# HAEMOGLOBIN $A_{1C}$, BLOOD PRESSURE AND LDL-CHOLESTEROL GOALS ATTAINMENT AND ITS ASSOCIATED FACTORS AMONG ADULTS WITH EARLY-ONSET TYPE 2 DIABETES IN TERENGGANU, 2023

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# HAEMOGLOBIN $A_{1C}$, BLOOD PRESSURE AND LDL-CHOLESTEROL GOALS ATTAINMENT AND ITS ASSOCIATED FACTORS AMONG ADULTS WITH EARLY-ONSET TYPE 2 DIABETES IN TERENGGANU, 2023


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## LIST OF ABBREVIATIONS

| | |
|---|---|
| ADA | American Diabetes Association |
| ABC | $HbA_{1c}$, blood pressure and LDL-C |
| BMI | Body Mass Index |
| CVD | Cardiovascular Disease |
| $HbA_{1c}$ | Hemoglobin $A_{1c}$ |
| HNF4A | hepatocyte nuclear factor 4A |
| IDMPS | International Diabetes Management Practices Study |
| JEPeM-USM | Human Research Ethics Committee of Universiti Sains Malaysia |
| JKNT | Jabatan Kesihatan Negeri Terengganu |
| LDL-C | Low-Density Lipoprotein-Cholesterol |
| NHMS | National Health Morbidity Survey |
| NMRR | National Medical Research Register |
| rs1800961 | T130I polymorphism |
| T2DM | Type 2 Diabetes Mellitus |
| T1DM | Type 1 Diabetes Mellitus |
| USM | Universiti Sains Malaysia |

## LIST OF SYMBOLS

| | |
|---|---|
| < | Less than |
| > | More than |
| % | Percentage |
| P | Proportion |
| d | Different |
| $Z_a$ | Z score associated with level of significant alpha |
| n | Number of samples |
| $P_0$ | The proportion of participant with exposure to factor without outcome |
| $P_1$ | The proportion of participant with exposure to factor with the outcome |
| m | The ratio of independent variables |
| α | Alpha |

**PENCAPAIAN SASARAN HEMOGLOBIN $A_{1C}$, TEKANAN DARAH, DAN KOLESTEROL LDL SERTA FAKTOR YANG BERKAITAN DALAM KALANGAN ORANG DEWASA PENGHIDAP DIABETES JENIS 2 PERMULAAN AWAL DI TERENGGANU, 2023**

## ABSTRAK

**Latar Belakang:** Peningkatan global dan tempatan dalam prevalens diabetes mellitus memberikan cabaran kesihatan awam yang ketara. Diabetes jenis 2 permulaan awal, yang didiagnosis antara umur 18 dan 45 tahun, semakin biasa dan dikaitkan dengan risiko komplikasi yang lebih tinggi. Oleh itu, mencapai matlamat ABC ($HbA_{1c}$ <7%, tekanan darah <140/90 mmHg, dan LDL-C <100 mg/dL) adalah penting untuk menguruskan diabetes dan mengurangkan komplikasi.

**Objektif:** Kajian ini bertujuan untuk menentukan pencapaian dua atau lebih matlamat ABC dan faktor yang berkaitan dalam kalangan orang dewasa dengan diabetes jenis 2 permulaan awal di Terengganu pada tahun 2023.

**Metodologi:** Reka bentuk kajian keratan rentas telah digunakan, menggunakan data sekunder orang dewasa dengan diabetes jenis 2 permulaan awal yang telah diaudit di *National Diabetes Registry* di Terengganu pada tahun 2023. Persampelan rawak mudah telah digunakan untuk memilih sampel yang diperlukan sebanyak 675. Data tentang ciri sosiodemografi, faktor gaya hidup, dan profil rawatan diabetes diekstrak dan dianalisis menggunakan SPSS versi 28. Statistik deskriptif dan regresi logistik berganda digunakan untuk meringkaskan data dan mengenal pasti faktor yang berkaitan dengan mencapai dua atau lebih matlamat ABC.

**Keputusan:** Purata umur peserta ialah 46.8 tahun (SD 7.86). Majoriti pesakit adalah perempuan (68.3%), etnik Melayu (97.9%), dan bukan perokok (95.4%). Proporsi pencapaian dua atau lebih matlamat ABC adalah 36.4%. Kajian mendapati bahawa wanita adalah 38% kurang berkemungkinan daripada lelaki untuk mencapai dua atau lebih matlamat ABC, dengan nisbah odds (OR) yang signifikan secara statistik

sebanyak 0.63 (95% CI: 0.44 hingga 0.88, p=0.007). Mengenai jenis rawatan, individu yang menjalani rawatan oral sahaja mempunyai kemungkinan 2.49 kali lebih tinggi untuk mencapai matlamat ini berbanding dengan kombinasi rawatan oral dan insulin (95% CI: 1.77 hingga 3.49, p<0.001). Selain itu, mereka yang tidak menggunakan sebarang rawatan mempunyai kemungkinan 2.76 kali lebih tinggi untuk mencapai matlamat berbanding dengan rawatan gabungan (95% CI: 1.11 hingga 6.91, p=0.030).

**Kesimpulan:** Penemuan ini menyerlahkan cabaran penting dalam kawalan diabetes komprehensif dalam kalangan orang dewasa dengan diabetes jenis 2 permulaan awal di Terengganu, dengan perbezaan berdasarkan jantina dan profil rawatan yang ketara dalam pencapaian matlamat. Pengurusan diabetes yang berkesan memerlukan menangani cabaran khusus jantina dan modaliti profil rawatan melalui kempen kesihatan awam, strategi antara disiplin dan penjagaan peribadi. Selain itu, pencapaian matlamat ABC yang disyorkan adalah lebih berkemungkinan pada pesakit yang mengambil lebih sedikit ubat untuk diabetes, menekankan potensi manfaat terapi ubat yang minimum dan pematuhan ubat yang lebih baik.

**Kata kunci:** Diabetes jenis 2 permulaan awal, pencapaian matlamat ABC, Cabaran kawalan diabetes, Ketaksamaan berdasarkan jantina, Profil rawatan

# HAEMOGLOBIN $A_{1C}$, BLOOD PRESSURE AND LDL-CHOLESTEROL GOALS ATTAINMENT AND ITS ASSOCIATED FACTORS AMONG ADULTS WITH EARLY-ONSET TYPE 2 DIABETES IN TERENGGANU, 2023

## ABSTRACT

**Background:** The global and local increase in prevalence of diabetes mellitus presents a significant public health challenge. Early-onset type 2 diabetes, diagnosed between ages 18 and 45 years, is increasingly common and associated with a heightened risk of complications. Therefore, achieving the ABC goals ($HbA_{1c}$ <7%, blood pressure <140/90 mmHg, and LDL-C <100 mg/dL) is essential for managing diabetes and reducing the complications.

**Objective:** This study aims to determine the attainment of two or more ABC goals and its associated factors among adults with early-onset type 2 diabetes in Terengganu in 2023.

**Methodology:** A cross-sectional study design was employed, utilizing secondary data of adults with early-onset type 2 diabetes who were audited in the National Diabetes Registry in Terengganu in 2023. A simple random sampling was applied to select the required sample of 675. Data on sociodemographic characteristics, lifestyle factors, and diabetes treatment profiles were extracted and analysed using SPSS version 28. Descriptive statistics and multiple logistic regression were used to summarize the data and identify factors associated with achieving two or more ABC goals.

**Results:** The mean age of the participants was 46.8 years (SD 7.86). The majority of the patients were female (68.3%), of Malay ethnicity (97.9%), and non-smokers (95.4%). The proportion of attainment two or more goals was 36.4%. Women are 38%

less likely than men to achieve two or more ABC goals, with a statistically significant odds ratio (OR) of 0.63 (95% CI: 0.44 to 0.88, p=0.007). Regarding treatment types, individuals on oral treatment alone have 2.49 times higher odds of achieving these goals compared to those on a combination of oral treatment and insulin (95% CI: 1.77 to 3.49, p<0.001). Additionally, those not on any treatment have 2.76 times higher odds of reaching the goals compared to those on the combination treatment (95% CI: 1.11 to 6.91, p=0.030).

**Conclusion:** These findings highlight significant challenges in comprehensive diabetes control among adults with early-onset type 2 diabetes in Terengganu, with notable sex-based disparities and treatment profiles in goal attainment. Effective diabetes management requires addressing gender-specific challenges and modality of treatment profiles through public health campaigns, interdisciplinary strategies, and personalized care. Additionally, achieving the recommended ABC goals is more likely in patients who take fewer medications for diabetes.

**Keywords**: Early-onset type 2 diabetes, ABC goals attainment, Diabetes control challenges, Sex-based disparities, Treatment profiles

# CHAPTER 1

# INTRODUCTION

## 1.1 Background of the study

Globally, the prevalence of diabetes mellitus (DM) has been steadily rising. Diabetes mellitus is a collection of physiological abnormalities marked by high levels of glucose in the blood due to either the body's resistance to insulin, insufficient synthesis of insulin, or excessive secretion of glucagon. There are two main types of diabetes mellitus: Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM). T1DM is a chronic and progressive autoimmune disease that affects around 1% of the population in affluent countries. The primary cause of hyperglycemia in T2DM is a combination of insulin resistance and decreased insulin production, which impacts around 8.5% of adults (Krause & De Vito, 2023).

The causes of diabetes may vary between T1DM and T2DM, however there may be shared characteristics that arise as the condition develops. Insulin resistance and dysfunction/death of β-cells may be present, leading to impairment of many tissues and cellular function and metabolism. In T2DM, hyperglycaemia, dyslipidaemia, and low-grade inflammation are significant contributors to the advancement of T2DM, and are commonly found in overweight individuals who are susceptible to developing T2DM (Banday, Sameer & Nissar, 2020). Over the last three decades, T2DM has become much more common in all nations, contributing to a public health burden that is linked to high medical expenses, increased morbidity, and early mortality. On a global scale, 462 million people are estimated to have diabetes (Khan *et al.*, 2020).

The prevalence of diabetes among persons aged 18 and older was 8.5% in the year 2014. One and a half million fatalities were directly attributed to diabetes in the year 2019. There was a three percent rise in the age-standardized death rates that were

caused by diabetes between the years 2000 and 2019. A thirteen percent rise in the death rate related to diabetes was seen in nations with lower-middle incomes (WHO, 2024).

According to National Health Morbidity Survey (NHMS) 2023 reports, the prevalence of diabetes in Malaysia stands at 15.6%, indicating that roughly 1 in 6 persons in Malaysia are affected by the condition (*NHMS*, 2023). This persistent ailment is a substantial public health issue in the nation, impacting a substantial segment of the populace. Furthermore, it is worth noting that 40% of adults with diabetes are uninformed of their illness, and a staggering 84% of young adults between the ages of 18 and 29 who have diabetes are unaware of their diagnosis (*NHMS*, 2023).

Terengganu is a constituent state of the federal government of Malaysia situated on the eastern coast of Peninsular Malaysia. The prevalence of diagnosed diabetes among individuals aged 18 years and older in Malaysia is 9.4% (95% confidence interval: 8.66, 10.20). In the specific case of Terengganu state, the prevalence of diagnosed diabetes in the same age group is much higher than the national prevalence, at 10.5% (95% confidence interval: 8.11, 13.41) (Awang *et al.*, 2022).

Over the past three decades, there has been a significant rise in the prevalence of T2DM among teenagers globally. Due to the increasing prevalence of T2DM among young individuals, it is expected that early-onset type 2 diabetes would become a prevalent feature among the diabetic population in both developed and developing countries (Sadat, 2023). Adults with early-onset type 2 diabetes are those who were diagnosed with T2DM between the ages of 18 and <45 years (Liu e*t al.*, 2022). It is reported that adults with early-onset type 2 diabetes are eighty percent more likely to begin insulin therapy than those with usual- onset T2DM (Liu *et al.*, 2022).

A study in Spain found that the T130I polymorphism (rs1800961) in the HNF4A (hepatocyte nuclear factor 4A) gene is linked to a decline in β-cell function and identified as a risk factor for T2DM. This polymorphism is inherited in an autosomal dominant manner. According to the study, carriers of the T130I mutation and noncarriers showed significant differences in glucose metabolism and lipid profile. These findings suggest that the T130I variant in HNF4A is a major susceptibility genotype associated with early-onset type 2 diabetes (Cieza-Borrella *et al.*, 2014).

Several Western countries have experienced a rise in the occurrence of adult with early-onset type 2 diabetes. Between 1990 and 2000, the prevalence of T2DM in youngsters in New York increased by a factor of 10 (Wilmot & Idris, 2014). Prescriptions for oral glucose lowering medication in the UK experienced an eightfold surge from 1998 to 2005. The UK has shown comparable rises in early-onset diabetes among adult specialist services, with T2DM representing 5% of the diabetes population under 30 years old in 2003. This percentage increased to 12% by 2006 and further expanded to encompass 24% of the diabetes population under 40 years old. The prevalence of childhood beginning T2DM in Japan increased twofold from the late 1980s to the early 1990s. As a result, a child in Japan who has new-onset diabetes is now statistically more likely to have T2DM rather than T1DM. Adult with early-onset type 2 diabetes has been documented in numerous nations worldwide, including Australia, Canada, China, India, Japan, Mexico, and Australia (Wilmot & Idris, 2014). Studies conducted recently reveal that compared to Western nations, Asian nations have a greater prevalence of adult with early-onset type 2 diabetes (Zou *et al.*, 2017).

The rising prevalence of adults with early-onset type 2 diabetes increases the risk of complications from the disease (Song & Hardisty, 2009; Wilmot & Idris, 2014). When comparing patients with usual-onset type 2 diabetes to those with early-onset

type 2 diabetes, the risk of developing complications like microalbuminuria was twice as high. When it came to the risk of developing a myocardial Infraction (MI) , adult with early-onset type 2 diabetes had a 14-fold higher risk than those with control subjects (Hillier & Pedula, 2003). The research conducted in Xinjiang, China unveiled those individuals with early-onset type 2 diabetes exhibited poorer lipid profiles and higher blood pressure. Moreover, over half of these patients had already encountered macro- and microvascular complications. In addition, women with early-onset type 2 diabetes faced a roughly threefold increased risk of atherosclerotic plaques compared to men (Zhang *et al.*, 2018).

Remarkably, a Chinese study highlighted those individuals diagnosed with early-onset type 2 diabetes displayed reduced levels of follicle-stimulating hormone (FSH), sex hormone-binding globulin, and total testosterone in their serum compared to those with late-onset type 2 diabetes. Given that testosterone regulates various aspects of men's health, including libido, bone density, fat distribution, muscle mass and strength, as well as the production of sperm and red blood cells, its significance cannot be overstated. The study further noted that early-onset type 2 diabetes patients exhibited impaired conversion of dehydroepiandrosterone (DHEA) to testosterone, potentially influenced by elevated blood glucose levels and decreased levels of 3β-hydroxysteroid dehydrogenase (3β-HSD) (Hu *et al.*, 2023).

Therefore, it is important to optimally manage diabetes among this category of diabetic patients. A crucial component of managing diabetes, according to clinical practice guideline diabetes mellitus 6$^{th}$ edition, is reducing multiple risk factors that are not limited to controlling glucose levels but also include blood pressure and cholesterol, namely ABC goals (Hemoglobin $A_{1c}$ less than 7%, blood pressure less than 140/90 mmHg, and low-density lipoprotein -cholesterol less than 100 mg/dl),

which have been shown to reduce complications (American Diabetes Association, 2015; MOH, 2020a).

The ABC goals in diabetes treatment are essential for properly managing the condition and minimizing the risk of complications. The target for Hemoglobin $A_{1c}$ ($HbA_{1c}$) in most non-pregnant individuals with diabetes is less than 7%. This target reflects average blood glucose levels over the past 2-3 months. Managing $HbA_{1c}$ levels is crucial to mitigating the risk of chronic complications associated with diabetes. The aim for blood pressure is to achieve a reading of less than 140/90 mmHg, although lower targets may be set for specific individuals. Controlling high blood pressure is critical because it increases the risk of heart disease, stroke, and kidney damage. Therefore, maintaining blood pressure within a healthy range is vital for overall well-being. The recommended low-density lipoprotein -cholesterol (LDL-C) level for most individuals with diabetes is below 100 mg/dL. High levels of LDL-C contribute to the development of atherosclerosis and elevate the risk of cardiovascular disease (CVD). Thus, effectively managing cholesterol levels is essential for maintaining heart health (American Diabetes Association, 2022).

Although attaining ABC goals is important, recent research indicates a low attainment rate for these objectives. A hospital study in Nepal found that only 37.8% of T2DM patients attain ABC goals, with younger patients showing superior blood pressure control (Baranwal *et al.*, 2020). This study highlights that a substantial fraction of patients failed to attain ABC goals, underscoring the need for further research to understand the underlying causes of this phenomenon.

## 1.2 Statement of problem

People with early-onset type 2 diabetes have a remarkably elevated lifetime risk due to the length of the disease, exposure to a hyperglycemic environment, and

atherogenic risk factors that are linked to it. Over the last thirty years, there has been a steady rise in the incidence of early-onset type 2 diabetes, which can hasten the onset of microvascular and macrovascular problems. The burden of complications associated with adults who have early-onset type 2 diabetes was found to be significant, with notable prevalence rates: 37.2% for CVD, 59.3% for retinopathy, and 53.1% for neuropathy. Moreover, adults within the early-onset group exhibited a higher rate of increase in these complications (Song & Hardisty, 2009). Based on this data, adults with early-onset type 2 diabetes are a high-risk population with unique problems and requirements, and diabetes will have a significant influence on a person's life, quality of care, and financial situation. In a multidisciplinary context, they should receive vigorous and supportive therapy to avoid serious morbidity developing during their most productive years.

The existing studies showed that attaining the treatment goals for diabetes yielded favourable effects in an incremental, dose-related manner. Compared to individuals with diabetes who met none of the goals, those who achieved one, two, or all three ABC goals experienced reduced CVD event rates by 36%, 52%, and 62%, respectively (Wong *et al.*, 2016). This is supported by a study in Japan that shows people who successfully attained two or more ABC goals compared to one or fewer ABC goals are associated with a lower rate of complications (Minato *et al.*, 2019).

However, up to date, only one study in Malaysia reported findings on the attainment of the three ABC goals among adults with diabetes (Kim *et al.*, 2021). The study revealed that only 4.5% of patients with T2DM successfully attained all three ABC goals, and 27.8% [U1]attained two or more goals. Those with early onset type 2 diabetes recorded the lowest proportion of achievement of these ABC goals. Thus, the study proposes implementing focused treatments for this specific subpopulation at

high risk. Therefore, it is crucial to investigate the attainment of two or more ABC goals within the local population and the associated factors, as understanding this attainment remains incomplete.

## 1.3 Rationale of the study

There is a clear association between the early development of T2DM and a higher likelihood of experiencing complications, coexisting medical conditions, and death. This study aims to provide data on the proportion of attainment of two or more ABC goals among adults with early-onset type 2 diabetes in Terengganu. These findings will provide valuable insights into achieving optimal diabetes care in Terengganu.

In addition, it will uncover the elements that are linked with the achievement of ABC goals in order to determine a more specific target population and provide best practices for improving diabetes care. Early detection and intervention can help reduce complications caused by T2DM in the early-onset group. This approach allows for the development of targeted therapies and allocation of resources to address the individual needs of diverse populations.

Ultimately, this study will provide information to assist the Terengganu State Health Department, a stakeholder in the study, in formulating policies and enhancing diabetes programmes. This will aid in the prevention or reduction of diabetes complications and enable the department to prioritise its approach and management of adults with early-onset type 2 diabetes. By doing so, it can enhance the overall well-being of individuals and populations, potentially leading to reduced healthcare costs and improved productivity.

## 1.4 Research questions

1. What is the proportion of adults with early-onset type 2 diabetes who attained two or more ABC goals in Terengganu in 2023?

2. What are the factors associated with attainment of two or more ABC goals among adults with early-onset type 2 diabetes in Terengganu in 2023?

## 1.5 Research objectives

### 1.5.1 General objective

To study the attainment of $HbA_{1c,}$ blood pressure and LDL-C (ABC) goals and its associated factors among adults with early-onset type 2 diabetes in Terengganu in 2023

### 1.5.2 Specific objectives

1. To determine the proportion of adults with early-onset type 2 diabetes who attained two or more ABC goals in Terengganu in 2023

2. To determine factors associated with attainment of two or more ABC goals among adults with early-onset type 2 diabetes in Terengganu in 2023

## 1.6 Research Hypothesis

There are significant associations between sociodemographic characteristics, lifestyle factors and diabetes profiles with attainment of two or more ABC goals among adults with early-onset type 2 diabetes in Terengganu in 2023

# CHAPTER 2

# LITERATURE REVIEW

The literature review was carried out utilizing a variety of web search engines, including PubMed, Google Scholar and Scopus databases. Only articles published between 2003 and 2023 were selected from the whole literature search. Several search techniques were used, including combining phrases and using Boolean operators (AND, OR, NOT). The keywords that apply during the search are ABC goals, attainment, $HbA1_C$, blood pressure and LDL-C, ADA, associated factors, early-onset diabetes, and T2DM.

## 2.1 Attainment of ABC goals

Previous reports indicated a consistent lack of achievement in meeting the ABC goals. According to the Joint Asia Diabetes Evaluation Programme, only 5.4% of individuals with diabetes in seven Asian nations were able to achieve the ABC targets (So *et al.*, 2011). The International Diabetes Management Practices Study (IDMPS) discovered that just 3.6% of individuals with diabetes from 17 countries across Europe, Asia, Latin America, and Africa were able to meet all of the ABC goals (Chan *et al.*, 2009).

Achieving the ABC goals is critical for managing diabetes and mitigating its complications. The American Diabetes Association (ADA) has established these targets to minimize the risk of long-term complications such as CVD, nephropathy, neuropathy, and retinopathy. Research indicates that attaining these goals significantly reduces the incidence of CVD and other diabetes-related complications. For instance, study demonstrated that meeting one, two, or all three ABC goals corresponded to reductions in CVD event rates by 36%, 52%, and 62%, respectively (Wong *et al.*,

2016). These findings underscore the importance of comprehensive management strategies in improving patient outcomes and preventing diabetes-related morbidity and mortality.

For those with diabetes, reaching the ABC goals is essential because it greatly raises quality of life by improving general health and wellbeing and enabling more active and satisfying lifestyles. Moreover, it facilitates customised treatment programmes and improved diabetes control by giving healthcare practitioners precise treatment targets and long-term health advantages (American Diabetes Association, 2022).

According to research in the USA comparing the proportion of ABC goals attainment among veterans with diabetes, 17.3% of patients in 2008–2009 fulfilled the three ABC goals. Additionally, the study discovered that, in comparison to the 2001–2002 evaluation, the percentage of patients meeting their specific LDL–C, blood pressure, and $HbA_{1c}$ targets increased dramatically in 2008–2009. All of this improvement in achieving ABC goals is due to the introduction of yearly clinician reminders, improved patient education, and program modifications—such as home-based telephone monitoring with diabetic case management (Vouri *et al.*, 2011). A similar study conducted in the United States similarly supports the aforementioned research. The study discovered that attaining the American Diabetes Association's ABC goals was a strong predictor of microvascular problems, but not macrovascular consequences, in persons with diabetes over a period of six years. Failing to achieve ABC targets significantly raised the likelihood of having microvascular problems (Bjornstad *et al.*, 2014).

## 2.2 Proportion of ABC goals attainment

In Brazil, among individuals with diabetes, 12.5% met all three ABC goals; 13.7% attained the blood pressure goal and $HbA_{1c}$ targets; 9.6% attained the LDL-C and blood pressure targets; and 8.9% attained the $HbA_{1c}$ and LDL-C targets. In just 20% of the sample, no goal was accomplished (dos Reis *et al.*, 2021). Another study in Brazil two years later showed improvement: around 600 (28.6%) achieved all three goals, 1364 (66.1%) reached $HbA_{1c}$ goal, 1596 (77.4%) reached blood pressure goal, and 1086 (52.7%) reached cholesterol goal (Chwal *et al.*, 2023). The research revealed that a greater body mass index (BMI) and longer duration of diabetes were associated with a lower likelihood of achieving at least two ABC goals.

In a study involving 808 T2DM patients who were not pregnant in United States, 23.7% of them attained all the three ABC goals, while 57.3% achieved the $HbA_{1c}$ goal, 65.6% the blood pressure goal, and 56.8% the LDL-C goal. Overall, 23.7% of the study sample achieved two ABC goals concurrently. On the other hand, 8.1% of them failed to fulfill any of the three goals. Reaching all three ABC goals was linked to more visits to medical providers. The study suggested that increased contact may be beneficial for people with T2DM who are unable to fulfill ABC goals (Shah *et al.*, 2015).

A recent study in Japan shows that 13 (7.7%) of the 168 patients did not meet any goals, while 47 (28.0%) of them met all the three ABC goals. Forty-five patients (26.8%) had attained dual goals, and 63 patients (37.5%) had single goal attained. The study shows that, there was a gradual decrease in the average and variability of fasting and post-breakfast plasma glucose, as well as $HbA_{1c}$ , when more ABC goals were attained (Kaori Kitaoka *et al.*, 2020).

Conversely, a study in Malaysia reported only 4.5% of patients achieved all three ABC goals (Kim *et al.*, 2021). The achievement of all three ABC goals by age groups showed that aged 18-44 years had the lowest proportion, 2.5% (95% CI: 1.8-3.4), followed by age group of 45-59 years, 3.6% (95% CI: 3.2-4.1), and ≥ 60 years, which was 5.7% (95% CI: 5.2-6.2). However, the study did not provide information on the achievement of two or more ABC goals based on age group. In conclusion, patients with early onset type 2 diabetes had the lowest proportion of all three ABC goals achievement.

## 2.3 Factors associated with attainment of ABC goals

A wide range of factors, including age, sex, ethnicity, smoking status, BMI, duration of diabetes, comorbidities like hypertension and dyslipidemia, complications like nephropathy, foot complications, cardiovascular disease, amputation, ischemic heart disease (IHD), and retinopathy, treatment profiles for diabetes, income status, educational attainment, physical activity, and unhealthy diet, may have an impact on achieving the ABC goals. These factors can be classified into sociodemographic factors, lifestyle and treatment profiles.

### 2.3.1 Sociodemographic characteristic

#### 2.3.1(a) Gender difference

There were studies reporting women to have a better diabetes control than men. The study conducted in the USA found more women than men (8.8% vs. 2.7%, $p<0.0001$) met all three ABC goals (Bjornstad *et al.*, 2014). Similar results from another study showed that men were far more likely to have uncontrolled goals in all areas (AOR = 1.71, 95% CI 1.10–2.66) (Alkandari *et al.*, 2022).

However, the opposite findings were also highlighted. A study conducted in the United States analyzed 808 individuals with type 2 diabetes who were not pregnant. The study revealed that 23.7% of these patients successfully attained the ABC goals simultaneously. The target attainment rates for ABC were lower among females, and one element that influenced the attainment of ABC goals was an increase in visits with healthcare providers. The study proposes that patients who are unable to achieve ABC goals may experience advantages from enhanced interaction with healthcare personnel (Shah *et al.*, 2015).

Another study in China investigated the differences in achieving lipid goals between male and female outpatients with type 2 diabetes and associated coronary heart disease. They also identified potential factors that may increase the risk of not reaching these goals. Utilizing data from a comprehensive epidemiological study that encompassed the entire nation, it was discovered that women had elevated levels of total cholesterol, LDL-C, and triglycerides in comparison to men. Nevertheless, their $HbA_{1c}$ levels were not elevated. Among the patients, the proportion of women who received lipid-lowering therapy was smaller, whereas the percentage of men who achieved LDL-C objectives was greater (Zhang *et al.*, 2017). The study proposes the implementation of a more assertive approach to managing lipids in women in order to address gender disparities. This is supported by other studies showing that women with T2DM faced challenges such as poorer lipid management, lower adherence to treatment regimens, and higher rates of nonadherence to statin therapy (Billimek *et al.*, 2015; Russo *et al.*, 2015; Alwhaibi *et al.*, 2019).

These disparities stem from factors including sex-based differences in medication response, healthcare satisfaction, and patient-provider communication (Anichini *et al.*, 2013; Xiang *et al.*, 2021). Strategies to address these gaps include

targeted interventions, public health campaigns, medication therapy management, and interdisciplinary approaches (Schroeder *et al.*, 2012; Currie & Delles, 2018). Precision medicine, which considers individual variability including sex, is increasingly recognized as crucial in diabetes care (Prasad & Groop, 2019).

Moving forward, efforts should focus on tailored treatment plans, gender-specific therapies, and individualized care to optimize diabetes treatment outcomes across genders (de Ritter *et al.*, 2020; Fourny *et al.*, 2021).

### 2.3.1(b) Ethnicity

Ethnicity may plan an important role in the attainment of ABC goals among diabetic patients. A study conducted in Kuwait evaluated the degree of glycemic, blood pressure, and cholesterol management in adult individuals with diabetes. The findings indicated only 7.4% of individuals were able to successfully manage and control all three ABC goals. Non-Kuwaitis had a significantly higher likelihood of having uncontrolled ABC factors compared to Kuwaitis, with nearly double the rate (Alkandari *et al.*, 2022). The study reported that just 1 out of every 13 individuals from Kuwait were able to attain satisfactory control over their glycemia, blood pressure, and cholesterol levels. There is an immediate need for a nationwide program focused on enhancing the quality of diabetes care and reducing the occurrence of long-term consequences.

In Malaysia, there was also a significant association between ethnicity and attainment of ABC goals. Patients of Chinese descent had greater odds to achieve all the three ABC goals as compared to Malays (AOR = 1.8, 95% CI 1.50–2.17) (Kim *et al.*, 2021). The result is similar to a study conducted in China from 2015 to 2017. The study consisted of 8401 adults who reported having diabetes and a sample of 3531 individuals who provided dietary information. The findings indicated that 64.1% of

individuals met each of the ABC goals, with 22.2% attainted the blood pressure target, 23.9% achieving the LDL-C target, and 32.2% achieving a BMI below 24 kg/m2 (Zhong *et al.*, 2023). The attainment of diabetes care targets set by guidelines in Chinese persons who self-reported having diabetes was extremely low. The results emphasize the urgency of implementing nationwide health initiatives to enhance diabetes management.

These disparities are influenced by factors such as genetic predispositions, cultural differences, and healthcare availability. The study indicates that additional investigation and focused interventions may be required to tackle these inequalities and enhance overall health results in varied populations.

#### 2.3.1(c) Income and education

A significant amount of research indicates that higher income disparities are linked to population health, with higher income (PR 1.26, 95% CI 1.10–1.45) was associated with a higher likelihood of achieving the ABC goals (Chwal *et al.*, 2023). The finding was explained by the relationship between higher income status with greater likelihood of having resources, suitable housing, access to primary healthcare, and sanitary conditions. A similar study in USA, also revealed that characteristics linked to poorer ABC controls included poverty, lack of health insurance, lower educational attainment, and race/ethnicity (Mercado *et al.*, 2021). The study demonstrates that there are significant sociodemographic gaps that affect the attainment of these goals and highlights the complex nature of managing diabetes. To enhance diabetes management, clinical and public health initiatives must develop customised approaches that take into account the various factors affecting persons with diagnosed diabetes, such as socioeconomic obstacles to healthcare and health-related prospects. The majority of those with known diabetes reaching the desired $HbA_{1c}$

levels of less than 7% was higher in knowledge gainers (46%) compared to non-gainers (29%) (Berikai *et al.*, 2007). A study conducted in Manitoba, Canada, revealed that diabetic patients with problems received a higher amount of social support income. However, they were twice as likely to be unemployed compared to individuals without diabetes (Kraut *et al.*, 2001).

### 2.3.2 Lifestyle factors

#### 2.3.2(a) Smoking

Nicotine and smoking have an impact on insulin sensitivity, pancreatic β cell function, and body composition, which ultimately affects diabetes management. Compared to non-smokers, active smokers have a 30% to 40% higher chance of developing T2DM (Maddatu, Anderson-Baucum & Evans-Molina, 2017). According to an Italian study, cigarette smoking exacerbates insulin resistance in diabetic individuals and regular smoking is a major contributor to the development of cardiovascular diseases and increased rates of illness and death (Campagna *et al.*, 2019). In order to mitigate these hazards, it is imperative to establish efficacious smoking cessation program and promote methods that discourage smoking. Medical practitioners and healthcare professionals should offer patients with information regarding the hazards associated with smoking and provide pharmaceutical interventions for the treatment of nicotine addiction. Advocating smoking cessation for individuals with diabetes is of utmost importance, since it has the potential to decrease the overall incidence of diabetes.

The World Health Organization supports quitting smoking as a lifestyle choice and acknowledges smoking as a preventable risk factor for T2DM. It also suggests that public health campaigns to address the worldwide diabetes epidemic must prioritize smoking cessation. Another study found a link between smoking and blood pressure,

with males 1.6 times more likely than women to have uncontrolled blood pressure and four times greater smoking rates (Alkandari *et al.*, 2022).

Individuals who engage in cigarette smoking have a 30%–40% higher likelihood of developing type 2 diabetes compared to those who do not smoke (CDCTobaccoFree, 2022). Individuals with diabetes who engage in smoking are at a higher risk compared to non-smokers when it comes to experiencing difficulties in accurately determining the appropriate amount of insulin and effectively controlling their disease (Centers for Disease Control and Prevention (US), National Center for Chronic Disease Prevention and Health Promotion (US), & Office on Smoking and Health (US), 2010).

The outcome is comparable to a retrospective cohort study conducted in Taiwan. This study examined the correlation between smoking and glycemic control in 3044 males who were recently diagnosed with type 2 diabetes (T2DM) in Taiwan between 2002 and 2017. At 3 months of follow-up, the estimated maximum difference in HbA1c reduction between smokers and non-smokers was 0.33% (95% CI, 0.05–0.62%) (Sia *et al.*, 2022). This suggests that, on average, non-smokers experienced a greater reduction in $HbA_{1c}$ levels than smokers, with the true difference likely falling between 0.05% and 0.62%. The results indicate that smoking has a detrimental effect on the regulation of blood sugar levels in males who have just been diagnosed with type 2 diabetes.[U2]

### 2.3.2(b) Physical activities and diet

Engaging in regular physical activity lowers blood pressure, lipids, insulin resistance, and $HbA_{1c}$ in people with T2DM (Colberg *et al.*, 2016). A systematic review and meta-analysis of randomized controlled clinical trials showed that people who did structured fitness training (23 studies) had lower $HbA_{1c}$ levels than people

who did not do fitness training. Engaging in structured aerobic exercise, structured resistance training, or a combination of both resulted in reductions in $HbA_{1c}$ levels (Umpierre *et al.*, 2011). The study determined that implementing a regimen of structured exercise training, which includes both aerobic and strength training, is linked to a decrease in $HbA_{1c}$ levels in individuals diagnosed with type 2 diabetes.

In addition, consuming salty foods, like soup, can raise body weight, which may contribute to the yearly rise in blood pressure, cholesterol, and $HbA_{1c}$ in people with T2DM (Sakamoto *et al.*, 2019). A comparative study conducted on Korean adults examined the impact of a vegan diet against a traditional diabetic diet on glycemic control. The findings revealed that vegan diets resulted in superior glycemic control compared to conventional diets (Lee *et al.*, 2016). The study revealed that both diets resulted in substantial decreases in $HbA_{1c}$ levels, while the vegan diet exhibited a more pronounced reduction. The positive impact of vegan diets remained significant even after accounting for variations in overall energy consumption or waist circumference during the 12-week period. The study proposes that dietary recommendations for individuals with type 2 diabetes should incorporate a vegan diet in order to enhance the control and therapy of the condition.

To achieve moderate and long-lasting weight loss, lifestyle modification—also referred to as behavioral weight control—involves nutrition, exercise, and behavioral therapy. Dietary guidelines advise cutting back on high-calorie foods and drinks, as well as reducing portion sizes. It is advised to eat a balanced diet high in whole grains, beans, and fiber. Research indicates that lowering calories while increasing physical activity can help improve glycemia and sustain $HbA_{1c}$ reductions. In one study, patients' mean $HbA_{1c}$ dropped from 8.8% to 7.4%, and all of them stopped either metformin or insulin as their previous type of diabetes therapy. A 5–10% decrease in

starting weight over several months is considered a successful diet; higher weight reduction is linked to improved risk variables including $HbA_{1c}$ and cardiovascular risk (George & Copeland, 2013).

Research indicates that individuals diagnosed with diabetes are actively implementing measures to enhance lifestyle aspects, including engaging in weight loss efforts, augmenting levels of physical activity, and decreasing calorie and fat consumption. However, in order to meet the ABC goals, it is necessary to enhance strategies that promote compliance with prescription drugs, engage in regular physical activity, make good dietary choices, and ensure access to support (Stark Casagrande *et al.*, 2013). The most effective way to minimise problems associated with T2DM may be achieved through the management of ABC goals. The study emphasises the significance of having access to healthcare, education, support for self-management, personal knowledge, behaviour, adherence to therapy, healthy settings, and the diversity in the underlying causes of diabetes.

### 2.3.3 Diabetes profiles

#### 2.3.3(a) Duration of diabetes

Research has shown that the length of diabetes is significantly associated with a higher risk of developing insulin resistance and that elevated $HbA_{1c}$ levels can result in long-term hyperglycemia and insulin insensitivity (Yousefzadeh, Shokoohi & Najafipour, 2014). It further emphasizes the challenge of treating diabetes over time and is consistent with other research findings that clearly imply that people with diabetes who have had the disease for more than five years also have a lower possibility of achieving ABC goals (Shah *et al.*, 2015).

The duration of diabetes significantly influences the ABC goals due to diabetes progresses, the body's ability to produce and utilize insulin often declines, making

blood glucose control more challenging. This progression can lead to more frequent and severe complications, necessitating adjustments in $HbA_{1c}$ goals to balance glycemic control with the risk of hypoglycemia. This individualized approach helps to optimize outcomes by considering the progressive nature of diabetes and the varying capacities of individuals to manage their blood glucose levels effectively over time (Stark Casagrande *et al.*, 2013; Kim *et al.*, 2021).

### 2.3.3(b) BMI

An increase in BMI is thought to be the primary cause of metabolic illness development. The idea that insulin resistance and β-cell dysfunction are most likely related is supported by the nonesterified fatty acids (NEFAs) released by adipose tissue. Body fat distribution is another important component that determines insulin sensitivity. Insulin resistance is linked to body mass index regardless of the extent of weight increase. Because of variations in body fat distribution, thin people also have radically different insulin sensitivity (Al-Goblan, Al-Alfi & Khan, 2014). A study conducted in Brazil shows there was an 18% (Model 2; PR = 0.82; 0.73–0.92) drop in the frequency of accomplishing at least two ABC goals for every 5 kg/m2 rise in BMI (dos Reis *et al.*, 2021).

A study conducted in the Western region investigates the correlation between a higher BMI and the onset of type 2 diabetes reveal that even a moderately elevated BMI significantly raises the likelihood of experiencing negative outcomes, such as reliance on insulin, cardiovascular issues, cerebrovascular problems, kidney-related complications, and lower extremity complications (Gray *et al.*, 2015; Yashi & Daley, 2024).

The association between BMI and diabetes is widely recognized. Elevated BMI, which indicates excessive weight or obesity, is linked to insulin resistance and

suboptimal glycemic control in persons diagnosed with type 2 diabetes mellitus. Attaining and sustaining a healthy BMI is essential for enhancing insulin sensitivity and successfully regulating blood glucose levels, hence increasing the attainment of ABC goals. Individuals with a BMI exceeding 23 kg/$m^2$ have a higher susceptibility to developing diabetes. Preventive strategies involve achieving a weight loss of 7% to 10% of the initial body weight during a period of 6 months. Weight management is a critical aspect of managing T2DM, where individuals should strive to decrease their body weight by a minimum of 5%-10% through limiting their calorie intake. It is recommended by clinical guidelines to measure and record the BMI and waist circumference in persons with diabetes who are overweight or obese. It is advised to make lifestyle changes such as following a low-calorie diet and engaging in regular physical activity in order to enhance glycemic control and facilitate weight loss (MOH, 2020a).

### 2.3.3(c) Complications

#### 2.3.1(c)(i) Kidney disease

Previous research has demonstrated that attainment of ABC goals can lower mortality and long-term consequences that persist after the intervention phase (MOH, 2020a). Attaining the ABC goals has been linked, in T2DM patients with maintained renal function, to both prospective and cross-sectional declines in chronic kidney disease (Minato *et al.*, 2019). According to a study, patients who achieved three or more goals had a 60% lower chance of end-stage renal disease and/or death compared to those who did not reach three goals, potentially saving money (Chan *et al*., 2019). In 2016 in Malaysia, 65% of new patients requiring dialysis had diabetic kidney

disease, which was the most common cause of end-stage kidney disease (MOH, 2020a).

#### 2.3.1(c)(ii) CVD

Research conducted in the United States found that attaining ABC goals at the same time is associated with a lower risk of events related to cardiovascular disease. According to the survey, 680 participants (33.7%) had accomplished two or more goals. These results highlight how crucial it is to fully manage modifiable risk variables in order to reduce the risk of CVD that remains in people with diabetes mellitus (Wong *et al.*, 2016).

Poor regulation of blood glucose levels is linked to a higher likelihood of experiencing cardiovascular disease. This is because consistently elevated blood sugar levels can promote malfunction in the endothelial cells and the creation of plaque in the arteries, ultimately contributing to the development of atherosclerosis. Controlling blood pressure is crucial in diabetic patients as hypertension greatly increases the likelihood of cardiovascular events, such as heart attacks and strokes. High blood pressure can place extra stress on the cardiovascular system, resulting in damage to blood vessels and increased strain on the heart (Rodriguez-Araujo & Nakagami, 2018).

Consistently monitoring blood pressure, cholesterol levels, and smoking habits, while also encouraging a healthy lifestyle that incorporates regular exercise and a well-balanced diet, are essential elements in managing cardiovascular risks in patients with diabetes (American Diabetes Association, 2022; ElSayed *et al.*, 2023). The ABC goals aim to lower the overall burden of cardiovascular disease in individuals with diabetes by focusing on these three areas. This approach ultimately leads to improved long-term health outcomes and quality of life (American Diabetes Association, 2022; CDC, 2024).

This was supported by a study in Singapore, which analyzed 665 patients with dyslipidemia and T2DM to determine if they achieved triple vascular treatment goals. Results showed that 66.3% achieved two or more ABC goals. However, eight out of ten patients did not meet their goals for glycemic control, blood pressure, and LDL-C levels, increasing their risk of vascular complications. Optimizing therapeutic interventions can help mitigate these risks (Goh *et al.*, 2018).

#### 2.3.1(c)(iii) IHD

A Chinese cross-sectional study involving 102 patients found that poor glycemic control was negatively correlated with endothelial dysfunction and IHD in patients with T2DM (Chen *et al.*, 2021). The study observed a higher prevalence of IHD among those with poor glycemic control. Maintaining optimal glucose regulation reduces the risk of atherosclerosis, defined as the buildup of fatty plaques in the arteries, a major cause of infarction. It also diminishes oxidative stress, inflammation, and endothelial dysfunction, which are all risk factors for IHD. These findings indicate that achieving blood glucose control objectives, such as those outlined in the ABC goals, can significantly lower the risk of IHD.

A related study conducted in Sweden investigated the incidence of IHD showed that diabetes increased the prevalence of IHD by an amount equivalent to ten years for men and twenty years for women (Wiréhn, Ostgren & Carstensen, 2008). Similar study in Thailand aimed to determine the prevalence of IHD and identify associated risk factors among patients with diabetes. In 2013, a cross-sectional survey was conducted across 831 public hospitals in Thailand, involving 25,902 patients. Among these patients, 918 (3.54%) were found to have IHD. The study identified, hypertension and hyperglycemic crises as significant risk factors for IHD (Sakboonyarat & Rangsin, 2018). The study further highlights the importance of

achieving optimal blood sugar levels and blood pressure control in reducing risk IHD among diabetic patients. Specifically, hypertension, a significant risk factor identified in the study, can be effectively managed through strict blood pressure control, which is a key component of the ABC goals. Similarly, hyperglycemic crises emphasize the critical need for maintaining proper glycemic control to prevent severe fluctuations in blood sugar levels that can lead to complications. By focusing on these ABC goals, healthcare providers can significantly reduce the prevalence of IHD and improve outcomes for patients with diabetes.

#### 2.3.1(c)(iv) Amputation

In Western Denmark, a 10-year follow-up study involving 118,78 diabetes patients examined the risk of peripheral neuropathy and peripheral artery disease in diabetes patients showed that patients with diabetes had a 9.5-fold higher risk. A significant association was identified between diabetes and amputation (Olesen *et al.*, 2021). While a retrospective observational study in India among 27 patients with poorly controlled diabetes with the aim of examining the mortality and amputation risk in people with diabetic foot shows that major lower limb amputations were frequent in diabetics receiving irregular treatment and inadequate management (Singh & Chawla, 2006).

According to research in Brazil, using secondary data registered, a quantitative, exploratory, cross-sectional study with a time series design was conducted. The sample included 64,196 patients, of which 85.2% had both diabetes mellitus and hypertension. Among these, 1.5% of individuals with type 2 diabetes and 2.2% of those with both diabetes and hypertension experienced diabetes-related amputations (Costa *et al.*, 2020). The study found that diabetic foot was associated with a higher incidence of