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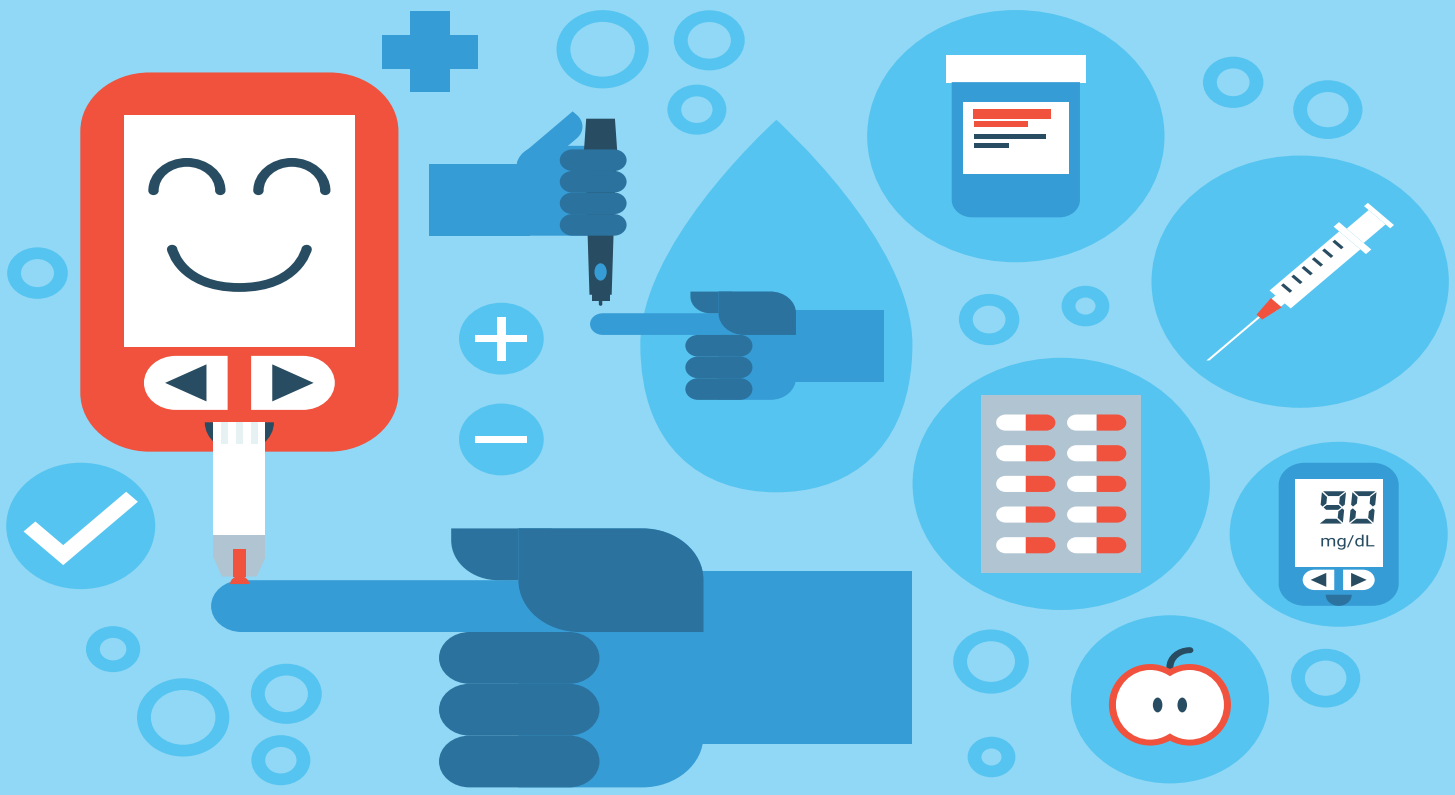
HEALTHCARE



PREDIABETES

The Economic Burden in Hong Kong

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About this report

Prediabetes is generally associated with glucose levels which are above normal but fall below the defined threshold for diabetes. In addition to likely progression to diabetes, prediabetes can put some people at greater risk for various health problems and complications. Given these risks and the often-asymptomatic nature of prediabetes, there is an increasing need to better understand the epidemiological and economic burden for more effective policy and action.

To address this need, the EIU conducted a research programme to illuminate the costs of inaction around prediabetes in Hong Kong, as well as the potential economic impact of interventions to delay the onset of type 2 diabetes (T2DM). For a full description of the methods, see Appendix 1.

Several key experts and stakeholders were engaged in the process. To note, the findings and views expressed in this report are those of EIU Healthcare and do not necessarily reflect the views of these contributors or project sponsors. We extend our sincere appreciation to the following for their time and contributions to this work:

- Dr Andrea Luk, Associate Professor, Department of Medicine & Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong
- Dr Quan Chao, Clinical Assistant Professor, School of Public Health, University of Hong Kong
- Dr Peter Tong, Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong

This work was commissioned by Merck Pharmaceutical and conducted independently by the EIU. The research was led by Gerard Dunleavy, with guidance from Rohini Omkar and Rob Cook. The economic modelling was performed by Dustin Hamalainen. The report was written by Amrita Namasivayam, and edited by Gerard Dunleavy and Rohini Omkar. André Comiran Tonon and Jocelyn Ho were contributing researchers.

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Executive summary

Diabetes is a major public health problem and the prevalence of the disease has reached epidemic proportions. Based on figures from the International Diabetes Federation (IDF), approximately 463 million adults between the ages of 20-79 years were living with diabetes in 2019, which amounts to 1 in every 11 adults.[1] Age-standardized diabetes prevalence increased from 4.3% in 1980 to 9.0% in 2014 in men, and from 5.0% to 7.9% in women in the same time period.[2]

Successful prevention of type 2 diabetes (T2DM) among high-risk individuals entails a multipronged approach including identification of risk factors, monitoring of plasma glucose levels, and the introduction of lifestyle interventions, with or without adjunctive pharmacological therapy.[3] A growing body of evidence now points to substantial benefits from early intervention at the prediabetes stage, when blood sugar levels are elevated (between 140–199 mg/dL, or 7.8–11.0 mmol/L 2 hours after eating), but are not high enough to be considered as diabetes.[4] Early diagnosis of prediabetes is therefore recommended as an important public health priority, particularly in terms of delaying the onset and progression of T2DM and reducing the heavy financial burden of the disease.[5]

South East Asia has seen a steep increase in diabetes in the last decade, with an estimated 96 million people having diabetes in the region.[6] Approximately 90% of this population have T2DM, which can be prevented or delayed if identified and treated early; however more than half of these cases remain undiagnosed[1]. According to IDF estimates, diabetes-related health expenditure in South East Asia amounted to more than *US$8bn* in 2019.[7] These figures underscore the urgency and importance of early diagnosis and intervention in the region, even more so at the prediabetes stage.

Key findings from this study indicate that the incidence of T2DM is increasing among younger adult populations in Hong Kong, implying that the costs of diabetes care and potential complications are bound to increase in the future, as a result of more people living with the condition for longer periods of time. Of greater concern is the large proportion of people for whom diabetes remains undiagnosed. At present, this is estimated to be approximately 50% of all T2DM cases, suggesting that even larger numbers of people with impaired glucose tolerance (IGT) or prediabetes have yet to be identified as being at high-risk for developing diabetes. Finally, early intervention in the diabetes pathway could result in cumulative cost savings of almost *US$19bn* by 2040. Increasing the awareness and recognition of prediabetes as a disease state, as well as drawing the attention of policymakers to the economic and social gains of early prediabetes identification through targeted screening of high-risk individuals, will be fundamental to reducing the economic burden of diabetes.

An introduction to diabetes and prediabetes

Diabetes is a chronic disease condition which involves either the cessation of insulin production by the pancreas (type 1 diabetes, T1DM) or the ineffective metabolism of insulin (T2DM). T1DM, also known as insulin-dependent diabetes, manifests in early childhood and is caused by an immune-mediated attack on beta islets in the pancreas; for this reason, T1DM is not yet preventable.[8] T2DM, which is the most common form of the disease—is an acquired and progressive disruption in glucose metabolism regulation that involves resistance to insulin. Its multifactorial aetiology encompasses genetic predisposition, excess body weight, physical inactivity, and other factors related to a sedentary lifestyle.[9] This, however, means that lifestyle modifications and pharmacological treatment can modify the progression of T2DM.

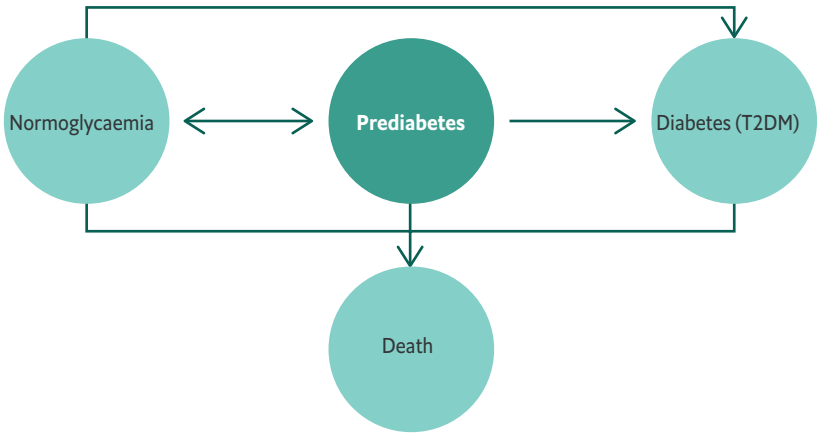
One of the biggest challenges with managing diabetes is the silent and progressive nature of the disease. The underlying pathophysiology of diabetes is hyperglycemia, a state of elevated blood glucose. Most people who are hyperglycemic are asymptomatic in the early stages, and for some, this may extend to later stages of the disease as well. Depending on the disease duration, hyperglycemia can lead to several adverse outcomes including blindness, thromboembolic events (e.g. heart attack, stroke), chronic kidney disease, and lower limb amputation.[10] Hence, if not diagnosed, managed, and controlled, diabetes may require constant medical care and hospitalization as a result of several comorbidities, many of which could lead to premature death[11].

In 2019, direct health expenditure for diabetes globally cost an estimated *US$760bn*.[12] Previous research estimates that the global economic burden of diabetes will be *US$2.5trn* in 2030, if past diabetes trends are to continue.[13] Therefore, strategies including primary prevention and early diagnosis of diabetes have been central goals of non-communicable disease (NCD) health programs and health surveillance worldwide.

The diabetes pathway and diagnostic criteria for prediabetes

Clinical glycemic control forms a spectrum with normoglycaemia on one end and diabetes on the other (Figure 1).

Figure 1: The diabetes pathway



Source: The Economist Intelligence Unit

An intermediate category, prediabetes, defined as IGT or impaired fasting glucose (IFG), was a term proposed in 1979 by the World Health Organization and the National Diabetes Data Group[14]; this classification seeks to identify individuals at risk for progression to diabetes and its complications as early as possible. The IDF report of 2019 describes a worldwide prevalence of IGT of 7.5% among adults (amounting to approximately 370 million people); this is projected to increase to 8.0% by 2030 and 8.6% by 2045.[15]

There has been much debate over the exact definition and terminology of prediabetes in the last several years, and across different international organisations and bodies. Table 1 shows the IDF clinical parameters used in the characterization of IGT or IFG. As of 2010, the American Diabetes Association (ADA) recommends diagnosing prediabetes as HbA1c values between 39 and 47 mmol/mol (5.7–6.4%) and IFG as fasting plasma glucose levels between 5.6 and 6.9mmol/L (100–125mg/dL).[3] An investigation of 25 communities across Mainland China, however, reports HbA1c levels between 5.8% and 6.2% (40–44 mmol/mol) to be more appropriate for Chinese populations, in accounting for genetic and ethnic differences.[16] While not all organisations and countries ascribe to these changes, the lower thresholds for prediabetes have substantially increased the number of people characterised as having prediabetes in countries that recognise and adopt these parameters in clinical practice.

Table 1: Prediabetes and diabetes diagnostic criteria

Glycaemic Status ↓	1. Fasting plasma glucose	2. Two-hour plasma glucose (following 75g oral glucose load)	3. HbA1c	4. Random Blood Glucose (with symptoms of hyperglycaemia)
Normoglycaemia	<6.1 mmol/L (<110 mg/dL)	<7.8 mmol/L (140 mg/dL)	<6.0%* (<42 mmol/mol)	Not applicable]
Prediabetes: Impaired Fasting Glucose- IFG	6.1-6.9 mmol/L (110-125 mg/dL)	<7.8 mmol/L (140 mg/dL)	6.0%- 6.4%* (42 to 47 mmol/mol)	
Prediabetes: Impaired Glucose Tolerance- IGT	<7.0 mmol/L (<126 mg/dL)	≥7.8 <11.1 mmol/L (≥140 to <200 mg/dL)		
Diabetes	≥7.0 mmol/L (≥126 mg/dL)	≥11.1 mmol/L (≥200 mg/dL)	≥6.5% (≥47 mmol/mol)	>11.1 mmol/mol (>200 mg/dL)

Notes on testing criteria: For normoglycaemia, any of the following criteria (1-3).
For prediabetes (IFG): Criteria 1, 1 and 2, or 3
For prediabetes (IGT): Criteria 1 and 2, or 3
For diabetes: One or more of criteria 1-4

*Note: The WHO does not currently recommend HbA1c testing for prediabetes.

Source: The Economist Intelligence Unit

While clinical intervention in the diabetes pathway is often only initiated once a patient is diagnosed with T2DM, there are salient benefits to earlier intervention at the prediabetes stage. Intensive lifestyle interventions have shown to produce a relative risk reduction of T2DM onset of 40-70%.[4] Beyond a higher likelihood of developing T2DM, individuals with prediabetes are shown to be at higher risk for cardiovascular disease, early-stage nephropathy, chronic kidney disease, diabetic retinopathy, and cancer.[17] Estimates suggest that 5-10% of people with prediabetes develop T2DM each year, with as much as 70% of people developing T2DM over their lifetime. However, with intervention and/or reduction in weight, it is possible to achieve a state of normoglycaemia after a prediabetes diagnosis, which reduces the risks associated with prediabetes.[18]

In this study, we focus on the economic burden of prediabetes in Hong Kong, with the aim to:

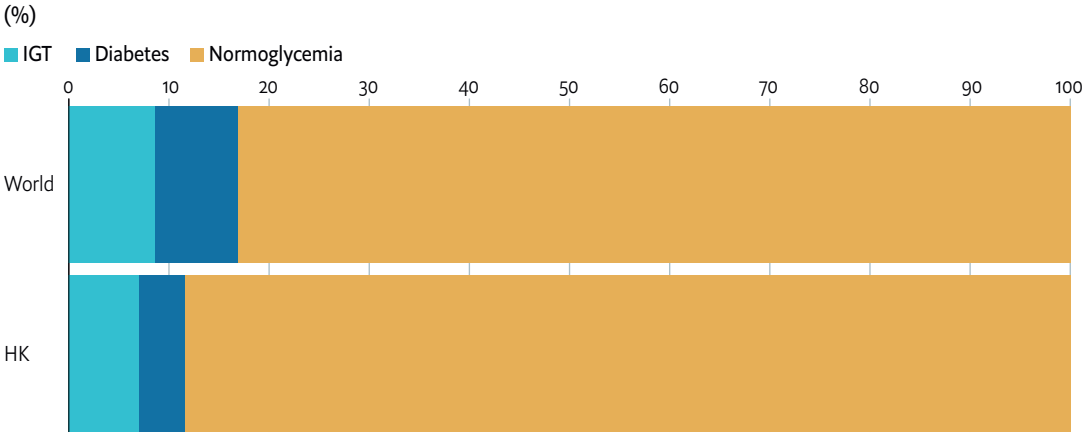
- Describe the current prevalence of prediabetes and diabetes in Hong Kong
- Describe existing programmatic and policy interventions that address diabetes
- Estimate the costs of action and inaction in addressing prediabetes and diabetes

Prediabetes in Hong Kong

Current prevalence and risk factors

One of the first reports documenting the prevalence of prediabetes in Hong Kong dates back to 1993, when 7.3% of 1,513 people had their diagnosis confirmed with an oral glucose tolerance test following the WHO 1985 criteria.[19] When this same sample was re-examined according to the ADA 1997 criteria, an additional 6.2% of people previously categorized in the normal fasting glucose group were then classified as prediabetic.[20] Subsequent studies report an overall higher prevalence of prediabetes, possibly due to the epidemiological transition with increasing cases of diabetes and prediabetes, and the shift from the WHO 1985 criteria to the ADA 1997 or WHO 1999 criteria, which considered a lower cutoff for the classification of prediabetes—thus including more people in this category.[21]

Figure 2: The age-adjusted percentage of population with diabetes (T2D) and impaired glucose tolerance (IGT) worldwide and in Hong Kong.



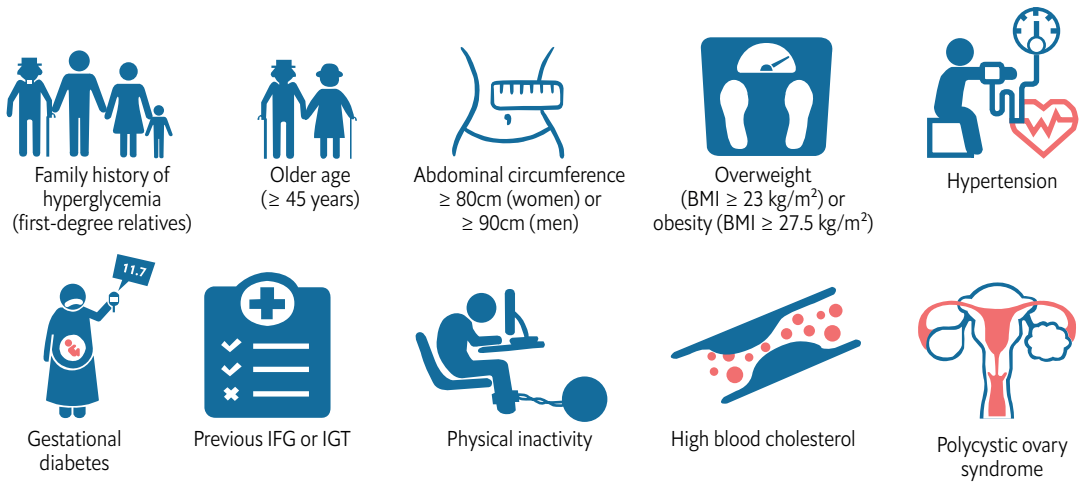
Source: The International Diabetes Federation (IDF) diabetes atlas 2019.

Based on the latest IDF estimates, Figure 2 illustrates the current prevalence of diabetes and IGT globally and in Hong Kong. However, Dr Tong of the Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong emphasised that the comparative prevalence might represent a significant underestimation of prediabetes and diabetes in Hong Kong, highlighting the difficulties in understanding the true extent and burden of these conditions.

In Hong Kong, the annual progression rates from IGT to diabetes are approximately 8.8–11.5%, and many studies have documented younger populations progressively becoming diabetic when their IGT remains undiagnosed and/or uncontrolled.[22-24] Not surprisingly, research has also reported an increasing trend of diabetes incidence among younger age groups (20-39 years), while incidence rates among people ≥60 years old have stabilized for men and declined for women.[25]

A plethora of research has uncovered a number of risk factors for the progression to T2DM among the Hong Kong population, illustrated in Figure 3 below. While family history and obesity are well-established risk factors for the development of impaired glucose regulation and diabetes,[26, 27] Dr Andrea Luk, Associate Professor, Department of Medicine & Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, highlighted that "about a third of patients with diabetes" at her hospital have a body mass index (BMI) of less than 23kg/m^2, which is the Asian BMI cut-off for being overweight.[28] Further highlighting the difficulties of identifying people with prediabetes and diabetes, she added, "these lean people are not being picked up for diabetes, because they don't have the sort of traditional phenotype of a diabetic person." To improve screening for T2DM, there needs to be greater awareness of the risk factors for the disease. "Family history of diabetes is not a well-recognized risk factor", according to Dr Luk. She elaborates, "it is not something that doctors would often ask a patient about."

Figure 3: Risk factors for prediabetes and diabetes in Hong Kong



BMI: body mass index; IFG: impaired fasting glucose; IGT: impaired glucose tolerance
Source: The Economist Intelligence Unit.

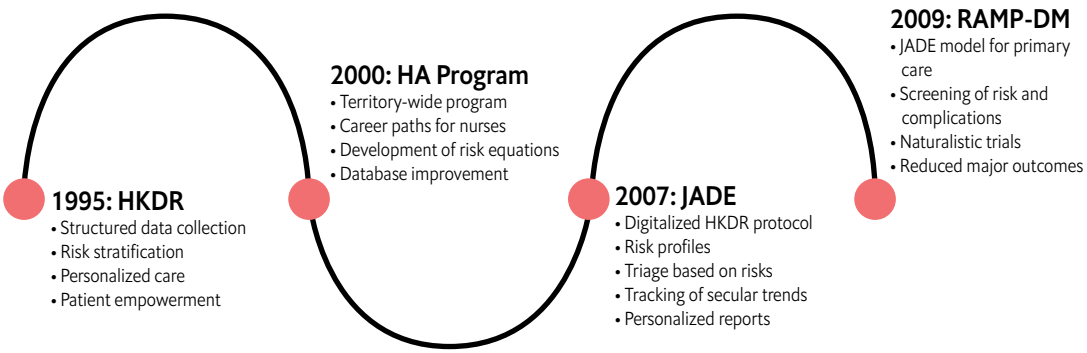
Health programs and policies centred around diabetes in Hong Kong

Starting in the early 1990s, the Hong Kong public health system implemented a series of subsidized, multidisciplinary programs that changed the course of diabetes in the territory, shown in Figure 4.[29]

The Hong Kong Diabetes Register (HKDR) was established in 1995, putting in place an annual or biannual assessment of all patient referrals for diabetes and a structured protocol aiming to stratify risk, screen for multiple complications, empower patients, and individualise treatment. The protocol of HKDR was adapted to an electronic version in 2007 to create the Joint Asia Diabetes Evaluation (JADE) program. JADE incorporated the data collected in the previous decade and designed risk profiles and algorithms for individualized follow-up of disease progression.

The successful establishment of the HKDR and JADE programs have enabled a consistent

Figure 4: Evolution of pioneer diabetes quality care programs in Hong Kong.



HA: Hospital Authority; HKDR: Hong Kong Diabetes Register; JADE: Joint Asia Diabetes Evaluation; RAMP-DM: Multidisciplinary Risk Assessment and Management Programme-Diabetes Mellitus.

Source: The Economist Intelligence Unit.

follow-up of high-risk individuals over time. Patients of the Private Public Partnership–Joint Asia Diabetes Evaluation (PPP-JADE) have experienced an approximately 50% decrease in the incidence of key outcomes such as chronic kidney disease, cardiovascular events, end-stage renal disease and death.[30] The learning and experience with hospital-based care from the JADE Program were then adapted to publically funded primary care settings (in a total of 73 clinics) with the creation of the RAMP-DM in 2009.

The effectiveness of JADE and RAMP-DM were recognised in the years after their establishment. For example, 47.5% of diabetic patients reached the goal of a HbA1c <7% in 2009; in 2013, this proportion increased to 56.5%.[31] When individuals were enrolled to the RAMP-DM treatment, they achieved greater reductions in all-cause mortality, hospitalizations, emergency attendance and specialist clinic attendance compared with those receiving standard care.[32] Over a period of 4.5 years, these improvements were able to save an average of US$7,294 per patient,[33] confirming the hypothesis that personalized care and individual empowerment contribute significantly towards the success rates of these initiatives in Hong Kong.

Where policy was concerned, the Hong Kong Department of Health published a strategic framework document titled "Promoting Health in Hong Kong: A Strategic Framework for Prevention and Control of Non-communicable Diseases" in 2008, in response to the World Health Organization launching a series of strategy and action plans for the prevention and control of NCDs between 2000-2008. The overall goal of the policy was to improve the health of the Hong Kong population, particularly in the context of transitioning from infectious diseases to NCDs. Following further international direction in 2018, the Hong Kong Department of Health formulated a strategy for the prevention and control of NCDs, with 9 targets to be achieved by 2025, defined in the publication "Towards 2025: Strategy and Action Plan to Prevent and Control Non-communicable Diseases in Hong Kong".[34] These targets have a direct impact on the management of diabetes and metabolic syndrome, and hence play a key role in preventing the progression of prediabetes to diabetes.

Challenges with prediabetes

Due to concerted programmatic and policy efforts over the last several decades, patients with diabetes, once diagnosed, are well managed in terms of treatment and follow-up. However, while diabetes management is a public health priority in Hong Kong, routine or targeted screening for diabetes is currently not part of preventive health programs in Hong Kong, and most diagnoses are made quite late in the pathway, only once complications arise. According to the Hong Kong Population Health Survey from 2014/2015, 54.1% of people diagnosed with diabetes had remained undiagnosed until the survey was conducted.[35]

Clinicians, particularly in the public sector, have to provide consultations for a large number of patients in a limited amount of time, and risk profiling for diabetes is not routinely conducted. While guidelines for screening do exist, they are not always consistently implemented across different settings, making the diagnosis of prediabetes even more challenging.

Dr Peter Tong, a physician in a private clinic, explains that there is no policy or guidance for the identification of people with prediabetes. "If I've got a patient with suspected prediabetes, I would not be able to refer the patient to a public hospital for further assessment. The hospital will not accept the referral because prediabetes is not regarded as a disease." IGT and prediabetes are not recognised as disease states or as a potential signal for early intervention in the diabetes pathway among the majority of policymakers, clinicians or patients. While Dr Luk acknowledges that "diabetes is definitely a public health priority in Hong Kong, and the condition is reasonably well managed in the public healthcare sector", she notes that the opposite is true for prediabetes.

> **Prediabetes has a low priority in Hong Kong and there is a lack of recognition amongst key stakeholders in the healthcare industry, and certainly amongst the public, for this condition.**
>
> Dr Andrea Luk, Associate Professor, Department of Medicine & Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong.

The lack of formal recognition of prediabetes has also meant less research is being done on possible screening or early interventions, and hence there is a scarcity of current data on prediabetes in Hong Kong. The paucity of research on the burden of prediabetes is both evidence of the lack of recognition of the condition, which further contributes to the lack of awareness of the disease. There was consensus among the experts interviewed for this report that greater research on the burden of prediabetes and the impact of screening is urgently needed in Hong Kong.

Dr Quan, Clinical Assistant Professor, School of Public Health, University of Hong Kong discussed how a number of contextual factors such as long working hours, sedentary routines, limited time for exercise and a culture of eating out in Hong Kong's fast-paced society make healthy lifestyle choices difficult to implement, particularly for younger working populations. Dr Quan, also described that "living spaces are small and crowded" in Hong Kong, and "people are less likely to eat at home, which typically results in the consumption of less healthy food."

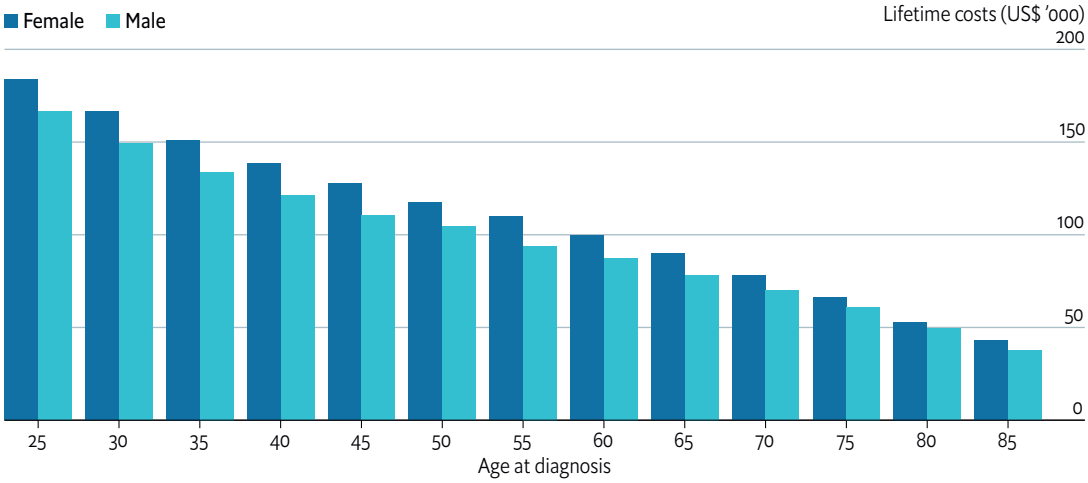
The ongoing COVID-19 pandemic has added further challenges. While the longer-term implications for diabetes management and care are yet to be determined, a fear of visiting clinics for routine tests and medication has been common in the last year,[36] particularly among diabetic patients for whom glycaemic control has deteriorated during the pandemic.[37] Eating and exercise routines have also changed; while lockdowns have presented the opportunity for more people to cook their meals at home,[38] the reliance on takeouts coupled with restrictions on exercising outdoors have led to more sedentary lifestyles, which could impact NCD incidence and prevalence in the years ahead.[39]

Costs of prediabetes in Hong Kong

Current and future health expenditure along the diabetes pathway

In 2014, annual direct health expenditure for diabetes amounted to approximately HK$2bn (US$ 257.8m) in Hong Kong.[40] More recently, Quan et al. estimated the lifetime cost of diabetes based on the age of diabetes diagnosis, from 25 to 85 years of age. The study highlighted that the younger an individual is when he or she develops T2DM, the higher the lifetime healthcare costs incurred; reaching as much as USD 166,409 and USD 183,651 for 25-year-old males and females, respectively.[41] Figure 5 describes the current lifetime costs for T2DM in Hong Kong, grouped by gender and age of diagnosis, based on the same study.[41] Higher costs for women are incurred due to longer life expectancy.

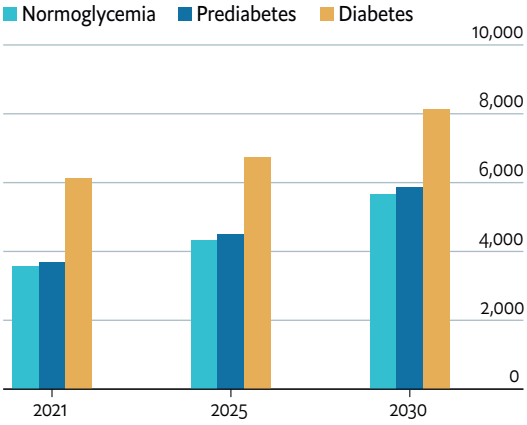
Figure 5: Lifetime costs for T2D care in Hong Kong (based on age at diagnosis and gender)
(US$ '000)



Based on: Quan J, et al, 2019.[41]

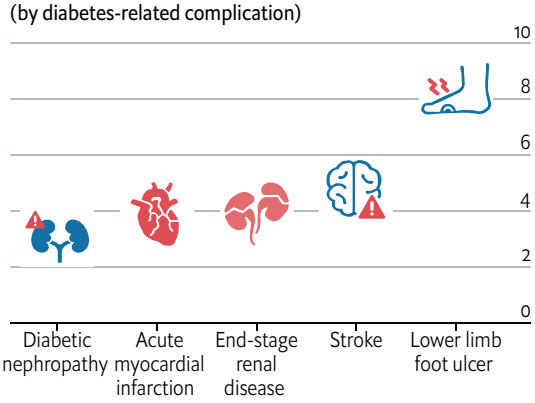
Based on EIU's modelling, projected costs over the next decade for people across different phases of the diabetes pathway in Hong Kong are shown in Figure 6. Costs for people with prediabetes are predicted to increase from US$3,700 to almost US$6,000 between 2021 and 2030. The cost increases for people with diabetes are even higher. The annual health care cost per person with diabetes is estimated to be more than US$8,000 by 2030, placing a significant economic burden on individuals and the wider health system in Hong Kong. At the population level, T2DM costs represent 0.7% of the nominal GDP in Hong Kong.

Figure 6: Per person total health resource use by glycaemic status
(US$)



Source: The Economist Intelligence Unit.

Figure 7: A new event of a lower limb ulcer increases public medical costs by 9.4 times in Hong Kong
Times increase in annual medical cost
(by diabetes-related complication)



Based on: Jiao F, et al, 2017.[42]

Current costs of complications related to diabetes

As T2DM is a chronic condition, the longer a person has the disease, the more prone they are to diabetes-related complications, another factor which could exponentially increase healthcare costs. Based on estimates from a study by Jiao F et al., the costs of diabetes-related complications in Hong Kong are shown in Figure 7.[42] Lower limb ulcers were associated with the biggest increase in direct medical costs, an almost 10-fold increase; end-stage renal disease and stroke increased the annual medical cost by 5 and 6 times, respectively.

Dr Quan remarked that there has been greater recognition in looking at the value of cost minimization through prevention of diabetes-related complications, "there is greater recognition of the value that prevention brings, particularly, diabetes-related complications, such as renal disease, which is incredibly expensive." He also highlights that some costly complications are more common in Asian populations compared to Western populations, "we get fewer heart attacks, but more strokes and renal disease."

It is encouraging to note that overall rates of diabetes-related complications in Hong Kong have declined significantly since 2001. However, of concern are the age-specific rates of complications: while the incidence of coronary heart disease, heart failure, stroke, hyperglycaemic crisis and lower-extremity amputation have decreased for all age groups above 45 years, across both women and men, there has not been a significant change for people with diabetes aged 20-44 years.[43]

Costs saved from early intervention

The EIU developed a Markov cohort simulation model that tracks how a patient cohort evolves over a nineteen-year period along the diabetes pathway. Using model parameters derived from peer-reviewed research and the best available data, we forecasted the prevalence of prediabetes and T2DM, which serve as inputs into our forward-

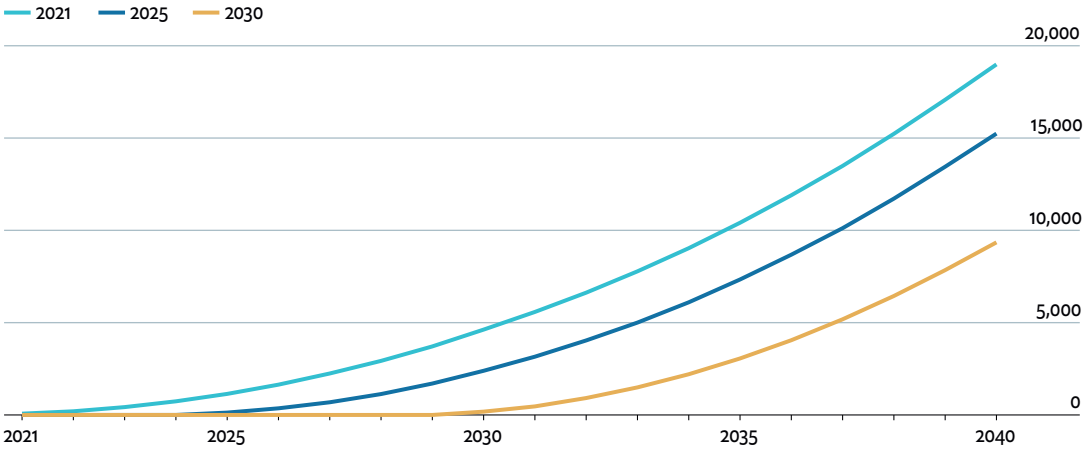
looking cost estimates. Historical prevalence rates are consistent with the 9th edition of the IDF Atlas.

By quantifying the current burden of prediabetes and estimating the impact of the delay of T2DM onset in Hong Kong, the model defines a baseline scenario of inaction, and captures a broad understanding of the value of intervening, without regard for specific treatments.

The projected cost savings over the next 19 years as a result of early intervention in the diabetic pathway are shown in Figure 8. Interventions modelled are treatment agnostic, and are therefore not specific to pharmacological or behavioural interventions. If an intervention was started in 2021, the cumulative costs saved would amount to almost US$19bn by 2040. If an intervention was delayed to the year 2025, the cost savings amount to US$15bn (over the 15 year period from 2025-2040), decreasing further to US$9bn if delayed till 2030 (for the 10 year period from 2030 to 2040).

Taken together, these estimates and projections highlight the significant cost savings over time from early screening and intervention at the prediabetes stage, as well as the health expenditure that would otherwise result from the current status quo.

Figure 8: Cumulative savings on costs of diabetes by year of intervention



Source: The Economist Intelligence Unit.

Conclusions and the way forward

The analyses presented in this brief highlight the economic impact of intervention and inaction pertaining to prediabetes in Hong Kong. In order to reduce the burden of cost, successful and early action will require a targeted focus on preventive and screening efforts for prediabetes among younger populations. Key conclusions indicate that:

The health and economic burden of T2DM will continue to increase.

T2DM is slated to remain a major public health issue in Hong Kong and Asia for the foreseeable future, and increasingly so among young adults.[44] The onset of T2DM in younger populations means that more people will be living with diabetes for longer in the decades to come, significantly increasing the burden on the health care system as well as the social and economic costs of managing the disease and its related complications.

There is no framework for diagnosing and treating prediabetes.

Prediabetes is not widely recognised by clinicians as a disease state or as a potential signal for early intervention in the diabetes pathway, and no proper framework exists for its diagnosis and treatment. Coupled with the lack of awareness of prediabetes among the general population as a consequence, this makes early diagnosis of prediabetes even more challenging.

Screening and management for diabetes should be extended to younger and prediabetic populations.

Proactive identification of high-risk patients are critical in preventing the transition from undiagnosed prediabetes to diabetes. Clinicians need to be more alert to the signs of prediabetes, particularly among people who are at a higher risk of diabetes, and policymakers need to be educated on the cost savings that could result from early diagnosis of prediabetic patients.

There are large cost-savings to be gained from early intervention for prediabetes.

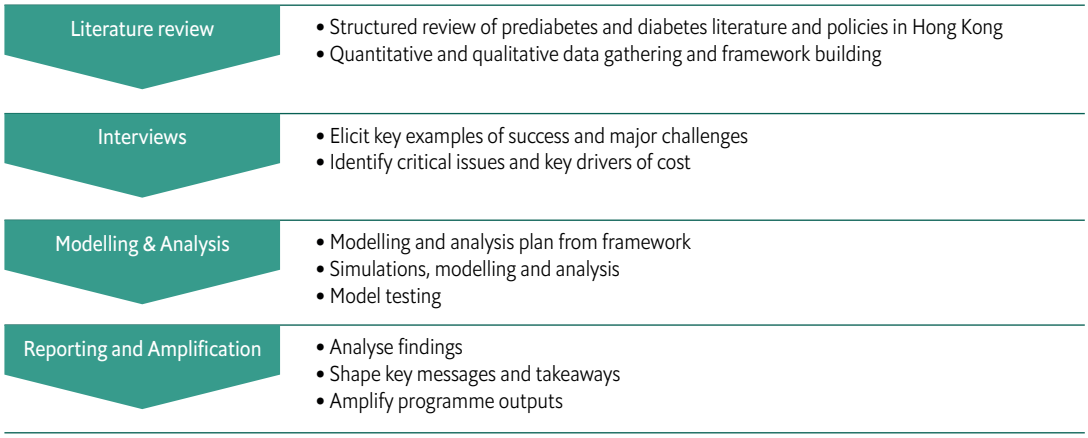
As a higher number of young adults are being diagnosed with T2DM, lifetime healthcare costs will increase dramatically in the future. With projected costs for diabetes care per person reaching US$8,000 by 2030, the potential savings from early, pre-emptive action are staggering, ranging from US$10-19bn over the next 19 years. Interventions that manage and reduce diabetes risk earlier in the diabetes pathway will be critical to effectively reducing the financial burden of the disease.

Appendix 1: methods and limitations

Our key aim with this programme was to provide actionable information which equips stakeholders with a clear understanding of the impacts of prediabetes, new perspectives on approaches to addressing its notable rise, and positions action on prediabetes as a strategy for wider macroeconomic growth at the national level.

The EIU's approach is comprised of the following components:

Figure A1. The EIU's methodology to build the cost of inaction around prediabetes.



Model definitions, parameters and assumptions

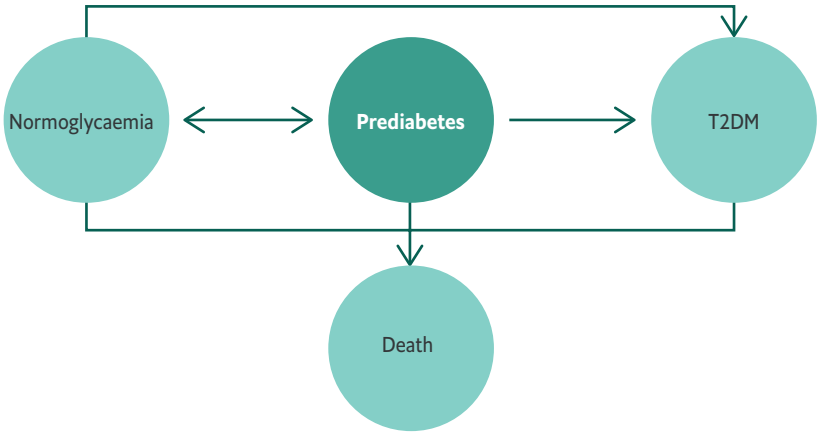
Building this model incorporated five key steps:

1. Defined data inputs and parameter assumptions
2. Forecasted overall health expenditures based on existing, country-specific, and long-term GDP forecasts
3. Modelled prevalence rates using a Markov cohort simulation
4. Calculated attributable health expenditures and forecasts
5. Repeated steps 1-4 for alternative parameter assumptions and calculated the attributable health expenditures under a range of delay of onset scenarios

At the outset of this programme, we defined a simplified "diabetes pathway" which outlines specific disease states that underpin this model (see Figure A2).

Figure A2. Simplified diabetes pathway

Figure A2. Transition rates across the diabetes pathway



Source: The Economist Intelligence Unit

Normoglycaemia—includes all people who do not meet the clinical criteria for prediabetes or diabetes below (see Figure A2 and Table A1)

Prediabetes—we use the International Diabetes Federation (IDF) clinical parameters for Impaired Glucose Tolerance (IGT) as our baseline for prediabetes prevalence and cost (see below).

Diabetes/Type II Diabetes Mellitus (T2DM)—see table below for clinical definition of diabetes. We aim to model T2DM where relevant, though where data is limited, we use data for all diabetes (types I & II, gestational) as a proxy where indicated.

Regression—refers to the transition between more advanced disease states to less advanced disease states. In this case, this refers to the rate of transition from a prediabetic state to normoglycaemia (see assumptions below).

Delay of onset/strength of intervention—early intervention in the prediabetic phase can delay or, in some cases, fully prevent the onset of T2DM. Delay of onset refers to the number of years delayed in which someone remains in the normoglycaemic or prediabetic state due to intervention.

Table A1: Prediabetes and diabetes diagnostic criteria

Glycaemic Status ↓	1. Fasting plasma glucose	2. Two-hour plasma glucose (following 75g oral glucose load)	3. HbA1c	4. Random Blood Glucose (with symptoms of hyperglycaemia)
Normoglycaemia	<6.1 mmol/L (<110 mg/dL)	<7.8 mmol/L (140 mg/dL)	<6.0%* (<42 mmol/mol)	Not applicable]
Prediabetes: Impaired Fasting Glucose- IFG	6.1-6.9 mmol/L (110-125 mg/dL)	<7.8 mmol/L (140 mg/dL)	6.0%- 6.4%* (42 to 47 mmol/mol)	
Prediabetes: Impaired Glucose Tolerance- IGT	<7.0 mmol/L (<126 mg/dL)	≥7.8 <11.1 mmol/L (≥140 to <200 mg/dL)		
Diabetes	≥7.0 mmol/L (≥126 mg/dL)	≥11.1 mmol/L (≥200 mg/dL)	≥6.5% (≥47 mmol/mol)	>11.1 mmol/mol (>200 mg/dL)

Notes on testing criteria: For normoglycaemia, any of the following criteria (1-3).
For prediabetes (IFG): Criteria 1, 1 and 2, or 3
For prediabetes (IGT): Criteria 1 and 2, or 3
For diabetes: One or more of criteria 1-4

*Note: The WHO does not currently recommend HbA1c testing for prediabetes.

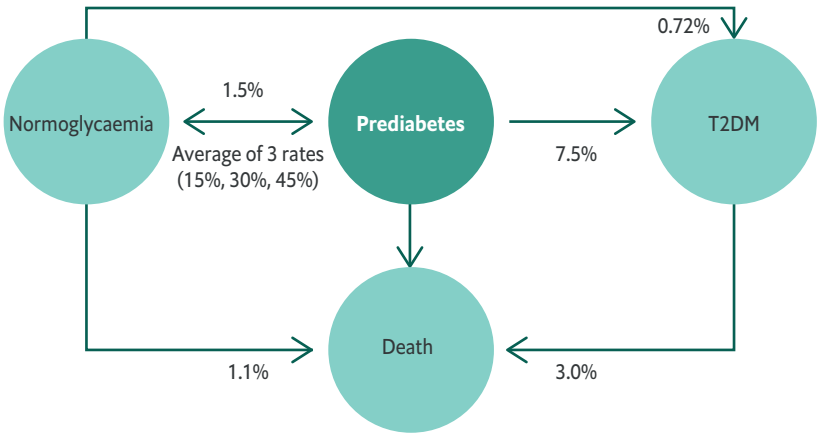
Source: The Economist Intelligence Unit

Model methods parameters

The EIU developed a Markov cohort simulation model that tracks how a patient cohort evolves over a nineteen-year period along the diabetes pathway, from normoglycaemia to death. Using model parameters derived from peer-reviewed research and the best available data, we forecasted the prevalence of prediabetes and T2DM, which serve as inputs into our forward-looking cost estimates. Historical prevalence rates are consistent with the 9th edition of the IDF Atlas.

We follow best practise in modelling disease progression as a Markhov process and include alternative parameter assumptions that reflect a range of baseline scenarios. Starting with a patient population whose disease states are distributed according to the current prevalence rates, our model simulates a patient's progression from normoglycemia through prediabetes and T2DM over a nineteen-year forecast horizon (see Figure A3).

Figure A3. Transition rates across the diabetes pathway



Source: The Economist Intelligence Unit

Iterating over thousands of scenarios gives a picture of what we can expect an average patient's disease progression to look like. We then compared treatment-agnostic impacts of interventions, modelling a conservative estimate of the delay of onset of T2DM across each country of focus. The year of intervention is the hypothetical start year for the intervention, while the strength of the intervention explores a conservative range of estimated years that the onset of T2DM would be delayed with intervention (1-10).

An intervention is assumed to affect the transition rates in two ways: first, by decreasing the prediabetes to T2DM transition rate; second, by increasing the prediabetes to normoglycaemia transition rate. The following table shows the percent change in these two ways, corresponding to the number of years that T2DM is delayed.

Table A2. Intervention assumptions for delay of onset model

Years of delay	1	2	3	4	5	6	7	8	9	10
% decrease in prediabetes to T2DM transition rate	5%	10%	20%	29%	39%	48%	56%	65%	72%	80%
% increase in prediabetes to normoglycaemia transition rate	7%	15%	15%	15%	15%	15%	15%	15%	15%	15%

Source: EIU Analysis

By quantifying the current burden of prediabetes and estimating the impact of the delay of T2DM onset in Hong Kong, the model defines a baseline scenario of inaction, and captures a broad understanding of the value of intervening, without regard for specific treatments.

Key assumptions

- *Population growth rates:* follow official estimates from EIU projections.[45]
- *Transition rates:* as a baseline for this model, we use transition rates between states within the diabetes pathway informed by best-available literature and data sources. Given wide ranges of variability in the literature for regression rates from the prediabetic state to normoglycemia (11% to 59%), the model toggles between 3 different regression rate scenarios (15, 30, 45%), and average of these three regression rates is used (see Figure A3).
- *Impact of Interventions:* published literature was referenced for a selection of impacts from known interventions for prediabetes. This model is treatment agnostic and therefore uses the average of expected impacts of interventions to produce the delay of onset estimations.
- *Cost ratios:* the model estimates health resource use among the population with prediabetes and diabetes in excess of resource use that would be expected in the absence of these conditions. Health expenditure is estimated and forecasted using an attributable fraction based on population averages. Overall relative cost ratios in this model are R= 1.04 for prediabetes and R=3 for diabetes, based on a review of the literature.

Attributable Fraction Method:

$$\sum_{a=1}^{6} \frac{P_a(R_a - 1)}{P_a(R_a - 1) + 1} U_a$$

where, for each age group a = {20-29, 30-39, 40-49, 50-59, 60+}, Pa is the diabetes (prediabetes) prevalence rate, Ua is the total projected health resource use for the given country, and Ra is the "relative cost ratio" (annual per-cap expenditures for people with diabetes/annual per-cap expenditures for people without diabetes).

Model limitations

Below are the key limitations of this model which should be considered when interpreting results:

1. *Intervention costs:* costs of intervention (lifestyle, pharmacological, etc.) are either highly variable or not captured in Hong Kong for this analysis and were thus out of scope for the model. Therefore, they were not subtracted from the savings projected in the delay of onset/ intervention scenarios. Further primary data collection and modelling would need to be done to address this gap.
2. *Assumptions:* this model is dependent on parameters (i.e. transition rates, inputs, etc.) for which there is little convergence in the literature. For instance, annual rates of regression from prediabetes to normoglycaemia ranged from 11% to 59%. As data improves, underlying assumptions of this model may need to shift to accommodate.
3. *Demographic changes:* this model assumes constant population growth over the forecast period, which means it is not sensitive to any changes in life expectancy or ageing.
4. *Cost ratios:* as most existing models also employ a consistent cost-ratio rate, this forced us to choose a relatively conservative "R value" for the model. This means that our cost estimates could be underestimated.

Data Input Summary

Key factors such as prevalence, transition rates and overall diabetes-related expenditure (age-segmented) have been captured in the model to allow for forecasting over a nineteen-year period, as follows:

Table A3. Data inputs and sources for EIU prediabetes model

Input Type	Input	Definition and sources/references
Demographic	Population growth rates	Number of people per country by age group over time[45]
	Prevalence rates	Proportion of the population with IGT or T2DM[46]
Cost (US $)	Normoglycaemia	Proxy: average public and private healthcare spend her head[47]
	Prediabetes	EIU assumption based on literature findings[48-51]
	Diabetes	Total cost of diabetes (incl. Type 1 and gestational)[52-61]
Transition rates	Normoglycaemia to prediabetes (and vice versa)	Proportion of people who transition between normoglycaemia and prediabetes over a defined period of time, validated by primary research[53, 49, 62-69]
	Normoglycaemia to T2DM	Proportion of people who develop T2DM without being diagnosed with prediabetes over a defined period of time, validated by primary research[49, 62, 64]
	Normoglycaemia to death	Mortality due to causes unrelated to diabetes[70] (EIU calculation)
	Prediabetes to T2DM	Global estimate of transition rates between prediabetes and T2DM[49, 63, 67, 71, 72]
	Prediabetes to death	Proportion of people that die from prediabetes related complications[61, 65]
	Effects on interventions at the prediabetes stage	The effects of pharmacotherapy and lifestyle interventions and the proportion of people that are either delayed or prevented from developing T2DM[48, 50, 73-78]
	T2DM to death	EIU calculation.

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