



Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Editorial

A patient-centric approach to optimise insulin therapy in Asia

1. Introduction

Diabetes is a global public health threat. The prevalence of diabetes, of which type 2 diabetes predominates, is expected to rise from 415 million in 2015 to 642 million by 2040 ([International Diabetes Federation](#)). While diabetes poses a huge economic burden to all nations, 75% of all cases occur in low- and middle-income countries ([International Diabetes Federation](#)). Western Pacific and Southeast Asia regions have the greatest number of people with diabetes in the world and the highest diabetes-related mortality rates. It is estimated that in Southeast Asia, almost half of people with diabetes are undiagnosed and are at increased risk of developing costly complications such as cardiovascular disease and end-stage renal failure, due to delayed diagnosis and inadequate treatment ([International Diabetes Federation](#); [Inzucchi et al., 2012](#)). Furthermore, the healthcare expenditure in 2015 due to diabetes was USD 7.3 billion in Southeast Asia and USD 106 billion in the Western Pacific region, compromising 12% and 10% of the total health budgets of each

region, respectively. By 2040 the healthcare expenditure in the Southeast Asian and Western Pacific regions is expected to increase to USD 12.9 and 133 billion, respectively ([International Diabetes Federation](#)).

Asian populations have a strong genetic predisposition to diabetes, characterised by early beta-cell dysfunction in the setting of insulin resistance ([Ma & Chan, 2013](#); [Ramachandran, Snehalatha, Shetty, & Nanditha, 2012](#); [Yoon et al., 2006](#)). They develop diabetes at a lower body mass index and waist circumference than their Caucasian counterparts ([Ramachandran et al., 2012](#); [Yoon et al., 2006](#)). Due to their young age of diagnosis and thus long disease duration, Asian populations demonstrate higher rates of morbidity and premature mortality compared with Caucasian populations ([Ramachandran et al., 2012](#)). The increasing number of Asians with diabetes can be attributed to urban population growth and ageing, rapid rates of urbanisation and increasing obesity, in part due to increased consumption of energy-dense foods (e.g. fast foods and sugar-sweetened beverages) and sedentary lifestyles, particularly among the younger generation ([Ramachandran et al., 2012](#)). Lack of access to specialist healthcare, insufficient clinical evaluation, delayed diagnosis, clinical inertia and suboptimal self-care are some of the challenges with regards to diabetes management in Asia ([Cramer, 2004](#); [Ko et al., 2010](#); [Mu et al., 2012](#)). Low levels of health literacy due to poor general education and insufficient health education in these countries further add burden to already under-resourced healthcare systems, which are unlikely to cope with the escalating costs of end-stage disease with rising prevalence of diabetes in Asia ([Grant, 2013](#); [Ringborg et al., 2009](#)).

National endeavours are urgently needed to raise diabetes awareness, detect subjects at high risk of developing diabetes so that diabetes can be prevented, and allow early intervention to prevent complications in people with diabetes ([Ramachandran et al., 2012](#); [Ringborg et al., 2009](#)). In 2015, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) published an update ([Inzucchi et al., 2015](#)) on a position statement regarding the management of hyperglycaemia in type 2 diabetes ([Inzucchi et al., 2012](#)). In this consensus statement, experts highlighted the need to individualise both treatment targets and treatment strategies, with an emphasis on patient-centred care and shared decision-making ([Inzucchi et al., 2015](#)).

This commentary discusses barriers pertinent to the management of diabetes in Asia and proposes possible solutions to design patient-centric healthcare models for overcoming these barriers. We shall highlight these challenges with special reference to timely insulin therapy, which may be particularly relevant to Asian patients given their predisposition to diabetes, the early onset of disease and

Conflicts of interest: The topic of using a patient-centric approach to treat type 2 diabetes was discussed at an Asian-focused Sanofi funded advisory board held in 2014. This article was subsequently developed as an entirely separate endeavour, based on the identified need for literature conveying the Asian perspective on this topic. The authors did not receive funding for this article. AV, RP and SB are employees of Sanofi and contributed in their capacity as diabetes subject matter experts. They did not exercise selective influence over the opinions expressed by other authors in this article. APK has served on advisory boards and received honoraria for consultancy or giving lectures from Abbott, AstraZeneca, Sanofi, Novo Nordisk, Eli Lilly, Merck Serono, Pfizer and Nestlé. CD has served on the advisory boards and speaker bureaus for AstraZeneca, Janssen, MSD, Novartis and Sanofi. His institution has received research support from Sanofi and AstraZeneca. EA has served on regional advisory boards for Sanofi and AstraZeneca and local advisory boards for AstraZeneca and Novartis. He has received speaker honoraria for Sanofi, Novartis, Eli Lilly, AstraZeneca, Boehringer Ingelheim and MSD. JC has served on the advisory boards and speaker bureaus for AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, MSD, Pfizer and Sanofi. Her institution has received research support from AstraZeneca, Bayer Healthcare, Boehringer Ingelheim, Eli Lilly, MSD, Pfizer and Sanofi. She is the Chief Executive Officer of the Asia Diabetes Foundation, a charitable organisation that developed the JADE Portal, on a *pro bono* basis. SG is a member of the local/regional advisory boards and has received honoraria for speaking engagements from Sanofi, Novo Nordisk, Boehringer Ingelheim, MSD and AstraZeneca. SJ has received grants, research support, served on advisory boards and received honoraria for consultancy or speaker support for Abbott, MSD, Novartis, Boehringer Ingelheim, Public Health Foundation of India, Novo Nordisk, Sanofi, USV, Sun Pharmaceutical Industries Ltd, Marico, Eli Lilly, Serdia, Pfizer, Johnson and Johnson Lifescan, Janssen, Dr Reddy's Laboratories, Cipla, Zydus Cadila, Bayer Zydus Pharma and Takeda. SK serves as an advisory board member and speaker for Sanofi Philippines and Novo Nordisk Philippines. ZH has served on local/regional advisory boards and has received honoraria for speaking engagements from Sanofi, Novo Nordisk, Eli Lilly, Novartis, Boehringer Ingelheim, MSD and AstraZeneca, Medtronic, APV, CYP, EH and NAK have no conflicts of interest to disclose.

Table 1
Pattern of glycaemic control and insulin usage in Asia.

Country	Patients not achieving glycaemic control (HbA _{1c} <7%), %	Rate of insulin usage (with or without OADs), %
China	58.9 (Pan, Yang, Jia, Weng, & Tian, 2009)	33.9 (Ji et al., 2013)
Hong Kong	55.2 (Yan et al., 2015)	20.6 (Yan et al., 2015)
India	62.3 (Nagpal & Bhartia, 2006)	35.2 (Mohan et al., 2014)
Korea	54.4 (Jeon et al., 2014)	16.4 (Korean Diabetes Association, 2015)
Malaysia	78.0 (Mafauzy, Hussein, & Chan, 2011)	21.4 (Ministry of Health: Malaysia)*
Philippines	85.0 (Jimeno, Sobreprena, & Mirasol, 2012)	41.9 (Jimeno et al., 2012)
Singapore	67.0 (Lee et al., 2001)	NR
Thailand	69.8 (Kosachunhanun et al., 2006)	25.3 (Kosachunhanun et al., 2006)†

OAD, oral antidiabetic drug; NR, not reported.

* Insulin usage exclusively in primary care clinics (insulin use in hospital-based diabetes clinics was 65.4% in the 2013 DiabCare study) (Ministry of Health: Malaysia).

† Insulin use exclusively in hospitals

increasing prevalence in this population (Ma & Chan, 2013; Ramachandran et al., 2012).

2. The importance of early insulin therapy

Both type 1 diabetes and type 2 diabetes are characterised by insulin insufficiency. Classic type 1 diabetes has an acute onset and is characterised by autoimmune beta-cell destruction that usually leads to absolute insulin deficiency (American Diabetes Association, 2014). Type 2 diabetes is caused by a combination of resistance to insulin action, often due to obesity and an inadequate compensatory insulin secretory response (American Diabetes Association, 2014).

The ADA and EASD recommend a glycaemic target of glycated haemoglobin (HbA_{1c}) <7% for most patients with diabetes and the aim of insulin therapy is to work towards this goal (Inzucchi et al., 2012, 2015). People with type 1 diabetes must take insulin every day and work closely with their healthcare provider to determine which insulin(s) is(are) most suited to them (American Diabetes Association). In type 2 diabetes, in addition to lifestyle modifications, oral antidiabetic drugs (OADs) are usually used to lower blood glucose, typically metformin followed by the addition of other OADs such as sulphonylureas, dipeptidyl peptidase 4 inhibitors, alpha glucosidase inhibitors, thiazolidinediones and sodium–glucose co-transporter 2 inhibitors. If there is inadequate glycaemic control with monotherapy, combination therapy with two or more therapeutic agents that target both insulin resistance and defects in insulin secretion is frequently used (Inzucchi et al., 2015). Clinical practice guidelines recommend early initiation of basal insulin as part of a combination regimen when adequate glycaemic control can no longer be achieved with OADs alone or in the case of severe hyperglycaemic conditions with acute metabolic derangement from the beginning (Goh et al., 2014; Inzucchi et al., 2012, 2015; Ko et al., 2011).

Timely and appropriate insulin therapy provides multifaceted economic and health-related benefits (Aloumanis, Benroubi, Sourmeli, & Drossinos, 2013; Levin, Zhou, Gill, & Wei, 2015; Owens, 2013; Raz & Mosenzon, 2013; Rosenstock et al., 2006; Woehl, Evans, Tetlow, & McEwan, 2008). Several studies have indicated that early insulin treatment may preserve beta-cell function by alleviating glucotoxic effects of hyperglycaemia, attain optimal glycaemic control and minimise the risk of long-term complications such as retinopathy and nephropathy (Ohkubo et al., 1995; Owens, 2013; Raz & Mosenzon, 2013). Asian patients, particularly those with young onset of disease and lean body mass, are likely to benefit from early insulin treatment due to the early beta-cell dysfunction that is characteristic of this patient population (Ma & Chan, 2013; Ramachandran et al., 2012; Yoon et al., 2006). Coupled with a long disease duration due to the earlier onset of disease, these subjects are at high risk of complications (Ramachandran et al., 2012; Yoon et al., 2006). The pronounced dysfunction in early insulin secretion found in Asian populations further emphasise the need for early insulin replacement (Fukushima, Suzuki, & Seino, 2004;

Matsumoto et al., 1997; Rattarasarn, Soonthornpan, Leelawattana, & Setasuban, 2006).

Intensive glycaemic control through early initiation of insulin therapy is cost-effective. Several studies have shown that improving glycaemic control results in medical cost-savings through a reduction in complications associated with diabetes, hospital admissions, physician visits, etc. (Gilmer, O'Connor, Manning, & Rush, 1997; Menzin, Langley-Hawthorne, Friedman, Boulanger, & Cavanaugh, 2001; Wagner et al., 2001). One study looked at whether sustained improvements in HbA_{1c} levels among patients with diabetes are followed by reductions in healthcare utilisation and costs (Wagner et al., 2001). Improvement in glycaemic control was defined as an HbA_{1c} decrease of 1% over the course of 1 year and a continuous decrease for another year. Patients who did not demonstrate this were classified as unimproved (Wagner et al., 2001). The study demonstrated that mean total healthcare costs were USD 685–950 less each year for patients who had improvements in glycaemic control compared to those who did not (Wagner et al., 2001). Another more recent study investigated the long-term cost savings of patients receiving primary care from clinical practices employing an “all-or-none diabetes system of care”. The study demonstrated an overall cost saving of 6.9% over the 8-year study period, despite an increase in outpatient and professional costs during the first year (Maeng, Yan, Graf, & Steele, 2016). Although the initial cost of treating diabetes was higher, the long-term benefits of receiving high-quality treatment resulted in cost saving (Maeng et al., 2016).

Despite the proven benefits and guideline endorsement of timely and appropriate insulin therapy, insulin use and glycaemic control remain suboptimal in Asia. The majority of patients fail to achieve a target HbA_{1c} <7% as recommended by the ADA and EASD (Inzucchi et al., 2012, 2015) and rates of insulin usage across the region are generally low (Table 1).

3. A patient-centric approach to timely and appropriate insulin therapy

A patient-centric approach for diabetes care is recommended by the ADA and the EASD (Inzucchi et al., 2012, 2015). This approach recognises the uniqueness of an individual's clinical profile (e.g. age, level of obesity, disease duration, presence of complications, level of cognition, psychological health and social support available) and treatment responses (e.g. mode of action and side effects). Thus, care must be tailored to the specific needs of an individual patient, taking into account his/her preferences, tolerance, needs and values (Inzucchi et al., 2012; Shah et al., 2010; Titchener, 2014). Where in other diseases, diagnosis and initiation of treatment are often the most critical success factors, in diabetes this is only the first step. Rather than being the recipient of care, the diabetes patient must contribute to initiating, intensifying and constantly adapting his/her care. There is good evidence to support this shared decision-making approach (Inzucchi et al., 2012; Shah et al., 2010).

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