

# FT Health

## Combating Diabetes

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# Unhealthy developments as burden of disease shifts

With poor medical provision and no visible signs of a cure, World Diabetes Day today offers scant cause for celebration, writes *Andrew Jack*

Barbara Young tuts as she points to a chart on her wall showing recent disease trends for four of the UK's most important diseases. Three – for heart attacks, stroke and cancer – are stabilising or dropping. The final one – for diabetes – continues to rise inexorably.

"Diabetes is the biggest cause of stroke, heart attack, blindness, amputation and kidney problems but the government is not taking it seriously enough," says Baroness Young, chief executive of Diabetes UK, the British charity.

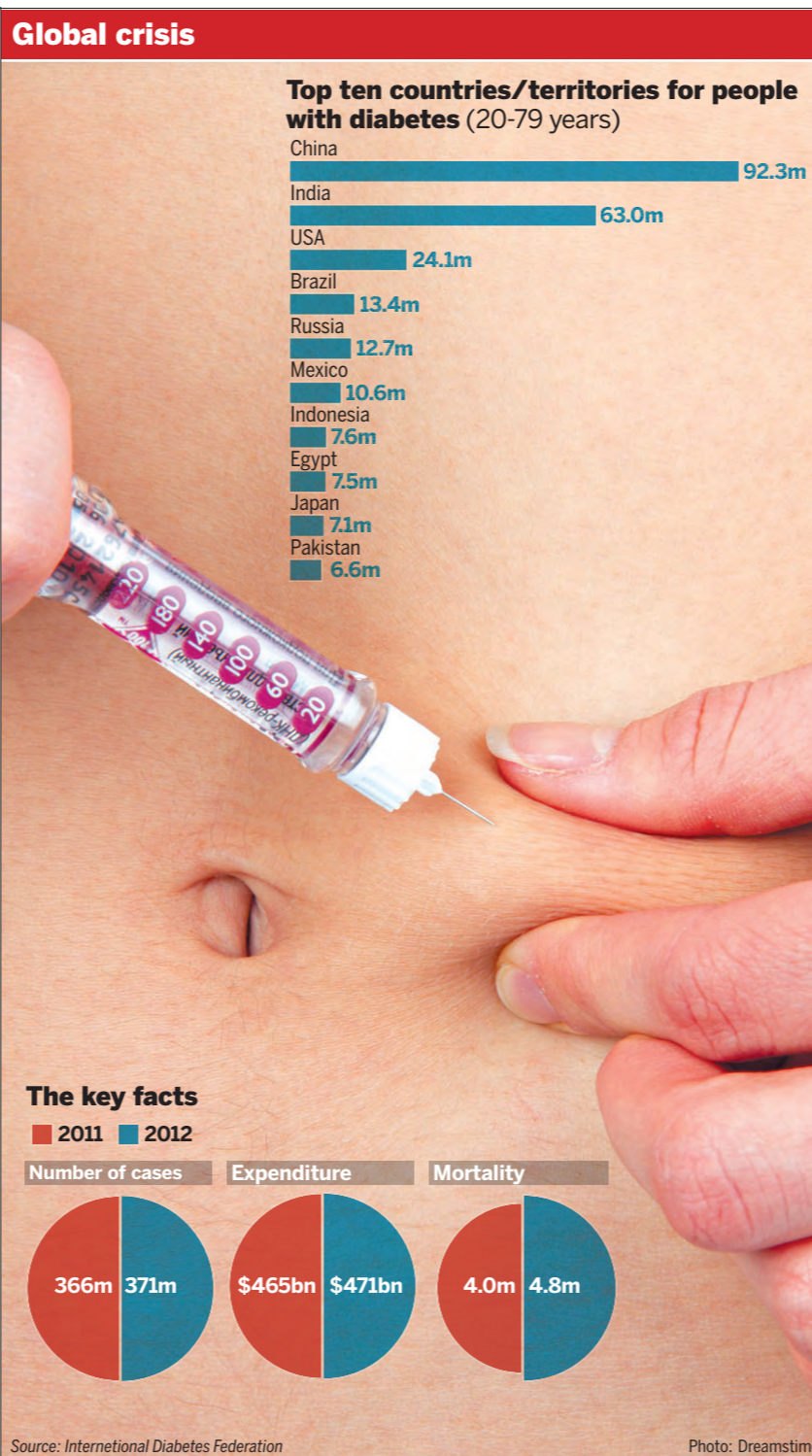
Her views are widely shared. The global trend for diabetes – a condition that means the body does not produce any (type 1) or sufficient (type 2) insulin adequately to control glucose levels in the body – is on the up, with few signs anywhere of a reversal. The situation is much improved on

90 years ago, when life-saving insulin was first developed for treatment. There are fresh signs of interest from policy makers, including the pioneering United Nations' resolution on non-communicable diseases issued last year, which targets the lifestyle factors behind type 2 diabetes.

But provision of and compliance with medicines are poor. There are no visible signs of a cure, diagnosis and supportive care is inadequate and efforts to prevent the onset of the condition remain in their infancy.

The latest estimate today – World Diabetes Day – from the International Diabetes Federation, an umbrella body for diabetes associations, suggests around 371m people now have the condition globally and nearly 5m will die from its complications each year.

In richer countries such as the US, the trend has long been recognised.



Yet the burden is shifting ever more into the developing nations, from the US's middle-income neighbour Mexico to some of the poorest African countries. Four-fifths of those with diabetes live in low and middle income countries.

"There is a strong correlation with economic growth and a change in lifestyle," says Jesper Høiland, head of international operations at Novo Nordisk, the Danish pharmaceutical group that is one of the world's largest producers of insulin and other diabetes products.

During his business travels, he says he was particularly shocked on a recent trip to a city in Indonesia, where he saw both a two-storey drive-through takeaway and a six-storey McDonald's fast food outlet. "Urban life is a big game-changer. People move from the fields to a sedentary

'There is a strong correlation with economic growth and a change in lifestyle'

job at a desk and fast food is seen as part of this lifestyle."

Some highlight the importance of genetic factors, with south Asians particularly vulnerable to diabetes. With body fat deposited internally, they are at risk with a much lower and less visible body-mass index than in the west.

Smaller family size and higher expectations for educational performance, spiralling urbanisation with more limited safe and attractive open space, less free time and greater heat may all be driving adults and their children to spend more time passively indoors, and eating unhealthy food.

In many regions, notably Africa, diabetes and other non-communicable diseases go undiagnosed, adding to the "double burden" with infectious illnesses from which they have long suffered. The fact they are now living

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## Sharing the burden of NCDs

Diabetes is devastating, debilitating and on the rise: by 2030, the number of people with diabetes worldwide is projected to reach 472 million<sup>1</sup>, most of whom will lack adequate healthcare. But the fight is far from over – and Lilly is playing its part.

Non-communicable diseases (NCDs), such as diabetes, cancer and heart disease, are the number one cause of premature death worldwide<sup>2</sup>. In 2008, they together killed a staggering 36 million people<sup>3</sup>, and in low- to middle-income countries they account for nearly 80 percent of all deaths<sup>4</sup>. Yet spending on NCDs accounts for less than three percent of all global health assistance in developing nations<sup>5</sup>.

As a pharmaceutical company driven by innovation, Lilly is committed to help. In late 2011, it launched the Lilly NCD Partnership to tackle the threat of NCDs in some of the world's most vulnerable communities. The initial focus is diabetes, and the Partnership aims to have a positive impact in three high-prevalence countries: India, Mexico and South Africa. There are also plans to extend the project to Brazil by early 2013.

The Lilly NCD Partnership was founded with an investment of US\$ 30 million over five years – a not-insubstantial sum, but a fraction of what is required to combat NCDs in developing countries. That's why Lilly's approach is different: the Lilly NCD Partnership aims to catalyse effective, replicable, and sustainable responses through collaborative, partner-based efforts.

The initiative is structured around three pillars: research, report, and advocate. The research will first investigate innovative new ways of tackling diabetes, and measure whether the programmes improve patient outcomes. The results will then be reported to a wide audience, including governments and healthcare organisations. Where a project has demonstrated clear benefits, the Lilly NCD Partnership will advocate for it to be replicated in other areas.

the *Lilly*  
**NCD**  
partnership

### India

India has an extraordinarily high incidence rate of diabetes, with an estimated 61 million people living with the disease<sup>6</sup>. Unchecked, this figure is projected to grow to more than 100 million by 2030<sup>7</sup>. Yet there are low levels of diabetes awareness and healthcare services are under intense pressure to adapt quickly in order to meet these growing needs. Additionally, due to the high cost of treatment and a lack of patient knowledge, adherence to treatment programmes is generally low.

To address this, the Lilly NCD Partnership is working with Public Health Foundation of India, Population Services International, and Project HOPE. The effort aims to reach 400,000 people in two locations: Sonapat, near Delhi; and Vizag, on the east coast. The project includes awareness activities, healthcare provider training, and interventions to insure people maintain their treatment regimens.

### South Africa

An estimated 14.7 million people suffer from diabetes in sub-Saharan Africa<sup>8</sup>, at least 78 percent of whom are yet to formally diagnosed<sup>9</sup>. The International Diabetes Federation calculates the number of people with diabetes could almost double by 2030<sup>10</sup>. In South Africa, the problem is exacerbated by the fact that the vast majority of the population rely on a public health system already stretched in its response to an array of health challenges, including tuberculosis and HIV.

As in India, the Lilly NCD Partnership is working with Project HOPE in South Africa to run a diabetes awareness, training and care programme, which operates from the newly-opened HOPE Centre in central Johannesburg. It also works closely with the Donald Woods Foundation in the rural Mbashe region to combine diabetes diagnosis and referral with an existing programme of home-based care for HIV and TB patients in remote and poorly serviced areas.

### Mexico

Diabetes is also a major killer in Mexico, causing 67,000 deaths in 2007<sup>11</sup>. Without taking significant steps to combat the disease, the prevalence of diabetes is projected to climb from fewer than four million people in 1995 to almost 12 million by 2025<sup>12</sup>. The nation's problems are compounded by treatment costs that rose by 26 percent during 2003-05<sup>13</sup>.

The Carlos Slim Health Institute is already working to improve the situation through Casalud, a comprehensive programme to improve diagnosis and care at the primary care level. The Lilly NCD Partnership is now collaborating with the Institute to demonstrate Casalud's effectiveness – firstly, it will help create a process manual to allow the Casalud model to be precisely replicated in other clinics. Secondly, an evaluator will assess implementation and record its impact. Thirdly, the evaluator will assess the long-term effect over several years, tracking patient outcomes and quality of life.

1 International Diabetes Federation, October 2009 <http://bit.ly/1TihjEE>, 2 NCD Alliance, April 2012 <http://bit.ly/1UdHxh>, 3, 4 World Health Organization, April 2011 <http://bit.ly/1Q42yeL>, 5 Center for Global Development, January 2010 <http://bit.ly/1Y5c5E>, 6, 7 Times of India, December 2011 <http://bit.ly/1PCTRIa>, 8, 9, 10 IDF Diabetes Atlas Fifth Edition, November 2011 <http://bit.ly/1UgawTu>, 11 Medical News Today, November 2007 <http://bit.ly/1S8TjwS>, 12, 13 Preventing Chronic Disease, January 2005 <http://1.usa.gov/V0KXSN>  
UKDBT01340, November 2012

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## FT Health Combating Diabetes

# Research may find route to repairing the sick pancreas

**Drugs** Although insulin is still the primary tool to control blood sugar, new treatments may delay complications, says *Alan Rapoport*

Diabetes is approaching epidemic proportions in the US, afflicting nearly a tenth of the population at a cost of billions of dollars per year, but growing awareness has been a boon for new research.

Diabetes is an excess of blood sugar, that comes about either because the body does not produce insulin, type 1; or because the body does not respond to the insulin that is produced, type 2. Researchers and drug companies are investing heavily in developing new treatments for both type 1 and type 2 diabetes, in the hope of slowing the disease's progression and delaying its debilitating complications.

Insulin, which reduces blood sugar levels, has been a backbone of treatment for both types of diabetes since Canadian researchers first discovered it in the pancreas in the 1920s.

The synthesised hormone is still central to treatment of type 1, but scientists are working on versions more responsive to sugar intake that can be administered less frequently.

Type 2 diabetes has been on the rise in the US as obesity has become a growing problem. Excess body weight and lack of exercise reduce the body's ability to produce insulin.

Novo Nordisk, the Danish drug company, is seeking regulatory approval for a long-acting insulin, which is intended to be effective for 24 hours, rather than the usual 12-hour half-life. The company is awaiting a final

approval from the US Food and Drug Administration but, if given the go-ahead, it is expected to be a blockbuster because of demand for an effective, long-acting insulin treatment.

"You can view insulin treatments as a form of hormone replacement treatment – a physician is creating a drug that the body cannot produce in a sufficient amount," says Alan Moses, chief medical officer at Novo Nordisk.

Generally, for patients with type 2 diabetes, doctors first prescribe lifestyle modifications such as diet and exercise to help reduce blood sugar levels, which spike after intake of carbohydrates or sugary foods. Secondary treatments include medications such as metformin or glyburide.

Metformin works by decreasing the amount of glucose the body produces and increasing its response to the insulin made by the pancreas, while glyburide boosts insulin production in the pancreas.

Drug companies are also studying the potential of medicines such as dapagliflozin, which lowers glucose levels by causing sugar to be excreted through urine. However, concerns exist about possible side-effects, such as bladder cancer.

Dr Moses says researchers are studying the relationship between obesity and diabetes, particularly looking at obese people who do not develop the disease to see what genetic characteristics they may have that protect them from its onset.



**Reducing pill: Metformin cuts the body's glucose production** Alamy

Because of the link between obesity and diabetes, doctors have been encouraged by the recent approval of Qsymia, a new diet drug that could be helpful for diabetics or pre-diabetics attempting to control their weight.

For patients with type 1 diabetes, insulin remains the primary treatment, because the pancreas is unable to produce it on its own.

However, Denise Faustman, director of the Immunobiology Laboratory at the Massachusetts General Hospital and an associate professor at Harvard, is working on a drug that could potentially reverse type 1 diabetes.

She is testing a generic vaccine that was used to prevent tuberculosis and has been shown in early trials to restore insulin production in type 1 diabetics by killing the cells that destroy the pancreas and increasing regulatory "T" cell levels.

"The goal is to get rid of bad white blood cells and see if the pancreas can

kick in on its own accord," says Dr Faustman.

Diabetes experts lament that many of the treatments for the disease have negative side-effects such as weight gain – which can be counterproductive – or heart and liver problems.

In spite of those concerns, studies by the US Centers for Disease Control found this year that the incidence of heart disease, strokes and lower limb amputations related to diabetes have all declined in recent years as treatments for diabetes and its common side effects have improved.

Ann Albright, director of CDC's Division of Diabetes Translation, says: "Taking care of your heart through healthy lifestyle choices is making a difference, but Americans continue to die from a disease that can be prevented. Although the cardiovascular disease death rate for people with diabetes has dropped, it is still twice as high as for adults without diabetes."

# Testing times in race to identify sufferers

## Diagnostics

The technology is improving but misconceptions are the big problem, says *Denise Roland*

Diagnosing a disease before serious symptoms become evident may sound a tall order. But health leaders are being asked to do just that, in a call to action from the International Diabetes Federation that says for every diabetic aware of their condition, another is undiagnosed.

Type two diabetes goes undetected for an average of 10 years in the UK. The disease's insidious progression means one or more of its serious complications – such as sight loss, heart disease and kidney disease – has already developed by the time of diagnosis.

Diabetes of all types is indicated by high blood sugar, a sign that the digestive hormone insulin is not working effectively.

But defining diabetes is not straightforward. Blood sugar levels vary on a sliding scale, leaving experts with the task of setting the cut-off point for diagnosis.

They face the challenge of including all those whose blood sugar is high enough to cause harm while not casting the net so wide that people suffer the stress and social stigma of a diagnosis when the benefits of treatment are not clear.

The World Health Organisation's blood sugar criteria are widely accepted, but no single test successfully identifies all cases, nor do any completely avoid false positives. Doctors minimise the risk of misdiagnosis by repeating tests or using two different methods.

The cheapest technique is measuring blood sugar after an eight-hour fast, but this approach alone is thought to miss around 30 per cent of people with diabetes.

An alternative is reading blood sugar two hours after a fixed intake of glucose. This may pick up cases of diabetes missed by the fasting test, but is less popular due to its higher cost and heavy time demands.

These two techniques were the standard approach for decades, but recently a newly approved method has become the procedure of choice. The HbA1c test, which uses the presence of an unusual form of the blood protein haemoglobin as an indicator of blood sugar levels, requires no preparation from patients, and allows doctors to test opportunistically.

Simon O'Neill, director of care, information and advocacy at charity Diabetes UK says: "Although HbA1c is not significantly better at diagnosing diabetes than the traditional blood tests, it is hugely more convenient, so the hope is that it will identify more cases because more people will be willing to be tested."

The HbA1c test's widespread adoption in the developed world cannot be emulated in many developing nations, however, due to its higher costs and unre-

liability in patients with conditions including malaria.

But misconceptions about diabetes, rather than the shortcomings of the tests, are largely the reason for such a high rate of under-diagnosis. A relaxed attitude towards the disease, even from within the medical profession, leaves people untested and unaware of their serious condition.

Mr O'Neill says: "There's a general belief about type two diabetes that it's a milder form than type one, fixed by simply not having sugar in your tea."

The challenge, he says, is both getting people at risk to approach a doctor, and convincing physicians that it is worth testing patients.

The potential to prevent millions of cases of diabetes when one in every 10 adults worldwide is predicted to have the disease by 2030 provides the drive for screening programmes such as the NHS Health Check initiative, which aims to identify all those at risk of lifestyle diseases.

And while the execution of this programme has been inconsistent, global discrepancies for diagnosis are starker still.

Eighty per cent of cases occur in low and middle-income countries, thanks to increasingly western lifestyles and a greater genetic propensity for the condition among some ethnicities.

Deaths due to diabetes compare to numbers killed by Aids, malaria and tuberculosis combined

## Post-marketing trials Debate simmers on usefulness of research after approval has been granted

It used to be that when a regulator requested more studies after initially approving an experimental drug, companies were reluctant to comply. But when it comes to new types of insulin, some seem all too keen to go far beyond what is required.

In an article in the British Medical Journal over the summer, Edwin Gale, emeritus professor of diabetic medicine at the University of Bristol, identified nearly 400,000 people who had been recruited for "post-marketing" trials of insulin analogues around the world in recent years. "The scientific value of such data might be doubtful, but the commercial rationale is good," he wrote.

Most clinical trials take place

before approval, designed to test safety and efficacy. But the trend today among regulators is to demand ever more "Phase 4" testing of medicines, and sometimes even to grant only a "conditional approval" with a requirement for subsequent data after launch to determine whether it should stay on the market.

When conducted well, such research can provide valuable additional information on safety and efficacy that extends far beyond the data derived from the small numbers of carefully selected patients in the idealised conditions of short-term closely-monitored trials.

Yet Prof Gale argues that the post-marketing "observational" trials

he examined were of limited value, with no "control arm" of cheaper insulins against which to compare the costlier new products, and a "deficit of data" collected over relatively short periods using unnecessarily large numbers of diabetics, notably in developing countries.

What they did provide was a way for the companies concerned to potentially influence recommendations of doctors (who are paid a fee) and the treatments of patients, with the potential that those introduced to the products studied remained on them once the research came to an end.

Philip Home, professor of diabetes medicine at Newcastle University and head of the global

advisory board for Alcheive, one such study in nearly 67,000 patients and funded by Novo Nordisk of Denmark, a diabetes specialist, defends the research.

"The findings were very useful," he says. "We found very good improvements in blood glucose control could be achieved everywhere. The quality of data in observational studies is undoubtedly below that in randomised clinical trials. It would be a very odd world if on occasion it didn't happen that a prescriber prescribed an inappropriate insulin."

"The world is not perfect. But we do have to do studies to decide whether agents are effective in different environments." Jesper Hoiland, Novo Nordisk's

head of international operations, argues that the data were useful and that the study was approved by ethics committees in every country where it was conducted.

"It's interesting that while academics can sit in Europe and decide what's right or wrong for Brazil," he says. "Does the western world know much better?"

Nevertheless, some European politicians are now calling for tougher rules akin to US legislation designed to avoid so-called "seeding studies" viewed as linked more to commerce than science.

Post-marketing research may be on the rise, but it will also come under much more scrutiny ahead.

Andrew Jack

# Apps hold promise to improve care and cut costs

## Remote monitoring

The ubiquity of mobile phones can be used for health, says *Sarah Murray*

For diabetes sufferers, mobile apps and electronic monitoring devices can help control the disease and manage lifestyle changes that create improvements in their condition. But while mobile devices are ubiquitous, the question is how to get more people to use them to manage diabetes and prevent pre-diabetes from developing into the full-blown disease.

The technology available for monitoring blood sugar levels has moved far ahead from the days when the system was to use finger sticks, a test strip, a pad of paper and a pen.

"The tools are much better," says Harry Greenspun, senior adviser for health-care transformation and technology at the Deloitte Centre for Health Solutions. "The technology has improved progressively." Diabetes monitoring technology is increasingly available via mobile phones. For

example, the iBGStar connects to iPhones and iPods. Designed and developed by AgaMatrix, a diabetes product maker, and commercialised by Sanofi, a healthcare company, the device displays results, analyses glucose patterns and offers graphs and statistics to help users track their disease.

The benefit of combining monitoring with mobile phones and apps is that it uses familiar and increasingly ubiquitous technology. In the US, 85 per cent of adults now have a cell phone, of which half are smart phones, according to new data from the Pew Research Centre's Internet & American Life Project.

Susannah Fox, an associate director of the project, says: "Those smart phones are capable of going online and running sophisticated apps. Which is just the sort of thing people are developing in the hope that patients will use them."

Devices also allow data to be transferred to health-care professionals. Wireless-enabled glucose meters automatically upload blood glucose levels to a database that can be accessed online. Even so, the new research from the Pew Research Cen-

tre suggests technology is not playing a huge role in helping people track their health. While 60 per cent of those polled said they kept track of their weight, diet and exercise, few were using technology to do so.

When asked about the most important indicator they tracked, half said they did it in their heads, a third said they used paper and a smaller group used software, a website, an app or a medical device such as a glucose meter.

Ms Fox says: "Technology still plays only a small supporting role when it comes to self-tracking health indicators."

This could change as more apps and devices come on to the market, and as diabetes sufferers are increasingly individuals for whom technology is an integral part of daily life. The challenge then will be what to do with patient-reported information. As the volume of data reaching healthcare professionals increases, so will the room for error.

"For any test, there are 50 ways you can have erroneous data," says Mr Greenspun. "It can be done improperly, it can be done at the wrong time or it can

be miscalibrated. And there are examples of people having other people take their tests for them."

Nevertheless, if doctors can manage their patients' conditions remotely, substantial cost savings can be made.

Shifts in the economics of healthcare delivery will support these savings, since payments to providers increasingly reward improved patient health, rather than numbers of hospital visits or medical interventions.

For policy makers, technology and remote monitoring offers broader benefits. With greater volumes of patient-reported data gathered, analytics tools could be used on diabetes levels across national populations, allowing for more informed policy decisions.

Technology can also support individuals in making the kinds of lifestyle changes needed to improve their condition.

In a 2011 trial, patients with type 2 received coaching via a mobile app developed by WellDoc, a technology-focused healthcare provider. Meanwhile, patients and their primary care providers had access to web portals.



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## FT Health Combating Diabetes



Workers on the insulin production line at a factory in Russia

Science Photo Library

# Deeper inquiry begins to shed light on causes

**Science** While diet and lifestyle affect the prevalence of type 2 diabetes, there are intriguing genetic factors, writes *Clive Cookson*

With diabetes becoming one of the most costly chronic diseases, the scientific effort to understand its fundamental biology and develop better diagnostic tests and treatments is gathering pace.

Rapidly increasing levels of obesity are associated with a worldwide surge in type 2 diabetes. An international study published in the *Lancet*, the medical magazine, last year found 347m adults had the disease, more than twice the number in 1980.

Although diabetes is clearly linked with obesity, it is not clear whether resistance to insulin – the defining characteristic of type 2 – is caused directly by obesity or whether some underlying factor, associated with unhealthy diet and lifestyle, causes obesity and diabetes. Or both.

Whatever the underlying reason, there is evidence that excessive fat cells accumulating in obesity may have a toxic effect on the body's response to insulin, the most important metabolic hormone, at least partly by triggering a damaging inflammatory response.

But, this cannot be the whole story because non-obese people sometimes develop type 2 diabetes too.

High-powered genetic studies, using the latest DNA sequencing technology, are proliferating through medical journals. Most are so-called genome-wide association studies, finding different mutations in people who do and do not have the disease.

These studies are just beginning to shed some light on the causes of type 2 diabetes and are unlikely to lead to treatments any time soon.

Matthew Hobbs, head of research at Diabetes UK, says: "About 60 genes have been linked to type 2 diabetes and there are undoubtedly more to find. There is no consensus on how

the genes interact and how they are affected by the environment.

"I think new drugs for type 2 will come from this research but a lot more work will be needed."

Beyond genetics, one of the most intriguing recent research findings came in an early stage clinical trial at Newcastle University in the UK, which showed that type 2 diabetes could be reversed by an extremely low calorie diet without drugs. Eleven people who cut their food consumption to just 600 calories per day – just above starvation – for two months became completely free of diabetes, and seven of them were still healthy three months after returning to a normal diet.

As usual with this sort of study, it is important to distinguish between correlation and causation

Dr Hobbs says: "We're hoping to fund some follow-up work on calorie-restricted diets, to find out whether they could be provided through the NHS [National Health Service]. We also want to know whether the weight loss on the extreme diet or the calorie restriction itself is having the effect."

Related research is showing that bariatric surgery, which reduces the size of the stomach, can relieve diabetic symptoms.

For example a study of 43 patients in Hyderabad, India, found that 20 of them no longer had type 2 diabetes 20 months after surgery and the other 23 needed smaller doses of medication. It seems that bypassing part of the stomach and gut had a beneficial effect even before the patients lost

weight, perhaps because the operation affected the cellular signalling system.

One of the main themes of metabolic research this year has been growing recognition of the role played by gut bacteria in disease. A healthy adult has about 1.5kg of bacteria in his or her intestine. These microbes normally live in healthy harmony with their host but if the equilibrium is disrupted disease may follow.

A Danish-Chinese collaboration between the University of Copenhagen and the Beijing Genomics Institute examined the intestinal bacteria of 345 people, half of whom had type 2 diabetes. They found clear evidence that diabetes sufferers had a more hostile bacterial environment, with more pathogens than the healthy controls.

But as usual with this sort of study it is important to distinguish between correlation and causation.

Karsten Kristiansen of University of Copenhagen says: "The big question now is whether the changes in gut bacteria can affect the development of type 2 diabetes or whether the changes simply reflect that the person is suffering from type 2 diabetes."

Parallels with other diseases are also important for understanding diabetes. One is cystic fibrosis.

Almost half of CF patients develop diabetes by the age of 30. It seems that the chloride channel protein, which is defective in CF, leads to a failure of insulin-producing cells in the pancreas.

There is also a potential link with Alzheimer's disease, possibly through a common inflammatory mechanism. The Alzheimer's Society is funding a study to see whether diabetes drugs help treat dementia, while Diabetes UK is supporting research from the opposite direction, on the effect of Alzheimer's drugs on diabetes.

### Type 1 diabetes Scientists explore artificial pancreas and islet cell transplants

While the increasing incidence of type 2 diabetes is linked to changing diet and rising levels of obesity, type 1 diabetes is also becoming more common – up by 3 to 5 per cent per year – and here the reasons are much less clear.

In type 1 diabetes the insulin producing cells are destroyed by an autoimmune reaction, usually in childhood or young adulthood. No one knows what is triggering this self-destructive process in more and more people, though in the broadest terms, environmental changes must be responsible because human genetics cannot change so fast.

Viral and/or bacterial infection may be an important factor. The "hygiene hypothesis" holds that, because modern life in advanced industrial societies is so clean compared with the conditions in which humans evolved, infants are not exposed to all the germs and dirt required to prime

the immune system to work well later. Then when the modern child does encounter pathogens, these may set off an autoimmune disease such as diabetes or asthma (which is also far more common than in the pre-industrial world).

Whatever the cause, diabetologists hope that medical engineering, in the form of an artificial pancreas, will help type 1 patients. The artificial pancreas is a device that measures blood glucose levels continuously and transmits the readings to an insulin pump that releases exactly the right amount of hormone into the patient, as and when needed.

Although both monitor and pump work well in patients separately, no one has yet put the two together into a robust and reliable system that patients can use routinely at home. Early clinical trials of artificial pancreas prototypes are, however, giving promising results.

Diabetes UK, for example, is supporting two projects at Cambridge university. One is aimed initially at pregnant women who are at particular risk of birth complications if their insulin and blood sugar levels are poorly controlled.

"The system works better in the lab than a glucose sensor and insulin pump working individually," says Matthew Hobbs, head of research at Diabetes UK. "The next stage is to move it out of the lab or hospital and show how it works when people are leading normal lives."

A more biological approach is to transplant insulin-producing islet cells into patients whose own pancreas has stopped working. This is already carried out successfully on a small scale, using islet cells from deceased organ donors but, since every patient needs the cells from three donors, transplantation is never going to become a routine treatment.

Clive Cookson

## DIABETES INNOVATION AND ADHERENCE

IMPROVES CARE AND REDUCES COSTS

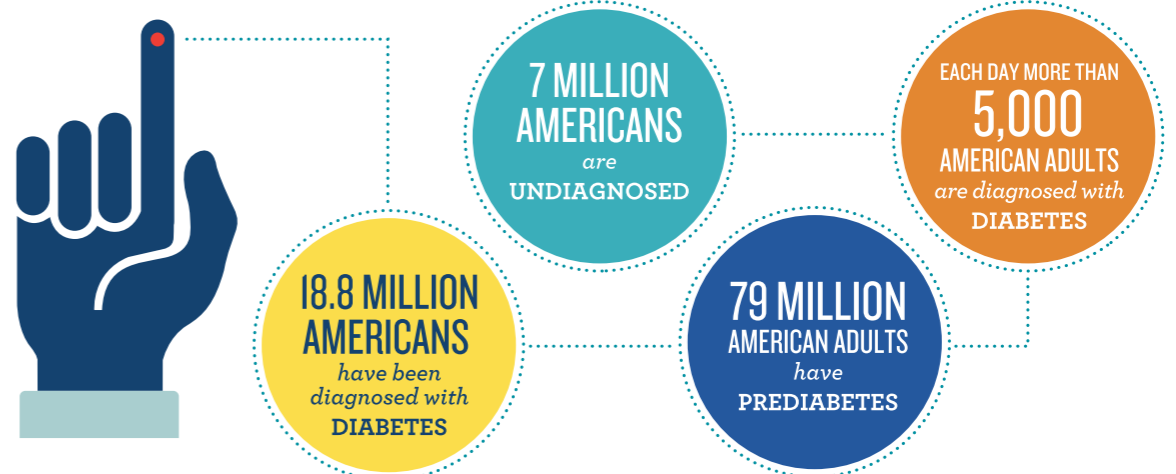
### MEDICINES IN DEVELOPMENT FOR DIABETES

BIOPHARMACEUTICAL RESEARCH COMPANIES ARE DEVELOPING MORE THAN **220 MEDICINES** TO TREAT DIABETES AND RELATED CONDITIONS

INCLUDING **130** FOR TYPE 2 DIABETES



### WHY ARE DIABETES MEDICINES IMPORTANT?



DIABETES AFFECTS NEARLY

**26 MILLION AMERICANS**

ABOUT ONE-QUARTER ARE UNAWARE THEY HAVE THE DISEASE



Uncontrolled diabetes can lead to many complications, including blindness, amputations, kidney failure, heart attacks, and stroke. In addition to the terrible human toll associated with these outcomes, the avoidable costs are enormous.

**NEARLY \$40,000**

The average cost of amputation surgery

**\$83,000**

A single year of dialysis for kidney failure patients

**AVERAGE \$31,000**

A hospital stay following a heart attack

**IN CONTRAST,**  
A YEAR SUPPLY OF THE MEDICINES that can help a patient avoid these outcomes typically runs about

**\$2,400**



### PATHWAYS TO CONTROL THE DISEASE



**CONTROL OF DIABETES IS POSSIBLE TODAY**

WITH THE PROPER TREATMENT PLAN, INCLUDING DIET, EXERCISE AND MEDICATIONS

### ADHERENCE IS KEY TO IMPROVED HEALTH

Patients with diabetes who **DID NOT** consistently take their diabetes medicines as prescribed were



**2.5 TIMES MORE LIKELY TO BE HOSPITALIZED** than those who followed their prescribed treatment regimens

### IMPROVED ADHERENCE TO DIABETES MEDICATION COULD RESULT IN:



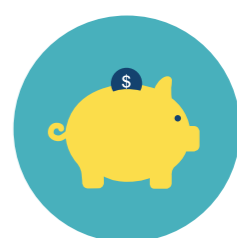
**1,082,000**

fewer emergency department visits



**618,000**

fewer hospitalizations annually



**\$8.3 BILLION**

in potential annual savings

### IMPROVED ADHERENCE AMONG PATIENTS WITH DIABETES OFFERS IMPROVED CARE AND REDUCED COSTS

Key goals for the health care system and policy makers.



## FT Health Combating Diabetes

# Battle to keep lawmakers sweet as sugary drinks targeted

**Food and drink** Nutrition is a battleground between producers, consumer groups and health professionals, writes *Louise Lucas*

Call it the battle of the bulge. Purveyors of sugary snacks, in order to keep selling their goods, are going on the defensive: reducing sugar and curbing marketing to keep policy makers sweet and stave off the threat of heavy-handed regulation.

So far, the strategy is having mixed success. Broadly in the US, the food and drink industry – and the advertising sector that in part lives off it – has managed to fight its corner, seeing off curbs to advertising and other restrictions thanks to heavy-duty lobbying.

But it has not been a home run. Some states have imposed a soda tax on sugary fizzy drinks. More radically, in September New York's board of health voted to approve a proposal made by Michael Bloomberg, New York mayor, that would prohibit restaurants, theatres and stadiums from selling sugary drinks in portions bigger than 16fl oz (475ml).

So incensed was the US beverage industry – among the biggest spenders on lobbying – that they are taking the administration to court in an attempt to block the rule, which is set to be imposed next spring.

While the more stringent curbs on advertising were fought off, in June Walt Disney, the media giant, said it would ban junk food ads on its children's TV programmes and websites by 2015.

In Europe the picture is similarly patchy. Various taxes have been imposed in Denmark, Hungary and France. More still are contemplating following suit as obesity levels escalate.

Denmark's pioneering "fat tax", introduced last year, has met a storm of controversy with opposition parties trying to have it rescinded.

In the UK, industry has opted to work hand-in-hand with government, claiming that co-operation leads to speedier, more efficient efforts.

Critics charge that the UK government's Responsibility Deals – a series of private/public sector arrangements in relation to various issues, including food – have put policymakers in the pockets of private companies who have the marketing muscle and spending clout to fend off draconian legislation.

The big fear for industry is that food becomes the next tobacco and subject to blanket bans on advertising and even packaging.

Which? the UK consumer body that sits on the food network's high level steering group, is among those underwhelmed by the government's approach, arguing that it is too reliant on voluntary deals rather than showing "real leadership".

One year after the Responsibility Deal was launched to help people eat healthily, a Which? survey showed just 28 per cent of people were satisfied that enough action was being taken.

"Despite the membership, the nature of the Deal means that the focus is on drafting pledges that food companies will be willing to sign up to," Which? said. "Issues are dealt with one by one, rather than as part of a more comprehensive strategy that tackles the main barriers to healthier eating."



If there is criticism in the developed world, it rages higher in emerging markets where – like tobacco before them – food and drink companies are accused of taking advantage of laxer laws and lower levels of concern over health.

Rejecting this, companies point to work they do in schools and running exercise clubs. Nestlé, the world's biggest food company by sales, started its Healthy Kids Global Programme in 2009, to "raise nutrition, health and wellness awareness of school-age children around the world".

The programme has not been without its difficulties. Some of the pilot schemes did not meet expectations and were scrapped. Others, especially in Africa, were delayed and the financial crisis was blamed for the removal of a Greek pilot programme.

Less controversially, manufacturers have sought to re-engineer their food and drinks to take out more sugar, calories and salt. This has not always been an unqualified success.

There was an outcry when HP Sauce, a staple condiment with Eng-

lish fried breakfasts, was made with less salt. Campbell Soups was forced into a U-turn last year when low salt soups proved unpopular with the great soup eating public.

Others, however, have managed to keep taste while making their products less unhealthy.

Cereal Partners Worldwide, Nestlé's joint venture with General Mills, has pledged to cut the sugar content of 20 Nestlé breakfast cereal brands popular with children and teenagers to 9g or less per serving by the end of 2015.

According to Nestlé, the changes mean breakfast cereals will have a sugar reduction of up to 30 per cent. Since 2003 it has removed more than 9,000 tonnes of sugar and almost 900 tonnes of salt from its recipes and added more than 3.4bn servings of whole grain.

Mars, the privately owned confectioner, claims to have removed 97 per cent of trans fats between 2002 and 2010. Some 15 per cent of saturated fats were cut from its Mars and Snickers bars in 2010 in Europe, compared with a 22 per cent cut in Australia.

**Supersize she: obesity linked to poor diet and lack of exercise is a factor in the growing incidence of type 2 diabetes**

# Education aims to cure ignorance

India

**Incidence of diabetes is spreading faster than awareness of it, writes Amy Kazmin**

For more than a decade, Yogesh Tyagi, a retired school teacher in New Delhi, has lived with diabetes. He tries to control his diet, especially his sweets intake, and takes exercise to keep the disease in check.

But even though Mr Tyagi's wife, Shashi, has spent years monitoring her husband's food intake, she has not been too conscious about her own eating habits, and how they could affect her long-term health.

"My mum takes care of my father and his diet, but she doesn't manage her diet very well," their 27-year-old daughter, Sakshi, also a teacher, says. "She has no prohibitions and is very fond of sweets."

This month, Sakshi Tyagi led her parents, brother, sister-in-law and their two children to a "mega-diabetes" screening at a Sikh temple in central New Delhi being held as part of a national diabetes awareness campaign.

"I thought it would be a good idea to get my mother and everybody screened," she says. "My family members have the tendency to develop diabetes because of the family history."

Her concerns were well-founded: the blood test showed her mother is a "borderline" diabetic who was advised to be much more careful about her diet to avoid serious health problems in the future.

Health educators also raised concerns about the two children, and their weight, urging them to spend more time playing outdoors.

"The schools give so much homework, they do not have time to play, and then they have TV and video games," says Ms Tyagi.

Along with the rapid economic growth and urbanisation of the past two decades, India is registering a sharp rise in the prevalence of diabetes – the result of diet changes, lack of exercise and sedentary lifestyle changes that have accompanied growing affluence.

According to the International Diabetes Federation, India has the second-highest diabetes burden in the world, with around 63m patients, or 9 per cent of the population (compared with 92.3m or 8.8 per cent for China) and another estimated 4.4m who may be living with the disease but have yet to be formally diagnosed.

Incidence of the disease in big cities is estimated at 12-13 per cent of the urban population.

"Lifestyles in India have become not so healthy," says Prathap Reddy, chairman of the Apollo Hospitals group, a national chain of private hospitals. "We are not eating healthily, we are not doing enough exercise and we have great stress."

But awareness about diabetes is not spreading nearly as fast as incidence of the disease.

Nearly half of India's newly identified diabetes

patients discover they have the illness when they seek treatment for some of its major complications, such as heart, kidney or vision troubles or difficulty walking.

But other tell-tale symptoms of diabetes – including excess hunger, extreme thirst and frequent urination – do not necessarily prompt many Indians to get tested for the disease.

"Diabetics do not know they have diabetes for a long time," Dr Reddy says. "The symptoms are clear, but unfortunately people ignore it."

Ignorance about diabetes even extends to families already touched by the disease, as was demonstrated in a study, released this month, by India's Health Education & Awareness League (known as the Heal Foundation) in Delhi, Mumbai and Bangalore.

The study, called India POLD (Perceptions Of people Living with Diabetes), surveyed 900 people, all of whom had one immediate family member with diabetes.

Of this group, fewer than half understood diabetes was caused by a lack of insulin, only 33 per cent knew obesity and heredity could contribute to the development of the disease, and 63 per cent were unaware of diabetes' potential long-term health consequences.

Even more revealing was that 85 per cent of respondents – who were all at high risk of the disease – said they did no blood sugar screenings, and 55 per cent said they did no exercise.

**Diet changes, lack of exercise and sedentary lifestyles have accompanied growing affluence**

In the run-up to World Diabetes Day today, the Heal Foundation, backed by the health ministry, Sanofi and other health sector and nutrition companies, has been running a huge, two-week diabetes awareness campaign, with screening camps in 20 cities.

Apollo is also rolling out a network of sugar-testing centres, with plans to offer free blood-sugar testing at its associated chain of pharmacies across India.

But it will take more than simply awareness to tackle the magnitude of India's diabetes challenge. R Santosh, a physician treating diabetics in Hyderabad, says India faces a serious shortage of experts to deal with management of advanced diabetes. The country has only between 350 and 400 trained endocrinologists.

Even after they have been diagnosed, patients are often alarmingly casual about the need for a different diet and more exercise.

"Patients don't tend to perceive diabetes as a major problem because it doesn't affect the body immediately," says Dr Santosh. "There is also a mentality of doctor shopping. Services are paid for by the patient and he is free to take a second, third or fourth opinion until he finds a treatment option that suits his lifestyle."

# Size of problem requires mass awareness-raising

US

**Tackling the disease will be crucial for the economy as well as sufferers, writes Sarah Murray**

In Philadelphia, Pennsylvania, and Knoxville, Tennessee, more than 300 people have been watching a new kind of reality TV show – Project Not Me – designed to reduce their risk of developing type 2 diabetes.

The 16 episodes follows six Minnesota adults with pre-diabetes as they go through the Diabetes Prevention Program.

The pilot programme of video-on-demand tutorials is part of efforts to extend delivery of diabetes prevention and slow the spread of a disease that, if unchecked, could affect more than one in three Americans by 2050.

In addition to the obesity epidemic, other factors lie behind the rise of diabetes in the US. With age increasing the risk of developing

type 2 diabetes, America's greying population is one.

Moreover a genetic predisposition to type 2 diabetes exists in Hispanics, African-Americans, Native Americans and Asians. In the US some of these communities have been growing rapidly in number.

The Centers for Disease Control and Prevention (CDC) predicts that one in three children who were born in 2000 will have diabetes in their lifetime, says Deneen Vojta, senior vice-president for business initiatives at UnitedHealth Group, which developed the show in partnership with Comcast, a cable operator.

She adds: "But if you look at the detail of that data, it's one in six white children and one in two children of colour."

Overall, the figures look stark. An estimated 26m Americans have diabetes, according to the CDC, while 79m adults have pre-diabetes, a condition that raises the risk of developing type 2 diabetes, heart disease and stroke.

Some positive news lies behind its increased preva-



Ann Albright: early action

lence. For a start, the proportion undiagnosed has fallen from half to a quarter of those known to be suffering. And people with diabetes are living longer. "We're getting to people earlier in the course of their disease," says Ann Albright, director of the CDC's Division of Diabetes Translation. "And that's good."

Set against this is the bad news. Dr Albright says: "We're having a big increase in incidence, that is, new cases of diabetes."

Because poor diet and lack of exercise are drivers

of the rising incidence of diabetes, the challenge is to find ways of delivering effective prevention.

Unlike other diseases, no immunisations are available. And while smoking-related illnesses can be addressed by helping people quit, as Dr Albright says: "You can't give up food."

Preventing people from eating unhealthily and leading sedentary lives is no simple task, particularly when a range of factors drives these behaviours.

In much of America, people get little exercise because urban lifestyles are designed around the car.

David Harlan, co-director of the Diabetes Centre of Excellence at UMass Memorial Medical Centre, says: "It's easy to say that we're eating more and exercising less, but the cultural societal factors promoting that are not well understood. It's very complex."

This is one of the reasons for initiatives such as the reality TV pilot. The show followed six adults going through a diabetes prevention programme, with each of the episodes featuring a

health and wellness coach helping viewers improve their diets and increase physical activity.

The show's content was modelled on the CDC-led National Diabetes Prevention Programme, a public-private initiative through which government agencies, community organisations, insurers, companies and healthcare centres are promoting lifestyle change programmes for people at high risk of developing type 2 diabetes.

Dr Albright argues that the multi-pronged approach is essential. "We have to do more than deliver it by healthcare," she says.

The other problem is reaching pre-diabetic individuals and the estimated 7m Americans who do not know they have the disease. Dr Harlan believes awareness-raising efforts can play a role – and he sees some parallels with antismoking campaigns.

He says: "As with cigarettes, we have to make it uncool not to be out exercising. Culture change is very difficult but achievable." Another barrier lies in

the nature of the US healthcare system.

Dr Harlan says: "Our system evolved at a time when what doctors did was fix broken bones, cut out appendices and treat pneumonia. Our entire reimbursement system is predicated on paying for these acute incidences."

This needs to change to tackle a disease such as diabetes, giving incentives to both providers and patients to promote healthy lifestyles.

But whether reaching pre-diabetics through reality TV or changing healthcare reimbursement schemes, finding ways of tackling diabetes will be critical for the US – not just for the millions of sufferers but also for the economy.

According to research by UnitedHealth's Dr Vojta and her colleagues, if no action is taken, diabetes could cost the US \$512bn annually by 2021, and \$3.5tn over the next decade.

"When you have 79m with pre-diabetes, that's a ticking time bomb," she says. "But that's still reversible."

# Unhealthy developments as burden shifts to emerging countries

Continued from Page 1

longer increases the risk they will develop such "lifestyle" conditions as diabetes.

The human and economic consequences are proving devastating. Uncontrolled or poorly-controlled diabetes leads to complications including pain, foot ulcers and blindness. Diabetics represent a large number of hospital admissions and the global healthcare costs alone are estimated at \$471bn a year.

Much remains unclear about the origins of diabetes. Particular mystery surrounds type 1, which affects about 10 per cent of those with the condition, typically starting in late childhood and destroying the

body's insulin producing cells.

There is early research on vaccines and speculation about infection as a cause triggering an auto-immune response but little clarity on how to prevent it. Type 2 also leaves many questions unanswered.

Ann Keeling, chief executive of the International Diabetes Federation, highlights research on early onset diabetes – sometimes confused with gestational diabetes in pregnant women – and its connection to infant nutrition. "Famine and revolution could provide a link, meaning diabetes is a development issue," she says.

Despite the difficulties, there has been undoubted

progress with treatment, which can slow acceleration and allow ever more convenient management of the condition to help boost patient compliance.

Philip Home, professor of diabetes medicine at Newcastle University, says: "There is still huge unmet need but in my career over three decades there has been a remarkable revolution in education, new insulins and oral agents and ways for people to monitor their own condition."

Three large pharmaceutical companies – Novo Nordisk, Sanofi and Eli Lilly – dominate insulin production but many others are active. The joint acquisition earlier this year of Amylin by Bristol-Myers Squibb

and AstraZeneca after a "beauty parade" highlighted the appetite for rivals for the therapy area.

Enrique Contorno, president of Eli Lilly's diabetes division, who stresses his company's interest in the full range of products, says there is scope to research therapies targeted for Asia; for the elderly; and for longer and more stable drugs for other groups such as Muslims who fast.

"Unfortunately I don't see a cure in five or 10 years' time but there are very important opportunities to help," he says.

There are tensions between doctors and industry. John Yudkin, emeritus professor of medicine at University College London,

argues that companies have pushed too far with a focus on costlier innovative drugs such as insulin analogues, especially in developing countries. "Pharma is rubbing its hands with glee at the explosion of diabetes, especially where there is a lot of money like the Middle East," he says.

In an echo of past advocacy around HIV, he says

**'Pharma is rubbing its hands with glee at the explosion of diabetes'**

John Yudkin of UCL

far better diabetes control would come by focusing efforts on wider use of generic products, rather than pushing expensive medicines that stretch poor countries' healthcare budgets or patients' savings.

To that effect, the International Insulin Foundation has launched the "100 Campaign" to achieve global coverage of insulin a century after its launch in 1922. It will require initiatives to encourage high quality competitive production and greater bargaining power by countries grouping together to place bulk orders, something the Pan-American Health Organisation is championing.

On both diagnosis and management of diabetes,

there is much scope for improved outcomes. This month, the UK parliament's Public Accounts Committee criticised the failure of the National Health Service to follow consistently existing guidelines to identify the early signs of diabetes and respond adequately.

Margaret Hodge, MP, the chair, warned: "There is no strong national leadership, no effective accountability arrangements for commissioners and no appropriate performance incentives for providers."

If such measures can help tackle the consequences of diabetes, attacking the causes remains still more problematic. Since last September's UN meeting on non-communicable diseases,

the drafting of targets and the creation of a monitoring mechanism to meet its goals have been repeatedly delayed.

There are signs of a reversal on pioneering "fat taxes" introduced in several European countries, and PepsiCo's chief executive has come under pressure from Wall Street for neglecting its core sugary and salty products.

Then again, McDonald's last week reported the first drop in sales for a decade, in a move analysts attributed in part to consumers' increased appetite for healthier food. Individuals will need to do more to take their fate – rather than hamburgers – into their own hands.