therapy in the Lipis district. Other than that, this study was done to find out the factors related to insulin therapy refusal.

Materials and methods

A cross-sectional study was conducted in five primary health clinics in Lipis district, Pahang Malaysia, namely Klinik Kesihatan (KK) Benta, KK Padang Tengku, KK Sungai Koyan, KK Merapoh and Klinik Bergerak Komuniti Lipis for two months from October to November 2017.

A self-administered questionnaire (Appendix 1) was developed by following a similar local study (Azmiah et al., 2011). The first part of the questionnaire included socio-demographic details. The patient's last HbA1c reading was also recorded. The second part of the questionnaire consisted of 20 items (18 negative items and 2 positive items). Scored on a five-point Likert Scale, where strongly disagree = 1, disagree = 2, unsure = 3, agree = 4, and strongly agree = 5. For calculation of the total score, the rating of the two positive items were in reverse, with strongly disagree = 5, disagree = 4, unsure = 3, agree

= 2, and strongly agree = 1. The total possible score for the questionnaire was 100. The higher the score indicated a more negative appraisal of insulin therapy. Data are presented as means \pm standard deviation (SD) (Chen et al., 2011).

Epi Info Version 7.2 Stac Calc was used to calculate the sample size for this study – Sample Size and Power with 95% Confidence level, 74.2% prevalence of rejecting insulin therapy, 5% precision and infinite population count (Tan et al., 2015). The minimum sample size required was 353 after a 20% allowance for non-responders. Respondent's inclusion criteria were those diagnosed with Type II diabetes mellitus (T2DM) with the last HbA1c reading ≥ 7.0 %, took two or more OGLDs for at least six months and never use insulin. Patients diagnosed with Type I diabetes mellitus, psychiatric disease or dementia and those with dexterity impairment were excluded from the study. Respondents were conveniently recruited when having follow-up for their T2DM and the consent form, which was adapted from the National Medical Research Register (NMRR), was disseminated to the selected study subjects (Appendix 2).

The prevalence of insulin refusal was calculated using the formula adapted from the Centres for Disease Control and Prevention website (Centres for Disease Control and Prevention. 2012). Data were analysed using Statistical Package for Social Sciences (SPSS) version 21.0. The Chi-square test was used to assess differences in proportion between those who accepted and those who rejected insulin therapy. Simple and multiple logistic regressions were utilised to study the factors related to insulin therapy refusal. A p-value of less than 0.05 was considered to be statistically significant.

The study was approved by the Medical Research Ethics Committee (MREC) Malaysia and registered with the National Medical Research Registry (NMRR ID: NMRR-17-1843-37560)

Results

A total of 201 patients were approached for the study but only 188 agreed to take part, yielding a response rate of 93.5%. Since a self-administered questionnaire was used as the study instrument for this study, those with low literacy refused to participate. The majority of the respondents were Malay (88.3%), single/widowed (70.2%), not working/retired (73.9%) with at least secondary education (50.5%) and an almost equal number of males and female participated in the study. Their mean age was 57.8 years and the average earning was RM1469.15 \pm 1270.76. The mean HbA1c reading was 9.17% \pm 1.60%.

Table 1: Patient's socio-demographic data and willingness to initiate insulin therapy (n=188)

Total	Willingness		
	n (%)	Willing (%)	Unwilling (%)
	188 (100.0)	101 (53.7)	87 (46.3)
Age	57.8* (11.5) ^v	55.3* (11.0) ^v	60.8* (11.3) ^v
Gender			
Male	85 (45.2)	27 (31.8)	58 (68.2)
Female	103 (54.8)	74 (71.8)	29 (28.2)
Ethnic			
Malay	166 (88.3)	86 (51.8)	80 (48.2)
Non-Malay	22 (11.7)	15 (68.2)	7 (31.8)
Marital Status			
Single/widowed	132 (70.2)	65 (49.2)	67 (50.8)
Married	56 (29.8)	36 (64.3)	20 (35.7)
Educational Level			
Not schooling/primary	56 (29.8)	46 (82.1)	10 (17.9)
Secondary	95 (50.5)	43 (45.3)	52 (54.7)
Tertiary	37 (19.7)	12 (32.4)	25 (67.6)
Working Status			
Not working	139 (73.9)	84 (60.4)	55 (39.6)
Working	49 (26.1)	17 (34.7)	32 (22.7)
Income			
RM0 – RM999	65 (34.6)	33 (50.8)	32 (49.2)
RM1000 – RM1999	82 (43.6)	44 (53.7)	38 (46.3)
RM2000 – RM2999	25 (13.3)	15 (60.0)	10 (4.0)
\geq RM3000	16 (8.5)	9 (56.2)	7 (43.8)
HbA1c	9.2* (1.6) ^v	8.8* (1.2) ^v	9.6* (1.6) ^v

*Mean ^vStandard deviation
HbA1c: glycated haemoglobin

The total possible score for the questionnaire is 100 and the higher the score indicates a more negative appraisal of insulin therapy. Table 2 showed the total score for both respondents' opinions regarding self-efficacy and insulin therapy (60.5 ± 8.2) indicating the respondents' perceptions were negative towards insulin therapy.

Table 2: Total Score for Self-Efficacy and Opinion Regarding Insulin

	Mean \pm SD
Opinion regarding self-efficacy	30.6 \pm 5.7
Opinion regarding insulin	29.9 \pm 4.1
Total Score:	60.5 \pm 8.2

The top three opinions regarding self-efficacy are feeling embarrassed to inject insulin in public (69.1%), the concern that hypoglycaemia would lead to permanent irreversible damage (60.1%) and fear of pain during insulin administration (57.4%).

Most respondents agreed that insulin might cause frequent hypoglycaemia (52.7%). Meanwhile, almost half admitted they were unsure about most of the information regarding insulin such as insulin and needles are more expensive than oral therapy (42.6%), whether insulin can be stopped once initiated (41.0%).

The prevalence of insulin refusal was presented in the figure below. Four of every ten patients reported unwilling to start insulin therapy (46.3%).

Simple logistic regression was conducted to analyse the association between insulin therapy refusal and socio-demographic data, hence deciding the factor(s) that might contribute to insulin refusal. Only factors with a p-value < 0.05 were deemed to be statistically significant. Six factors that fulfilled the criteria, namely age, gender, educational level, employment status, and HbA1c were further investigated with multiple logistic regressions.

After analysing multiple logistic regressions, only gender, educational level, age, and HbA1c remained significantly associated with the tendency to accept insulin therapy. While controlling for other factors, women were 20 % more likely to accept insulin therapy, compared to

male respondents (adjusted OR 0.20, 95 % CI 0.10-0.40, $p = <0.001$). Respondents who received tertiary education were 83% more likely to resist insulin therapy compared to those who received only primary education or with no formal education (adjusted OR 0.17, 95 % CI 0.06-0.50, $P = 0.001$). Age and HbA1c were inversely associated with insulin therapy acceptance. For every one-year increase in age, respondents were 1.04 times more likely to reject insulin therapy (adjusted OR 1.04, 95 % CI 1.01-1.08, $p = 0.012$). Similarly, for every 1.0% increment in HbA1c level, subjects were 1.33 times more reluctant to initiate insulin therapy (adjusted OR 1.33, 95 % CI 1.07-1.67, $p = 0.013$).

Discussion

It is important to address a patient's perception of insulin therapy as many patients were hesitant to use insulin due to their negative beliefs about insulin injection (Hassan et al., 2013). The current study found out that the respondents have a prominent negative belief towards insulin therapy (total score 60.5 ± 8.2). This finding was comparable to a previous study where their insulin naive T2DM respondents scored 62.9 ± 7.1 indicating negative perceptions towards therapy (Ghadiri-Anari et al., 2013). This was understandable as patients tended to worry about the unfamiliar forms of treatment and become a barrier for the patient to start the treatment. By recognizing the patient's hurdle, psychological insulin refusal (PIR) can be overcome. Providing the information and introducing the possible need for insulin early in treatment can improve patient's perceptions towards insulin in general and overcome PIR (Polonsky et al., 2011).

The majority of respondents admitted that they feel embarrassed to inject insulin in public (69.1%). It can be inconvenient and embarrassing as insulin needs to be injected at a certain time. This was supported by a previous finding where more than half of the subjects (55.9%) expressed that injecting insulin in public was embarrassing (Azmiah et al., 2011). The absence of a private area may cause them to inject too early or might entirely omit the dose and eventually resulting in hypo/hyperglycaemia (Chen et al., 2011; Hunt et al., 1997). However, feeling embarrassed to inject insulin in public was the least worrying reason for patients in a previous study done in Kubang Pasu, Kedah (17.5%) (Tan et al., 2015).

Table 3: Opinion Regarding Self-Efficacy

No.	Statements	Mean \pm SD	Number (%)		
			Disagree	Unsure	Agree
1	Feel embarrassed to inject insulin in public	3.8 \pm 1.2	34 (18.1)	24 (12.8)	130 (69.1)
2	Concern that hypoglycaemia would lead to permanent irreversible damage	3.6 \pm 1.0	41 (21.8)	34 (18.1)	113 (60.1)
3	Fear of pain during insulin administration	3.1 \pm 1.1	70 (37.3)	10 (5.3)	108 (57.4)
4	Fear of injection	2.9 \pm 1.3	79 (42.0)	9 (4.8)	100 (53.2)
5	Injecting insulin makes one feel as if he/ she is a drug addict.	3.1 \pm 1.5	71 (37.8)	21 (11.2)	96 (51.0)
6	Lack of confident in injecting insulin	3.1 \pm 1.2	66 (35.1)	45 (23.9)	77 (41.0)
7	Unable to arrange/ adjust daily activities as needed in insulin therapy	3.0 \pm 1.3	81 (43.1)	36 (19.1)	71 (37.8)
8	Worry about hypoglycaemia	2.6 \pm 1.4	103 (54.8)	20 (10.6)	65 (34.5)
9	Unable to arrange/ adjust diet as needed in insulin therapy	2.5 \pm 1.1	109 (57.9)	16 (8.5)	63 (33.5)
10	Lack of time to inject insulin systematically	2.4 \pm 1.3	128 (68.1)	6 (3.2)	54 (28.7)

Table 4: Opinion Regarding Insulin Therapy

No.	Statements	Mean \pm SD	Number (%)		
			Disagree	Unsure	Agree
1	Insulin causes hypoglycaemia frequently.	3.4 \pm 1.0	37 (19.7)	52 (27.7)	99 (52.7)
2	Insulin contains illegal substances.	2.9 \pm 1.4	79 (42.0)	31 (16.5)	78 (41.5)
3	Insulin causes a lot of adverse effects in the future.	2.9 \pm 1.0	75 (39.9)	45 (23.9)	68 (36.2)
4	Insulin and needles are more expensive than oral hypoglycaemic agents.	3.2 \pm 0.9	40 (37.2)	80 (42.6)	68 (36.2)
5	Insulin leads to renal failure.	2.9 \pm 1.5	75 (39.9)	51 (27.1)	62 (33)
6	Insulin therapy leads to dependency.	2.8 \pm 1.2	72 (38.2)	54 (28.7)	62 (33)
7*	Insulin prevents long-term complications of uncontrolled diabetes.	3.1 \pm 1.2	66 (35.1)	72 (38.3)	50 (26.6)
8	Insulin therapy cannot be stopped once initiated.	2.7 \pm 0.9	78 (41.5)	77 (41.0)	33 (17.5)
9*	Insulin is more effective than oral hypoglycaemic agents.	3.4 \pm 0.9	95 (50.5)	62 (33.0)	31 (16.5)
10	Insulin leads to blindness.	2.1 \pm 0.9	113 (60.1)	65 (34.6)	10 (5.3)

*Questions 7 and 9 are the positive questions.

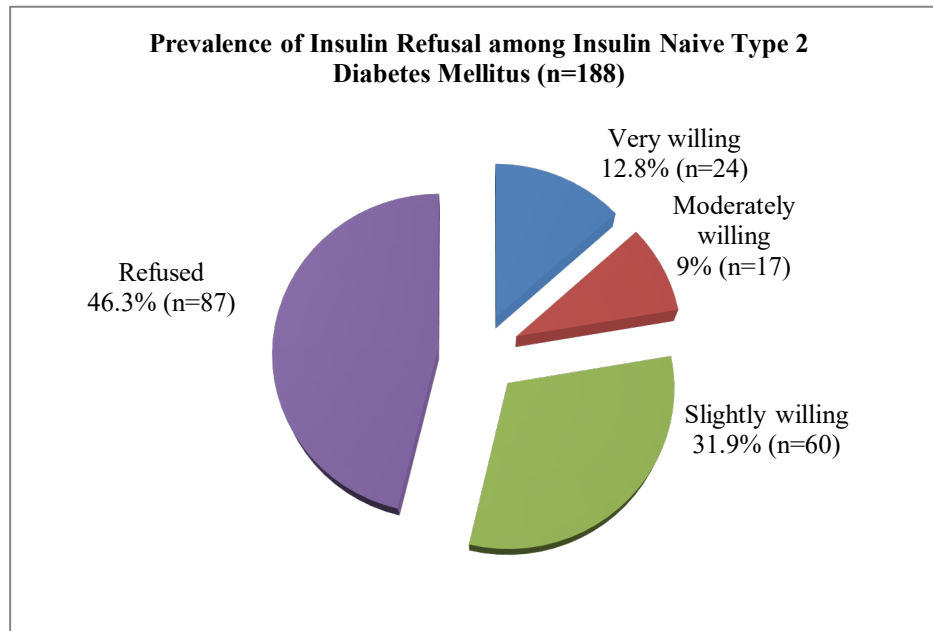


Figure 1: Prevalence of Insulin Refusal among Insulin Naive Type 2 Diabetes Mellitus in Public Patients in Primary Care Clinics PKD Lipis (n=188; 58.2% female; 93.1% Malay)

Fear of problematic hypoglycaemia was found to be a secondary concern in the current study as most of the patients afraid that hypoglycaemia would lead to permanent irreversible damage (60.1%) and agreed that insulin can cause hypoglycaemia frequently (53.7%). One of the contributing factors could be because most of the respondents lived alone (70.2% of patients were single/widowed) and thus intensified the fear. The DAWN study addressed the fear of hypoglycaemic events as one of the patients' factors that contribute to a poor sense of well-being and thus affecting overall diabetes outcomes (Korytkowski, 2002). The result was comparable to the findings in previous studies where 59.6% and 47.8% of patients respectively admitted that they refused insulin due to the fear of problematic hypoglycaemia (Azmiah et al., 2011; Tan et al., 2015).

In the current study, 46.3% of patients with Type 2 diabetes mellitus who visited public clinics in Lipis denied insulin if the treatment was given to them. This percentage was comparable with previous studies done by Khan et al., (2008) and Azmiah et al., (2011) as 42.5% and 50.7% of their respondents respectively unwilling to initiate the treatment. Meanwhile, higher refusal rates were recorded in previous studies done in various countries ranging from 60 to 80% of refusal rate (Wong et al., 2011; Tan et al., 2015; 1999; Kaur et al., 2018). However, Polonsky et al., (2004) reported the

lowest rate with 28.2% of refusal. Due to geographic factor as the current study was done in a rural setting, health promotion activities to patients are restricted, causing insufficient exposure to health information. Urban populations have a better acceptance of insulin treatment and better access to health information related to disease and treatment (Rubino et al., 2007).

The current study found out that age was inversely associated with insulin therapy acceptance. For every one-year increase in age, respondents were 1.04 more likely to reject insulin therapy ($p=0.012$). However, a different finding was observed in previous literature as elderly respondents were more accepting of insulin therapy ($r=-0.153$, $p<0.05$) (Rubino et al., 2007). Treating the elderly with diabetes is challenging as they are at an increased risk rate of concomitant illnesses such as hypertension, renal impairment, and heart diseases. Polypharmacy is also one of the concerns as patients will be more concerned regarding possible drug-drug interaction and the idea of adding insulin into the treatment will cause more worries and cause them to refuse the therapy (Ministry of Health, 2015). However, several previous studies found no significant difference between age groups and willingness to start insulin therapy (Tan et al., 2015; Ghadiri-Anari, et al., 2013; Batais et al., 2016).

Some previous studies discovered that male patients were more likely to accept the insulin initiation which male patients were said to be naturally less fearful of injection (Polonsky et al., 2004; Hassan et al., 2013; Kaur et al., 2018). A local study was done by Azmiah et al., (2011) also found out that female patients were 2.7 times more likely to refuse insulin initiation. However, in the current study female respondents were 20% more expected to accept insulin therapy, compared to males ($p = <0.001$).

As found in previous studies, patients with higher educational backgrounds were less likely to refuse insulin initiation. Wong et al., (2011) revealed that patients with tertiary level of education were more willing to start insulin therapy. Same finding was observed in local study in which patient with at least a secondary education was 55.0% less likely to refuse insulin as patients with higher education are expected to be more receptive towards knowledge on disease and insulin therapy (Tan et al., 2015). However, the current study found out that respondents who received tertiary education were 83.0% more likely to resist insulin therapy ($p=0.001$) and supported by a previous study done in Saudi Arabia as those with tertiary education were 48% unwilling to initiate insulin therapy ($p=0.023$) (Batais et al., 2016).

The recent study reported HbA1c level was related to the refusal as for every 1.0% increment in HbA1c level subjects were 1.33 times more reluctant to initiate insulin therapy ($p=0.013$). Similar findings were recorded in previous studies where a significant relationship was found between patient's willingness for insulin initiation with HbA1c level (Azmiah et al., 2011; Tan et al., 2015). A different finding was observed by Wong et al., (2011) in which those who were reluctant to start the treatment were among the lower mean HbA1c group. Compared to the other studies, patients with HbA1c $>7\%$ were recruited in the recent study. According to previous literature patient with higher HbA1c tends to refuse insulin therapy more than those with lower HbA1c as a higher dose of insulin initiation is needed and thus higher concern for hypoglycaemia (Hayward, 1997; Abaira et al., 1995).

However, some limitations should be noted. The current study has a limited number of respondents as those with the last HbA1c reading $< 7.0\%$ were excluded from the study. The minimum sample size required was 353 after a 20% allowance for non-responders. However, only 188 respondents agreed to participate in the study, causing difficulty to identify significant relationships from the data. The

questionnaire given was self-administered. Thus, those with low literacy tended to avoid participating in the study.

Conclusion

Overall, insulin naive T2DM patients in primary care clinics in the Lipis district demonstrated a high level of negative perception towards insulin therapy (mean score = 60.5 ± 8.2). Almost half of them (46.3%) were reluctant to start insulin therapy when being suggested by their doctors. Most patients still have negative opinions regarding insulin and self-efficacy which resulted in a great influence on their willingness to start the therapy. In the future, factors that might be associated with insulin refusal should be addressed possibly in every patient so that the refusal rate can be reduced.

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Conflict of Interest

The authors whose names are listed above certify that they have NO affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in the manuscripts.

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