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Pathophysiology of type 2 diabetes: A focus on the metabolic differences among southeast Asian, Chinese and Indian populations and how this impacts treatment

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Abstract

The prevalence of type 2 diabetes has been rising in China, India and Southeast Asia for decades, challenging their healthcare systems. With region-specific determinants such as genetics, lifestyle transition and early-life environment, people with type 2 diabetes showed their unique phenotypes, including being, on average, younger in age, with lower BMI but higher percentage body fat mass, higher postprandial glucose and poorer beta-cell function at onset. These features invalidated the implementation of some trial evidence from the Caucasian population when informing guideline recommendations and clinical decision-making. For example, α-glucosidase inhibitors and DPP4 inhibitors, targeting postprandial glucose, showed greater effectiveness and acceptability in Chinese people with type 2 diabetes. The indispensable use of insulin in people with severely impaired beta-cell function is common in China, India and Southeast Asian countries but induces the accumulation of body fat mass, which further worsens the prognosis of the people. GLP-1 receptor agonists show strong weight-lowering effects and cardiovascular protection and provide additional benefits for Asian people compared to Caucasians with the same levels of BMI. Adding GLP-1 receptor agonists to people receiving insulin may neutralise the adverse effect of body weight gain. Clinicians and patients should consider the unique features of the population before making decisions, and policymakers should be aware of the pragmatic determinants during the implementation of the overseas evidence. The adoption of international trials to the region by adjusting their distinct features may improve the relevance of evidence and the treatment response at the individual level.

KEYWORDS
diabetes complications, insulin resistance, insulin secretion, type 2 diabetes

1 | INTRODUCTION

Type 2 diabetes and its complications are challenging the global healthcare system. The International Diabetes Federation (IDF) estimated that 589 million people are suffering from type 2 diabetes in 2024, and projected 853 million in 2050.[1] China, India and Southeast Asia, with the most rapidly developing population, economics and infrastructure, account for 47.7% of world people with type 2 diabetes. The large population highlights the substantial management burden of type 2 diabetes in these developing countries. Although the

obesity pandemics and population ageing are well-established drivers of global diabetes growth, they may not fully explain the sharp rise observed in Asia over the past few decades. People with type 2 diabetes in China, India and Southeast Asia show unique phenotypes compared with Caucasians, including more severe beta-cell dysfunction, early onset of type 2 diabetes and lower BMI at diagnosis. These features suggest the distinction of the pathophysiology of type 2 diabetes in these regions. In this review, we synthesised the latest evidence of metabolic differences and treatment for people with type 2 diabetes among Chinese, Indian and Southeast Asian.

2 | EPIDEMIOLOGY

In the past few decades, the prevalence of type 2 diabetes is growing rapidly in China, India and Southeast Asia (see Table 1). In China, the age-standardised prevalence of type 2 diabetes rose from 0.674% in 1980 to 11.9% in 2024, affecting 148 million people.[1,2] In India, it increased from 2.1% in 1975 to 10.5% in 2024, affecting 89.8 million people.[1,4] In Malaysia, the adult prevalence even exceeded 20% in 2024.[1] Asia transformed from a low-burden region into an area where prevalence now equals or exceeds the global level (4.3% in 1980 and 11.9% in 2024).[1,13] However, the increase of type 2 diabetes in Asia showed no signs of slowing, unlike the stabilisation observed in Western populations. In China, the incidence of type 2 diabetes increased 60% in 2021 compared with 1990, while that in the UK decreased 3%–4.1% between 2004 and 2014.[14,15]

The large number of affected people imposes a substantial burden, including money spent and lives lost on these developing countries. For example, in 2015, diabetes costs $22 billion in India (1% of GDP) and $7.18 billion in Malaysia (2.4% of GDP).[16] In 2020, the total costs of diabetes reached $250.2 billion in China, equivalent to 1.58% of the country's GDP.[17] Compared with Western populations, type 2 diabetes in China, India and Southeast Asia affects people at different ages and with different patterns of complications. Asian populations tend to develop type 2 diabetes at a younger age. According to the Joint Asia Diabetes Evaluation (JADE) cohort, 18% of people in Asia with type 2 diabetes were diagnosed before the age of 40,[11] compared with only 4.8% in the UK.[12] South Asians were on average 9–10 years younger at the onset of type 2 diabetes than Caucasians.[18] Asians, especially those with early-onset type 2 diabetes, frequently develop diabetes-related complications. According to the China National HbA1c Surveillance System, 11% of people with type 2 diabetes developed non-fatal cardiovascular disease. The risk of non-fatal cardiovascular disease is 91% higher in people with early-onset type 2 diabetes than those with late-onset. Much of this risk could be attenuated by adjusting the duration of type 2 diabetes, which implies the higher risk in early-onset people is mostly attributable to a longer duration of diabetes.[19] Similarly, people with early-onset diabetes face a higher risk of microvascular disease compared with those with late-onset diabetes. Among individuals with early-onset diabetes, 5.1% developed nephropathy and 7.1% developed retinopathy, compared with 1.5% and 2.7% in those with late-onset diabetes.[20] Diabetes

TABLE 1 Epidemiology of type 2 diabetes in China, India, Southeast Asia and UK.[1]

	China	India	Malaysia	Indonesia	UK	US
Previous reported prevalence	1980: 0.674%[2] 2000–2001: 5.5%[3]	1972–1975: 2.1% in urban population; 1.5% in rural population[4] 1999–2002: 3.3%[5]	2000: 4.85% (IDF crude)	2000: 4.53% (IDF crude)	1991: 1.32%[6] 2011:5.2% (IDF)	2000: 8.04%
Recent prevalence (IDF 2024)	13.79%	9.48%	19.86%	11.03%	9.15%	15.70%
Recent age-standardised prevalence	2018:12.4%[7] 2024: 11.9% (IDF)	2024: 10.5% (IDF)	2024: 21.1% (IDF)	2024: 11.3% (IDF)	2024: 7.4% (IDF)	2024:13.7% (IDF)
Predicted age-standardised prevalence	2050: 13.9% (IDF)	2050: 12.8% (IDF)	2050: 23.5% (IDF)	2025:12.6%	2050: 8.5% (IDF)	2050: 15.2% (IDF)
Age-standardised prevalence of IFG (IDF 2024)	9.9%	11.7%	5.9%	7.7%	5.4%	14.2%
Isolated IFG	2.4% (2017[8])	10.1% (2020[9])	-	13.4% (2023[10])	-	-
Age-standardised prevalence of IGT (IDF 2024)	13.3%	11.9%	16.3%	16.3%	9.5%	11.5%
Isolated IGT	11.5% (2017[8])	3.3% (2020[9])	-	18.6% (2023[10])	-	-
Prevalence at younger age (before 40)	18% Asian people according to JADE (2007–2012)[11]				4.8% of all type 2 diabetes under the age of 80 in England and Wales (2021–2022).[12]	

complications contribute significantly to morbidity and mortality. In 2021, an estimated 0.9 million deaths were attributed to type 2 diabetes and hyperglycaemia in China.[14] In 2024, diabetes-related deaths accounted for 10.6% of all deaths in China, 5% in India and 8.4% in Indonesia.[1] These patterns suggest a despairing trend of diabetes complications in the following decades in the region.

3 | FEATURES AND POTENTIAL MECHANISMS

Tables 2 and 3 show phenotypes and determinants of type 2 diabetes in Asia in comparison with Western countries (taking the UK as an example).

3.1 | Beta-cell function and insulin resistance

Compared with other ethnic groups insulin secretion, the core pathophysiological mechanism of type 2 diabetes, is the lowest among the Indian and Chinese population.[35] A meta-analysis compared beta-cell function of people with normal glucose tolerance in different ethnic groups. The study used the increment above basal level of insulin concentrations during the first peak to measure the acute insulin response to glucose (AIR_g). The AIR_g in Africans was approximately four times that of East Asians, and in Caucasians was 1.5 times that of East Asians.[36] By contrast, the insulin sensitivity index in Asians, as measured by FSIGT with MINMOD analysis, was 1.5 times that of Caucasians. These findings suggest less insulin resistance and more pronounced impaired insulin secretion in Asians relative to non-Asians. This severely impaired insulin secretion may reduce individuals' ability to compensate for insulin resistance. They develop type 2 diabetes at a lower level of insulin resistance compared with non-Asians. Beta-cell dysfunction may be a more important contributor than insulin resistance in the development of type 2 diabetes among Asians. A prospective study reported that the age-BMI-adjusted HOMA-IR was 2.3 μIU/mL/mmol/L in Indians, 3.45 μIU/mL/mmol/L in African Americans and 2.59 μIU/mL/mmol/L in Caucasians. The association between HOMA-IR and the incidence of type 2 diabetes was weaker in South Asians compared with Caucasians. A per standard deviation increase in HOMA-IR increased the risk of type 2 diabetes by 1.67 times in Indians, compared with 33.64 times in Caucasians.[37] Among individuals with severe resistance, the HOMA-β level is among half that of those from India compared to people from Sweden.[35]

Although impaired insulin secretion is a common feature among Asian populations, the pathways of type 2 diabetes may differ among them. Among individuals with prediabetes, higher postprandial glucose levels are more common in Chinese (prevalence of isolated impaired glucose tolerance (IGT): 11.5% vs. isolated impaired fasting glucose (IFG): 2.4%),[8] while higher fasting glucose is more common in India (isolated IFG:10.1% vs. isolated IGT: 3.3%).[9] IFG and IGT are different states of insulin resistance and differ in their sites of insulin resistance. People with isolated IFG present severe hepatic insulin resistance and normal or near-normal muscle insulin sensitivity, whereas those with IGT are characterised by marked muscle insulin

TABLE 2 Features of type diabetes in China, India, Southeast Asia (Indonesia) and UK.

	China[21]	India[22]	Indonesia[23]	Malaysia[24]	UK[25]
Age	55.30	52.1 ± 9.2	55.6 ± 9.8	58.3 ± 11.27	52.0 ± 8.5
Duration of type 2 diabetes	-	8.6 ± 5.6	-	5.9 ± 5.56	Newly diagnosed
BMI	25.09	27.2 ± 4.6	26.4 ± 4.4	27.28 ± 5.96	29.1 ± 5.5
Fasting blood glucose (mmol/L)	8.13	7.9 ± 2.8	9.8 ± 3.3	8.59 ± 3.41	11.8 ± 3.7
Postprandial glucose (mmol/L)	14.56	11.4 ± 4.0	13.9 ± 4.6	13.24 ± 4.77	-
HOMA-B	-	-	-	-	49.9 (30.6–73.5) HOMA2
HOMA-IR	-	-	-	-	1.6 (1.1–2.2) HOMA2
Triglycerides (mmol/L)	2.03	-	2.1 ± 2.1	1.94 ± 1.25	1.73 (1.25–2.48)
LDL cholesterol (mmol/L)	2.92	-	3.3 ± 1	3.19 ± 1.10	3.7 ± 1.1
Systolic blood pressure	134.20	-	127.7 ± 17.2	136.72 ± 19.53	136.0 ± 19.5
Complications	Nephropathy 14.4% Cardiovascular disease 14.6%[26]	Nephropathy 18.8% Macrovascular complications 2.3%	Nephropathy 8.2% Cardiovascular complication 22.5%[27]	Nephropathy 7.3% Ischaemic heart disease 3.2%	Nephropathy 2.02%

TABLE 3 Determinants of type 2 diabetes in Asian people compared with Western people.

	China	India	Southeast Asia	Europe/US
Body composition	Higher body fat percentage compared with Caucasian at a given BMI[28]	Higher fat mass and abdominal fat mass, lower lean mass	Higher body fat percentage compared with Caucasian and Chinese at a given BMI	Lower body fat percentage at same BMI compared with Asians[28]
Body composition[29]	Higher fat mass (Indians: 32.1 kg in women; 29.3 kg in men); higher abdominal fat mass (Indians: 2.76 kg in women; 2.85 kg in men) Lower fat free mass (Indians: 39.9 kg in women; 55.8 kg in men)			Lower fat mass (28.3 kg in women; 22.9 kg in men) Lower abdominal fat mass (2.23 kg in women; 2.1 kg in men) Higher fat free mass (43.8 kg in women; 62.5 kg in men)
Early life environment (epigenetics)	Thrifty phenotype induced poor development of pancreatic beta-cell mass and function			-
Insufficient physical activity among adults in 2022[30]	23.8%	49.4%	40.4%	19%
Lifestyle and transitions	The consumption of grains, and dietary fibre declined while consumption of refined grains, fat, refined carbohydrates increased[31,32,33] Decreased level of physical activity and energy expenditure			-
Obesity prevalence trends[34]	2.5% in 2002	2.1% in 2002	2.4% in 2002	20.5% in 2002
	4.5% in 2012	4.1% in 2012	4.6% in 2012	24.8% in 2012
	8.3% in 2022	7.3% in 2022	8% in 2022	26.8% in 2022

resistance and only mild hepatic insulin resistance.[35] Intervention of 6-month lifestyle modification can reduce 31% diabetes risk in individuals with isolated IGT and 12% diabetes risk in individuals with isolated IFG.[38]

3.2 | BMI and body composition

Severe beta-cell dysfunction, along with limited tolerance to insulin resistance, may partially explain the lower BMI observed at diabetes diagnosis in Asians. Average BMI values in Asians remain lower than those in the UK. For example, the average BMI of adults with type 2 diabetes is 25.09 kg/m^2 in China, 27.2 kg/m^2 in India, 26.4 kg/m^2 in Indonesia, 27.28 kg/m^2 in Malaysia, compared with 29.1 kg/m^2 in the UK.[21–25] In the recent global and Indian obesity guidelines,[39,40] the criteria of obesity shifted from relying solely on BMI threshold to considering organ functions. A fixed BMI cutoff may be of limited relevance, especially in Asian populations, where type 2 diabetes can occur at lower BMI levels. Another reason is that BMI, although a useful measure of general adiposity, cannot discriminate between fat mass and lean mass, which affect the risk of type 2 diabetes in different ways. The fat mass in Indian with BMI of 24 kg/m^2 in men and 26 kg/m^2 in women are similar with that Europeans with the BMI of 30 kg/m^2.[29] According to previous studies, a distinct pattern of body composition characterised by "high body fat, low muscle mass at normal weight" is more common in Asians. Among men adjusted for age, height and weight, Indians demonstrated 28% higher fat mass, 36% higher abdominal fat mass and 11% lower fat free mass than Europeans.[29] Compared with Caucasians at given BMI, the body fat percentage was 5% to 7% higher in Indian men, 8% higher in Indian women, 5% higher in Indonesian men and 7% higher in Indonesian women from Malay ancestry.[28] Numerous studies reported the different influence of fat mass and skeletal muscle mass on development of type 2 diabetes. High fat mass is a risk factor, per standard deviation increases in fat mass increase 71% risk of type 2 diabetes in women and 70% risk in men.[41] In contrast, higher skeletal muscle mass would be a protective factor, each standard deviation increase in skeletal muscle mass was associated with 21% lower risk of type 2 diabetes in women and 42% in men with diminished muscle mass.[42] Abdominal fat, especially the subcutaneous abdominal adipose tissue, is a key driver of insulin resistance.[43] Therefore, the high body fat, high abdominal fat mass and low skeletal muscle mass are likely important contributors to the development of type 2 diabetes among Asian people.

The specific phenotypic characteristics of Asians were confirmed in cluster analysis. In the Swedish All New Diabetics in Scania (ANDIS) cohort,[44] type 2 diabetes was classified into severe insulin-deficient diabetes mellitus (SIDD), severe insulin-resistant diabetes mellitus (SIRD), mild obesity-related diabetes mellitus (MOD) and mild age-related diabetes mellitus (MARD). SIDD is more common in India and China than in Sweden (India: 26.5%; China: 24.8%; Sweden: 17.5%), and these people develop type 2 diabetes at a younger age (India: 42.5 years; China: 50.5 years; Sweden: 56.7 years), lower BMI (India: 24.9 kg/m^2; China: 22.5 kg/m^2; Sweden: 28.9 kg/m^2), lower

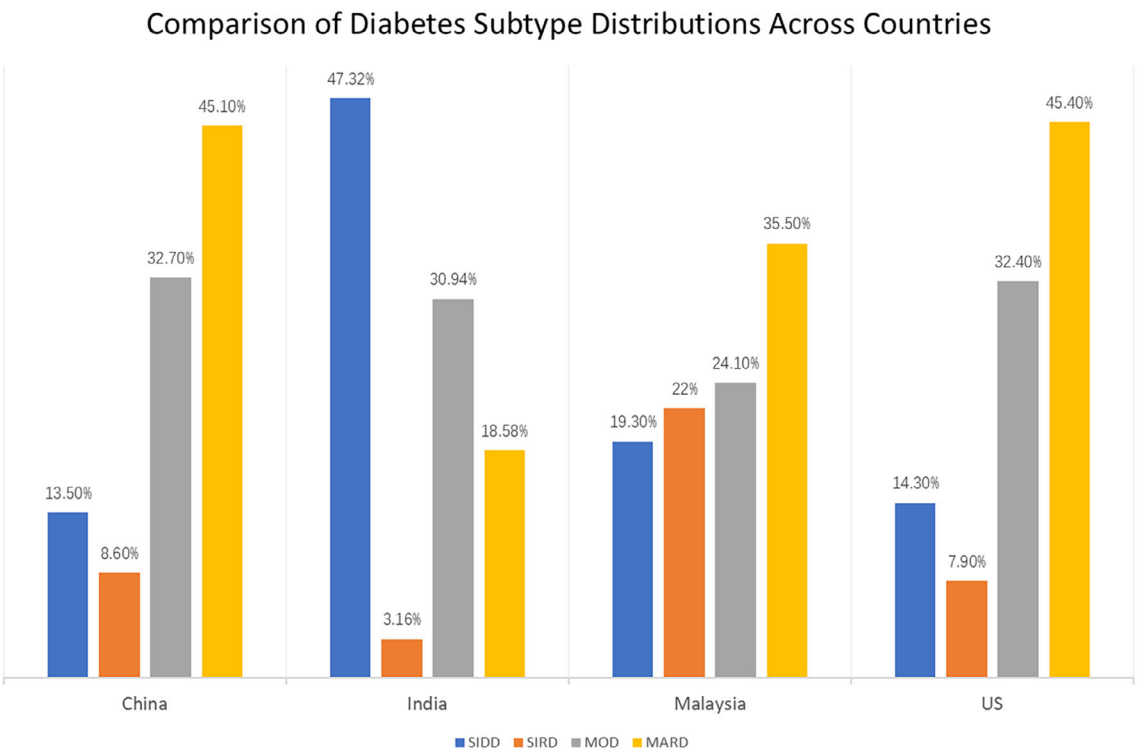

FIGURE 1 Comparison of diabetes subtype distributions across countries.[47–49] MARD, mild age-related diabetes; MOD, mild obesity-related diabetes; SIDD, severe insulin-deficient diabetes; SIRD, severe insulin-resistant diabetes. The figure illustrates the subtype distributions across countries. The treatment principles are likely to differ by subtypes. For example, insulin therapy may be more beneficial for SIRD. Weight loss through GLP-1 agonists could be effective for MOD. Managing complication risks should be a major target for MARD, with potentially less stringent glucose control.

HOMA-beta (India: 38.8; China: 20.2; Sweden: 47.6) and lower HOMA-IR (India: 2.8; China: 1.1; Sweden: 3.2).[44–46] The cohort in India also identified two subtypes, insulin-resistant obese diabetes (IROD) and a unique combined insulin-resistant-deficient diabetes (CIRDD). The CIRDD subtype was characterised by the lowest HDL cholesterol (31.6 mg/dL) and highest serum triglycerides (414 mg/dL).[45] However, the distribution of diabetes subtypes varies across different Asian regions (Figure 1).[47–49]

These studies further highlighted the distinct phenotypes of type 2 diabetes in Asian populations, including more severe beta-cell dysfunction, lower insulin resistance, younger age at diagnosis and a body composition pattern characterised by higher fat mass, lower lean mass, yet lower BMI. To better explain the sharp rise and distinct features of Asian type 2 diabetes in the past four decades, it is essential to consider the contribution of genetic predisposition, early-life environment and rapid lifestyle transitions.

4 | OTHER CONTRIBUTORS

4.1 | Genetics

Most identified genetic variants associated with type 2 diabetes are similar in Asians and non-Asians. However, some genetic variations might partly explain the distinct phenotype of Asians. Genetic variants associated with a lower risk of type 2 diabetes but higher body fat and BMI appear less frequent in Indians than in Europeans,[50] which may explain the body fat distribution and its relationship with disease observed in Indians. Variants in PAX4, which increase the susceptibility to early-onset type 2 diabetes,[51] are associated with a 31% higher risk of type 2 diabetes in Asian people,[52] but these variants are rare or monomorphic in Europeans.[53] Despite similar gene variants and effects, the allele frequencies may differ among Asians and non-Asians. For example, the risk allele frequency of variant rs7903146 in TCF7L2, which is associated with beta-cell response to GLP-1 and increased susceptibility to type 2 diabetes,[54] differs between East Asians (frequency of 5%) and Europeans (frequency of 30%).[55] Although genetic factors may play a role in predisposing Asians to the development of type 2 diabetes, these factors cannot fully explain the sharp rise.[56] Other risk factors may play a far more important role in the rise of type 2 diabetes in these regions.

4.2 | Lifestyle transitions and thrifty phenotype

Asian countries experienced rapid economic development, and massive rural-to-urban migration occurred. For example, the urbanisation rate increased from 17.9% to 66.2% in the past four decades in

China.[57] Urbanisation led to substantial shifts in lifestyle and dietary structure, which are strongly associated with health outcomes.[58] Calorie intake increased in many Asian countries, primarily from carbohydrates. The energy contribution from carbohydrates in the Chinese population declined from over 70% in the 1980s to 53% in 2015.[59] From 1982 to 2015 in China, grain intake decreased from 498 to 281.1 g/reference man/day, vegetables decreased from 298 to 255.1 g/reference man/day and dietary fibre decreased from 13.3 to 9.9 g/reference man/ day (from 1992 to 2015).[31] A similar trend occurred in India; the intake of grains, vegetables and dietary fibre declined while animal fat and refined increased.[32] According to The Prospective Urban and Rural Epidemiology study, the median glycaemic index was 88.9 in the Chinese diet, 88.2 in Southeast Asia, 88 in Africa, compared with 80 in North America and Europe. The glycaemic load of the South Asian diet was highest at 346 g/day, followed by China at 304.6 g/day, compared with North America and Europe at 177.1 g/day. However, a higher glycaemic index diet was associated with a 15% higher risk of type 2 diabetes when comparing the highest quintile to the lowest. Similarly, a diet with a higher glycaemic load was associated with a 21% higher risk of type 2 diabetes when comparing the highest quintile to the lowest.[60] The economic development resulted in more sedentary behaviour and fewer physical activities than previously. According to the Global Health Observatory data in 2022, 23.8% of adults had insufficient physical activities in China, 49.4% in India, 40.4% in Southeast Asia and 19% in the UK.[30] These lifestyle changes contributed to the rise of type 2 diabetes and obesity in these countries.

With lifestyle transitions, the prevalence of obesity increased from nearly 2% to 8% in Asian countries from 2002 to 2022.[34] The diabetogenic effect of obesity adds to individuals with poor early growth and may further increase the susceptibility to the development of type 2 diabetes, especially for Asians.[61] According to the thrifty genotype hypothesis, poor foetal or early natal nutrition influences the epigenetic modification, causes impaired development of the endocrine pancreas to adapt to the current nutritional conditions. However, the following good or over-nutrition may exceed the metabolic capacity of the endocrine pancreas and increase the susceptibility to type 2 diabetes.[35] Evidence from the Dutch Hunger Winter suggested that poor nutrition in utero is associated with decreased glucose tolerance in adults. Compared with the non-exposed population, the mean 2-h glucose concentration was 0.5 mmol/L higher among participants exposed to famine during late gestation.[62] This factor is particularly important for Asian developing countries, many of which experienced great famines—such as the Chinese famine (1959–1961), Bengal famine (1943) and Java famine (1944–1945)—and rapid economic development accomplished with increased nutritional conditions. Those exposed to malnutrition during foetal development are facing three times the higher risk of hyperglycaemia and another six times the higher risk if adopting a Western diet in their later lives.[63]

Other factors may also contribute to type 2 diabetes pathogenesis. For example, gut microbiota may affect the risk of type 2 diabetes and response to the glucose-lowering drugs, while infection may increase insulin resistance by activating inflammatory mediators.[35]

5 | TREATMENT OF TYPE 2 DIABETES IN ASIA

Multiple classes of pharmacological agents are available for glycaemic control and complications reduction in people with type 2 diabetes. Recommendations for drug treatment of type 2 diabetes are summarised in Table 4.[64–68] Guidelines recommendations for most oral antidiabetic agents are similar across countries. However, the response and the real-world use of these drugs may be different in Asian people with type 2 diabetes compared with Western people.

5.1 | Metformin and sulphonylureas

Although the prescription of metformin started to decline in the US since 2022,[69] with the rise of SGLT2 inhibitors and GLP-1 receptor agonists, metformin, in guidelines from most Asian countries, remains the first medication for newly diagnosed type 2 diabetes, with sulphonylureas as an alternative or the second.[64–68] In Hong Kong, the prescription rate of metformin rose from 41.1% in 2002 to 58.7% in 2019, with the rate of sulphonylureas declining from 52.3% in 2002 to 31.1% in 2016.[70] In China's mainland, the use of metformin increased from 53.7% in 2014 to 59.5% in 2024, and the use of sulphonylureas decreased from 70.2% to 9.4%.[71,72] 86.6% diagnosed within 2 years were on metformin therapy in India.[73] In the US, the use of metformin increased from 33% in 2003–2004 to 74% in 2015–2016,[74] and decreased from 76% in 2022 to 64% in 2023; that of sulphonylureas decreased to 2%.[69] Metformin was the most preferred drug in the past decades, but the use decreased in the US and is lower in China than in other regions, despite continuous increase. The use of sulphonylureas decreased, but is more common in China.

Sulphonylureas increase insulin level by stimulating insulin secretion from pancreatic beta cells, suitable for Asians with beta cell function. However, concerns exist regarding sulphonylureas-induced beta-cell apoptosis.[75] Metformin remains the most widely used antidiabetic medication after the rise of SGLT-2 inhibitors and GLP-1 receptor agonists, largely due to its affordability, safety and accessibility, especially in low-income regions. The lower use of metformin in China may partly reflect patients' attitudes toward body weight. Metformin is associated with moderate weight loss ranging from 4.62 to 0.72 kg.[76] Many Asian people, especially Chinese, are concerned about its body weight loss effect as they do not think they are big in size.

5.2 | SGLT-2 inhibitors

Sodium-glucose cotransporter-2 (SGLT-2) inhibitors gained traction due to their benefits in reducing the risk of cardiovascular and chronic kidney disease.[77–79] Guidelines recommended these drugs for second-line or combination therapy, especially for people with high cardiovascular and kidney risk.[80] The effect of SGLT-2 inhibitors on HbA1c and cardiovascular benefits appears consistent across ethnic

TABLE 4 Guidelines of type 2 diabetes in China, India, southeast Asia and US.

Drugs	CDS guideline 2024 (China)[66]	ICMR guideline 2018 (India)[67]	MEMS guideline 2020 (Malaysia)[65]	IMOH guideline 2020 (Indonesia)[68]	ADA guideline 2025 (US)[64]
Metformin	First-line monotherapy	First-line monotherapy	First-line monotherapy	First-line monotherapy	First-line
Sulphonylureas	Combination therapy	First-line combination therapy	Second-line monotherapy; combination therapy	Second-line monotherapy; combination therapy	-
α-Glucosidase inhibitors	Combination therapy	Second-line combination therapy	Second-line monotherapy; combination therapy	Second-line monotherapy; combination therapy	Not recommended
SGLT2 inhibitors	Second-line therapy; combination therapy	First-line combination therapy	Second-line monotherapy; combination therapy	Second-line monotherapy; combination therapy	Second-line
GLP-1 receptor agonists	Second-line therapy; combination therapy	Second-line combination therapy	Second-line monotherapy; combination therapy	Second-line monotherapy; combination therapy	Second-line
DPP4 inhibitors	Combination therapy	First-line combination therapy	Second-line monotherapy; combination therapy	Second-line monotherapy; combination therapy	Second-line
Insulin therapy	For newly diagnosed type 2 diabetes with symptomatic hyperglycaemia; when combination therapy is not effective for target blood glucose	Recommend for symptomatic hyperglycaemia	Not adequately controlled on maximum oral glucose lowering drugs ± GLP-1 receptor agonists	Combination therapy	As part of any combination medication plan when hyperglycaemia is severe

groups. A meta-analysis reported an HbA1c reduction of 0.65% among Asians and 0.60% among non-Asians.[81] Risk reduction for major adverse cardiovascular events (MACE) was 19% in Asians and 10% in Caucasians.[82]

The American Diabetes Association (ADA) did not recommend these drugs until 2018. In the US, the use of SGLT-2 inhibitors increased from 1%–4% before 2022 to 7% in 2023.[69] Due to the cardiovascular and kidney benefits, as well as the availability of low-cost options, SGLT-2 inhibitors also gained rapid popularity in the treatment of type 2 diabetes across Asia. In Hong Kong, the use of SGLT-2 inhibitors increased from 0.04% in 2015 to 0.4% in 2016[83] and 6% in 2019.[70] In Singapore, the use of SGLT-2 inhibitors increased from 0.5% in 2007 to 7.4% in 2017.[84] In India, the use was about 10% in 2017,[73] while in China, it reached 38.9% in 2024.[72]

Precision medicine should be considered to choose the right treatment for each person, especially those with cardiorenal risks.[85] In addition to the risk of genital infections, the potential for ketoacidosis and loss of lean body mass with SGLT2 inhibitor use needs attention.[86] Both SGLT - 2 inhibitors and low-carbohydrate diets stimulate ketogenesis; the restriction of carbohydrate may increase the risk of developing SGLT-2 inhibitor-induced euglycaemic diabetic ketoacidosis.[87,88] A meta-analysis suggested the changes in body weight and lean mass from using SGLT-2 inhibitors; the loss of lean mass accounted for between 10% and 40% of the body weight lost, with an average of around 30%. Compared with other antihyperglycaemic drugs, SGLT-2 inhibitors result in approximately 0.8 kg greater reduction in lean mass.[89]

5.3 | GlP-1 receptor agonists

Guidelines recommended glucagon-like peptide 1 (GLP-1) receptor agonists for second-line or combination therapy. GLP-1 receptor agonists exert anti-inflammation and antioxidant effect to prevent endothelial dysfunction and arterial stiffening, and improve cardiovascular and possible renal outcomes in people with diabetes.[90] From 2022 to 2023, GLP-1 receptor agonists increased from 6% to 18% in the US.[69] According to studies from the 2010s, GLP-1 receptor agonists were not commonly used in Asia.[71,91] In China, the use of GLP-1 reached 14.9% in 2024.[72]

Evidence suggests GLP-1 receptor agonists are more effective among Asians. The HbA1c reduction with GLP-1 receptor agonists was 0.32% greater in Asian-dominant studies. In Asians, the number of people achieving target HbA1c ≤ 7.0% was five times higher in the

GLP-1 receptor agonists group than in the control group. In non-Asians, the number of people achieving target HbA1c ≤ 7.0% was two times higher in the GLP-1 receptor agonists group than in the control group.[92] Cardiovascular benefits of GLP-1 receptor agonists were also greater in Asians with type 2 diabetes than in non-Asians, with MACE risk reductions of 8% in Caucasians, 22% in Africans and 75% in Asians.[93]

Moreover, GLP-1 receptor agonists provide greater benefit for people with obesity. Considering the worse beta-cell function, the benefit threshold for BMI can be lower among Asians. However, 25%–40% of the weight lost consists of lean mass.[94] It is necessary to introduce the bioelectric impedance analysis or body composition in deciding if GLP-1 receptor agonists are needed.

5.4 | DPP-4 inhibitors

Guidelines recommended dipeptidyl peptidase-4 (DPP-4) inhibitors for second-line or combination therapy. With a similar mechanism to that of GLP-1 receptor agonists, these agents show similar ethnic differences of effects. Like GLP-1 receptor agonists, they appear to be more effective in Asians, with an additional HbA1c reduction of 0.26% compared to non-Asians.[95] The GLP-1 receptor agonists and DPP-4 inhibitors reduce blood glucose by enhancing insulin secretion and inhibit glucagon secretion in a glucose-dependent manner, which may be especially effective for the defect of insulin secretion in Asian people.

DPP-4 inhibitors use rapidly rises in Asia. In China, the use of DPP-4 inhibitors was 0.8% in 2014,[71] and 16.8% in 2024.[72] In Singapore, the use increased from 1.2% in 2008 to 31.2% in 2017.[84] During 2015–2016 in the US, one-fifth of people received DPP-4 inhibitors, most as combination therapy,[74] however, the first-line use decreased from 2% in 2022 to 1% in 2023.[69] The use of newer agents consistently increases in Asia, replacing traditional agents, such as sulphonylureas.

5.5 | α-Glucosidase inhibitors

α-Glucosidase inhibitors (AGIs) reduce blood glucose by inhibiting carbohydrate absorption. In Asian countries, they are recommended as an alternative first-line pharmacotherapy, particularly for people with a high carbohydrate diet and high postprandial blood glucose. The ADA guideline did not specifically recommend this drug. Acarbose use in Asia reached 29.2% in China,[72] 18.6% in India[22] and 25.18% in Indonesia.[27] However, it is rarely reported in the US.

AGIs are agents that specifically impact on postprandial hyperglycaemia. HbA1c reduction effect of Acarbose is greater in east and Southeast Asian people compared with South Asian people and European people.[96] HbA1c reductions were 1.54% in populations consuming an Eastern diet versus 0.52% with a Western diet.[97] The MARCH randomised trial suggested that acarbose is comparable to metformin in effectiveness among Chinese people for initial therapy; HbA1c reduction at week 48 was −1.11% in acarbose and −1.12% in metformin.[98] The enhanced response of acarbose may be partly explained by the higher proportion of dietary carbohydrates consumed in this population compared with Western people.

5.6 | Insulin therapy

Insulin therapy is recommended in cases of symptomatic hyperglycaemia or when combination oral therapy fails to achieve target glucose control. Real-world data suggested a higher insulin use rate in Asian countries compared with Western countries. The use of insulin was 36.8% in China in 2024,[72] and 17.2% in India between 2015 and 2017.[73] In Singapore, the insulin use increased from 24.4% in 2007 to 57.9% in 2017.[84] In the US, the use of insulin increased from 17.1% in 2006 to 23% in 2013, primarily driven by the adoption of basal insulin analogues and rapid-acting insulin analogues.[99]

Under insulin therapy, HbA1c reduction from baseline was −1.46% in Asian people compared with −2.17% in Caucasians.[100] The insulin requirement of Asians is higher than that of Caucasians; for twice-daily insulin lispro mix 75/25, the dose reached 0.67 U/kg for non-Asians, 0.91 U/kg for Asian Indians and 0.53 U/kg for East Asians.[101] These differences may be related to worse insulin secretion capacity. Leaner people are more likely to need insulin. A study reported insulin use was 49% in lean type 2 diabetes and 44% in obese individuals. The insulin use in people diagnosed within 1 year was 35% in lean individuals and 25.8% in obese individuals.[102] This may reflect the more severe beta-cell dysfunction in lean diabetes. Chinese people preferred injections in relation to meals and did not prefer injections irrespective of meals; the possible reason may be that patients' belief in injections in relation to meals could bring better blood glucose control.[103]

Insulin may not be suitable for people with obesity or invisible obesity. But still, some people with obesity still need insulin to prevent acute complications. In this situation, the combined therapy of GLP-1 receptor agonists is necessary to neutralise the adverse effects of weight gain. For those without obesity, GLP-1 receptor agonists may prevent weight gain. The fixed combination of GLP-1 receptor agonists and insulin provides a conventional option for such people.[104] Free and fixed-ratio combinations of basal insulin and GLP-1 receptor agonists provide a better effect in glucose lowering than basal insulin intensification.[105] More multiple injections of insulin for better insulin control—it may be dangerous for people with cognitive impairments and living alone. Once daily insulin for convenience fits better for more people; alternatively, twice daily insulin of single may also work.

6 | CONCLUSIONS

China, India and Southeast Asia are facing a rapid rise of type 2 diabetes, leading to substantial burden in both cost and mortality. Population ageing and obesity epidemic alone cannot fully explain this sharp

rise, with distinct features in type 2 diabetes. Genetic predisposition, early environment and lifestyle changes accompanying economic development contribute to the rapidly rising and special phenotypes—younger age of onset, lower BMI and worse beta-cell function. These distinctions may provide insights into unique therapy for Asian people, such as AGIs and insulin. Although most countries follow similar treatment guidelines, drug response and usage patterns vary significantly across ethnic groups. Further studies are needed to explore the unique therapy for people with type 2 diabetes in China, India and Southeast Asia.

AUTHOR CONTRIBUTIONS

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The authors declare no conflict of interest.

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REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 11th ed. 2025 Accessed May 29, 2025. https://diabetesatlas.org/
2. Zhong XL. Diabetes mellitus survey in China. *Chin Med J (Engl)*. 1982;95(6):423-430.
3. Gu D, Reynolds K, Duan X, et al. Prevalence of diabetes and impaired fasting glucose in the Chinese adult population: international collaborative study of cardiovascular disease in Asia (InterASIA). *Diabetologia*. 2003;46(9):1190-1198.
4. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. *Indian J Med Res*. 2007;125(3):217-230.
5. Sadikot SM, Nigam A, Das S, et al. The burden of diabetes and impaired fasting glucose in India using the ADA 1997 criteria: prevalence of diabetes in India study (PODIS). *Diabetes Res Clin Pract*. 2004;66(3):293-300.
6. Holden SE, Jenkins-Jones S, Morgan CL, Peters JR, Schernthaner G, Currie CJ. Prevalence, glucose control and relative survival of people with type 2 diabetes in the UK from 1991 to 2013. *Diabet Med*. 2017;34(6):770-780.
7. Wang L, Peng W, Zhao Z, et al. Prevalence and treatment of diabetes in China, 2013-2018. *JAMA*. 2021;326(24):2498-2506.
8. Li Y, Teng D, Shi X, et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American Diabetes Association: national cross sectional study. *BMJ*. 2020;369:m997.
9. Anjana RM, Unnikrishnan R, Deepa M, et al. Metabolic non-communicable disease health report of India: the ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17). *Lancet Diabetes Endocrinol*. 2023;11(7):474-489.
10. Ministry of Health of the Republic of Indonesia. *Indonesian Health Survey 2023: National Report*. Health Development Policy Agency MoH RI; 2024.
11. Yeung RO, Zhang Y, Luk A, et al. Metabolic profiles and treatment gaps in young-onset type 2 diabetes in Asia (the JADE programme): a cross-sectional study of a prospective cohort. *Lancet Diabetes Endocrinol*. 2014;2(12):935-943.
12. NHS England Digital. *National Diabetes Audit 2021–22, Young People with Type 2 Diabetes—Detailed Analysis Report*. NHS England Digital; 2023. Accessed May 22, 2025. https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-audit-yt2/young-people-with-type-2-diabetes-detailed-report-2021-22
13. Zhou B, Rayner AW, Gregg EW, et al. Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants. *Lancet*. 2024;404(10467):2077-2093.
14. Zhang H, Jia Q, Song P, et al. Incidence, prevalence, and burden of type 2 diabetes in China: trend and projection from 1990 to 2050. *Chin Med J (Engl)*. 2025;138(12):1447-1455.
15. Magliano DJ, Islam RM, Barr ELM, et al. Trends in incidence of total or type 2 diabetes: systematic review. *BMJ*. 2019;366:l5003.
16. Bommer C, Sagalova V, Heesemann E, et al. Global economic burden of diabetes in adults: projections from 2015 to 2030. *Diabetes Care*. 2018;41(5):963-970.
17. Liu J, Liu M, Chai Z, et al. Projected rapid growth in diabetes disease burden and economic burden in China: a spatio-temporal study from 2020 to 2030. *Lancet Reg Health*. 2023;33:100700.
18. Wright AK, Welsh P, Gill JMR, et al. Age-, sex- and ethnicity-related differences in body weight, blood pressure, HbA1c and lipid levels at the diagnosis of type 2 diabetes relative to people without diabetes. *Diabetologia*. 2020;63(8):1542-1553.
19. Huo X, Gao L, Guo L, et al. Risk of non-fatal cardiovascular diseases in early-onset versus late-onset type 2 diabetes in China: a cross-sectional study. *Lancet Diabetes Endocrinol*. 2016;4(2):115-124.
20. Li L, Ji L, Guo X, et al. Prevalence of microvascular diseases among tertiary care Chinese with early versus late onset of type 2 diabetes. *J Diabetes Complications*. 2015;29(1):32-37.
21. Yang W, Lu J, Weng J, et al. Prevalence of diabetes among men and women in China. *N Engl J Med*. 2010;362(12):1090-1101.
22. Das AK, Mithal A, Joshi S, et al. Baseline characteristics of participants in the LANDMARC trial: a 3-year, pan-India, prospective, longitudinal study to assess management and real-world outcomes of diabetes mellitus. *Endocrinol Diabetes Metab*. 2021;4(3):e00231.
23. Soeatmadji DW, Rosandi R, Saraswati MR, Sibarani RP, Tarigan WO. Clinicodemographic profile and outcomes of type 2 diabetes mellitus in the Indonesian cohort of DISCOVER: a 3-year prospective cohort study. *J ASEAN Fed Endocr Soc*. 2023;38(1):68-74.
24. Mastura I, Chew BH, Lee PY, et al. Control and treatment profiles of 70,889 adult type 2 diabetes mellitus patients in Malaysia—a cross

sectional survey in 2009. *Int J Collab Res Intern Med Public Health*. 2011;3(1):98-113.
25. Lin B, Coleman RL, Bragg F, Maddaloni E, Holman RR, Adler AI. Younger-onset compared with later-onset type 2 diabetes: an analysis of the UK prospective diabetes study (UKPDS) with up to 30 years of follow-up (UKPDS 92). *Lancet Diabetes Endocrinol*. 2024;12(12):904-914.
26. Ji L, Hu D, Pan C, et al. Primacy of the 3B approach to control risk factors for cardiovascular disease in type 2 diabetes patients. *Am J Med*. 2013;126(10):925.e911-925.e922.
27. Soewondo P, Sidartawan S, Suastika K, Pranoto A, Soeatmadji DW, Tjokroprawiro A. The DiabCare Asia 2008 study – outcomes on control and complications of type 2 diabetic patients in Indonesia. *Med J Indones*. 2010;19(4):235-244.
28. Wulan SN, Westerterp KR, Plasqui G. Ethnic differences in body composition and the associated metabolic profile: a comparative study between Asians and Caucasians. *Maturitas*. 2010;65(4):315-319.
29. Rush EC, Freitas I, Plank LD. Body size, body composition and fat distribution: comparative analysis of European, Maori, Pacific Island and Asian Indian adults. *Br J Nutr*. 2009;102(4):632-641.
30. WHO. Global Health Observatory (GHO) Data. Prevalence of Insufficient Physical Activity. Accessed May 15, 2025. https://www.who.int/data/gho/data/themes/topics/indicator-groups/insufficient-physical-activity-indicator-group
31. Yu D, Zhao L, Zhao W. Status and trends in consumption of grains and dietary fiber among Chinese adults (1982–2015). *Nutr Rev*. 2020;78(suppl_1):43-53.
32. Hills AP, Arena R, Khunti K, et al. Epidemiology and determinants of type 2 diabetes in south Asia. *Lancet Diabetes Endocrinol*. 2018;6(12):966-978.
33. Jiang H, Zhang J, Du W, Su C, Zhang B, Wang H. Energy intake and energy contributions of macronutrients and major food sources among Chinese adults: CHNS 2015 and CNTCS 2015. *Eur J Clin Nutr*. 2021;75(2):314-324.
34. WHO. Prevalence of Obesity Among Adults, BMI >= 30 (Age-Standardized Estimate) (%). Accessed May 15, 2025. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/prevalence-of-obesity-among-adults-bmi--30-(age-standardized-estimate)-(-)
35. Ke C, Narayan KMV, Chan JCN, Jha P, Shah BR. Pathophysiology, phenotypes and management of type 2 diabetes mellitus in Indian and Chinese populations. *Nat Rev Endocrinol*. 2022;18(7):413-432.
36. Kodama K, Tojjar D, Yamada S, Toda K, Patel CJ, Butte AJ. Ethnic differences in the relationship between insulin sensitivity and insulin response: a systematic review and meta-analysis. *Diabetes Care*. 2013;36(6):1789-1796.
37. Narayan KMV, Kondal D, Daya N, et al. Incidence and pathophysiology of diabetes in South Asian adults living in India and Pakistan compared with US blacks and whites. *BMJ Open Diabetes Res Care*. 2021;9(1):e001927.
38. Weber MB, Ranjani H, Staimez LR, et al. The stepwise approach to diabetes prevention: results from the D-CLIP randomized controlled trial. *Diabetes Care*. 2016;39(10):1760-1767.
39. Misra A, Vikram NK, Ghosh A, Ranjan P, Gulati S. Revised definition of obesity in Asian Indians living in India. *Diabetes Metab Syndr*. 2025;19(1):102989.
40. Rubino F, Cummings DE, Eckel RH, et al. Definition and diagnostic criteria of clinical obesity. *Lancet Diabetes Endocrinol*. 2025;13(3):221-262.
41. Lee DH, Keum N, Hu FB, et al. Comparison of the association of predicted fat mass, body mass index, and other obesity indicators with type 2 diabetes risk: two large prospective studies in US men and women. *Eur J Epidemiol*. 2018;33(11):1113-1123.
42. Liu D, Li N, Zhou Y, et al. Sex-specific associations between skeletal muscle mass and incident diabetes: a population-based cohort study. *Diabetes Obes Metab*. 2024;26(3):820-828.
43. Grover B, Misra A. Abdominal obesity and adipose tissue depots: focus on intra-abdominal versus subcutaneous adipose tissue depots in Asian Indians. *Metabolic Syndrome*. Elsevier; 2024:635-645.
44. Ahlqvist E, Storm P, Käräjämäki A, et al. Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables. *Lancet Diabetes Endocrinol*. 2018;6(5):361-369.
45. Anjana RM, Baskar V, Nair ATN, et al. Novel subgroups of type 2 diabetes and their association with microvascular outcomes in an Asian Indian population: a data-driven cluster analysis: the INSPIRED study. *BMJ Open Diabetes Res Care*. 2020;8(1):e001506.
46. Li X, Yang S, Cao C, et al. Validation of the Swedish diabetes re-grouping scheme in adult-onset diabetes in China. *J Clin Endocrinol Metab*. 2020;105(10):e3519-e3528.
47. Zou X, Zhou X, Zhu Z, Ji L. Novel subgroups of patients with adult-onset diabetes in Chinese and US populations. *Lancet Diabetes Endocrinol*. 2019;7(1):9-11.
48. Yajnik CS, Wagh R, Kunte P, et al. Polygenic scores of diabetes-related traits in subgroups of type 2 diabetes in India: a cohort study. *Lancet Reg Health Southeast Asia*. 2023;14:100182.
49. Kazlauskaite R, Ellermeier N, Ngongo C, et al. Associations between type 2 diabetes subtypes and complications: analysis of the Malaysia National Diabetes Registry. *J Endocrinol Metab*. 2023;14(1):1-12.
50. Yaghootkar H, Whitcher B, Bell JD, Thomas EL. Ethnic differences in adiposity and diabetes risk – insights from genetic studies. *J Intern Med*. 2020;288(3):271-283.
51. Kwak SH, Chae J, Lee S, et al. Nonsynonymous variants in PAX4 and GLP1R are associated with type 2 diabetes in an east Asian population. *Diabetes*. 2018;67(9):1892-1902.
52. Cheung CYY, Tang CS, Xu A, et al. Exome-chip association analysis reveals an Asian-specific missense variant in PAX4 associated with type 2 diabetes in Chinese individuals. *Diabetologia*. 2017;60(1):107-115.
53. Hosoe J, Suzuki K, Miya F, et al. Structural basis of ethnic-specific variants of PAX4 associated with type 2 diabetes. *Hum Genome Var*. 2021;8(1):25.
54. Yako YY, Guewo-Fokeng M, Balti EV, et al. Genetic risk of type 2 diabetes in populations of the African continent: a systematic review and meta-analyses. *Diabetes Res Clin Pract*. 2016;114:136-150.
55. DIAbetes Genetics Replication And Meta-analysis (DIAGRAM) Consortium, Asian Genetic Epidemiology Network Type 2 Diabetes (AGEN-T2D) Consortium, South Asian Type 2 Diabetes (SAT2D) Consortium, et al. Genome-wide trans-ancestry meta-analysis provides insight into the genetic architecture of type 2 diabetes susceptibility. *Nat Genet*. 2014;46(3):234-244.
56. Unnikrishnan R, Anjana RM, Mohan V. Diabetes mellitus and its complications in India. *Nat Rev Endocrinol*. 2016;12(6):357-370.
57. National Bureau of Statistics of China. China statistical yearbook 2023. 2023 Accessed June 20, 2025. https://www.stats.gov.cn/sj/ndsj/2023/indexch.htm
58. Zhao Y, Yang H, Jiao R, et al. Phenotypic age mediates effects of Life's essential 8 on reduced mortality risk in US adults. *Precis Clin Med*. 2024;7(3):pbae019.
59. Xu Y, Lu J, Li M, et al. Diabetes in China part 1: epidemiology and risk factors. *Lancet Public Health*. 2024;9(12):e1089-e1097.
60. Miller V, Jenkins DA, Dehghan M, et al. Associations of the glycaemic index and the glycaemic load with risk of type 2 diabetes in 127 594 people from 20 countries (PURE): a prospective cohort study. *Lancet Diabetes Endocrinol*. 2024;12(5):330-338.

61. Sattar N, Misra A. Adiposity at the core of the rising tide of young-onset type 2 diabetes worldwide. *Diabetes Metab Syndr*. 2025;19(5):103249.
62. Ravelli ACJ, Meulen J, Michels RPJ, et al. Glucose tolerance in adults after prenatal exposure to famine. *Lancet*. 1998;351(9097):173-177.
63. Li Y, He Y, Qi L, et al. Exposure to the Chinese famine in early life and the risk of hyperglycemia and type 2 diabetes in adulthood. *Diabetes*. 2010;59(10):2400-2406.
64. Committee ADAPP. 9. Pharmacologic approaches to glycemic treatment: standards of Care in Diabetes—2025. *Diabetes Care*. 2024;48-(suppl 1):S181-S206.
65. Malaysia Endocrine & Metabolic Society. *Management of Type 2 Diabetes Mellitus*. 6th ed. Malaysia Endocrine & Metabolic Society; 2021.
66. Chinese Diabetes Society. Guideline for the prevention and treatment of diabetes mellitus in China (2024 edition). *Chin J Diabetes Mellitus*. 2025;17(1):16-139.
67. Tandon N, Mohan V. *ICMR Guidelines for Management of Type 2 Diabetes*. Indian Council of Medical Research; 2018.
68. Ministry of Health of the Republic of Indonesia. National Medical Service Guideline on Adults Type 2 Diabetes Management. 2020
69. Do D, Lee T, Peasah S, Inneh A, Patel U, Good C. Trends in first-line glucose-lowering medication use among US adults with type 2 diabetes from 2019 to 2023. *J Manag Care Spec Pharm*. 2025;31(5):520-526.
70. Yang A, Wu H, Lau ESH, et al. Glucose-lowering drug use, glycemic outcomes, and severe hypoglycemia: 18-year trends in 0·9 million adults with diabetes in Hong Kong (2002-2019). *Lancet Reg Health West Pac*. 2022;26:100509.
71. Ji L, Lu J, Weng J, et al. China type 2 diabetes treatment status survey of treatment pattern of oral drugs users. *J Diabetes*. 2015;7(2):166-173.
72. Wu H, Cai X, Yang W, et al. 848-P: the antidiabetic medication treatment patterns in Chinese patients with type 2 diabetes—real-world evidence from ICaReMe China registry study. *Diabetes*. 2025;74(Supplement_1):848.
73. Borgharkar SS, Das SS. Real-world evidence of glycemic control among patients with type 2 diabetes mellitus in India: the TIGHT study. *BMJ Open Diabetes Res Care*. 2019;7(1):e000654.
74. Le P, Chaitoff A, Misra-Hebert AD, Ye W, Herman WH, Rothberg MB. Use of antihyperglycemic medications in U.S. adults: an analysis of the National Health and nutrition examination survey. *Diabetes Care*. 2020;43(6):1227-1233.
75. Maedler K, Carr RD, Bosco D, Zuellig RA, Berney T, Donath MY. Sulfonylurea induced β-cell apoptosis in cultured human islets. *J Clin Endocrinol Metab*. 2005;90(1):501-506.
76. Shi Q, Nong K, Vandvik PO, et al. Benefits and harms of drug treatment for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. *BMJ*. 2023;381:e074068.
77. Wang S, Li S. Type 2 diabetes, heart failure and the treatment of their comorbidity. *Minerva Med*. 2025;116(2):141-155.
78. Ye W, Han K, Xie M, et al. Mitochondrial energy metabolism in diabetic cardiomyopathy: physiological adaption, pathogenesis, and therapeutic targets. *Chin Med J (Engl)*. 2024;137(8):936-948.
79. Pan X, He H, Bao Y, et al. Chinese expert consensus on the management of hypertension in adults with type 2 diabetes. *J Evid Based Med*. 2024;17(4):851-864.
80. Agarwal A, Mustafa R, Manja V, et al. Cardiovascular, kidney related, and weight loss effects of therapeutics for type 2 diabetes: a living clinical practice guideline. *BMJ*. 2025;390:e082071.
81. Cai X, Gao X, Yang W, et al. No disparity of the efficacy and all-cause mortality between Asian and non-Asian type 2 diabetes patients with sodium–glucose cotransporter 2 inhibitors treatment: a meta-analysis. *J Diabetes Investig*. 2018;9(4):850-861.
82. Lee MMY, Ghouri N, McGuire DK, Rutter MK, Sattar N. Meta-analyses of results from randomized outcome trials comparing cardiovascular effects of SGLT2is and GLP-1RAs in Asian versus white patients with and without type 2 diabetes. *Diabetes Care*. 2021;44(5):1236-1241.
83. Yang A, Wu H, Lau ESH, et al. Trends in glucose-lowering drug use, glycemic control, and severe hypoglycemia in adults with diabetes in Hong Kong, 2002–2016. *Diabetes Care*. 2020;43(12):2967-2974.
84. Tan YZ, Cheen MHH, Goh SY, et al. Trends in medication utilization, glycemic control and outcomes among type 2 diabetes patients in a tertiary referral center in Singapore from 2007 to 2017. *J Diabetes*. 2019;11(7):573-581.
85. Li S, Shi Q, Litvin V, Manski CF. Precision medicine in cardiorenal and metabolic diseases with routinely collected clinical data: a novel insight. *Precis Clin Med*. 2022;5(4):pbac025.
86. Nong K, Jeppesen BT, Shi Q, et al. Medications for adults with type 2 diabetes: a living systematic review and network meta-analysis. *BMJ*. 2025;390:e083039.
87. Tay J, de Bock MI, Mayer-Davis EJ. Low-carbohydrate diets in type 2 diabetes. *Lancet Diabetes Endocrinol*. 2019;7(5):331-333.
88. Rosenstock J, Ferrannini E. Euglycemic diabetic ketoacidosis: a predictable, detectable, and preventable safety concern with SGLT2 inhibitors. *Diabetes Care*. 2015;38(9):1638-1642.
89. Zhang S, Qi Z, Wang Y, Song D, Zhu D. Effect of sodium-glucose transporter 2 inhibitors on sarcopenia in patients with type 2 diabetes mellitus: a systematic review and meta-analysis. *Front Endocrinol (Lausanne)*. 2023;14:1203666.
90. Alharbi SH. Anti-inflammatory role of glucagon-like peptide 1 receptor agonists and its clinical implications. *Ther Adv Endocrinol Metab*. 2024;15:20420188231222367.
91. Singla R, Bindra J, Singla A, Gupta Y, Kalra S. Drug prescription patterns and cost analysis of diabetes therapy in India: audit of an endocrine practice. *Indian J Endocrinol Metab*. 2019;23(1):40-45.
92. Kim YG, Hahn S, Oh TJ, Park KS, Cho YM. Differences in the HbA1c-lowering efficacy of glucagon-like peptide-1 analogues between Asians and non-Asians: a systematic review and meta-analysis. *Diabetes Obes Metab*. 2014;16(10):900-909.
93. Kang YM, Cho YK, Lee J, et al. Asian subpopulations may exhibit greater cardiovascular benefit from long-acting glucagon-like peptide 1 receptor agonists: a meta-analysis of cardiovascular outcome trials. *Diabetes Metab J*. 2019;43(4):410.
94. Conte C, Hall KD, Klein S. Is weight loss-induced muscle mass loss clinically relevant? *JAMA*. 2024;332(1):9-10.
95. Kim YG, Hahn S, Oh TJ, Kwak SH, Park KS, Cho YM. Differences in the glucose-lowering efficacy of dipeptidyl peptidase-4 inhibitors between Asians and non-Asians: a systematic review and meta-analysis. *Diabetologia*. 2013;56(4):696-708.
96. Weng J, Soegondo S, Schnell O, et al. Efficacy of acarbose in different geographical regions of the world: analysis of a real-life database. *Diabetes Metab Res Rev*. 2015;31(2):155-167.
97. Zhu Q, Tong Y, Wu T, Li J, Tong N. Comparison of the hypoglycemic effect of acarbose monotherapy in patients with type 2 diabetes mellitus consuming an Eastern or Western diet: a systematic meta-analysis. *Clin Ther*. 2013;35(6):880-899.
98. Yang W, Liu J, Shan Z, et al. Acarbose compared with metformin as initial therapy in patients with newly diagnosed type 2 diabetes: an open-label, non-inferiority randomised trial. *Lancet Diabetes Endocrinol*. 2014;2(1):46-55.
99. Lipska KJ, Yao X, Herrin J, et al. Trends in drug utilization, glycemic control, and rates of severe hypoglycemia, 2006–2013. *Diabetes Care*. 2016;40(4):468-475.
100. Davidson JA, Wolffenbuttel BH, Arakaki RF, Caballero AE, Jiang HH, Hardin DS. Impact of race/ethnicity on efficacy and safety of two starter insulin regimens in patients with type 2 diabetes: a posthoc analysis of the DURABLE trial. *Ethn Dis*. 2013;23(4):393-400.

101. Ji L, Min KW, Oliveira J, Lew T, Duan R. Comparison of efficacy and safety of two starting insulin regimens in non-Asian, Asian Indian, and East Asian patients with type 2 diabetes: a post hoc analysis of the PARADIGM study. *Diabetes Metab Syndr Obes*. 2016;9:243-249.
102. Coleman NJ, Miernik J, Philipson L, Fogelfeld L. Lean versus obese diabetes mellitus patients in the United States minority population. *J Diabetes Complications*. 2014;28(4):500-505.
103. Huang Y, Huang Q, Xu A, Lu M, Xi X. Patient preferences for diabetes treatment among people with type 2 diabetes mellitus in China: a discrete choice experiment. *Front Public Health*. 2021;9:782964.
104. Balena R, Hensley IE, Miller S, Barnett AH. Combination therapy with GLP-1 receptor agonists and basal insulin: a systematic review of the literature. *Diabetes Obes Metab*. 2013;15(6):485-502.
105. Maiorino MI, Chiodini P, Bellastella G, et al. Free and fixed-ratio combinations of basal insulin and GLP-1 receptor agonists versus basal insulin intensification in type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Obes Metab*. 2018;20(9):2309-2313.

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