



STORIES OF PROGRESS:

DIABETES

Improving quality of life through management of a complex disease

TRANSFORMING LIVES

PRESENT DAY...

HARU'S LIFE WITH DIABETES

Haru lives comfortably with type 2 diabetes and manages his condition through an insulin pump and medication to control blood glucose.

*FORTY YEARS AGO...*

In 1978, Haru's condition would have meant more complicated treatment. He would have used traditional syringes and animal insulin, without a mechanism for monitoring blood glucose levels himself.

IN THE FUTURE...

Haru hopes that people with diabetes will access cell treatment to restore the normal pancreas function. He wants to ensure his children have a healthier, lower risk lifestyle and can prevent diabetes with physical exercise and good nutrition.

One in 11 adults have diabetes, which represents 425 million patients globally. Together with cardiovascular diseases, cancers and chronic respiratory diseases, diabetes is one of the world's four major NCDs, and one of the only chronic diseases that continues to increase in prevalence. It refers to a group of disorders whereby the body is unable to regulate blood sugar. It is a lifelong illness that requires complex, delicate management of glycemic control and targeted prevention of long-term complications.

Today, diabetes is categorized as Type 1 or Type 2. Patients with Type 1 diabetes (often called insulin-dependent diabetes) are unable to produce insulin in the pancreas due to an auto-immune disease. Patients with Type 2 diabetes (often called adult-onset diabetes), have lost their ability to produce insulin and often develop the disease in adulthood as a result of excessive body weight and insufficient exercise.

Type 2 diabetes has been distinguished from Type 1 since the 1970s. Rates of Type 2 diabetes have risen rapidly, driven largely by lifestyle factors including growing obesity rates. Because sophisticated laboratory tests are required to distinguish between Type 1 and Type 2 diabetes, separate global estimates of diabetes are challenging, but estimates suggest that Type 2 diabetes accounts for 90-95% of cases worldwide. Although Type 1 diabetes is not preventable, patients can avoid complications through proper diagnosis and treatment to regulate blood sugar. In contrast, Type 2 diabetes can be prevented and reversed through targeted lifestyle interventions.

Poorly managed diabetes can lead to serious complications for patients, including heart attack, stroke, blindness, amputation, kidney failure - and early death. Patients with weak or compromised immune systems as a result of diabetes are three times higher risk of developing TB. By some estimates, only about 6% of patients will live free of diabetes-related complications.

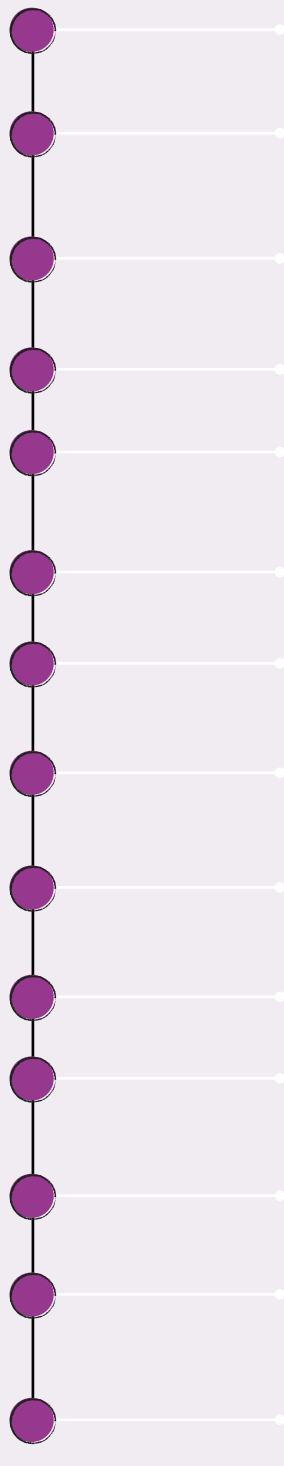
Since 1980, age-standardized diabetes prevalence has more than doubled in men and increased by 60% in women worldwide with millions dying from diabetes or higher-than-optimal blood glucose. The global economic burden of diabetes and its associated complications was estimated to be USD 1.3 trillion in 2015, or 1.8% of gross domestic product. Two thirds of these costs were direct medical costs (USD 857 billion) and one third were indirect costs, such as lost productivity. Diabetes, therefore, is not only a worldwide health issue because of its effect on mortality, morbidity, and quality of life, it also has a significant impact on national economies. With global diabetes rates on the rise, the economic burden is expected to increase USD 2.2 trillion by the year 2030.

Rates of diabetes are growing in LMICs, with nearly 80% of people with diabetes living there. Improving economic status and associated rise in poor diets and lack of exercise, drives the incidences of diabetes to unprecedentedly high levels and creates a mounting health challenge.

Patients can now live with diabetes and manage its symptoms, but not everyone is diagnosed and treated.



KEY MILESTONES

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- 1973:** Invention of the first wearable insulin infusion pump.
 - 1978:** Synthetic 'human' insulin is produced using recombinant DNA techniques, the first human protein to be manufactured through biotechnology.
 - 1982:** Regulatory and marketing approval for human insulin, was granted in the UK and the US, made possible through cooperative efforts between physicians and scientists working in research institutions, universities, hospitals, and the pharmaceutical industry.
 - 1985:** Launch of the first manufactured insulin pen.
 - 1989:** St Vincent Declaration: WHO and International Diabetes Federation effort for multi-stakeholder agreement on goals for the care of people with diabetes.
 - 1990s:** Development of multiple anti-diabetic medicines to improve blood glucose control, including oral antidiabetic agents such as Alpha-glucosidase inhibitor, meglitinides and thiazolidinediones.
 - 2000:** Insulin glargine, a first long-acting human recombinant insulin, is launched.
 - 2002:** World Diabetes Foundation founded, a leading funding mechanism dedicated to preventing and treating diabetes in developing countries, which has provided USD 137 million in funding to date.
 - 2005:** The approval of the first GLP-1 receptor agonist therapy, exenatide, which lowers blood sugar in Type 2 diabetics.
 - 2011:** WHO issues new guidelines recommending HbA1C as a diabetes screening tool which offers greater stability by monitoring glucose levels over several months.
 - 2012:** The first SGLT-2 inhibitor, dapagliflozin, is approved, which reduces blood sugar and demonstrates cardiovascular benefits.
 - 2013:** University of Cambridge develops an artificial pancreas that pairs the technology of an insulin pump with a continuous glucose monitor.
 - 2014:** Inhalable insulin is approved by the FDA, facilitating fast-acting pre-measured insulin.
 - 2015:** Launch of the SDGs, including the target to reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being by 2030.

50 YEARS OF INNOVATION TO IMPROVE DISEASE MANAGEMENT

THE THERAPIES THAT HAVE BEEN DEVELOPED OVER THE LAST COUPLE OF DECADES FOR THE TREATMENT OF DIABETES...THE PROGRESS HAS BEEN TERRIFIC. THERE HAVE BEEN MAJOR CHANGES IN THE KINDS OF INSULIN THAT ONE CAN TAKE, IN TERMS OF HOW QUICKLY THEY MAY ACT OR INSULIN THAT LASTS FOR A WHOLE DAY TO GIVE 24 HOUR COVERAGE.

William Chin,
Chief Medical Officer, Frequency
Therapeutics

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The quality of life of people with diabetes has changed considerably since 1968 thanks to evolution in types of insulin, mechanisms for delivering it, as well as tools to monitor and more accurately control blood glucose levels. Since the development of synthetic human insulin as the primary treatment for diabetes, innovation has made insulin easier to use, faster acting, and longer lasting. Treatment has transformed diabetes into a disease that patients can live with. Side effects and long-term complications have been reduced, and the choice of treatments for patients expanded. Appropriate treatment, close monitoring and behavioral changes can delay or prevent its progression.

The first insulin pen was introduced in 1985. It improved patient ease of use and adherence. Accuracy of treatment led to reduced diabetes care costs, compared with using a vial and syringe. Pens can now record the date, time, and amount of previous doses so that patients and healthcare providers can see exactly how much insulin the patient last took and when. Improvements in insulin pumps have also improved the quality of life of patients. Features include the ability to connect wirelessly to a blood glucose meter or under-the-skin sensors which monitor and regulate insulin semi continuously. A new trend in the design of insulin pumps is the tubing-free patch pump that adheres directly to the skin.

There are currently hundreds of medicines to manage diabetes being developed that could further improve insulin delivery. For instance, researchers are exploring a slow-dissolving molecule which could keep insulin in a patient's body for over two weeks. If successful, it has the potential to replace daily shots altogether. Similarly, a once-a-week natural hormone could effectively regulate blood sugar, as might modulating genes responsible for insulin sensitization. A cream has also been developed.

In addition to insulin, people with diabetes often rely on multiple other anti-diabetic drugs to adequately control blood glucose. Metformin is a popular first-line oral anti-diabetic drug (OAD) developed in the 1920s and understood to treat Type 2 diabetes from the 1970s. However, because diabetes is progressive, first-line treatments like metformin may eventually fail to control sugar levels, meaning second-line, and eventually third or fourth-line therapies may be required. Many new classes of OADs have been developed over the past decades. For example, dipeptidyl peptidase-4 inhibitors (DPP4), first discovered in 1967, lowers sugar levels in novel ways which means it can be used in combination with other medication. The introduction of second-generation sulfonylurea agents, which are more potent than first-generation agents, allowed patients to take smaller and less frequent doses per day. Most recently, the approval of the novel sodium-glucose cotransporter 2 (SGLT-2) inhibitors, have proven to significantly reduce blood sugar and blood pressure while also leading to weight loss and important cardiovascular benefits. There have been advances in injectable drugs also. Glucagon-like peptide-1 (GLP-1) receptor agonists such as exenatide, a synthetic version of a protein found in the saliva of a species of the Gila monster, help to lower blood sugar levels in people with Type 2 diabetes.

The progressive nature of the disease underscores the need for innovative medications with improved efficacy to provide additional therapeutic benefit and lower risks for certain complications in diabetic patients.

Identifying diabetes early is key to effective treatment, and approaches have evolved for earlier and more precise diagnosis for patients. The traditional diagnostic method of testing of blood glucose, a fasting plasma glucose (FPG) test, is a relatively inexpensive ‘finger-prick’ for patients. However, this test fails to diagnose approximately 30% of previously undiagnosed diabetes. The oral glucose tolerance test is more sensitive and substantial, able to detect specific types of prediabetes which FPG cannot. Random plasma glucose tests can be more convenient for patients as they are completed without fasting in advance. Some blood tests can complement basic tests by looking specifically for antibodies, which might be a sign of Type 1 diabetes. In 2011, WHO issued new guidelines recommending a diabetes screening tool that offers greater stability by monitoring glucose levels over several months. Many non-invasive tests have been developed which measure glucose without the need to draw blood, and recently, researchers have attempted to use patient saliva as a non-invasive method test.

COLLABORATIONS TARGET RISK FACTORS

Helping people lead healthy lifestyles is a means to reversing the rise in diabetes. Type 2 diabetes is largely preventable through healthy diet and regular physical activity. Actions to prevent diabetes are most effective before birth and in early childhood.

Sanofi’s Diabetes in Schools partnership in Turkey has been effective at enhancing early diagnosis of Type 1 diabetes in school age children, as well as in raising awareness among children and teachers of childhood obesity and the importance of healthy eating habits in preventing diabetes. IFPMA works with the International Federation of Red Cross and Red Crescent Societies in the promotion of ‘4 Healthy Habits’: healthy eating, moderate consumption of alcohol, physical activity and not smoking.

A focus on prevention, screening, early diagnosis and managing hyperglycemia in pregnancy is critical to reducing maternal, perinatal, and neonatal mortality. Not to mention, preventing diabetes in the next generation. Novo Nordisk’s program Changing Diabetes® in Pregnancy focuses on the link between gestational diabetes and maternal and new-born health through capacity building, screening of pregnant women and awareness-raising. It partners with local health authorities and global partners such as the International Federation of Gynecology and Obstetrics, Women Deliver, and Management Sciences for Jhpiego.

Many partnerships use new technologies to promote healthy behaviors. For example, IFPMA partner with International Telecommunications Union’s Be He@lthy Be Mobile initiative on the mDiabetes program which uses SMS technology to promote prevention and control of diabetes. The program has reached 8.5 million people in India, over 200,000 people in Egypt and over 150,000 people in Senegal, with

quantitative evaluation of the program demonstrating a positive influence on the intervention group.

Urbanization is also a lens for addressing diabetes risk factors. The Cities Changing Diabetes program launched in 2014 by three global partners (Steno Diabetes Centre Copenhagen, University College London, and Novo Nordisk) accelerates the global fight against urban diabetes. Today, the program features local partnerships in 10 cities to address the social factors and cultural determinants that can increase vulnerability of Type 2 diabetes among certain people living in cities.

BETTER HEALTH SYSTEMS KEY TO IMPROVED DIAGNOSIS AND CARE

KEEPING UP WITH SUCH PROGRAMS ENABLES US AS UPCOMING PHYSICIANS TO BE ABLE TO TREAT OUR PATIENTS ACCORDING TO THE MOST RECENT DEVELOPMENTS. ”

Cheryl Tikolo,
medical student on the Merck
Capacity Advancement Programme

Improved health infrastructure enables awareness raising, early diagnosis and better care management. Nearly one in two people that have diabetes are undiagnosed. In many cases, they are unaware they have the disease, which can result in complications and early death.

Trained health care workers and sophisticated laboratory tests are usually required to diagnose and manage the disease. Education is crucial to creating a health workforce which can effectively care for patients with diabetes. The Capacity Advancement Programme, led by Merck KGaA in partnership with ministries of health, universities, and local diabetes associations across five African countries, focuses on strengthening health systems to enable more effective prevention, diagnosis, and management of diabetes. The program expects to have trained over 50,000 by the end of 2018. Students are equipped with understanding of the most recent advancements in diabetes, allowing patients to benefit from the latest knowledge and techniques.

The growth of Type 2 diabetes in poor regions can only be tackled by context-specific interventions. Eli Lilly and Company, through the Lilly Global Health Partnership, specifically tackles rising diabetes in countries of Brazil, China, India, Mexico, South Africa, and the US. The partnership works with governments and local partners to bring care closer to primary level and improve health outcomes by tackling key pain points in the cascade of care, with the ultimate ambition of increasing early detection, intervention, and treatment.

Targeting serious and specific diabetes-related risks is also where industry and others are active. For instance, one frequently encountered complication of diabetes is neuropathy, particularly affecting the feet. Sanofi works to prevent diabetes amputations through early intervention strategies as part of its Diabetes Africa Foot Initiative.

In Type 2 diabetes, prevention, early detection, early control, and early access to the right interventions can deliver significant improvements in patient outcomes. AstraZeneca takes a unique look at youth and primary prevention. 70% of premature deaths from the most common non-communicable diseases, of which diabetes is one, can be linked to risk behaviors that started in youth. Through its Young Health Programme, AstraZeneca has reached more than 2.25 million youth with health

information on the importance of physical activity, healthy eating and avoiding tobacco use.

The lack of access to affordable insulin also remains a key impediment to successful treatment and management. Novo Nordisk's Access to Insulin Commitment since 2001 (updated in 2017) means the company supplies human insulin in least developed countries and other low-income countries at a price that does not exceed 20% of the average realized price for Europe, the US, Canada, and Japan. Others, such as Novartis through Novartis Access – also commit to differential pricing in LMICs to widen the availability of treatments.

Affordably priced insulin and generic treatment often does not reach patients in LMICs due to lack of healthcare financing, weak supply chains, and health care infrastructure. Ultimately, reducing rates of diabetes and reaching patients with care will rely upon improved health systems and infrastructure.

FUTURE FOCUS ON DISEASE MANAGEMENT AND TENTATIVE STEPS TOWARDS A CURE

The WHO projects that diabetes will be the seventh leading cause of death in 2030, with an expected increase of 205 million additional cases by 2035 if appropriate action is not taken. Huge strides have been made in managing the disease and improving quality of life. The ultimate goal of all efforts must be to improve outcomes of patients through vaccines and ultimately, a cure.

Research into the development of an artificial pancreas brings the world one step closer to a developing a cure. The University of Cambridge developed an artificial pancreas in 2013 that pairs the technology of an insulin pump with a continuous glucose monitor. Described as 'a bridge to a cure', it delivers both insulin and glucagon every five minutes as required, connecting via Bluetooth to a smartphone app to calculate the required doses needed.

R&D has also been strongly focused on cell therapy, injecting or inserting living cells into a patient to take over the function of the faulty cells. This brings the hope of potentially restoring the normal function of the pancreas, reducing the need for insulin therapy to only the most severe cases.

Preventing Type 1 diabetes is another area of interest, specifically immunotherapy. A patient's own immune system can be re-educated not to attack beta cells, potentially delaying the clinical onset of the disease.