Review of insulin-associated hypoglycemia and its impact on the management of diabetes in Southeast Asian countries

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ABSTRACT
Although the incidence of diabetes is rising in Southeast Asia, there is limited information regarding the incidence and manifestation of insulin-associated hypoglycemia. The aim of the present review was to discuss what is currently known regarding insulin-associated hypoglycemia in Southeast Asia, including its known incidence and impact in the region, and how the Southeast Asian population with diabetes differs from other populations. We found a paucity of data regarding the incidence of hypoglycemia in Southeast Asia, which has contributed to the adoption of Western guidelines. This might not be appropriate, as Southeast Asians have a range of etiological, educational and cultural differences from Western populations with diabetes that might place them at greater risk of hypoglycemia if not managed optimally. For example, Southeast Asians with type 2 diabetes tend to be younger, with lower body mass indexes than their Western counterparts, and the management of type 2 diabetes with premixed insulin preparations is more common in Southeast Asia. Both of these factors might result in higher rates of hypoglycemia. In addition, Southeast Asians are often poorly educated about hypoglycemia and its management, including during Ramadan fasting. We conclude there is a need for more information about Southeast Asian populations with diabetes to assist with the construction of more appropriate national and regional guidelines for the management of hypoglycemia, more closely aligned to patient demographics, behaviors and treatment practices. Such bespoke guidelines might result in a greater degree of implementation and adherence within clinical practice in Southeast Asian nations.

INTRODUCTION
The present article seeks to explore what is currently known about the problem of insulin-associated hypoglycemia in the populations with diabetes of members (Indonesia, Malaysia, the Philippines and Singapore) of the Association of South East Asian Nations (ASEAN), with a view to establishing guidelines for its avoidance and management. This is an important undertaking because the prevalence of type 2 diabetes is high and rising in these nations, and there are some potentially important cultural and etiological differences between ASEAN populations and those of the predominantly Caucasian nations for which some of the standard global guidelines have been developed. To assess what is known about insulin-associated hypoglycemia in these Southeast Asian countries and related issues of local significance, published scientific articles of potential relevance were identified by a PubMed search using search terms including ‘hypoglycaemia/hypoglycemic,’ ‘insulin/cost/quality of life’ and countries/nationalities; for example, (Hypoglycaemia OR Hypoglycemia) AND insulin AND (Indonesia or Indonesian). The search results assessed were limited to recent publications (2000–2016), and the countries included were Indonesia, Malaysia, the Philippines and Singapore. The present review provides a narrative account of the subject based on the relatively few articles identified, supplemented where necessary by information from international studies.

PREVALENCE OF DIABETES IN THE SOUTHEAST ASIA REGION
There is limited information regarding actual rates of diabetes in Southeast Asia, owing to a lack in many countries of regular population surveys that utilize appropriate methodology; that is,
utilization of household interviews and measurements of fasting blood glucose in those not previously diagnosed as diabetic at the time of survey. While Malaysia carries out a national health and morbidity survey, and has reported the prevalence of diabetes in adults at 17.5% in 2015, this information is lacking for other countries and relies on estimates. In Indonesia, Malaysia, the Philippines and Singapore, the estimated prevalence of diabetes (based on oral glucose tolerance tests) in adults was 6.2, 16.6, 6.1 and 12.8%, respectively, and since the 1980s there has been a large increase (1.5- to 5.2-fold) in the prevalence of diabetes. The highest increases in this prevalence are in urban areas, with Southeast Asia seeing some of the highest rates of global urbanization. Although rates of diabetes are increasing globally, there is a mismatch between the projected estimated increases in prevalence (1.5-fold) and spending (1.2-fold) from 2015–2040, due to the fact that 75% of the global population with diabetes lives in low-to-middle-income countries, which contribute just 19% to global diabetes-related health expenditure. However, in the Southeast Asian nations, diabetes-related health costs are predicted to escalate much higher than the global average of 8% total health expenditure. In 2010, Indonesia, the Philippines, Singapore and Malaysia spent, respectively, 7.0, 11.0, 15.0 and 16.0% of their total national health expenditure on diabetes, and by 2030 it is predicted that costs in these countries will rise 1.7- to 1.8-fold. A contributor to this health expenditure is the prevalence and type of therapeutic treatment offered to patients in Southeast Asia. For example, a high proportion of patients with type 2 diabetes in Indonesia, the Philippines, Singapore and Malaysia take at least one oral antidiabetic drug (OAD) (57.2-85.0%), with a smaller proportion of patients taking insulin (3.0-19.3%) alone or in combination with OADs (8.0-19.4%; Table 1). Comparing these limited data with data from the USA, the use of OADs appears more common in Asia, with insulin used less frequently in some countries (particularly in combination with OADs) than in the USA.

**INSULIN-ASSOCIATED HYPOGLYCEMIA**

Insulin therapy is the primary therapeutic intervention for patients with type 1 diabetes, and in many countries this is also true for patients with type 2 diabetes who become inadequately controlled with lifestyle changes and OADs. The goal of insulin therapy is to regain glycemic control, which is generally assessed by success in achieving target glycated hemoglobin (HbA1c) concentration. However, successful management also requires monitoring of hypoglycemia, the most common side-effect of insulin and many other glucose-lowering therapies. In pursuit of glycemic targets, while minimizing patient risk of hypoglycemia, insulin is dosed according to self-monitoring of blood glucose (SMBG) levels, and is measured more frequently when patients are closer to glycemic target, at greater risk of hypoglycemia or symptomatic for low blood glucose. Rates of hypoglycemia differ across the different treatment options for the first insulin prescribed, with higher rates of hypoglycemia associated with bolus and premixed insulins compared with basal insulin. Intensified basal–bolus regimens inevitably result in higher rates of hypoglycemia compared with basal-only insulin regimens, and premixed insulins have been associated with a greater incidence of hypoglycemia than basal–bolus regimens. The experience of hypoglycemia can be at best unpleasant and at worst life-threatening for the patient, hence the fear of repeated episodes can lead patients and their carers to become overly cautious in their treatment of diabetes – potentially to the detriment of the patient’s long-term prognosis. Hypoglycemia is therefore an important consideration when constructing individualized glycemic targets. Despite high awareness among patients and physicians that hypoglycemia is a significant barrier to the effective treatment of diabetes, it is feared that there is vast underreporting of hypoglycemia rates. This might therefore mask the scale of the problem, and potential differences between insulin products and regimens.

**INCIDENCE OF HYPOGLYCEMIA IN SOUTHEAST ASIA**

There is a paucity of information regarding the incidence of hypoglycemia in Southeast Asia, particularly for patient-reported data from clinical practice. In contrast, there are a number of European and North American observational studies and surveys in patients with type 1 diabetes and type 2 diabetes reporting rates of non-severe hypoglycemia, but their comparability with South Asian countries might be questionable. The scarcity of hypoglycemia data for Asians was partly addressed after the completion of the A1chieve study – a non-interventional, observational study of 66,726 insulin-experienced (started on insulin detemir, insulin aspart or

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**Table 1 | Diabetes treatment patterns of patients from Southeast Asia and the USA**

| Treatment       | Indonesia (type 2 diabetes)  | Malaysia (DM)  | Philippines (DM)  | Singapore (type 2 diabetes) | USA (DM) |
|-----------------|-------------------------------|----------------|-------------------|-----------------------------|---------|
| OADs            | 61.9%                         | 79.1%          | 85.0%             | 57.2%                       | 50.3%   |
| Insulin         | 17.3%                         | 25.1%          | 15.0%             | 3.0%                        | 17.8%   |
| OAD and insulin | 19.4%                         | NA             | 8.0%              | 9.0%                        | 13.0%   |
| Other           | 0.3%                          | 0.5%           | NA                | NA                          | NA      |

1 Oral antidiabetic drugs (OADs) used without injectables. 2 Traditional or complementary medicine. 3 Using at least one oral drug of which 97% were OADs. DM, diabetes mellitus; NA, not available; OAD, oral antidiabetic drug.
biphasic insulin aspart) and insulin-naïve patients with type 2 diabetes, in 28 countries across four continents36. A1chieve® showed that initiation of, or switch to, insulin therapy using modern insulin analog products decreased the rates of hypoglycemia in patients with type 2 diabetes27–29. However, although A1chive® might provide reassurance about the clinical efficacy/safety profiles of particular insulin analogs, gaps remain in the reporting of hypoglycemia rates for patients with type 1 diabetes in each of the countries within the ASEAN region (e.g., data for Malaysia and Singapore are lacking), and for all diabetes patients taking other insulin regimens, such as basal and premix. Apart from A1chive®, there are few publications reporting the rates of hypoglycemia for exclusively South-east Asian populations, with many studies reporting rates from multinational populations where Asian and Western populations are mixed30–32. With a lack of comprehensive data regarding rates of hypoglycemia from Southeast Asian countries, it is difficult to quantify the potential impact of hypoglycemia in this region. However, there is a wealth of information from Western countries, which can be discussed alongside the available data detailing the impact of hypoglycemia in Southeast Asia. Collectively, the evidence shows that the impact of hypoglycemia is wide and far reaching, affecting the morbid burden of patients, treatment adherence and thereby diabetic complications. These in turn have health economic implications.

**IMPACT OF HYPOGLYCEMIA**

*Impact on patient health, well-being and treatment adherence*

Before insulin is even initiated, patients and physicians have misconceptions about hypoglycemia, creating a fear of insulin therapy that can result in reduced adherence once insulin is initiated33,34, and in some cases, refusal to initiate it35. A study in Malaysia reported that non-adherent patients felt their healthcare professional (HCP) had not properly explained the risks and benefits of insulin to them36, and some patients perceived that advice from their HCP was biased towards the benefits, with the risks of insulin therapy only explained once patients had agreed to start treatment27. In addition, 54.3% of Malaysians with type 2 diabetes, using insulin, were worried about the risk of hypoglycemic events, and 61.3% of those not currently using insulin were worried about starting insulin treatment36. This ‘fear factor’ about hypoglycemia has a negative impact on the management of diabetes, metabolic control and health outcomes39. Episodes of hypoglycemia, when symptomatic, lead to unpleasant and distressing symptoms including pounding heart, trembling, hunger, sweating and difficulty in concentrating39. In severe cases, this can lead to confusion/disorientation, seizures and loss of consciousness requiring third-party assistance41. The trauma created by hypoglycemia translates into a tangible fear of hypoglycemia and, although this has not been quantified in Southeast Asia, one Singaporean study of patients with type 1 diabetes or type 2 diabetes taking insulin for at least 1 year has validated the use of a fear-of-hypoglycemia survey42 in patients who had at least one episode of mild (56%), moderate (51%) or severe hypoglycemia (31%) in the month, 6 and 12 months before the survey. Although patient fear has not been quantified to date, it is clear that severe episodes of hypoglycemia can result in medical complications43, associated with increased risk of falls, fall-related morbidity44,44 and increased risk of mortality45–47. Such symptoms and consequences contribute to an overall decrease in patients’ health-related quality of life48–50, and studies such as A1chive® have shown that if rates of hypoglycemia can be improved upon, so can health-related quality of life51–54.

The fear of hypoglycemia works as a limiting factor to the achievement of glycemic control, preventing HCPs from intensifying insulin therapy20, particularly in older patients with comorbidities55, thus placing them at an increased risk of complications such as cardiovascular disease56. For this reason, both the American Diabetes Association and the European Association for the Study of Diabetes guidelines advise that the target level of glycemic control is individualized based on a patient’s risk of hypoglycemia, duration of disease, comorbidities and life expectancy17,18. This individualized approach to treatment translates to hypoglycemia being a common reason for patients with type 2 diabetes changing or switching insulin therapy57, and severe cases of hypoglycemia can lead to termination of insulin therapy58.

*Health economic impact*

Severe hypoglycemia accounts for significant medical expenditure as a result of hospitalization59–61 and loss of productivity62, with lower blood glucose/more severe hypoglycemia being associated with increased length of stay and increased risk of mortality63. Furthermore, economic costs increase in patients with micro-and macrovascular complications arising from poor glucose control64, which is likely to occur in patients receiving less intensive glucose-lowering therapies and those with reduced adherence to medications due to fear of hypoglycemia. One potential driver of increased economic cost in patients at high risk of hypoglycemia is the more frequent use of SMBG65, but as SMBG is poorly utilized by patients in Asian countries, such as Malaysia66,67 (despite incorporation into type 2 diabetes treatment guidelines68), the economic costs of hypoglycemia in Southeast Asia are more likely to be impacted by its underutilization and the economic consequences derived from poorer glycemic control69. The economic impact of hypoglycemia also differs among different insulins as a result of differences in their kinetic profiles, and because different doses might be required to reach the same glycemic target. For example, a cost-effectiveness analysis in Singaporean patients with type 2 diabetes estimated that the costs of treating complications, including severe hypoglycemia, were $5,450 and $2,800 per patient for those using neutral protamine Hagedorn or insulin glargine over a 5-year period70. However, this cost-effectiveness analysis requires validation with local outcomes data, as the rates of severe hypoglycemia (1.30 and 0.57 per patient-year for neutral protamine Hagedorn insulin and insulin glargine) were extrapolated from a study of Western patients with type 1 diabetes71.
In summary, there is a scarcity of information regarding the true incidence and impact of hypoglycemia in Southeast Asia and, as a result, diabetes guidelines have been based on information taken from global studies that have informed Western guidelines. However, the Southeast Asian population is characterized by demographic, etiological and cultural differences from Western populations, as well as treatment differences, and these might have different consequences on both the incidence and impact of hypoglycemia.

DEMOGRAPHIC AND ETIOLOGICAL ISSUES PERTAINING TO SOUTHEAST ASIAN PATIENTS
Southeast Asian patients often present with type 2 diabetes at a younger age and with lower body mass index than their Caucasian counterparts, and with a phenotype characterized by loss of prandial insulin secretory reserve. These factors in turn result in some differences between Southeast Asian and Western nations in the use of insulin therapy, and all of these issues can impact the risk, manifestation and appropriate management of hypoglycemia. For example, predictive factors for hypoglycemia include previous hypoglycemia, >2 injections per day, body mass index <30 kg/m² and duration of insulin therapy >10 years/longer duration of therapy. In contrast to the incidence of type 2 diabetes, type 1 diabetes is less common in Asia compared with other regions, hence the following discussion will predominantly focus on issues concerning type 2 diabetes.

Southeast Asians might be genetically predisposed to developing type 2 diabetes as, despite having a greater adiposity than Western populations, there is a tendency for those with type 2 diabetes to be younger and have a lower body mass index compared with Western populations with type 2 diabetes. This might also explain the finding that Asians have type 2 diabetes characterized primarily by β-cell dysfunction/reduced insulin secretion rather than insulin resistance, with greater post-prandial rises in glycemia.

The notion that type 2 diabetes presents differently in people of Asian descent is supported by studies conducted outside of Asia. For example, in an observational study in the UK, people with a South Asian ethnicity experienced a smaller improvement in HbA1c, independent of treatment type or social deprivation, and a finding that might have been explained by the earlier onset of diabetes in Asian ethnicities, and the tendency for HbA1c control to become more challenging with duration of diabetes.

CULTURAL ISSUES PERTAINING TO SOUTHEAST ASIAN PATIENTS
Educational differences in Southeast Asia

The available evidence suggests there are communication/educational issues that might impact the manifestation of hypoglycemia in Southeast Asian populations. A survey examining communication between patients and physicians found that patients with type 2 diabetes in Asia had a poorer understanding of the symptoms and causes of hypoglycemia compared with other regions. While 53% of Europeans did not understand that medication is a cause of hypoglycemia, this was 72% in Asia. Furthermore, 74% of surveyed Asians reported that it would be extremely useful to discuss hypoglycemia more frequently with their physician.

Ramadan
Ramadan is a period of fasting of approximately 29 days based on the lunar calendar, where food is not consumed during daylight hours, and is typically divided by a light pre-dawn meal and a post-sunset large meal. As patients with increased daily activity and/or irregular eating habits (decrease, delay or omission of meals) are at increased risk of hypoglycemia, such behaviors represent a particular concern in Southeast Asia because of the high proportion of Muslim patients who practice Ramadan. In 2013, the total populations of Indonesia, Malaysia, the Philippines and Singapore were, respectively, 249, 30, 99 and 5 million people, but because of a lack of any recent census data in many Southeast Asian countries, the sizes of the Muslim populations are unknown. However, a study from the year 2000 by Pew Research Center’s Forum on Religion & Public Life placed the proportion of Muslims in Indonesia, Malaysia, the Philippines, and Singapore at 88.2, 60.4, 51.1 and 14.9%, respectively.

In Malaysia, 89.8% of patients with type 2 diabetes fast for at least 15 days during Ramadan, and this fasting places Asians at a greater risk of both hypo- and hyperglycemia, as shown by the Epidemiology of Diabetes and Ramadan study. The Epidemiology of Diabetes and Ramadan study assessed the effect of fasting on treatment patterns of patients with diabetes during Ramadan from 13 different countries, including some from Southeast Asia. It showed that 42.8 and 78.7% of patients with type 1 diabetes or type 2 diabetes fasted for ≥15 days, and during Ramadan there was a significant increase in the incidence of severe hypoglycemia in patients with type 2 diabetes. Furthermore, significant associations between change in insulin dose and severe hyperglycemia were found during Ramadan, with 27.7% of patients with type 2 diabetes either decreasing (24.7%) or stopping insulin (3.0%)77. These findings are concerning, and highlight that there might be a need to improve patient education and awareness of the risks of fasting with diabetes. Additionally, as specific guidelines have been developed for the Southeast Asian countries with the highest proportion of Muslims (Indonesia and Malaysia), there could also be a need to increase awareness and adherence to these guidelines amongst HCPs. Both the Indonesian and Malaysian guidelines for patients with type 2 diabetes advise that special education about hypoglycemia and SMBG should be provided 2–4 months before Ramadan, and that during Ramadan patients should take care to ensure adequate hydration (≥1,500 mL/day), appropriate levels of exercise, and to make adjustments to the timing and dose of insulin if there are changes in meal times. Furthermore, recent international guidelines for the...
management of diabetes during Ramadan state that patients need careful blood glucose monitoring and if necessary such treatment regimens may be adjusted, because patients treated with sulfonylureas and insulin are at the highest risk of hypoglycemia. However, just 68 and 62% of patients with type 1 or type 2 diabetes from the Epidemiology of Diabetes and Ramadan study received advice from HCPs regarding fasting and diabetes. Insulin use is a particular concern in pregnant women (with either type 1 or type 2 diabetes) during Ramadan in Southeast Asia, with one Malaysian study showing that 20.8% of pregnant women were unable to fast for more than 15 days without hypoglycemia or fetal demise. It is therefore of no surprise that recommendations suggest that physicians consider offering patient education, more regular SMBG and dose adjustment to minimize the risk of hypoglycemia in the weeks preceding Ramadan.

INSULIN TREATMENT DIFFERENCES IN SOUTHEAST ASIA AND WESTERN PRACTICE

Differences in the manifestation of type 2 diabetes have inevitably led to some differences in approach to insulin treatment between Southeast Asian and Western populations. Although the proportions of Southeast Asians using insulin appears to be similar to the West/USA, with the exception of Singapore (Table 1), the type of insulin preferred in these continents might differ. For example, while the first insulin to be used in the regimen of Westerners is most often a basal insulin, Asian patients are more often started with a premix (Figure 1), as this addresses postprandial glucose as well as fasting plasma glucose control. Premixed insulins being more popular in Asia might result in higher rates of hypoglycemia compared with Western populations using basal insulins. As hypoglycemia is a greater concern during Ramadan fasting, a South Asian consensus guidelines has been developed for the use of insulin during Ramadan, with different insulin doses recommended during fasting and at mealtime to minimize hypoglycemia and postprandial hyperglycemia, respectively. Additionally, these consensus guidelines recommend use of insulin analogs during Ramadan to help reduce the risk of hypoglycemia in insulin-treated patients. The guidelines recommend that those on premix use 30 U of 70:30 (bolus:basal) in the evening with dinner and 10 U at predawn/morning; alternatively, an inverted dual regimen (30:70 or 25:75 and 50:50 in the evening) can also be used. For those using basal–bolus insulin, the consensus guidelines recommend using a full dose of bolus insulin in the evening and a half dose in the morning, whereas basal insulin should be converted to a regimen of half a dose in the morning (neutral protamine

![Figure 1](http://onlinelibrary.wiley.com/journal/jdi)

**Figure 1** | Reported insulin use from DiabCare Indonesia, Malaysia, the Philippines, and in UK patients with type 2 diabetes
Hagedorn insulin) or a full dose before bedtime, but given as a basal analog insulin. Furthermore, Indonesian guidelines for the management of type 2 diabetes during Ramadan 2015 state that patients should change from premix insulin to basal plus or bolus to avoid hypoglycemia.

**GUIDELINES**

With so few studies of hypoglycemia in Southeast Asia, there is a lack of data on which bespoke guidelines can be constructed and therefore clinical practice guidelines have historically been based, and are heavily reliant, on data and guidelines from Western populations.

In a 2013 literature search for non-Western (including the ASEAN region) country diabetes guidelines, only the Philippines lacked national guidelines for type 1 and type 2 diabetes. However, whilst Indonesia, Malaysia and Singapore had diabetes guidelines, a large proportion (30-55%) of non-Western guidelines are reliant on statements and definitions from the World Health Organization, International Diabetes Federation and American Diabetes Association. For example, in Indonesia, Malaysia, the Philippines and Singapore, HbA1c targets are similar to those in the West, with targets individualized to the patient, but a target of <6.0% or <7.0% recommended for most patients.

Furthermore, as 70% of non-Western countries had guidelines that include recommendations for the management of hypoglycemia, a proportion of these would have based hypoglycemia guidelines on the Western population data referenced by the World Health Organization, International Diabetes Federation and American Diabetes Association – rather than data from their home nation and/or region. Comparing the guidelines that are available for Indonesia, Malaysia, the Philippines and Singapore, with the exception of Ramadan, there is an absence of guidelines that address the concerns for HCPs in this region, namely the rise of diabetes, and the costs that will accompany an aging population that, on average, will have had diabetes longer than Western populations. As in the West, several of the guidelines recommend an individualized HbA1c target, with frequent monitoring of blood glucose to minimize the risk of hypoglycemia in patients using insulin. In addition, Indonesian and Singaporean guidelines emphasize the need to educate patients about hypoglycemia, and how insulin administration and glucose monitoring can help patients adjust their insulin dose, food intake and exercise levels to minimize the risk.

However, although some countries cover some of the needs of South Asian patients, there is the additional problem created by the poor implementation and adherence. For example, in a recent report in Indonesia, despite a high awareness among GPs of the type 2 diabetes treatment guidelines, a large number neither adopted nor adhered to these guidelines in their treatment practice. This was particularly prominent regarding adherence to screening guidelines for type 2 diabetes, with just 2% of GPs adhering to these, perhaps explaining the large deficit in diabetes awareness in Indonesia where two-thirds remain unaware of their condition. In addition, non-adherence to dosing guidelines in Indonesia could go some way to explain why 68% of patients with type 2 diabetes in Indonesian hospitals have poor glycemic control.

**FUTURE PERSPECTIVES/CONCLUSIONS**

The main finding of this review is that, at present, there is a scarcity of data in the ASEAN and indeed Southeast Asian populations regarding the incidence and impacts of hypoglycemia. There are little to no data regarding the incidence of hypoglycemia in Southeast Asian patients with insulin-treated diabetes, especially in those managed according to real-world clinical practice. In addition, the present review has highlighted that there are several reasons to believe Southeast Asians might be of a different risk profile for hypoglycemia compared with Western populations because of physiological/etiological differences in the presentation of type 2 diabetes, gaps in patient knowledge of hypoglycemia, the high proportion of patients who practice Ramadan (exposing them to increased risk of hyper- and hypoglycemia), and a preference for human insulin and premix insulin regimens over regimens with lower associated rates of hypoglycemia, such as those based on modern insulin analogs. With no available data quantifying the impact of hypoglycemia in Southeast Asian populations, specifically based on the risks outlined above, it is difficult to envisage that there would not be considerable benefit in future studies focused on collecting real-world hypoglycemia data in this population.

Collecting data from South Asian populations will provide valuable information to assist in the construction of more appropriate national guidelines, which can then be more closely aligned to the national patient demographics, behaviors and treatment practices, and might result in a greater degree of implementation and adherence within clinical practice. This in turn could lead to improvements in the management of diabetes, and reduce the risk of hypoglycemia in insulin-treated patients.

As in the West, with healthcare improving in Asian countries, the demographic of patients with diabetes is shifting towards older age groups that have both impaired responses to hypoglycemia and are at greater risk of severe hypoglycemia. With Asian patients often developing type 2 diabetes at an earlier age than those in the West, and with so few (<30%) reaching glycemic targets (or even monitoring plasma glucose with SMBG), Asians are at a unique risk of diabetes-related adverse events and complications, thus making it all the more important to effectively educate and manage patients, and develop more appropriate guidelines for this purpose.

One study that could help address the lack of data and aid development of new guidelines is the non-interventional International Operations Hypoglycemia Assessment Tool; this is a Novo Nordisk-sponsored study with the aim of assessing the incidence of hypoglycemia among patients with insulin-treated (premix, short-acting and long-acting) diabetes.
results have been presented for some companies, and a full publication of the global study results was published in 2016\textsuperscript{15}.

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**DISCLOSURE**

Dr Su-Yen Goh is on the local advisory boards of the following companies: Novo Nordisk, Sanofi Aventis, AstraZeneca, Boehringer Ingelheim and Eli Lilly. Dr Zanariah Hussein is an advisory board member for AstraZeneca, Boehringer Ingelheim, Lilly, Sanofi-Aventis and Novo Nordisk; is currently participating in, and has participated in for the past 2 years, clinical trials with Novartis, Novo Nordisk and MSD; and receives research support from Medtronic. Professor Achmad Rudijanto has received research support from Novo Nordisk, and has received speaker fees from Novo Nordisk, Sanofi Aventis and AstraZeneca.

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