

Cost-effective solutions for the prevention of type 2 diabetes



International
Diabetes
Federation

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Foreword

Diabetes is a global epidemic that affects everyone. The numbers are staggering: 415 million people were living with diabetes in 2015, another 318 million people were at high risk of developing type 2 diabetes, and diabetes was responsible for 5 million deaths. Worryingly, the epidemic shows no signs of relenting, with the number of people living with diabetes expected to reach 642 million by 2040. Diabetes has an enormous human, social and economic impact, with one in eight health dollars currently spent on treating the disease and its associated complications.

Despite these alarming statistics, cost-effective solutions exist to reduce the global burden that diabetes currently poses. Much can be done to prevent the onset of type 2 diabetes, as outlined in this *“Cost-effective solutions for the prevention of type 2 diabetes”* report, published by IDF to provide an overview of the latest evidence on the different programmes available to tackle the rise of the most prevalent form of diabetes. The wide range of options presented and their cost-saving implications give cause for optimism that the current situation can be reversed.

Intensive lifestyle modification, involving the adoption of healthy diets and increased physical activity, remains the cornerstone for the prevention of type 2 diabetes. This report discusses in detail the components of a successful lifestyle modification programme, the benefits of using certain medications for primary prevention, and provides an analysis of different public health measures to promote healthier behaviours.

The intention of this report is to provide policy makers and diabetes advocates with an accessible and comprehensive summary of the current data on the clinical effects of primary prevention programmes, the costs associated with their delivery, and the resulting benefits for our societies. Evidence on actionable solutions is also included to inform policy development. IDF is very grateful to all the researchers who produced the evidence that made this report possible.

Successful prevention of type 2 diabetes will only be achievable through concrete and effective action at the community level. We hope that the practical solutions outlined in this report will help those active on the ground to change the diabetes landscape to achieve a healthier future for all.

Dr Shaukat Sadikot

President, International Diabetes Federation

Cost-effective solutions for the prevention of type 2 diabetes

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Executive summary



Background

Public health systems are subject to substantial financial pressures and need to allocate finite resources in a cost-effective and evidence-based manner.

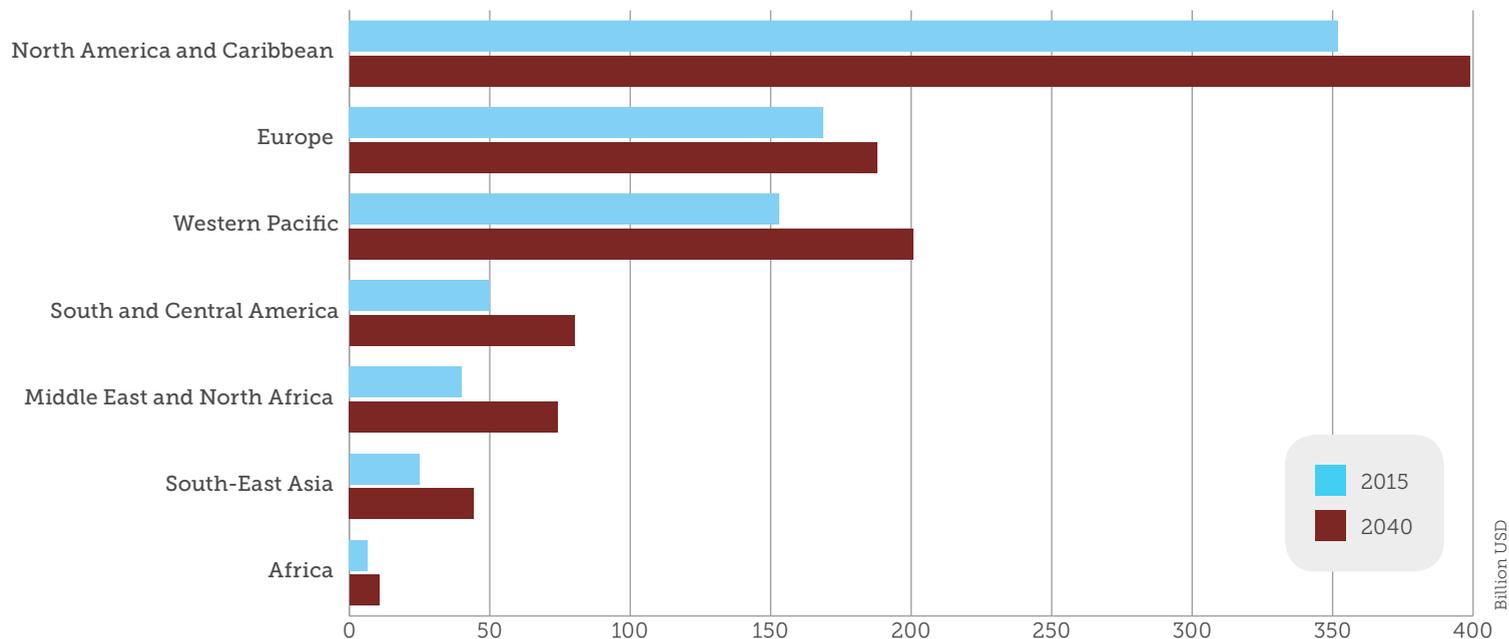
Among the largest economies in the world, the share of resources dedicated to health has increased substantially since the beginning of this century, despite the economic slowdown¹. This trend will continue as a result of demographic challenges faced in many countries.

The latest estimates indicate that worldwide, diabetes alone was responsible for USD 673 billion in healthcare spending in 2015, which represents 11.6% of the total amount spent on health².

Based on the combination of factors previously presented, it is crucial to identify which strategies can be used in order to respond to the healthcare needs of the largest possible share of population.

Diabetes-related complications are the major driver of diabetes health expenditure³. Preventing people from developing type 2 diabetes will substantially reduce the risk of people having complications such as cardiovascular disease, retinopathy, and kidney failure⁴. Type 2 diabetes mellitus accounts for more than 90% of all diabetes cases⁴⁻⁷. There is evidence that the vast majority of cases of type 2 diabetes can be prevented or delayed⁸⁻¹⁰.

Figure A Total health expenditure on diabetes per IDF region



Nevertheless, it is still necessary to identify which prevention programmes can provide better health outcomes, and the resources needed to provide these programmes to different target groups; and based on that, select the programmes that offer the best value for money.

Objective

This report provides a summary of cost-effectiveness studies conducted on programmes for the prevention of type 2 diabetes, in order to support evidence-based policy that will most effectively reduce the human and economic burden of type 2 diabetes.

Diabetes

Diabetes is a chronic condition that occurs when the body cannot produce enough insulin or cannot use insulin¹¹, and is diagnosed by observing raised levels of glucose in the blood.

Over time, the resulting high levels of glucose in the blood (known as hyperglycaemia) causes damage to many tissues in the body, leading to the development of disabling and life-threatening health complications.

There are three main types of diabetes:

Type 1 diabetes:

Caused by an auto-immune reaction in which the body's defence system attacks the insulin-producing beta cells in the pancreas. As a result, the body can no longer produce the insulin it needs.

Type 2 diabetes:

The most common type of diabetes. It usually occurs in adults, but is increasingly seen in children and adolescents.

With type 2 diabetes, there is a combination of inadequate production of insulin and the body's inability to respond fully to insulin (insulin resistance).

Gestational diabetes:

Hyperglycaemia that is first detected at any time during pregnancy is classified as either:

- gestational diabetes mellitus
- diabetes mellitus in pregnancy

Women with slightly elevated blood glucose levels are classified as having gestational diabetes, whilst women with substantially elevated blood glucose levels are classified as having diabetes mellitus in pregnancy.

Prevention of type 2 diabetes

The cornerstone of the prevention of type 2 diabetes is the adoption of a healthy diet and increased physical activity. In the last 20 years, several randomised control trials conducted in different parts of world have shown that the risk of developing type 2 diabetes can be significantly reduced by adopting healthier lifestyles, with or without the use of inexpensive medications¹²⁻¹⁴.

Cost-effectiveness analysis

The aim of cost-effectiveness analysis is to evaluate the costs and health effects of specific interventions. Most frequently, it is used to compare studies of prospective new interventions with current practice, other alternative interventions, or with a fixed price cut-off point representing the assumed social willingness to pay for an additional unit of health.

Methods

In order to summarise the available data on the cost benefits of primary prevention of type 2 diabetes, a systematic literature review was conducted.

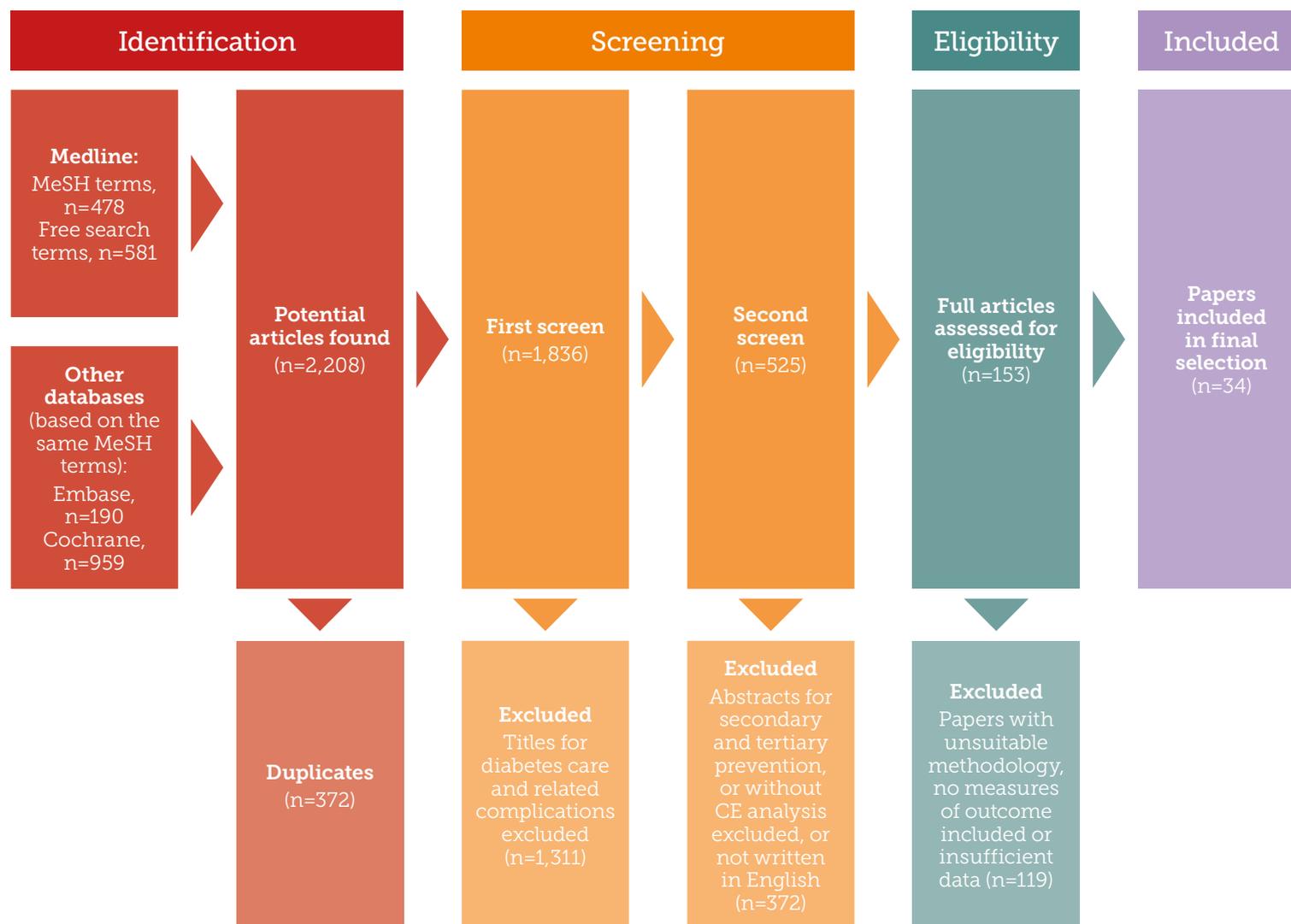
Initially, 2,008 articles were identified as potentially relevant. After a first review, duplicates and papers that assessed the effectiveness of programmes and therapies for diabetes care, and for diabetes-related complications were excluded, leading to 525 articles for abstract review.

During the abstract review, papers that targeted patients diagnosed with diabetes or aimed to prevent and control

the development of diabetes-related complications, were also excluded, as were abstracts that did not specify any cost-effectiveness outcomes.

The next step was the full review of 153 scientific papers. During the full review the methodological quality of the papers were assessed, leading to a final sample of 34 papers.

Figure B Study selection



Results

Through this literature review, it was possible to identify 34 scientific papers from 13 countries that assessed the cost-effectiveness of primary prevention of type 2 diabetes between the years 2005 and 2015.

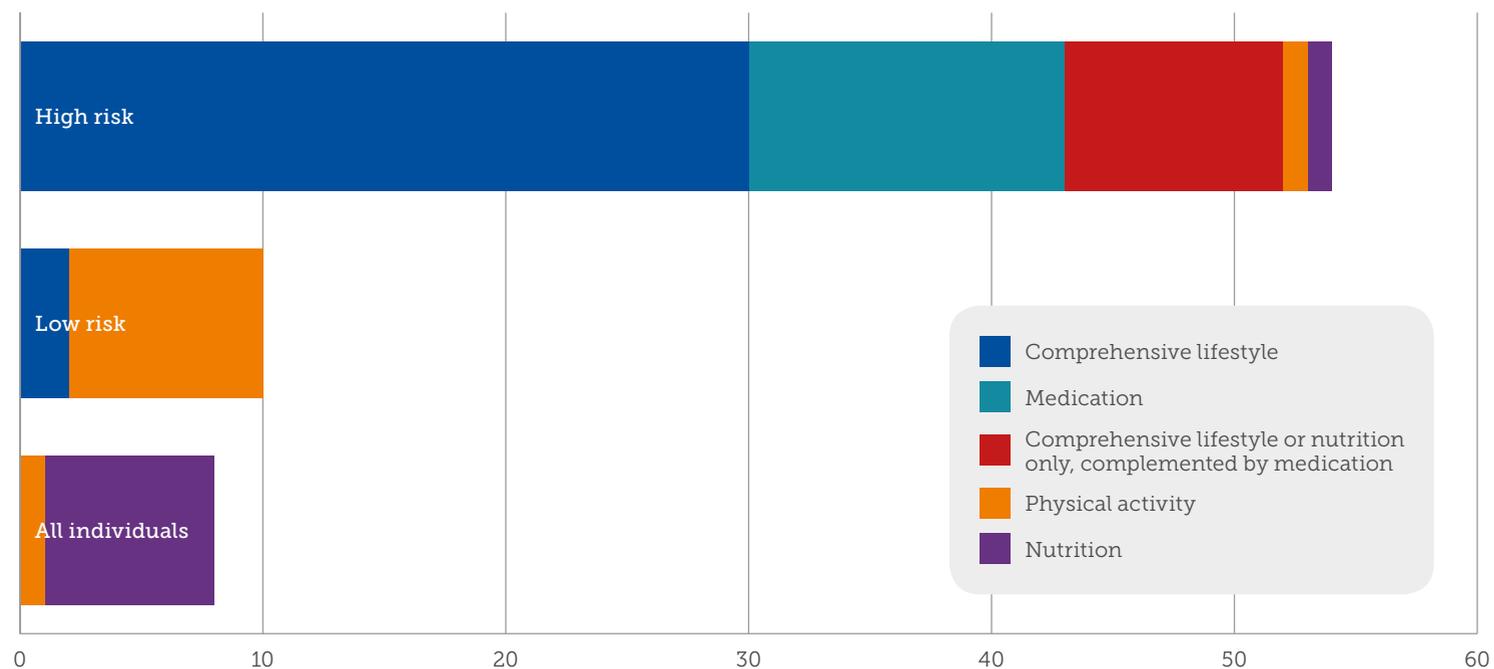
In the 36 studies on primary prevention of type 2 diabetes, 71 interventions were analysed. This was possible because in several cases, one research study looked at multiple interventions aiming to achieve the same objective: prevent the onset of type 2 diabetes. Of these, nearly half focused on comprehensive lifestyle interventions (n=33), which were programmes that aimed to prevent the development of type 2 diabetes by encouraging participants to lose weight through an increase in physical activity and in the consumption of healthier food.

The second most common type of intervention was the use of medication to prevent type 2 diabetes. A total of 15 studies examined the effectiveness of medications such as Metformin, Orlistat, and Acarbose.

Three quarters of the interventions (n=54) focused on people at high risk of developing type 2 diabetes. High-risk patients were considered as those diagnosed with impaired glucose tolerance or impaired fasting glucose, women with previously diagnosed gestational diabetes or participants with a combination of risk factors such as a family history of diabetes, obesity, and old age.

Of the interventions analyzed, 14% were judged to be cost-saving, meaning that better health outcomes can be achieved and at the same time health funds can be saved, while 67% interventions were evaluated as

Figure C Number and type of interventions by target population



cost-effective, meaning that the Incremental Cost-Effectiveness Ratio (ICER) obtained was below ID 50,000 after adjusting to 2016 values, and for purchasing power differences between countries.

Comprehensive lifestyle programmes generally aim to achieve and maintain a reduction of 5-7% body weight, and a minimum of 150 minutes of moderate to intense physical activity per week, with a similar intensity to that of brisk walking. Of those that provided the cost per QALY gained (ID) from a health system perspective, the majority of interventions were found to be highly cost-effective with an ICER lower than ID 20,000. One study was found to be cost-saving.

Of the nine studies that assessed the cost per QALY gained of using metformin from a health system perspective, eight had an ICER below 50,000 ID per QALY gained, with two being cost-saving, while one – metformin therapy for those diagnosed with impaired fasting glucose – was not cost-effective.

Programmes focusing on individuals considered to have a high risk of developing type 2 diabetes were more cost-effective than those targeting low risk individuals.

Studies comparing the cost-effectiveness of group interventions versus individual counselling showed that those delivered to groups of participants were more cost-effective.

Regarding public health measures promoting healthier lifestyles, only seven such interventions were identified for this analysis. The most cost-effective among these seven was a modelling study conducted in the USA that estimated that more than 100,000 diabetes person-years, and 20,000 deaths due to cardiovascular disease could be saved through a taxation on sugar-sweetened beverages (SSB).

The IDF calls for countries to consider the following recommendations:

1. Comprehensive lifestyle programmes for people with impaired glucose tolerance, that are cost-effective from a health system perspective, and potentially cost-saving from a societal perspective¹⁵⁻¹⁶.
2. Local adaptations of comprehensive lifestyle programmes are good alternatives for lower-resource settings, as they can reduce the overall costs of programme provision, while still ensuring clinical effectiveness. Such adaptations may include optimising the number of activities and implementing group sessions rather than individual-level interventions¹⁷⁻¹⁸.
3. Metformin is an inexpensive drug for the management of type 2 diabetes, and can provide sustainable health gains. It could be considered as a cost-effective strategy for type 2 diabetes prevention, alongside comprehensive lifestyle programmes¹⁵.
4. Public health measures to promote healthier diets, such as a tax on sugar sweetened beverages, show promising results regarding cost-effectiveness for primary preventions of type 2 diabetes¹⁹.

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Introduction



What is diabetes?

Diabetes is a chronic condition that occurs when the body cannot produce enough insulin or cannot use insulin¹, and is diagnosed by observing raised levels of glucose in the blood. Insulin is a hormone produced in the pancreas; it is required to transport glucose from the bloodstream into the body's cells where it is used as energy. The lack, or ineffectiveness, of insulin in a person with diabetes means that glucose remains circulating in the blood. Over time, the resulting high levels of glucose in the blood (known as hyperglycaemia) causes damage to many tissues in the body, leading to the development of disabling and life-threatening health complications.

There are three main types of diabetes:

There are also other less common types of diabetes such as: Monogenic diabetes and secondary diabetes.

Type 1 diabetes

Type 1 diabetes is caused by an autoimmune reaction, in which the body's defence system attacks the insulin-producing beta cells in the pancreas. As a result, the body can no longer produce the insulin it needs. The disease can affect people of any age, but onset usually occurs in children or young adults. People with this form of diabetes need insulin every day in order to control the levels of glucose in their blood. Without insulin, a person

with type 1 diabetes will die. Why this autoimmune reaction occurs is not fully understood, and current technologies are not capable of preventing it². Despite this, people with type 1 diabetes, when provided with adequate care, can live a healthy life and avoid the complications associated with diabetes³. Symptoms of type 1 diabetes can appear rapidly, and include excessive thirst and frequent urination.

Figure 1 Symptoms of type 1 diabetes



What is diabetes?

Diabetes is a chronic condition that occurs when the body cannot produce enough insulin or cannot use insulin¹, and is diagnosed by observing raised levels of glucose in the blood. Insulin is a hormone produced in the pancreas; it is required to transport glucose from the bloodstream into the body's cells where it is used as energy. The lack, or ineffectiveness, of insulin in a person with diabetes means that glucose remains circulating in the blood. Over time, the resulting high levels of glucose in the blood (known as hyperglycaemia) causes damage to many tissues in the body, leading to the development of disabling and life-threatening health complications.

There are three main types of diabetes:

There are also other less common types of diabetes such as: Monogenic diabetes and secondary diabetes.

Type 2 diabetes

Type 2 diabetes is the most common type of diabetes. It usually occurs in adults, but is increasingly seen in children and adolescents. In type 2 diabetes, there is a combination of inadequate production of insulin and the body's inability to respond fully to insulin (insulin resistance).

The symptoms of type 2 diabetes may be similar to those of type 1 diabetes but are often less severe, and may develop slowly. Symptoms may include frequent urination, excessive thirst, and blurred vision.

Figure 2 Symptoms of type 2 diabetes



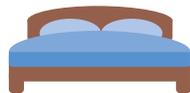
Excessive thirst and a dry mouth



Frequent and abundant urination



Lack of energy, extreme tiredness



Sexual issues



Blurred vision



Tingling or numbness in hands and feet



Recurrent fungal infections in the skin



Slow-healing wounds

What is diabetes?

Diabetes is a chronic condition that occurs when the body cannot produce enough insulin or cannot use insulin¹, and is diagnosed by observing raised levels of glucose in the blood. Insulin is a hormone produced in the pancreas; it is required to transport glucose from the bloodstream into the body's cells where it is used as energy. The lack, or ineffectiveness, of insulin in a person with diabetes means that glucose remains circulating in the blood. Over time, the resulting high levels of glucose in the blood (known as hyperglycaemia) causes damage to many tissues in the body, leading to the development of disabling and life-threatening health complications.

There are three main types of diabetes:

There are also other less common types of diabetes such as: Monogenic diabetes and secondary diabetes.

Many people with type 2 diabetes remain unaware of their condition for a long time because the symptoms are usually less marked than in type 1 diabetes and may take years to be recognised. However, during this time the body is already being damaged by excess blood glucose. As a result, many people already have evidence of complications when they are diagnosed with type 2 diabetes (see Diabetes complications).

Although the exact causes for the development of type 2 diabetes are still not known, there are several important risk factors. The most important are excess body weight, physical inactivity and poor nutrition. Other factors that play a role are ethnicity, a family history of diabetes, a past history of gestational diabetes and advancing age.

The number of people with type 2 diabetes is growing rapidly worldwide. This rise is associated with ageing populations, economic development, increasing urbanisation, less healthy diets and reduced physical activity⁴.

In contrast to people with type 1 diabetes, most people with type 2 diabetes do not require daily insulin treatment to survive. The cornerstone of treatment of type 2 diabetes is the adoption of a healthy diet and increased physical activity. In the last 20 years, several randomised control trials conducted in different parts of world have shown that the risk of developing type 2 diabetes can be significantly reduced by adopting healthier lifestyles, with or without the use of inexpensive medications⁵⁻⁷. If blood glucose levels continue to rise however, people with type 2 diabetes may be prescribed insulin.

What is diabetes?

Diabetes is a chronic condition that occurs when the body cannot produce enough insulin or cannot use insulin¹, and is diagnosed by observing raised levels of glucose in the blood. Insulin is a hormone produced in the pancreas; it is required to transport glucose from the bloodstream into the body's cells where it is used as energy. The lack, or ineffectiveness, of insulin in a person with diabetes means that glucose remains circulating in the blood. Over time, the resulting high levels of glucose in the blood (known as hyperglycaemia) causes damage to many tissues in the body, leading to the development of disabling and life-threatening health complications.

There are three main types of diabetes:

There are also other less common types of diabetes such as: Monogenic diabetes and secondary diabetes.

Gestational diabetes

Hyperglycaemia that is first detected at any time during pregnancy is classified as either⁸:

- gestational diabetes mellitus
- diabetes mellitus in pregnancy

Women with slightly elevated blood glucose levels are classified as having gestational diabetes, which tends to occur from the 24th week of pregnancy, whilst women with substantially elevated blood glucose levels are classified as having diabetes mellitus in pregnancy. Previously unknown diabetes should be detected as early as possible in the pregnancy.

Women with hyperglycaemia during pregnancy can control their blood glucose levels through a healthy diet, gentle exercise and blood glucose monitoring. In some cases, insulin or oral medication may also be prescribed.

Gestational diabetes normally disappears after birth. However, women who have been previously diagnosed are at higher risk of developing gestational diabetes in subsequent pregnancies and type 2 diabetes later in life. Nevertheless this risk can be halved through lifestyle and pharmacological interventions⁹. Babies born to mothers with gestational diabetes also have a higher risk of developing type 2 diabetes in their teens or early adulthood¹⁰.

Impaired glucose tolerance and impaired fasting glucose

People with raised blood glucose levels that are high enough to be diagnosed as diabetes are considered to have impaired glucose tolerance (IGT), and/or impaired fasting glucose (IFG). These conditions are often described as prediabetes as they represent a high risk of transiting to diabetes.

Impaired glucose tolerance is diagnosed following a glucose tolerance test. This involves measuring the blood glucose concentration two hours after a drink containing 75g of glucose. In impaired glucose tolerance, the glucose level is higher than normal, but not high enough to make a diagnosis of diabetes (i.e. between 7.8 and 11.1mmol/l (140 to 200 mg/dl)). Impaired fasting glucose is diagnosed when the fasting glucose level is higher than normal, but not high enough to make a diagnosis of diabetes (between 6.1 and 7 mmol/l (110 and 125 mg/dl)). Raised levels of HbA1c in the non-diabetic range can also be used to identify people at risk of developing type 2 diabetes.

People with intermediate hyperglycaemia are at increased risk of developing type 2 diabetes. This shares many characteristics with type 2 diabetes, and is associated with advancing age and the body's inability to use the insulin it produces. Not everyone with intermediate hyperglycaemia goes on to develop type 2 diabetes; lifestyle interventions – healthy diet and physical activity – can work to prevent the progression to diabetes.

In the table below, the 2006 World Health Organization diagnostic criteria for classifying diabetes, IGT and IFG are presented.

Table 1 2006 World Health Organization diagnostic criteria for classification of diabetes, IGT, and IFG¹⁰

Diabetes should be diagnosed if **one or more** of the following criteria are met:

- Fasting plasma glucose ≥ 7.0 mmol/L (126 mg/ dl)
- Two-hour plasma glucose ≥ 11.1 mmol/L (200 mg/dl) following a 75g oral glucose load

Impaired Glucose Tolerance (IGT) should be diagnosed if **both** of the following criteria are met:

- Fasting plasma glucose < 7.0 mmol/L (126 mg/dl)

- Two-hour plasma glucose 7.8-11.1 mmol/L (140 -200 mg/dl) following a 75g oral glucose load

Impaired Fasting Glucose (IFG) should be diagnosed if **both** of the following criteria are met:

- Fasting plasma glucose 6.1-6.9 mmol/L (110-125 mg/dl)
- Two-hour plasma glucose < 7.8 mmol/L (140 mg/dl) following a 75g oral glucose load

Diabetes complications

People with diabetes are at higher risk of developing a number of disabling and life-threatening health problems compared to people without diabetes. Consistently high blood glucose levels can lead to serious diseases affecting the heart and blood vessels, eyes, kidneys, and nerves (Figure 3).

People with diabetes are also at increased risk of developing infections. In almost all high-income countries, diabetes is a leading cause of cardiovascular disease, blindness, kidney failure and lower-limb amputation. The growth in prevalence of type 2 diabetes in low- and middle-income countries means that without effective strategies to support better management of diabetes, it is likely that there will be large increases in the rates of these complications.

Diabetes complications can be prevented or delayed by maintaining blood glucose, blood pressure and cholesterol levels as close to normal as possible. Many complications can be picked up in their early stages by screening programmes that allow treatment to prevent them becoming more serious.

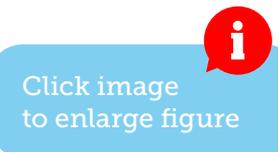
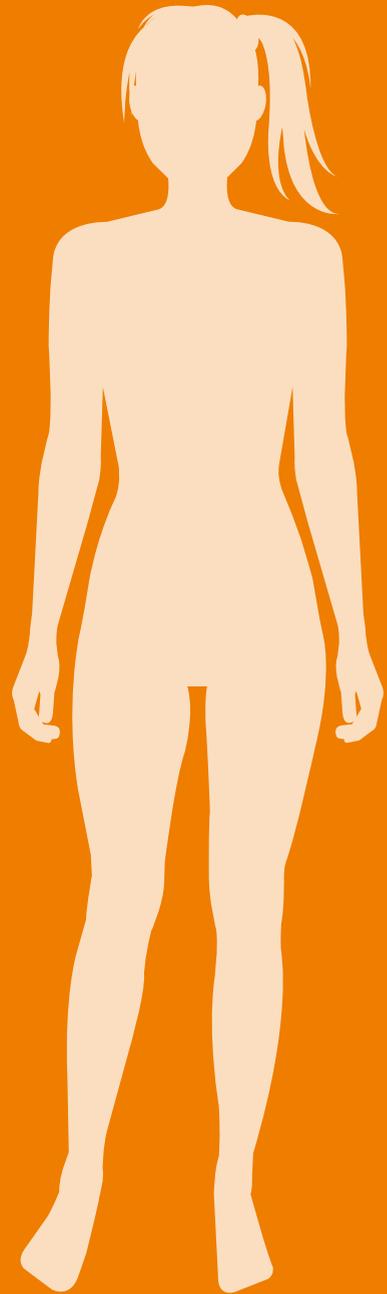


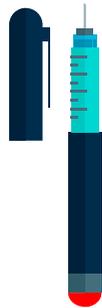
Figure 3 Diabetes-related complications



Hover over icons for
more information

Medication

People with diabetes require medication to control their blood glucose levels blood pressure and blood lipids. Below are the main medications available for the different types of diabetes presented.



Medication for type 1 diabetes

It is essential that everyone with type 1 diabetes has an uninterrupted supply of high-quality insulin. There are several different types of insulin available, but as a minimum, regular quick-acting human insulin and longer-acting NPH-insulin should be available to everyone in all parts of the world.

Medication for prevention of type 2 diabetes

Despite lifestyle programmes being the most important intervention for prevention of type 2 diabetes, there are also a number of pharmacological therapies for the management of type 2 diabetes. These therapies can also be beneficial for primary prevention in high risk populations. Among the medications with proven benefits are metformin, thiazolidinediones, and alpha-glucosidase inhibitors¹². In any case it is important to remark that despite the benefits observed, regulatory authorities have not yet approved medications for prevention of type 2 diabetes¹³.



Medication for management of type 2 diabetes

There are a number of medications for type 2 diabetes. Metformin is well-established and one of the most effective. Gliclazide is a sulfonylurea, which increases insulin secretion in type 2 diabetes. Both medications

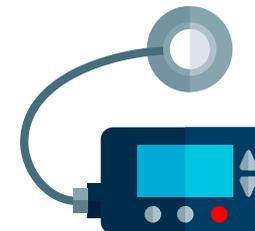
are on the World Health Organization list of essential medicines for diabetes. They should both be available and accessible to all people with type 2 diabetes worldwide, according to need. Other commonly used treatments for type 2 diabetes include GLP-1 analogues (injectable treatments that are not insulin) and DPP4 inhibitors. These treatments both enhance the body's natural response to ingested food, reducing glucose levels after eating. The SGLT2 inhibitors are a new class of drug that acts by increasing the excretion of glucose in the urine.



Medication for gestational diabetes

A healthy diet and lifestyle change are the mainstay of treatment in gestational diabetes. If medication is required, then insulin is the standard treatment. Some studies have shown that glyburide (glibenclamide) and metformin can be safe and effective as a treatment for gestational diabetes¹⁴.

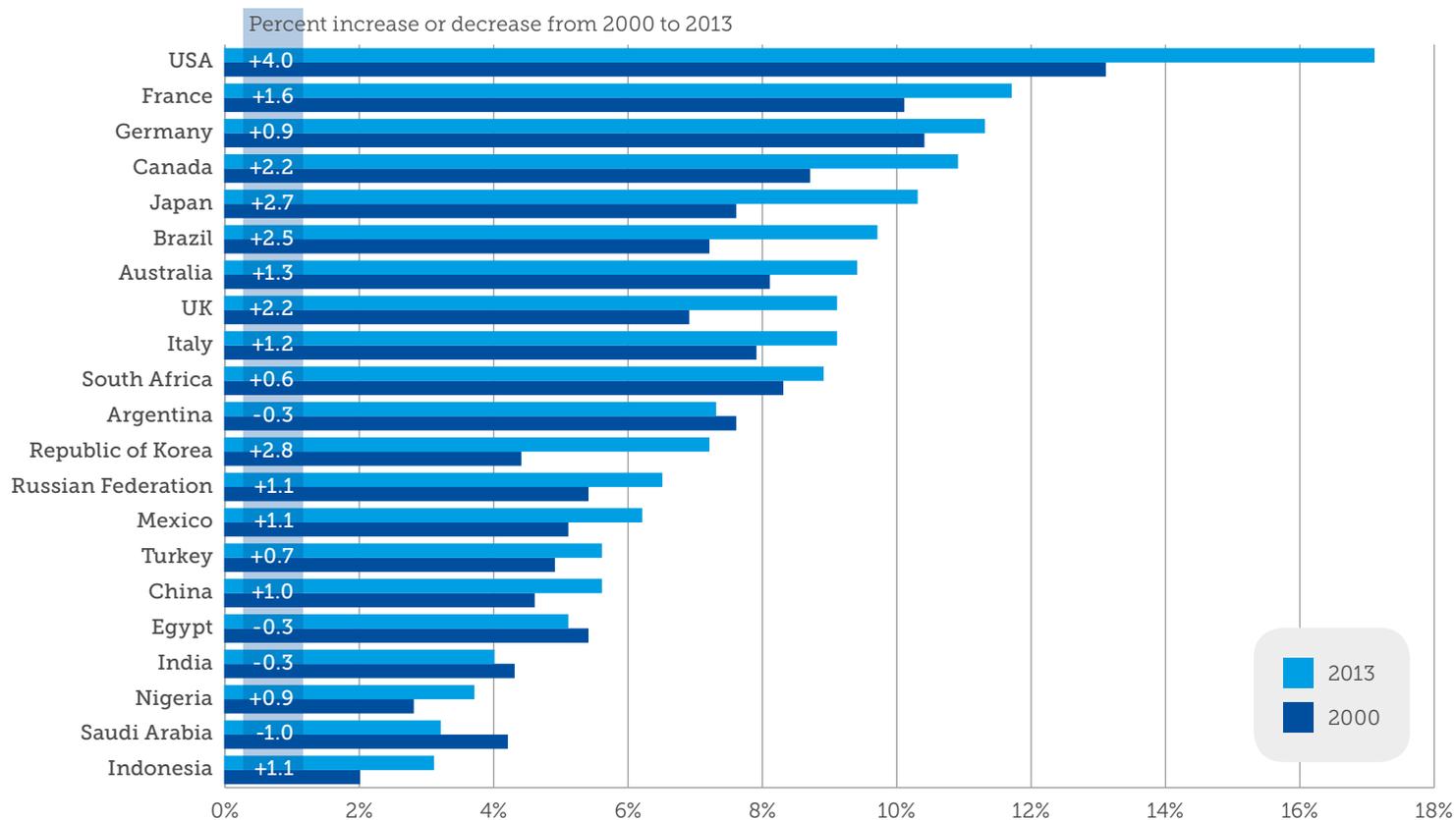
In addition, people with all types of diabetes may need access to medications to control blood pressure and cholesterol levels in order to reduce their risk of vascular complications.



The challenge ahead

Public health systems are subject to substantial financial pressures and need to allocate finite resources in a cost-effective and evidence-based manner. Among the largest economies in the world, the share of resources dedicated to health has increased substantially since the beginning of this century, despite the economic slowdown¹⁵. This trend will continue as a result of demographic challenges faced in many countries (Figure 4). The share of public funds allocated to the healthcare sector has increased in most countries (Figure 5).

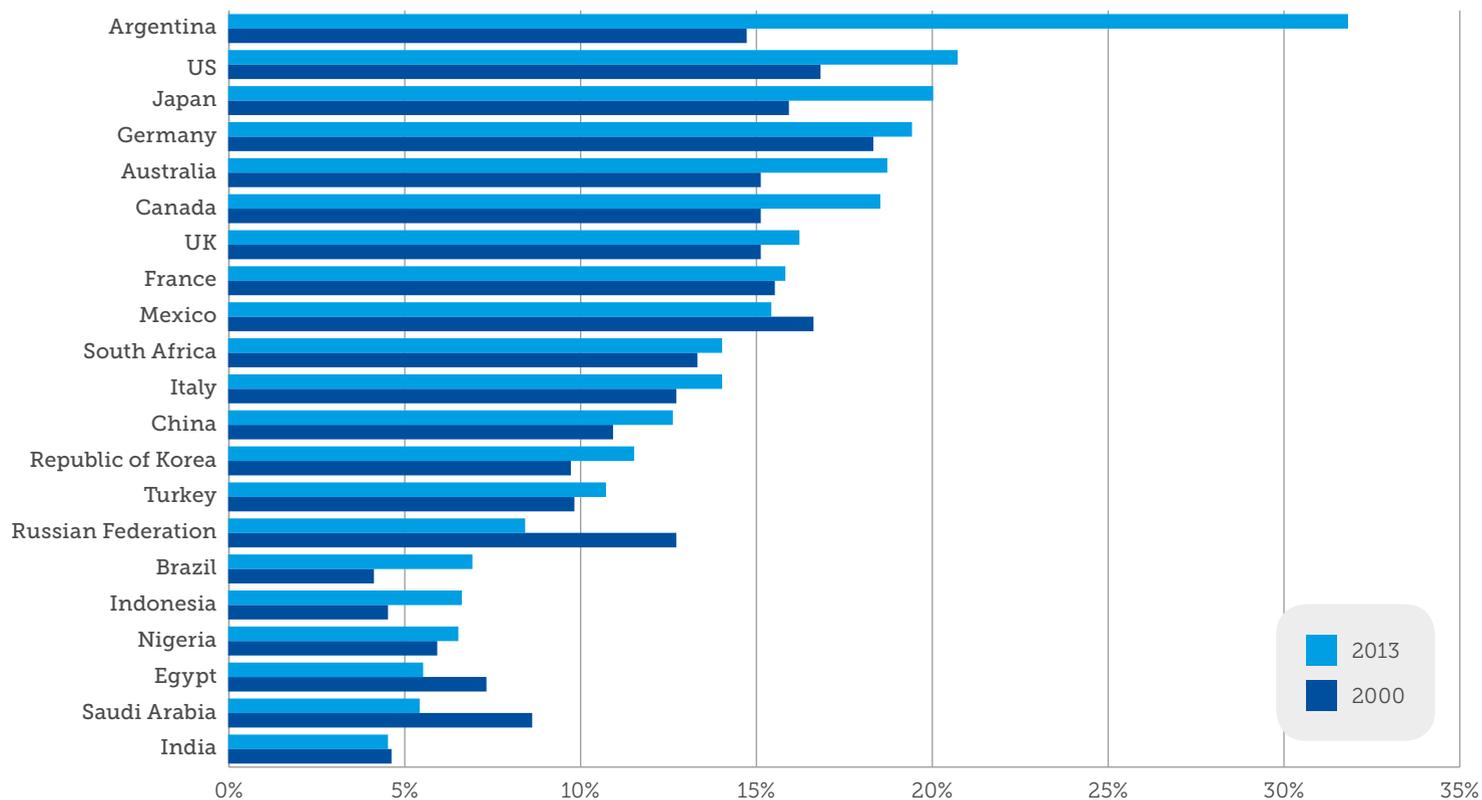
Figure 4 Total expenditure on health as a percentage of gross domestic product



The challenge ahead

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Figure 5 General government expenditure on health as a percentage of total government expenditure



Based on the combination of factors previously presented, it is crucial to identify which strategies can be used in order to respond to the healthcare needs of the largest possible share of population.

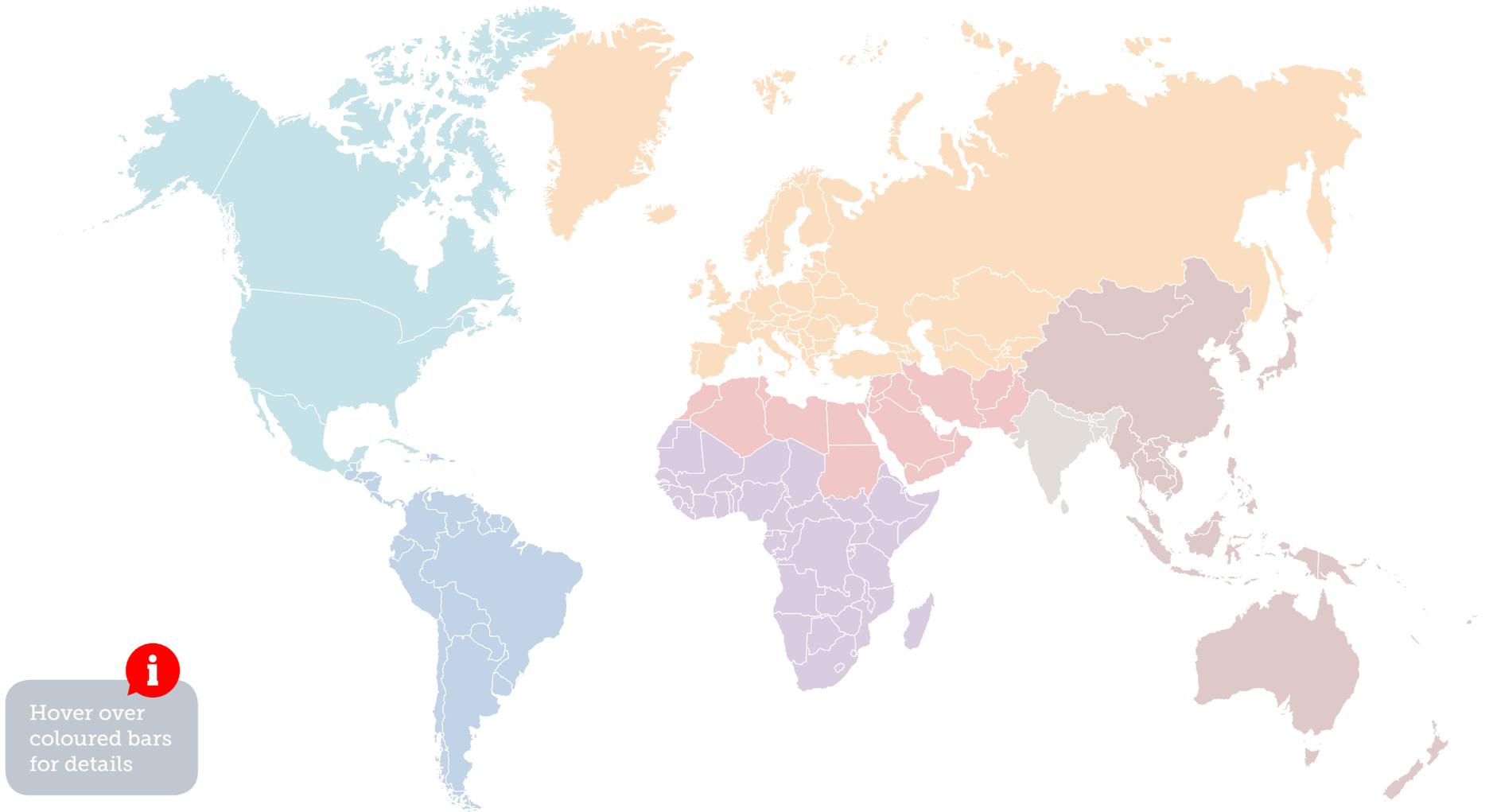
In 2015, it was estimated 415 million adults had diabetes worldwide, and this number is predicted to increase to 642 million adults by 2040¹⁶. Moreover, diabetes imposes a large economic burden on individuals, families, national health systems, and on countries due to increased use of health services, loss of productivity, and disability¹⁷⁻²⁰. The latest estimates indicate that diabetes was responsible for USD 673 billion in healthcare spending in 2015 worldwide, which represents 11.6% of the total amount spent on health¹⁶.

The International Diabetes Federation stratifies countries into seven geographical regions: Africa, Europe Middle East and North Africa, North America and Caribbean, South and Central America, South-East Asia and the Western Pacific Region.

Health expenditure on diabetes is expected to rise in the next 25 years in every region of the world, reaching USD 802 billion in 2040 (Figure 3). Currently the region with the highest expenditure on diabetes is the North American and Caribbean Region, estimated at USD 348 billion in 2015. On the other hand, the Africa Region has the lowest total expenditure on diabetes: USD 3.4 billion. In the next 25 years, the Middle East and North Africa Region will observe the highest growth (81%) in the total health expenditure on diabetes, while the Europe Region will have the lowest growth (11%).



Figure 6 The seven regions of the International Diabetes Federation



The amount spent on diabetes becomes even more meaningful when comparing it to the total health expenditure. Diabetes was responsible for 12% of the total amount spent on health worldwide in 2015. This varies regionally: the IDF region with the highest share of expenditure spent on diabetes in 2015 was the Middle East and North Africa Region (15%), followed by the North America and Caribbean Region (14%). On the other hand, the African Region, and the European Region spent the least with 7%, and 9% respectively.

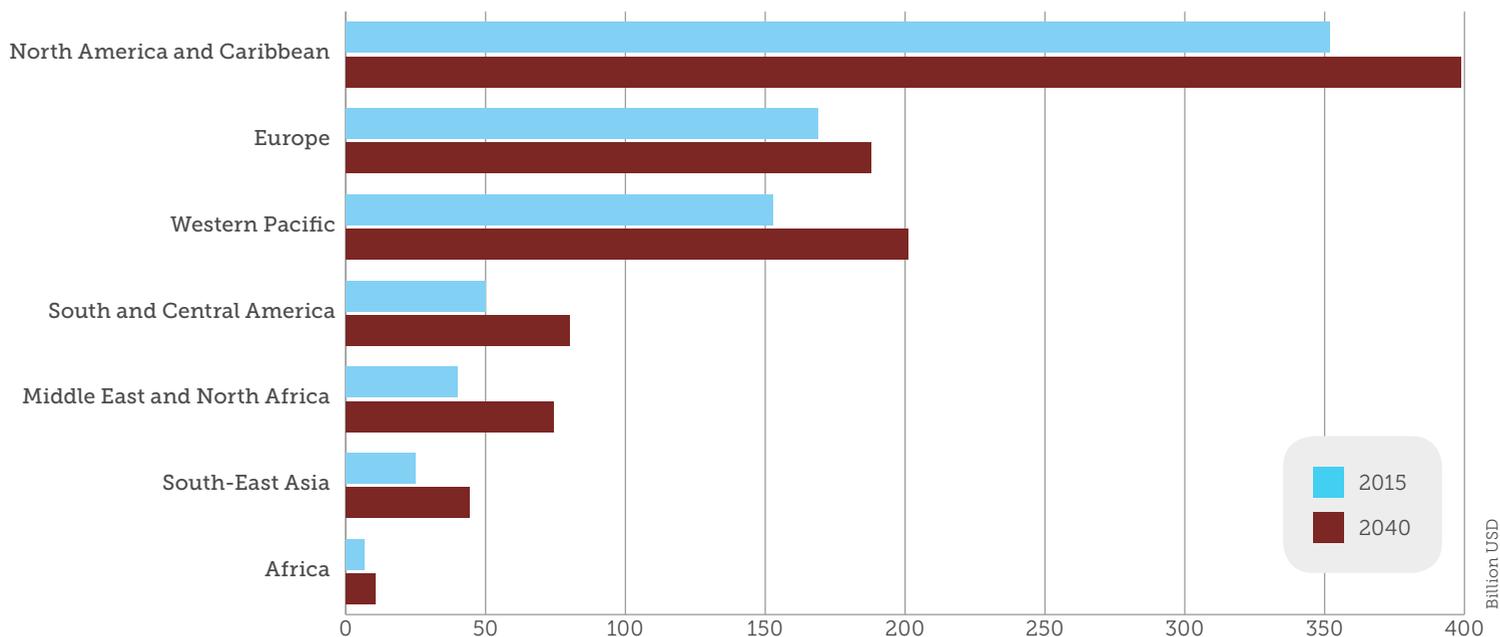
Diabetes-related complications are the major driver of diabetes health expenditure¹⁸. Preventing people from developing type 2 diabetes will substantially reduce the risk of people having complications such as cardiovascular disease, retinopathy, and kidney failure³.

Type 2 diabetes mellitus accounts for more than 90% of all diabetes cases²¹⁻²⁴. There is evidence that the vast majority of cases of type 2 diabetes can be prevented or delayed²⁵⁻²⁷. There is also evidence that gestational diabetes can be prevented by lifestyle modification.

Nevertheless, it is still necessary to identify which prevention programmes can provide better health outcomes, and the resources needed to provide these programmes to different target groups; and based on that, select the programmes that offer the best value for money.

This report provides a summary of cost-effectiveness studies conducted on programmes for prevention of type 2 diabetes, in order to support evidence-based policy that will most effectively reduce the human and economic burden of type 2 diabetes.

Figure 7 Total health expenditure on diabetes per IDF region



The amount spent on diabetes becomes even more meaningful when comparing it to the total health expenditure. Diabetes was responsible for 12% of the total amount spent on health worldwide in 2015. This varies regionally: the IDF region with the highest share of expenditure spent on diabetes in 2015 was the Middle East and North Africa Region (15%), followed by the North America and Caribbean Region (14%). On the other hand, the African Region, and the European Region spent the least with 7%, and 9% respectively.

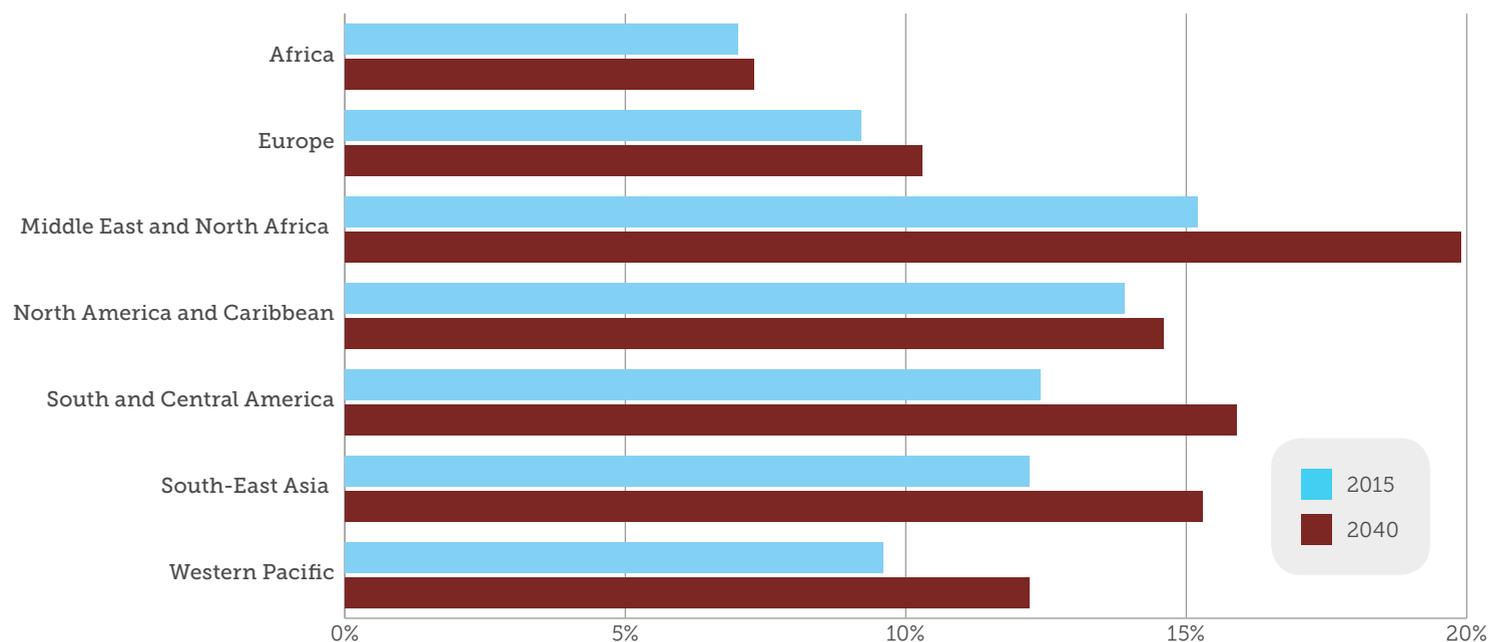
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Figure 8 Proportion of health expenditure spent on diabetes



Cost-effectiveness analysis



Cost-effectiveness analysis

The objective of health economics is to improve the health of the population through the efficient use of resources. Economic analysis is potentially useful for comparing methods for prevention, screening, risk assessment, diagnosis, monitoring, rehabilitation and follow-up, as well as treatment. Economic evaluation is usually conducted in the form of a cost-effectiveness analysis, with the health effects being measured using an appropriate non-monetary outcome indicator, such as life years gained, or cases prevented²⁸.

The aim of cost-effectiveness analysis is to evaluate the costs and health effects of specific interventions. Most frequently, it is used to compare studies of prospective new interventions with current practice, other alternative interventions, or with a fixed price cut-off point representing the assumed social willingness to pay for an additional unit of health²⁹.

At the centre of health economics is the idea that resources should be allocated across interventions and population groups to generate the highest possible overall level of population health²⁹.

In cases where calculations show that some current interventions are relatively cost-ineffective, and that others that are not being adopted are relatively more cost-effective, resources could be reallocated across interventions to improve health from a population perspective²⁹.

Incremental Cost-Effectiveness Ratio (ICER)

The indicator most widely used for assessing the interventions is the Incremental Cost Effectiveness Ratio (ICER); the ICER is expressed as the ratio of the difference in cost between two strategies to the difference in their effectiveness. This can be interpreted as the cost of obtaining an extra unit of effectiveness, and it quantifies the trade-offs between patient outcomes gained and resources spent³⁰.

$$ICER = \frac{(Cost\ of\ intervention\ a - Cost\ of\ intervention\ b)}{(Effectiveness\ of\ intervention\ a - Effectiveness\ of\ intervention\ b)}$$

As an illustrative example, imagine that a local policy maker wants to implement a diabetes prevention programme with the objective of promoting healthy lifestyles in a community, and that the choice is between the only two possible options: a physical activity programme and a healthy eating programme, both targeting the same population group and with the same duration (three years).

In this example, the physical activity programme has an implementation cost of USD 150,000 whereas the

healthy eating programme costs USD 100,000. However, the (more expensive) physical activity programme is estimated to prevent 20 people from dying, while the healthy eating one is expected to prevent only 18 deaths.

In this example, the ICER of the physical activity programme compared to the healthy eating one is the ratio between the difference of the implementation costs (USD 50,000), and the difference of the interventions' effectiveness (two lives saved) which is USD 25,000 per life saved, i.e.

$$ICER = \frac{(150,000 - 100,000)}{(20 - 18)} = \frac{50,000}{2} = 25,000$$

The effectiveness of different interventions can be measured with different indicators, such as:

Traditionally the effectiveness of healthcare interventions was measured in reduction of mortality rates. This approach has one crucial limitation as it does not differentiate between extending a life by one year or by several years³¹.

The years of life gained (YLG) provide a solution where the effectiveness of the intervention is calculated based on the life years gained associated with the average life expectancy at different life stages. This calculation could lead to priority being given to interventions for younger rather than older individuals. To account for this, a discount rate of 3-5% per extra year gained is

included, meaning later years gained are given a lower value compared to the years immediately after the intervention³¹.

Using the previous example, instead of quantifying the health outcomes on deaths averted, we assume there are 100 people in each intervention group. The physical activity programme increases life expectancy by four years, and the healthy eating programme by two years. In this case, the physical activity programme represents 200 extra years compared to healthy eating. Based on that, the ICER is USD 250 per year of life gained.

$$ICER = \frac{(150,000 - 100,000)}{(100 \times 4 - 100 \times 2)} = \frac{50,000}{200} = 250$$

The effectiveness of different interventions can be measured with different indicators, such as:

Despite the usefulness of the years of life gained as indicator for assessing healthcare interventions, one limitation is that YLG does not account for the impact of morbidity, or in other words the quality of life experienced in the years after intervention. The QALYs provide an answer for this problem by combining premature death and morbidity. This is achieved by associating a weight between 1 (perfect health) and 0 (death) to the health status experienced by people (quality of life) at different stages of their life and multiplying these weights by the number of years lived with the respective status (quantity of life). The weight or quality of life associated to each health status is based on dimensions such as: mobility, pain, self-care ability,

anxiety, and capacity to perform activities such as studying, work or leisure³².

Going back to the previous example, the life expectancy is expected to increase by four years through physical activity and two years through healthy eating. In an example where the morbidity weights are 0.2, and 0.1 respectively, the physical activity programme is associated with a gain of 3.2 QALYs gained per person ($4 \times (1 - 0.2)$), and the healthy eating to 1.8 QALYs gained per person ($2 \times (1 - 0.1)$). Since each programme enrolled 100 participants, in this case the ICER is USD 357 per QALY gained.

$$ICER = \frac{(150,000 - 100,000)}{(100 \times 4 \times (1 - 0.2) - 100 \times 2 \times (1 - 0.1))} = \frac{50,000}{100 \times 3.2 - 100 \times 1.8} = \frac{50,000}{140}$$

The effectiveness of different interventions can be measured with different indicators, such as:

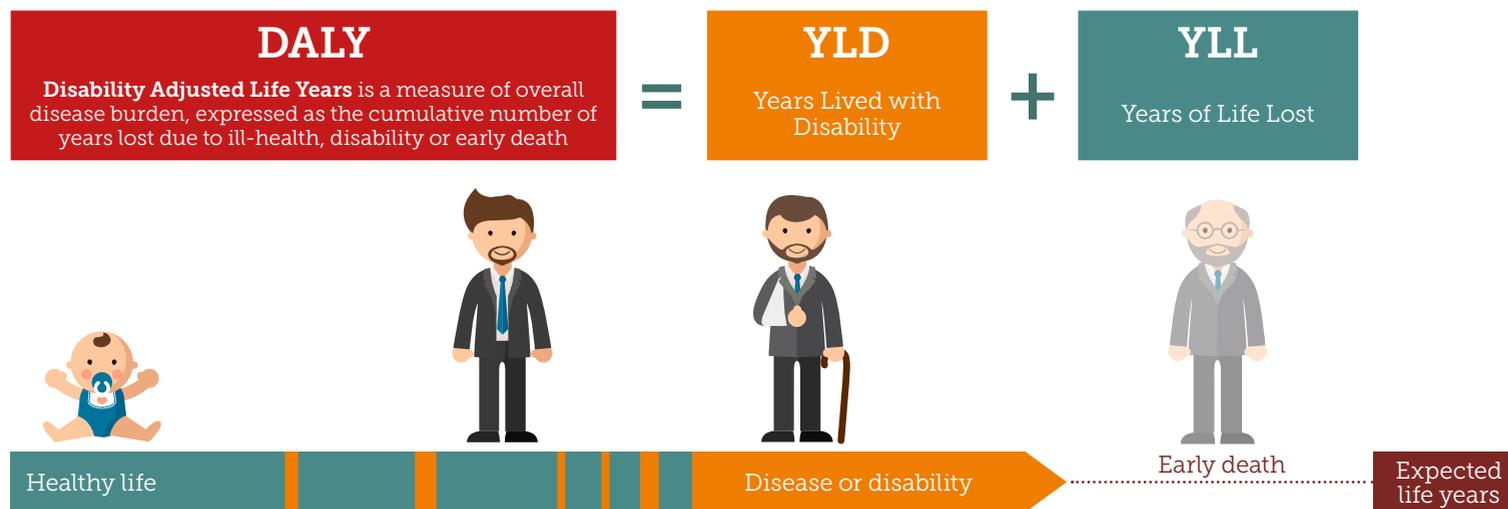
The DALY was first introduced by the World Bank, and quantifies the healthy years of life lost due to the mortality and morbidity of a specific condition compared to the ideal health situation where the entire population lives to an advanced age, free of disease and disability^{31,33} (Figure 6).

Applying this concept to the example previously used in this section, one can say DALYs are the other side of the coin of QALYs. Assuming average life expectancy in that community is 75 years, and average healthy

life expectancy is 70. If neither the physical activity, nor the healthy eating programme is put in place, life expectancy would drop to 70 years, and healthy life expectancy to 60 years. The commonly used weight associated to years lived with disability is 0.5. Therefore, the disease burden associated to diabetes per person in this example is ten DALYs (table 2).

$$\begin{aligned}
 \text{DALYs per person} &= \\
 \text{YLL (YLD x disability weight)} &= \\
 5 + (10 \times 0.5) &= 10
 \end{aligned}$$

Figure 9 Disability Adjusted Life Years (DALYs), Years Lived with a Disability (YLD) and Years of Life Lost (YLL)



The effectiveness of different interventions can be measured with different indicators, such as:

Table 2: Illustrative example of Years of Life Lost (YLL) and Years Lived with Disability (YLD) due to diabetes

	Life expectancy	Healthy life expectancy
National average	75	70
Unfollowed in a person with untreated diabetes	70	60
Years of life lost (YLL)	5	
Years lived with disability (YLD)		10

As mentioned earlier, in this example the physical activity programme increases life expectancy by four (morbidity weight of 0.2) years while healthy eating only two years (morbidity weight of 0.1). Therefore, in this case the DALYs associated with the physical activity programme are 6.8, compared to 8.2 for healthy eating.

Table 3: DALYs avoided with diabetes prevention programmes

	DALYs avoided	DALYs
No intervention	0	10
Physical activity programme	3.2	10 – 3.2 = 6.8
Healthy eating	1.8	10 – 1.8 = 8.2

This means that the implementation of the physical activity programme represents a reduction of 140 DALYs for the total community in comparison with the healthy eating programme (100 x 6.8 – 100 x 8.2 = -140), with an ICER of USD 357 per DALY avoided.

$$ICER = \frac{(150,000 - 100,000)}{(100 \times 6.8 - 100 \times 8.2)} = \frac{50,000}{-140} = -357$$

The effectiveness of different interventions can be measured with different indicators, such as:

Figure 10 Relationship between Quality Of Life Years (QALYs) and Disability Adjusted Life Years (DALYs)
– source: Bjarne Rabberstad 2005



The effectiveness of different interventions can be measured with different indicators, such as:

Another possible method to quantify the incremental value of one intervention is through the number of cases of a certain disease prevented. This method can be particularly useful when analysing interventions for primary prevention, as the reduction of disease incidence is often the primary outcome of such programmes. Despite its straightforward concept, which is easy to understand by policy makers, there are important limitations to consider such as the non-inclusion of the morbidity dimension, or the long-term sustainability of the outcomes.

For the example used in this section, assuming that out of 100 people of the target group, the physical activity programme prevents 40 of them developing diabetes in the next ten years, while the healthy eating programme prevents only 30 cases in the same timeframe. Therefore, in this case the ICER is USD 5,000 per case avoided.

$$ICER = \frac{(150,000 - 100,000)}{(40 - 30)} = \frac{50,000}{10} = 5,000$$

The effectiveness of different interventions can be measured with different indicators, such as:

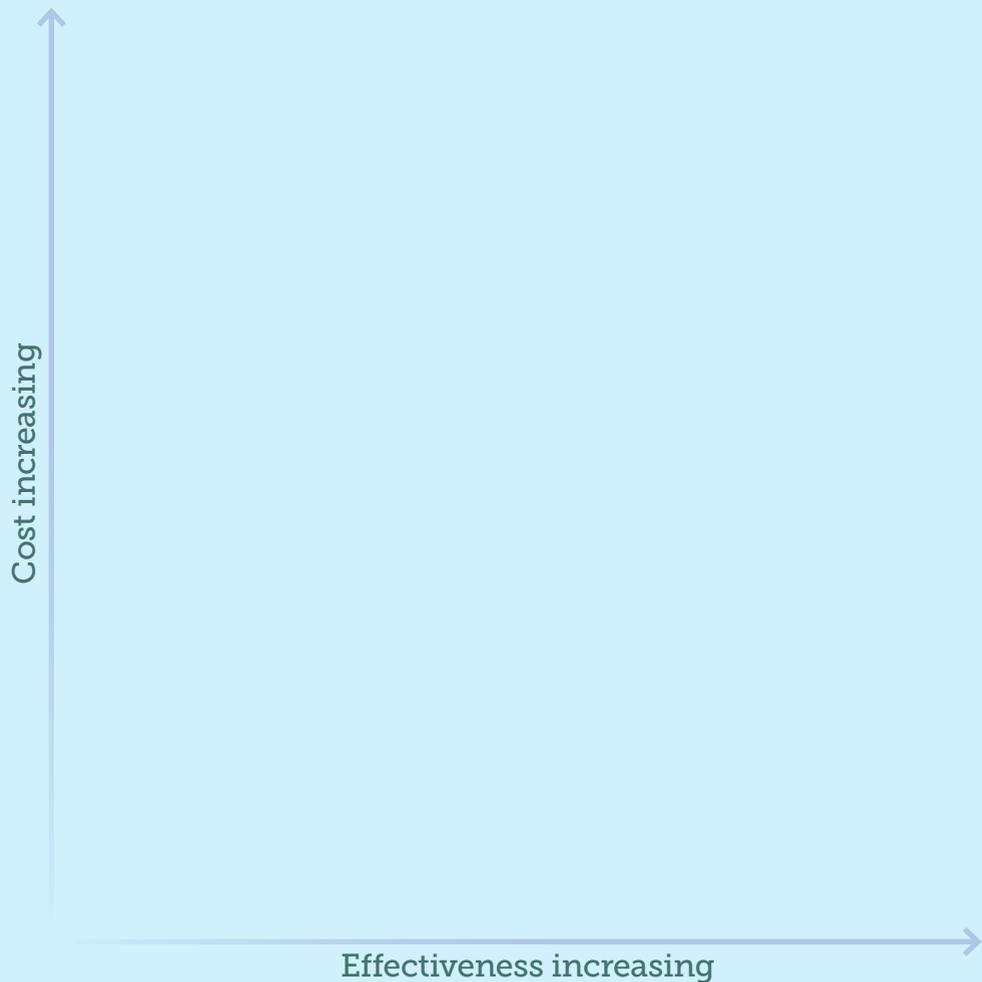
Finally, the last outcome measure presented here is the total number of cases identified. This indicator is used for comparing the effectiveness of different screening interventions, or it can also be found as a secondary outcome measure in more comprehensive programmes that include screening as one of its components.

Support for decision making

The examples previously presented exemplified that by providing the additional costs of achieving a certain health improvement (ICER), cost-effectiveness analysis can support decision makers in comparing interventions and allocating resources effectively.

Figure 11 illustrates the typical results framework of cost-effectiveness analysis between two interventions, and how it can help decision makers with resource allocation.

Figure 11 Cost-effectiveness of decision making



Perspective of analysis

In order to ensure comparability in assessing cost-effectiveness, it is important to define the perspective that is to be used as the basis for the analysis of each study. The perspective determines the relevant costs that need to be accounted for. The most commonly used perspectives are those of society, the health system, the payer and the patient. The outcomes observed will therefore vary depending on the perspective chosen as they differ substantially (Table 4).

The health system perspective is the traditional approach used in cost-effectiveness studies. Despite its narrow approach, the main advantage of this approach is its straightforward concept. On other hand, the societal

perspective is the most comprehensive perspective. This perspective takes in consideration the costs and benefits of all stakeholders which can be medical, or non-medical, direct and indirect costs.

Table 4 Health economics perspectives of analysis

Society	Health Systems	Payer	Patient's perspective
All costs incurred by society as a whole (including those of health system, and patient) in delivering health services, includes indirect costs such as productivity losses due to medical leave of patients, and informal care givers	All provider costs in service delivery: <ul style="list-style-type: none"> • Salaries of healthcare professionals • Costs of medications • Equipment • Consumables • Fixed assets • Social care givers 	This perspective can vary from country to country: <ul style="list-style-type: none"> • Countries with universal health coverage – Similar to health system perspective • Countries based on risk-pooling – Costs paid by insurance companies or sickness funds • Other countries – similar to the patient's perspective 	All costs borne by a patient when seeking care: <ul style="list-style-type: none"> • Out-of-pocket payments • Co-payments • Costs of transport • Costs of taking time off work

Methodology



Methodology

In order to summarise the available data on the cost benefits of primary prevention of type 2 diabetes, a systematic literature review was conducted. The scientific databases used were Medline (Medical Literature Analysis and Retrieval System Online), EMBASE (Excerpta Medica), and Cochrane Central.

In order to identify the relevant studies – a search strategy based on medical subject headings (MeSH) was developed (Table 5). For the three databases, all the combinations were tested and after that, the term “cost-effectiveness diabetes prevention” was used for free search as well.

Table 5 Search strategy based on medical subject headings (MeSH)

MeSH Terms		MeSH Terms	
1	Diabetes mellitus	17	Health Promotion
2	Pre-diabetes	18	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
3	1 or 2	19	Clinical Trial
4	Technology Assessment, Biomedical	20	Evaluation Studies
5	Comparative Effectiveness Research	21	Meta-Analysis
6	Cost-benefit analysis	22	Government Publications
7	Models, Economic	23	Review
8	Value of Life	24	Comparative Study
9	4 or 5 or 6 or 7 or 8	25	Observational Study
10	Prevention, Primary	26	Validation Studies
11	Diet therapy	27	Journal Article
12	Nutrition Therapy	28	Randomized Controlled Trial
13	Risk Reduction Behaviour	29	Technical Report
14	Health Services, Preventive	30	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
15	Physical activity	31	3 and 9 and 18 and 30
16	Health Education	32	Limit 31 to (humans and year="2005-2015")

The inclusion criteria for studies identified from the search were (Figure 12):

1. Primary prevention studies (studies on patients with diagnosed diabetes were excluded)
2. Study outcomes needed to provide clear information on the effectiveness and cost of the intervention (cost per QALY gained, cost per DALY avoided, or other type of ICER)
3. Original articles (other literature reviews were excluded)
4. Articles published in English, between January 2005 and April 2015

Initially 2,008 articles were identified as potentially relevant for the purpose of this report. After a first review, 372 duplicates were excluded, as were papers that assessed the effectiveness of programmes and therapies for diabetes care, and for diabetes-related complications (see Diabetes complications section) leading to 525 articles for abstract review.

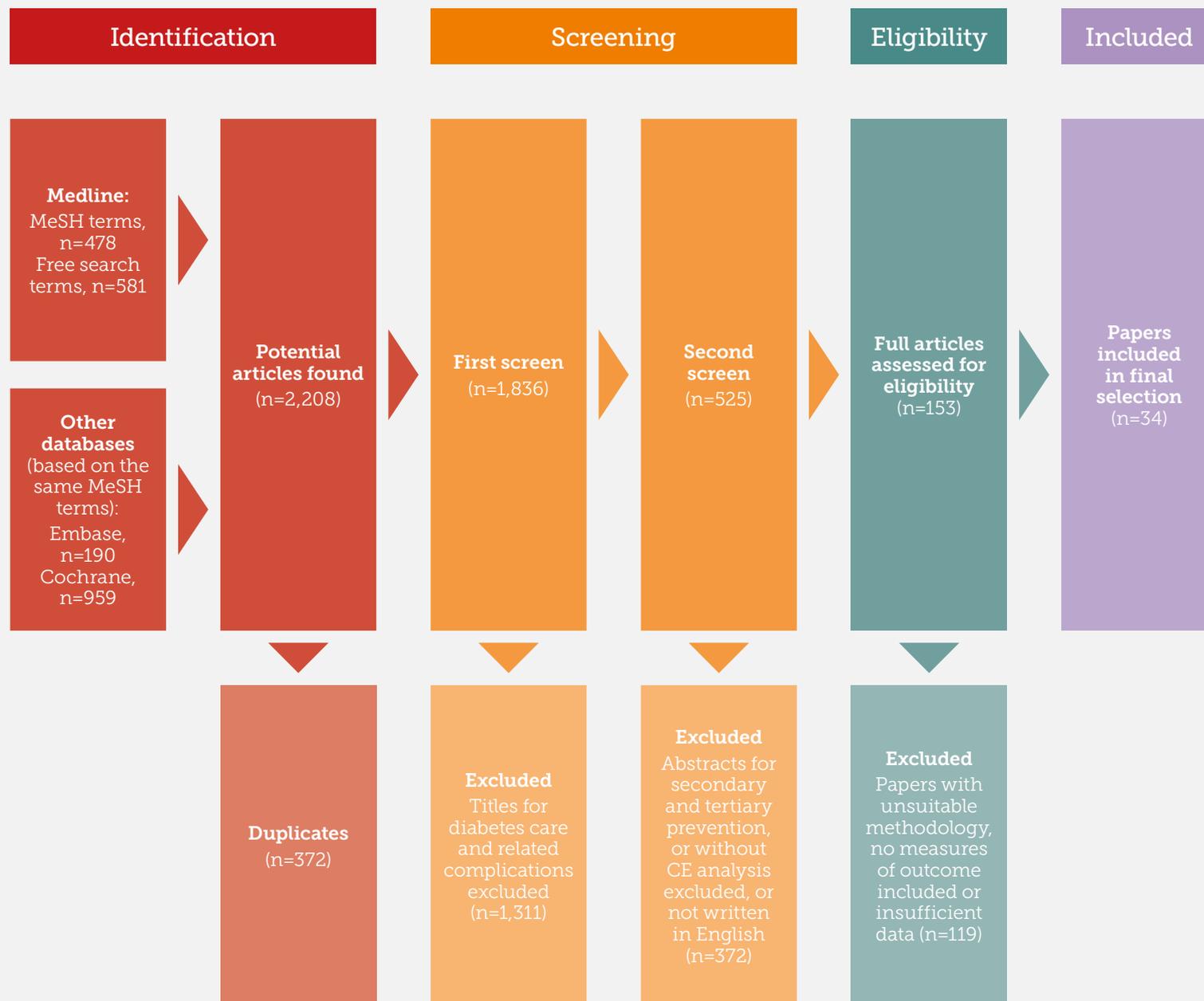
During the abstract review, papers that had a target group of patients with diagnosed diabetes or those aiming to prevent and control the development of diabetes-related complications, were also excluded, as were abstracts that did not specify cost-effectiveness outcomes.

The next step was the full review of 153 scientific papers. During the full review, the methodological quality of the papers was assessed, leading to a final sample of 34 papers. The criteria for exclusion included lack of data on the research methods used, insufficient evidence on the outcomes observed, quantification of the outcomes based on multiple non-communicable diseases rather than only diabetes, or outcomes measured solely in terms of reducing diabetes risk factors such as weight loss.

Studies were defined as cost-effective based on the 50,000 International dollars (ID) per QALY, which represents a threshold used often by policy makers to decide whether an intervention offers good value for money, cost of the interventions analysed were converted to international dollars.

ID are a hypothetical currency with the same purchasing power parity (PPP) of USD in the United States of America at a given point in time, and is used to make comparisons both between regions and over time. PPP can be used as conversion factor to convert different economic aggregates from different countries and territories into the common currency unit of ID. ID are calculated by dividing the amount of national currency by the PPP exchange rate. As an example, the PPP between the USA and Germany is the number of euros that has the same purchasing power in Germany as 1 USD in USA³⁴.

Figure 12 Study selection



Results



Results

Through this literature review it was possible to identify 34 scientific papers from 13 countries that assessed the cost effectiveness of primary prevention of type 2 diabetes between the years 2005 and 2015.

Geographic distribution

The European Region had the highest number of studies (n=17), followed by the North American and Caribbean Region (n=11). Together, they accounted for 78% of the studies identified. No studies were found in the Africa Region, Middle East and North Africa Region, or South and Central America Region.

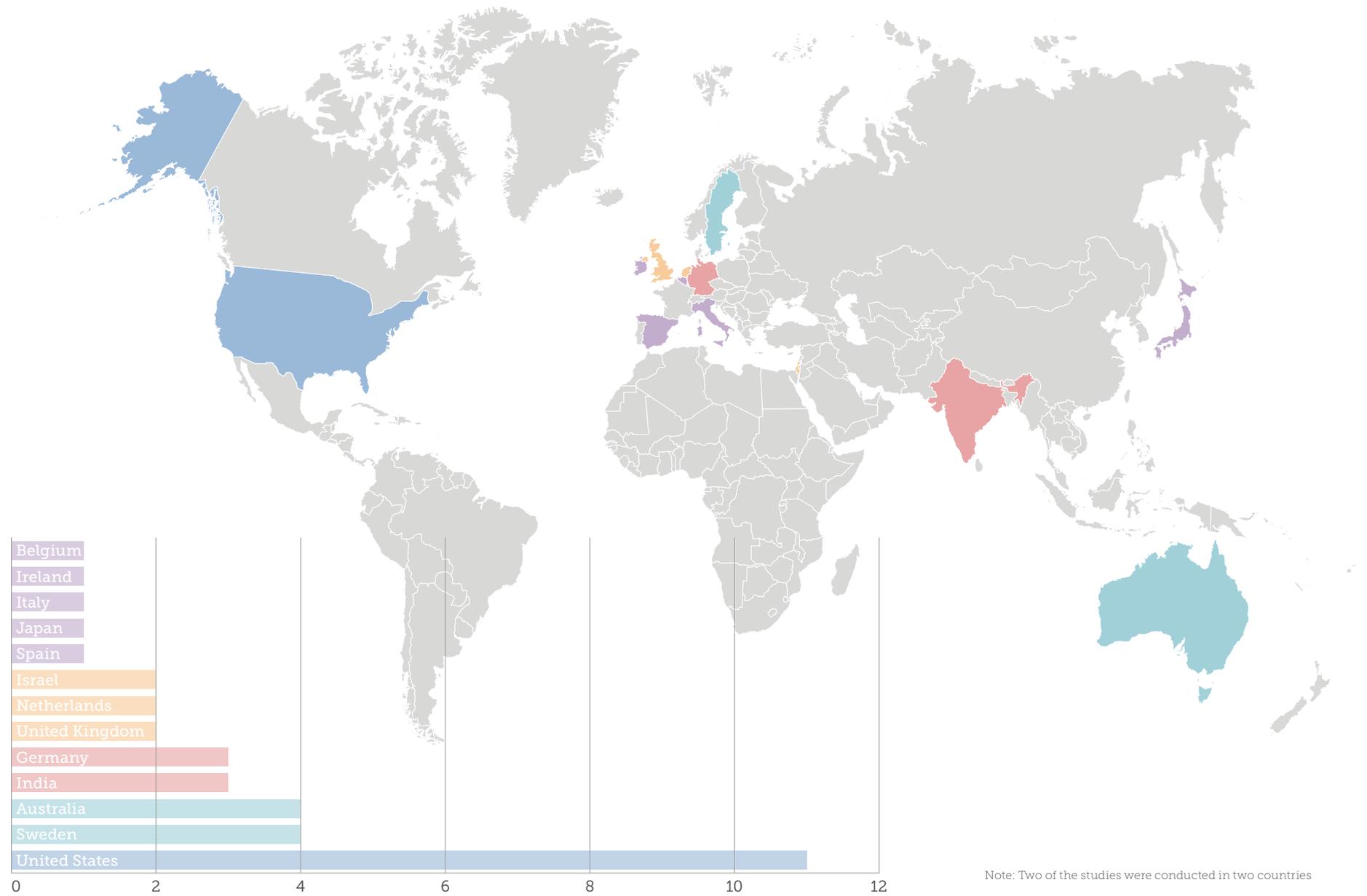
The country with most of studies conducted on the cost-effectiveness of primary prevention of type 2 diabetes was the United States of America (n=11),

followed by Australia, and Sweden (n=4). In Figure 13 the total number of studies is 36, because in two of the studies conducted two countries were analysed (India, and Israel).

Based on the classification used by the World Bank³⁵, there were 33 studies from high-income countries, three studies were found from a lower-middle income country (India), and no studies from low-income countries.



Figure 13 Number of studies identified per country



Type of intervention

In the 36 studies on primary prevention of type 2 diabetes, 71 interventions were analysed. In several cases, one research study looked at multiple interventions aiming to achieve the same objective: prevent the onset of type 2 diabetes.

Of these 71 interventions, nearly half focused on comprehensive lifestyle interventions (n=33), that is programmes that aimed to prevent the development of type 2 diabetes by encouraging participants to increase physical activity and to eat healthier food, with the aim of achieving weight loss.

The second most common type of intervention was the use of medication to prevent type 2 diabetes. A total of 15 studies examined the effectiveness of medications such as Metformin, Orlistat, and Acarbose. A further seven studies examined interventions that combined a lifestyle

programme with medication such as Metformin, Orlistat, and Voglibose.

There were also nine interventions focusing solely on increasing the physical activity levels of participants, and seven intervention focusing solely on nutrition, with the aim of encouraging participants to have healthier diets.

In the majority of the interventions, screening programmes to identify those at risk of developing diabetes were included in the analysis (70%).



Figure 14 Number of studies by country and type of intervention

Target group

The interventions described in this report were targeted at three types of individuals: (1) those at high risk of developing type 2 diabetes, (2) those at low risk and (3) all individuals.

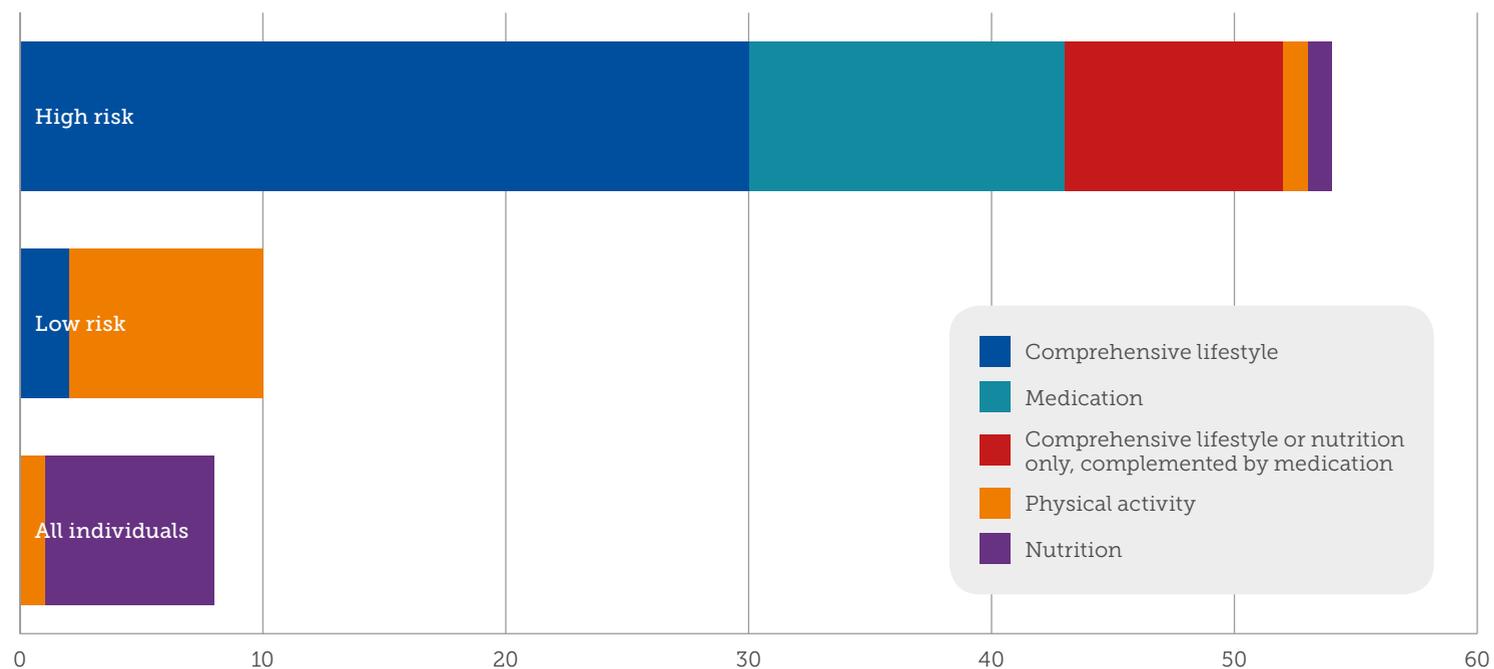
Three quarters of the interventions (n=54) focused on people at high risk of developing type 2 diabetes. High-risk patients were considered as those diagnosed with impaired glucose tolerance or with impaired fasting glucose, women with previously diagnosed gestational diabetes or participants with a combination of risk factors such as family history of diabetes, obesity, and older age.

The second most researched target group were people at low risk of developing diabetes (n=10), which was

defined as those individuals without diagnosed impaired glucose tolerance or impaired fasting glucose, those not previously diagnosed with gestational diabetes, or with no diabetes risk factors.

The remaining seven interventions were directed to all individuals regardless of their risk of developing type 2 diabetes. These were public health measures such as incentives to increase vegetable consumption, or the construction of green areas for leisure activities.

Figure 15 Number and type of interventions by target population



How cost-effective is primary prevention of type 2 diabetes?

Out of the 71 interventions analysed, ten (14%) were judged to be cost-saving, meaning that better health outcomes can be achieved and at the same time health funds can be saved. Moreover, these cost-saving interventions were from each of the types of intervention analysed, which illustrates the variety of effective options available for policy makers regarding the primary prevention of type 2 diabetes.

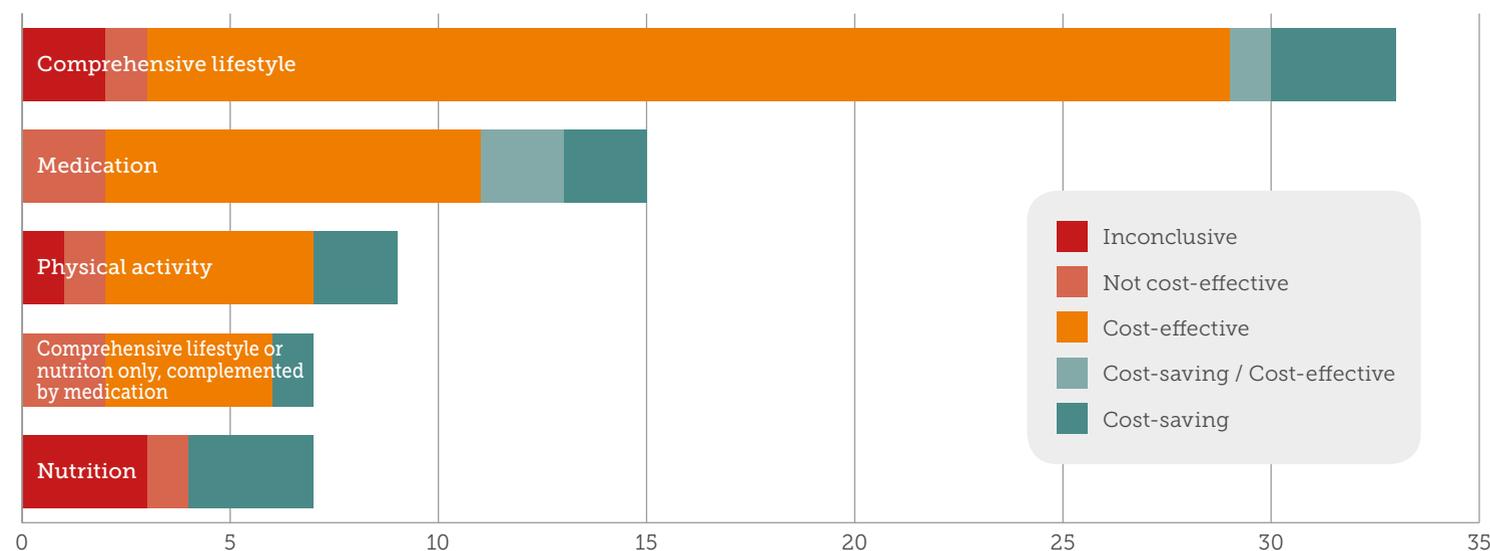
Forty-eight (67%) interventions were evaluated as cost-effective, meaning that the ICER obtained was below ID 50,000 after adjusting to 2016 values, and for purchasing power differences between countries. In the case of three of these interventions they could still be potentially cost-saving.

Seven (10%) interventions were not cost-effective, meaning the ICER was higher than ID 50,000; a further

six (8%) yielded inconclusive findings e.g. no significant results, or insufficient data provided to determine ICER.

It is important to emphasise that categorising an intervention as cost-effective or not cost-effective depends on the societal willingness to pay for healthcare. This will determine whether the acceptance threshold is ID 50,000, or higher or lower.

Figure 16 Cost-effectiveness by type of intervention, based on ID 50,000 acceptance threshold



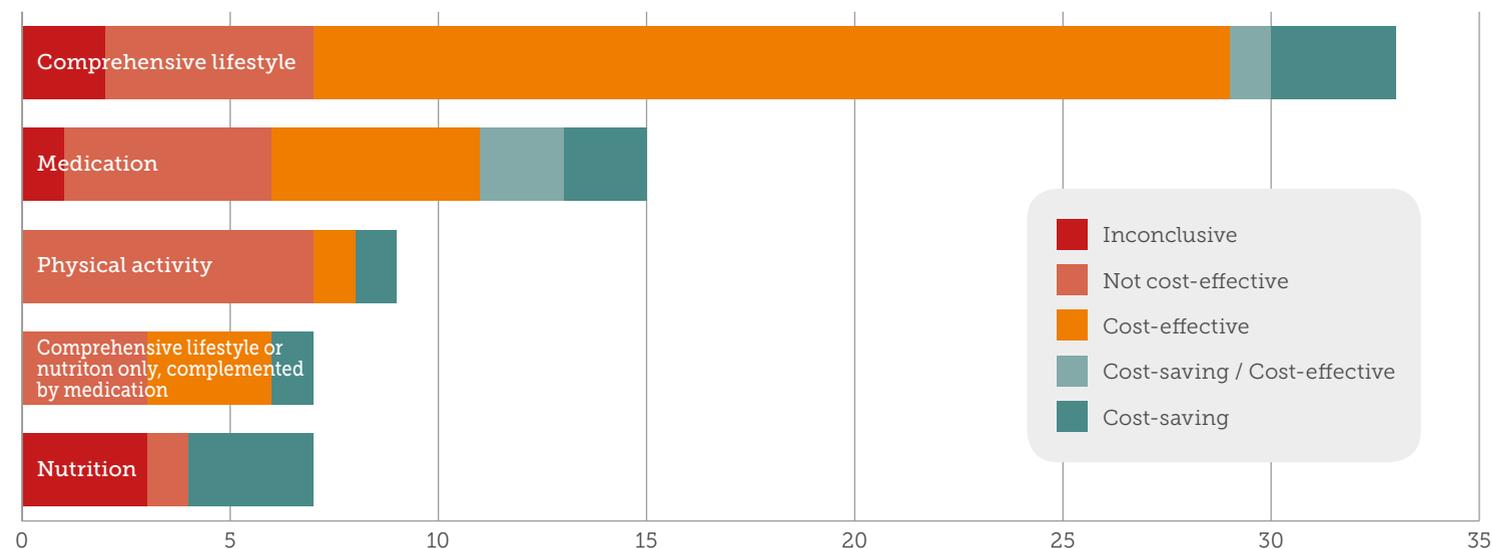
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For the same list of interventions, if an ICER of ID 25,000 is used instead of the ID 50,000 used throughout this report, the overall results would differ substantially. The number of cost-saving interventions remains the same, ten (14%), but the number of cost-effective

interventions drops to thirty-four (48%), while the number of not cost-effective interventions triples, from seven to 21 (30%). At this threshold, most comprehensive lifestyle interventions remain cost-effective, whereas those based on physical activity become less so.

Figure 17 Cost-effectiveness by type of intervention, based on ID 25,000 acceptance threshold



Recommendations

The initial objective of this research was to identify which interventions, from a cost-effectiveness perspective, should be prioritised by local policy makers regarding the primary prevention of type 2 diabetes.

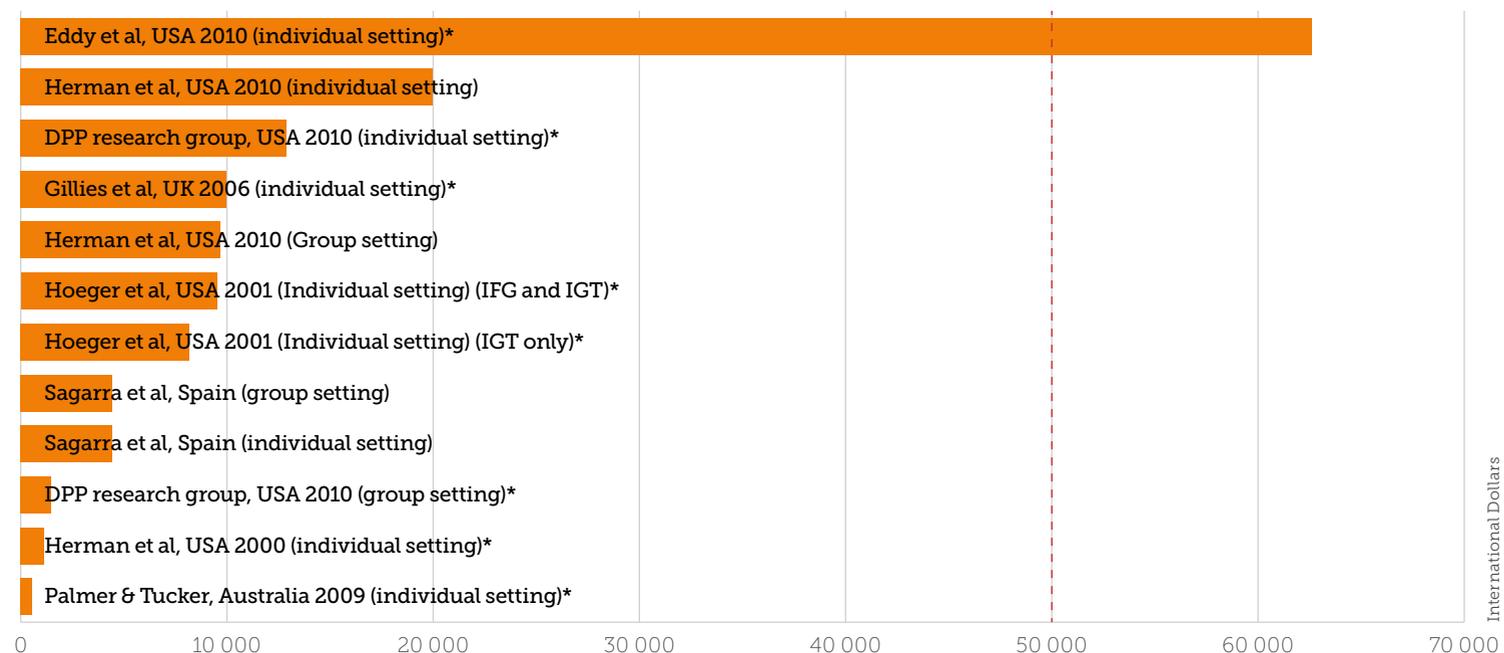
1) Cost-effectiveness of comprehensive lifestyle programmes to prevent or delay type 2 diabetes

Large randomised control trials, such as the Diabetes Prevention Program (DPP)⁵, the Diabetes Prevention Study (DPS)⁷, and the Da Qing Study⁶, have

systematically proven that the majority of cases of type 2 diabetes can be prevented or delayed.

In this review, 56 (79 %) interventions were based on similar lifestyle programmes, or included a lifestyle change component, and 28 of these interventions

Figure 18 Cost per Quality Of Life Year (QALY) gained from comprehensive lifestyle programmes to prevent type 2 diabetes from a health system perspective



*Modelling studies

followed the approaches of the trials, such as the DPP, and DPS.

Comprehensive lifestyle programmes generally aim to achieve and maintain a reduction of 5-7% body weight, and a minimum of 150 minutes of per week of moderate intensity physical activity with similar intensity to brisk walking. The methods to achieve these goals vary between interventions, but often include: 1) lifestyle coaching and individual case management, 2) structured courses on behavioural self-management strategies, 3) physical activity sessions, 4) regular follow-up sessions complemented by adherence strategies, and 5) adaptation of content according to local culture.

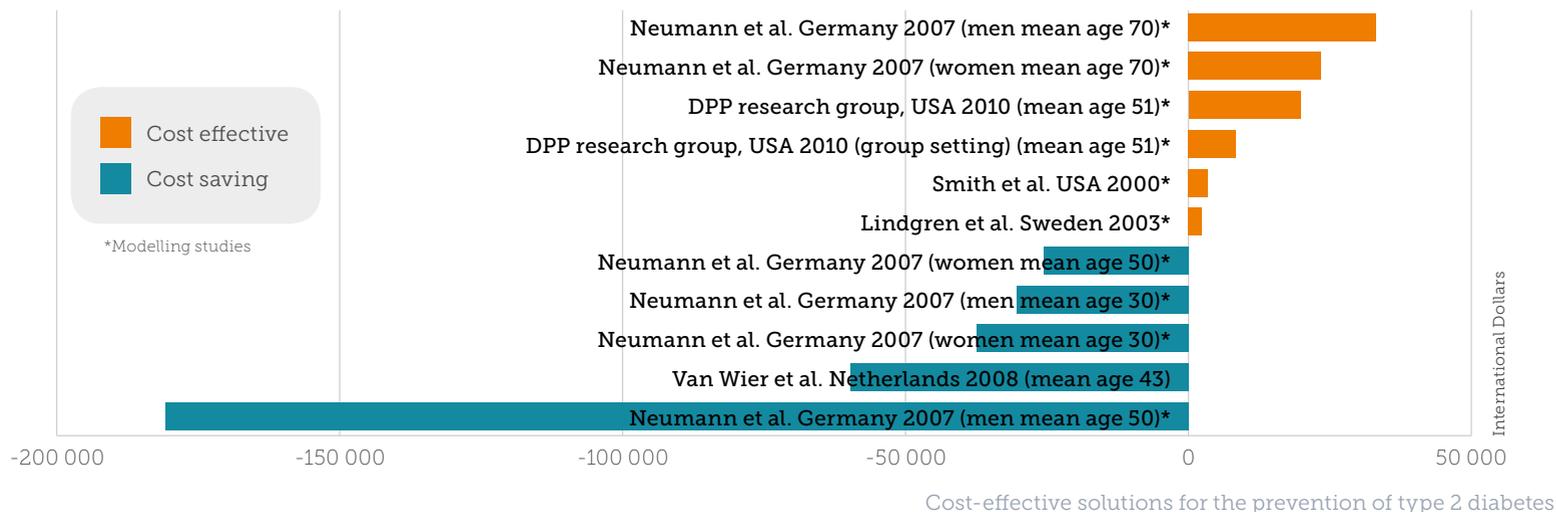
Depending on the setting, local policy makers may adapt programmes to their local needs by choosing only some of the components of the intervention, or by arranging the programme to be delivered either in group, or individual sessions³⁶.

In this analysis, the studies included demonstrated that such lifestyle programmes are not only highly effective in preventing the onset of type 2 diabetes, but they also offer excellent value for money, and can be cost-saving.

Of those studies that provided the cost per QALY gained (ID) from a health system perspective, the majority of interventions were found to be highly cost-effective with an ICER lower than ID 20,000. One study was found to be cost-saving, which modelled the American Diabetes Prevention Program in Australia³⁷, and would lead to savings of ID 500 per QALY gained. There was also one study that was not found to be cost-effective³⁸. In this study, the health benefits of the lifestyle intervention were similar to other studies, however the control group did not experience a significant decrease in health related quality of life and therefore the incremental health value was lower. Furthermore, the total health costs associated with the lifestyle programme were substantially higher than in the other studies (Figure 18).

Note that primary prospective studies generally confirmed the findings of studies based on economic modelling from secondary data, although some modelling studies of individual and group interventions were more cost-effective (and in one case cost-saving) than any prospective study. This suggests a degree of caution should be advised when interpreting modelling studies which suggest very high cost-effectiveness compared to 'real-world' studies.

Figure 19 Cost per quality of life year (QALY) gained from comprehensive lifestyle programmes to prevent type 2 diabetes from a society perspective



As might be expected, studies that compared the cost-effectiveness of group versus individual interventions showed that those delivered to groups of participants were more cost-effective (Table 6).

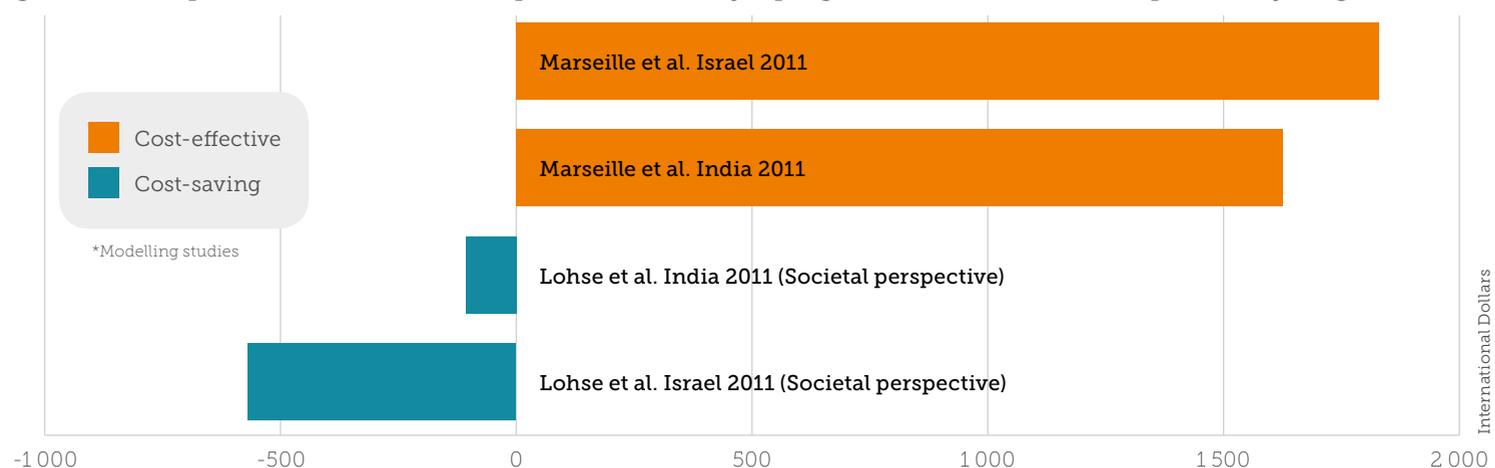
When expanding the analysis to the costs and benefits faced by society as a whole, the results were even more positive, with all interventions being either cost-saving or cost-effective, with the ICER ranging from savings of ID 181,000 to an ICER of ID 33,000 per QALY gained⁴²). The earlier participants were enrolled in these comprehensive lifestyle programmes, the higher the benefits (Figure 18).

Table 6 Studies that compared individual and group intervention, with cost per QALY gained from a health system perspective

Study	Individual setting	Group setting
DPP research group ³⁹	12 878	1 478
Sagarra et al. ⁴⁰	8 181	4 452
Herman et al. ⁴¹	19 990	9 960

In most of the comprehensive lifestyle programmes analysed, the target group included individuals with either impaired fasting glucose, impaired glucose tolerance, or in some cases both. There were four cases where comprehensive lifestyle interventions were tested by modelling their cost-effectiveness in women with a previous history of gestational diabetes. One of these studies analysed the cost-effectiveness in India and in Israel from a societal perspective, and in both cases results suggest the intervention was cost-saving with a negative ICER of 100 and ID 600 per DALY avoided. The other study focused on the same countries, although the study perspective was not described. Here the ICER was ID 1,600 for India, and 1,800 for Israel (Figure 20). Confirmation of these findings in prospective studies would suggest such an approach should be widely adopted to support healthy behaviours in this group.

Figure 20 Cost per DALY avoided of comprehensive lifestyle programme for women with previously diagnosed GDM



Medication as a complement to lifestyle programmes

Although lifestyle programmes conveyed the most benefit in prospective trials, the use of off-label medications has also been shown to be of benefit in the prevention of type 2 diabetes^{5,27}.

In our review, there were seven studies that examined the effect of medication as a complement to lifestyle programmes. Four studies used Orlistat as a complement to an intervention to modify diet only, while two analysed the cost-effectiveness of metformin as a complement to lifestyle, and one tested Voglibose combined with lifestyle.

Metformin is the first line medication for management of type 2 diabetes, and is on the World Health Organization List of Essential Medicines⁴³. Orlistat is

a lipase inhibitor, used as a therapy against obesity, while Voglibose is alpha-glucosidase inhibitor used for lowering post-prandial blood glucose levels.

From the seven interventions analysed, one using Voglibose was cost-saving, while four interventions were cost-effective: three using Orlistat and one using Metformin (Figure 20). The other two interventions were classified as non cost-effective due to an ICER higher than ID 50,000. This may be a result of the high cost of these drugs at the time the studies were conducted. A re-evaluation may be needed as prices for these drugs have decreased substantially since these studies were conducted⁵⁰.

Figure 21 Costs-effectiveness of lifestyle intervention complemented by medication

	Medication	Target group	Perspective	ICER (ID)	Cost-effectiveness
Iannazzo, Italy, 2008 ^{*44}	Orlistat	Obese	Society	89,000 per QALY gained	Not cost-effective
Iannazzo, Italy, 2008 ^{*44}	Orlistat	IGT	Society	25,000 per QALY gained	Cost-effective
Lacey et al., Ireland, 2003 ^{*45}	Orlistat	Obese	Health system	15,000 per QALY gained	Cost-effective
Hertzman, Sweden, 2003 ^{*46}	Orlistat	Obese	Health system	12,000 per QALY gained	Cost-effective
Ramachandran et al., India, 2006 ⁴⁷	Metformin	IGT	Health system	116 per case prevented	Cost-effective
Bertram, Australia, 2003 ^{*48}	Metformin	IGT	Health system	65,000 per DALY avoided	Not cost-effective
Ikeda, Japan 2009 ^{*49}	Voglibose	IGT	Payer	-9,000 per life year gained	Cost-saving

2) Metformin can be a cost-effective medication for primary prevention of type 2 diabetes

There were 15 interventions that analysed the cost-effectiveness of different types of medication as a sole therapy to prevent the onset of type 2 diabetes. Most of these studies assessed the costs and benefits of Metformin (n=12), while two studies focused on Acarbose, and one on Orlistat.

Despite not being as effective as lifestyle intervention, metformin has been proven to be effective in the primary prevention of type 2 diabetes⁵. This combined with the relative low cost of metformin, opens interesting opportunities in terms of cost-effectiveness.

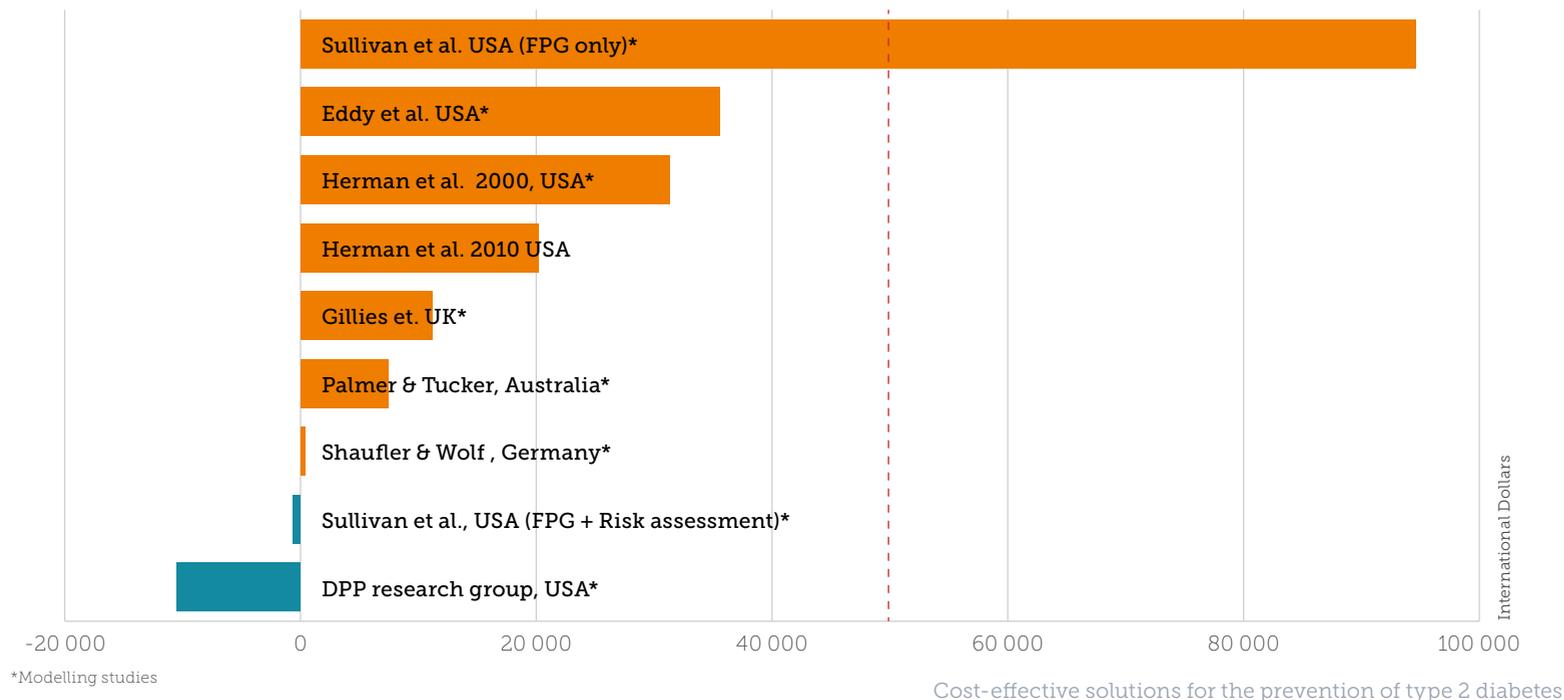
Of nine studies that assessed the cost per QALY gained of using metformin from a health system perspective, eight had an ICER below ID 50,000 per QALY gained, with two being cost-saving, while one, metformin therapy for those diagnosed with impaired fasting

glucose was not cost-effective⁵¹. This was the only metformin intervention that targeted this population group, while all the others have focused on individuals with impaired glucose tolerance, which can justify the discrepancy of results (Figure 22).

The remaining three metformin studies used other methodologies for estimating the ICER. In two of them, the cost per case of diabetes prevented was ID 93 in India, and ID 21,000 in Germany respectively, while the other estimated a cost per DALY averted in Australia ID 18,000.

In the case of Orlistat the ICER was ID 82,000 per DALY avoided and therefore not cost-effective. However, this was based on the cost of Orlistat therapy being AUD 1,290 in 2003 for one year of therapy. In contrast, Orlistat can now be purchased in the UK at less than GBP 275 (AUD 470 / USD 350) per year and therefore its cost-effectiveness has most likely increased. In the case of Acarbose the ICER was of ID 30,000 per DALY avoided.

Figure 22 Cost per QALY gained of metformin therapy



3) Cost-effectiveness of population-based interventions to prevent or delay type 2 diabetes

Despite the effectiveness and cost benefits of interventions and therapies designed for individuals at high risk of developing type 2 diabetes, these require substantial investment and resource allocation from health systems, and a proportion of individuals targeted will still develop diabetes. Therefore, a number of studies have examined the potential impact of strategies that promote healthier lifestyles to the whole population, or to individuals with a low risk of developing diabetes, as a means of primordial prevention of type 2 diabetes.

In this systematic review, ten interventions targeting low risk individuals, and seven interventions targeting the whole population were identified. These two groups represented one quarter of all interventions analysed.

Public health measures

In the seven interventions targeting the whole population, six were from a study that explored a variety of nutrition policies that could be adopted as part of the Supplemental Nutrition Assistance Program (SNAP), that aims to improve dietary habits in the USA⁵². The nutrition policies tested were: 1) ban of sugar sweetened beverages (SSB) from the nutrition assistance programme, 2) introduction of a tax on SSB, 3) subsidy to promote vegetable consumption, 4) monetary reward on the purchase of vegetables through SNAP, while 5) and 6) looked at effects of an increase on the overall SNAP budget. Only three of these interventions were conclusive, the ones tackling SSB were cost-saving, while subsidising vegetable purchases was not cost-effective (Table 7).

Table 7 Cost per QALY gained from various nutrition policies, from a health system perspective

Intervention	Cost per QALY gained
Sugar-sweetened beverage ban	- ID 2 900
Tax on sugar-sweetened beverages	- ID 513 000
Subsidy on vegetables	+ ID 880 000
Monetary reward on purchase of vegetables	Not significant
Budget increase	Not significant

The other study analysed the diabetes prevention benefits of a major urban planning project in the UK⁵³. It assessed the impact on individuals' physical activity of greater availability of green spaces for leisure. This study on the benefits of physical activity, from a public health perspective, concluded the cost per case of diabetes prevented would be ID 36,000 per DALY avoided.

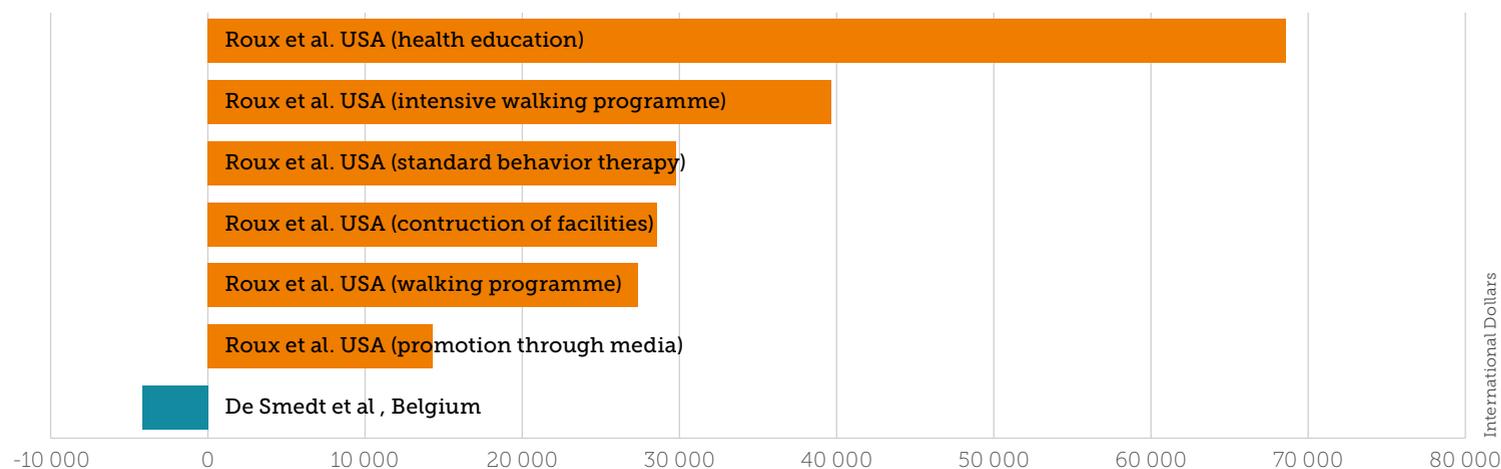
Interventions targeting low risk individuals

Of the ten interventions that targeted low-risk individuals, seven used strategies to promote an increase in physical activity (Figure 23), while the other three followed a more comprehensive approach (Table 8).

These interventions were based on cohorts of healthy individuals only, while the studies in the previous section used cohorts representative of the country's population.

Of the seven physical activity interventions, one programme was assessed as cost-saving with a negative ICER of ID 4,200 per QALY gained, five were cost-effective with ICER ranging between ID 14 and 40,000 per QALY gained, and one was not cost-effective (Figure 23).

Figure 23 Cost per QALY gained of physical activity interventions, from a society perspective



Of the three interventions targeting low-risk individuals through comprehensive lifestyle programs, two were considered cost-effective, as the ICER was below ID 50,000 per QALY gained, though in one of them, Roux

et al.⁵⁴, the cost benefits were marginal. The other intervention, Johansson et al.⁵⁵, was conducted in three Swedish communities, and the results varied from being cost-saving, to not cost-saving.

Table 8 Comprehensive lifestyle programs for low-risk population

Comprehensive lifestyle programmes	Perspective	Cost per QALY gained ID	Cost-effectiveness
Johansson et al. Sweden, DPP for low risk, community 2, women	Society	-46,400	Cost-saving
Johansson et al. Sweden, DPP for low risk, community 1, women	Society	-26,400	Cost-saving
Jacobs-Van der Bruggen et al. Netherlands	Health system	4,400	Cost-effective
Roux et al. intensive lifestyle, USA	Society	46,900	Cost-effective
Johansson et al. Sweden, DPP for low risk, community 2, men	Society	Less effective	Not cost-effective
Johansson et al. Sweden, DPP for low risk, community 3, men	Society	Less effective	Not cost-effective
Johansson et al. Sweden, community 3, women	Society	Less effective	Not cost-effective
Johansson et al. Sweden, DPP for low risk, community 1, men	Society	N/A	Inconclusive

Discussion



Discussion

Different types of interventions have been identified that can help prevent the onset of type 2 diabetes. Moreover, the vast majority of these interventions provide good value for money.

The largest group of interventions analysed were comprehensive lifestyle programmes, aimed at improving nutrition and physical activity. Despite their generally positive outcomes, their cost-effectiveness varied. This variation can be attributed to different

factors such as the age of participants, participants' risk of developing diabetes, and whether the format of the lifestyle modification programme was aimed at a group or individuals.

Figure 24 Cost-effectiveness of comprehensive lifestyle programmes, cost per QALY societal perspective

Intervention	Gender participants	Mean age of participants	Target group	Group/ individual intervention	Cost per QALY gained
Neumann et al. 2007 ⁴²	Men	50	High-risk individuals	Group	-181,000
Van Wier et al. 2008 ⁵⁷	Both	44	High-risk individuals	Individual	-60,000
Johansson et al. 2004, community 2 ⁵⁵	Women	55	Low-risk individuals	Group	-47,000
Neumann et al. 2007 ⁴²	Women	30	High-risk individuals	Group	-37,000
Neumann et al. 2007 ⁴²	Men	30	High-risk individuals	Group	-30,000
Johansson et al. 2004, community 1 ⁵⁵	Women	55	Low-risk individuals	Group	-26,000
Neumann et al. 2007 ⁴²	Women	50	High-risk individuals	Group	-26,000
Herman et al. 2000 ⁵⁸	Both	51	High-risk individuals	Individual	1,200
Lindgren et al. 2003 ⁵⁹	Both	56	High-risk individuals	Individual	2,300
Smith et al. 2000 ⁶⁰	Both	55	High-risk individuals	Group	3,400
DPP research group, 2010 ³⁹	Both	51	High-risk individuals	Group	8,400
Herman et al. 2010 ⁴¹	Both	51	High-risk individuals	Group	9,700
DPP research group, 2010 ³⁹	Both	51	High-risk individuals	Individual	20,000
Herman et al. 2010 ⁴¹	Both	51	High-risk individuals	Individual	20,000
Neumann et al. 2007 ⁴²	Women	70	High-risk individuals	Group	23,000
Neumann et al. 2007 ⁴²	Men	70	High-risk individuals	Group	33,000
Roux et al. 2004 ⁵⁴	Both	70	Low-risk individuals	Individual	47,000
Johansson et al. 2004, community 1 ⁵⁵	Men	57	Low-risk individuals	Group	Less effective than comparator
Johansson et al. 2004, community 2 ⁵⁵	Men	56	Low-risk individuals	Group	Less effective than comparator
Johansson et al. 2004, community 3 ⁵⁵	Women	55	Low-risk individuals	Group	Less effective than comparator

Programmes focusing on individuals considered to have a high risk of developing type 2 diabetes were more cost-effective than those targeting low risk individuals. This finding is justified by the lower number of patients needed to prevent one case of diabetes in the high risk groups, than in the low risk ones (Figure 24).

Regarding the age of participants, within those at high risk, studies targeting older patients have shown worse cost-effectiveness results, than those with younger patients. This could be explained by lower adherence rates, lower incremental benefits due to life expectancy, and age being positively correlated with higher risk of type 2 diabetes.

Finally, looking at studies that analysed the delivery of comprehensive lifestyle programmes in a group format, compared to individual counselling^{39,41}, those using a group format provided substantially better value for money. This is mainly due to efficiency gains, leading to cost savings.

Other studies have shown promising results using group-based interventions in achieving significant health benefits at a very low cost, compared to individual counselling^{61,62}. In a community programme developed in the USA, intensive lifestyle modification based on group sessions led by professional lifestyle coaches on topics such as food consumption and physical activity, participants managed to achieve similar weight loss (5% of body weight) as with the Diabetes Prevention Program. In this program the average delivery cost was ID 400⁶².

Another study delivered a local diabetes prevention programme led by community health workers in a group setting. With similar objectives to the Diabetes Prevention Program, this programme participants lost 4% of body weight compared to usual care. The programme costs were ID 708 per person, and results suggest savings of ID 1600 per participant, when analysed from a societal perspective⁶¹.

As previously demonstrated, the effectiveness of lifestyle modification programmes is dependent on identifying the right individuals to be targeted. Thus it is important to identify which screening methods are most effective. One of the studies included in this report's analysis looked at the effectiveness of four different screening strategies followed by intense lifestyle modification in an Australian prevention programme⁶³. In three of the strategies, a non-invasive Diabetes Risk Score, AUSDRISK was used, followed by a fasting blood glucose test, while the other study focused on blood testing only.

The AUSDRISK is the Australian type 2 diabetes risk assessment tool, which consists of ten questions to help individuals assess their risk of developing type 2 diabetes over the next five years.

Within the three strategies that included the risk assessment tool, the variations were whether the threshold of high risk should be set at a 5-year risk (derived from AUSDRISK) of developing type 2 diabetes of 2.5%, 5.5%, or 2.5% followed by a second risk assessment after blood testing.

This study demonstrated that the AUSDRISK Diabetes Risk Score was more cost-effective than using a fasting plasma glucose test alone. This is largely due to the use of resources required to perform blood tests on people with low risk of developing diabetes⁶³. Moreover, performing a second risk assessment after blood testing – this time only those at a risk of 4% or higher are invited to take part in the lifestyle programme – seems to be more cost-effective than enrolling patients in lifestyle modification right after fasting plasma glucose testing (Figure 25).

Figure 25 Cost per case prevented for four screening strategies

Criteria for Prevention Programme Enrolment in AusDiab ⁶³	Cost per case prevented in ID
DRS threshold at 5.5% and FPG below 7.0 mmol/l	10,600
DRS threshold at 2.5% and FPG between 5.6 and 6.9 mmol/l	10,580
DRS threshold at 2.5% and FPG below 7.0 mmol/l invited for second AUSDRISK, if DRS higher than 4%	9,560
No AUSDRISK, and if FPG between 5.7 and 6.9 mmol/l	12,220

A number of the interventions analysed the effectiveness of medication, as support for a weight-loss diet, to prevent the onset of type 2 diabetes. The medications studied were licenced type 2 diabetes therapies that are often prescribed, off-label, to prevent the onset of diabetes in individuals at high risk. All of these medications are now off patent and are potentially available as low-cost generic drugs. Thus further analysis should be conducted in order to assess the cost-effectiveness of such therapies based on current pricing.

One of the initial objectives of this report was to identify evidence on the most effective practices from a public health perspective. One of the public health measures regularly proposed is the implementation of taxes on unhealthy foods, particularly on sugar-sweetened beverages (SSB). Despite the increasing efforts in this field, only seven such interventions were identified for

this analysis. The most cost-effective of these seven was a modelling study conducted in the USA that estimated that more than 100,000 diabetes person-years, and 20,000 CVD deaths could be saved through a taxation on SSB⁵². A recent study that analysed the potential impact of a tax imposed on SSB in Mexico in 2014, suggested it will lead to a reduction of 189,000 cases of type 2 diabetes, 20,000 fewer strokes, and 19,000 fewer deaths, while also saving USD 983 million⁶⁴. Other countries, such as Denmark, Finland, France, Hungary, and the UK have also adopted similar policies. In a report published by the World Health Organization Regional Office for Europe, such policies have shown to be feasible, and can influence consumption and purchasing patterns with a significant impact on dietary and health-related behaviour⁶⁵.

Public health policies should not be restricted to price-related measures alone. Other measures to create healthy food environments include: promotion of healthy diets in schools and kindergartens; prominent food labelling; and improvements in the regulation of marketing of foods⁶⁶.

As described in the results section, there were nine interventions that focused on physical activity programs. These interventions varied from community-based programmes aiming to promote more active lifestyles^{54,67}, to the construction of public infrastructures⁵³. From a public health perspective, policies that seek to promote the use of public transportation reduce the car traffic inside cities, and increase walkability should be tested, and evaluation conducted in order to assess the most effective strategies to tackle the diabetes epidemic⁶⁸.

Conclusion



Conclusion

Comprehensive lifestyle programmes for people with impaired glucose tolerance and/or impaired fasting glucose, are cost-effective from a health system perspective, and potentially cost-saving from a whole societal perspective^{39,47}

Local adaptations of comprehensive lifestyle programmes are good alternatives for lower-resource settings, as they can reduce overall costs of programme provision, while still ensuring clinical effectiveness. Such adaptations may include optimising the number of activities and implementing group sessions rather than individual-level interventions^{55,61}

Metformin is an inexpensive drug for the management of type 2 diabetes, and can provide sustainable health gains. It could be considered as a cost-effective strategy for type 2 diabetes prevention, alongside comprehensive lifestyle programmes³⁹.

Public health measures to promote healthier diets, such as a tax on sugar sweetened beverages, show promising results regarding cost-effectiveness for primary preventions of type 2 diabetes⁵².

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