

COMPANY AND COMPANY-SUPPORTED PROGRAMMES WITH A COMPONENT OF DONATED INSULIN IN LOW- AND MIDDLE-INCOME COUNTRIES

April 2018

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April 2018

Published by

Health Action International
Overtoom 60 (2) | 1054 HK Amsterdam
The Netherlands | +31 20 412 4523
www.haiweb.org

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The ACCISS Study is supported by The Leona M. and Harry B. Helmsley Charitable Trust and Stichting ICF. The analysis included in this report is that of the authors alone and does not necessarily reflect the views of The Helmsley Charitable Trust or Stichting ICF. All references and conclusions are intended for educational and informative purposes and do

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Acknowledgements

This study was performed with financial support of The Leona M. and Harry B. Helmsley Charitable Trust, Health Action International, and the University Medical Centre Groningen, University of Groningen (Netherlands). The Access to Medicine Foundation generously provided access to information in their databases not covered by a non-disclosure agreement with the relevant companies. Jayasree K Iyer, Catherine Gray, Graham Ogle, Richard Laing, David Beran and Marg Ewen provided valuable comments to earlier versions of the report. The analysis included in this report is that of the authors alone and does not necessarily reflect the views of The Helmsley Charitable Trust.

Acronyms

ACCISS	Addressing the Challenge and Constraints of Insulin Sources and Supply
AMPATH	Academic Model Providing Access to Healthcare
ATM	Access to Medicine
BMI	Body mass index
BoP	Base of the Pyramid
CDiC	Changing Diabetes® in Children
CDiP	Changing Diabetes® in Pregnancy
CSR	Corporate social responsibility
GDM	Gestational diabetes mellitus
HbA _{1c}	Glycated haemoglobin (A1c)
HCP	Health care professional
IDF	International Diabetes Federation
IFPMA	International Federation of Pharmaceutical Manufacturers and Associations
LDC	Least-developed countries
LFAC	Life for a Child
LMICs	Low- and middle-income countries
NCD	Non-communicable disease
SEF	Sanofi Espoir Foundation
UN	United Nations
WDF	World Diabetes Foundation
WHO	World Health Organization

Executive Summary

The Addressing the Challenge and Constraints of Insulin Sources and Supply (ACCISS) Study was started in 2015 to identify the barriers to equitable access to insulin in low- and middle-income countries (LMICs). Such a study is not complete without consideration of the supply of donated insulin through corporate social responsibility and other programmes by the three main insulin-producing companies (Eli Lilly and Company [hereafter Eli Lilly], Novo Nordisk, and Sanofi), and by the most relevant foundations (the World Diabetes Foundation [WDF], the International Diabetes Federation [IDF], Life for a Child [LFAC] and the Sanofi Espoir Foundation [SEF]). The study attempts to identify, describe and estimate the magnitude and impact of these insulin donation programmes in LMICs.

Methods

The main source of data on the donation programmes was publicly available information from the three main insulin-producing companies and the most relevant diabetes organisations, supplemented with information from the Access to Medicine Index Foundation. Other web searches were performed to check that no important programmes and initiatives had been overlooked. Information on the public health impact of the programmes was obtained from peer-reviewed literature, conference presentations, and discussions with a number of experts and programme staff from sub-Saharan countries during the Third African Diabetes Congress in Cameroon (19–22 April, 2017). All stakeholders had a chance to comment on earlier drafts of this report.

Results

The six companies and organisations studied run at least 25 different diabetes-related initiatives in over 70 LMICs. Many of these programmes focus on disease awareness, patient screening, education, training, and improving health systems; some include a component of differential pricing or insulin donations.

Three multi-year programmes with a component of free insulin for persons with type 1 diabetes (mostly children) in LMIC were identified. These are LFAC, Changing CDiC and WDF (Table 2). The estimated annual number of recipients of donated insulin in 43 LMICs grew from 8193 in 2009 to 35,382 in 2015 (Table 3 and Figure 1). Very little public information is available on differential pricing and discounts on human insulin.

In 2015, there were about 542,000 children below the age of 15 living with type 1 diabetes. LFAC estimates that 112,000 of these children are in need of support. Our estimates indicate that about one-third of these children are now covered by programmes with a component of insulin donation.

Some of these programmes have had a considerable public health impact. In some countries, the number of enrolled (and surviving) children has increased dramatically. For example, in Rwanda, the programme started with 25 people in 2004 and included 699 people in 2014. Other programmes report similar increases in the number of treatment centres or participating health facilities. For example, the national programme in Tanzania started with one diabetes clinic in 2003 and has recently rolled out to 187 district hospitals. A 2016 LFAC factsheet shows that 20 LFAC country programmes now claim near-universal national coverage of children with type 1 diabetes.

The health impact of these programmes has been studied in ten countries (Bolivia, Cameroon, Guinea, Ghana, Haiti, Northern India, Mali, Nepal, Rwanda and Tanzania). Several of these countries report an increase in mean body weight (e.g., from 53 to 61 kg in Cameroon) and body mass index (e.g., from 15.4 to 19 kg/m² in India), a reduction in mortality (e.g., from 24.5 to 2/1000 patient years in Uzbekistan), a reduction in average HbA1c values (median starting value 11.5 percent, median current value 8.5 percent), and a reduction in the frequency of acute and chronic complications (e.g., a reduction in serious keto-acidosis from 10 percent in 2011 to 0.6 percent in 2014 in Tanzania). Some studies report on the performance of children in school with mixed results.

In several countries, especially those where the programme is able to diagnose and treat most new cases of type 1 diabetes, the diabetes programmes have become a visible and recognised part of the national health system, although not always fully integrated with other services. Several programmes report that the donation programmes have delivered a very important proof of concept: that it is possible that children with type 1 diabetes can successfully be diagnosed and treated in LMIC, and that most (up to 80–90 percent) can survive into young adulthood. The programmes have also proven that it is possible to arrange for regular HbA1c testing—usually in a few designated centres in the country.

In an evaluation of the LFAC programme in 2014, 31 (78 percent) country programmes indicated that they cannot support individuals beyond their age of eligibility (18–21 years with CDiC and 25 years with LFAC). This is a serious ethical issue. Various solutions are being tried in different countries with some success. Several programmes include activities to train adolescents to earn a living and ultimately pay for their own treatment. The transition into adult treatment is possible, but must be planned in advance and needs additional investment.

The general sustainability of donation programmes is another challenge. Recently, the CDiC programme was extended beyond its original target date of 2015, to cover 20,000 children by 2017 (the latest figure was 13,700 children in 2015). Insulin donations to the LFAC programme are assured until 2018. There are no signals that the major donors are considering withdrawing their support; CDiC recently expanded into five new countries (Cambodia, Ivory Coast, Myanmar, Senegal, and Sudan).

Public reporting on the programmes is widely scattered, largely incomplete, and sometimes inconsistent; most financial information provided to the Access to Medicines Index is covered by confidentiality agreements. The level of detail varies greatly between programmes, countries and years. When medicine donations are mentioned, the types and quantities of the different products are rarely specified. Where financial amounts are disclosed, it is not clear whether these amounts are based on retail sale prices in Organisation for Economic Co-operation and Development (OECD) countries, or on international not-for-profit wholesale prices. For most insulin donation programmes, whether the patients receive human or analogue insulin is not officially published, although informal contacts with several programmes have revealed that most donations—especially those through LFAC and CDiC—are human insulin. There is even less information available for the various differential pricing programmes, as information on the relevant countries, type of product(s), quantities per country, and any conditions, restrictions and sustainability provisions, is rarely provided, or done so confidentially.

It is only in recent years that an increasing number of papers have described the health impact of the support programmes. The scientific quality of these papers and,

therefore, the strength of the evidence they present, is not very high. None of the papers had a control group, about two-thirds were simple “pre-post” studies, reporting key health statistics before and after a certain period. The other studies were “post-only”, reporting on current health indicators.

Conclusion

Despite the incomplete, scattered and often low-quality information publicly available, we can conclude that company and company-supported programmes with a component of donated insulin, such as LFAC and CDiC, have made a considerable impact on the lives of over 35,000 children with type 1 diabetes in 40 LMICs. These individuals owe their lives to these programmes. The huge rise in the number of people being served and treatment centres would likely not have taken place—or not yet have taken place—without the external support from these programmes. Yet, only one-third of children with type 1 diabetes in need globally are currently covered by these programmes, and the overall health outcomes for these children are still far from ideal. As such, these support programmes have not yet reached their maximum potential.

Recommendations

Despite the considerable progress that has been made in the diagnosis, treatment and survival of children with type 1 diabetes, several challenges remain. These can be divided into challenges in quality of care, health system performance, and financing, and sustainability (see main body of the report). It is acknowledged that many challenges identified in the published literature, and by the national programmes staff consulted, relate to diabetes programmes in general, and often go far beyond the aspect of insulin donations only. However, donation programmes cannot and should not be seen in isolation from national diabetes programmes. Secondly, programmes with a component of donated insulin have often filled a void in national health systems and have thereby generated, often for the first time, valuable experiences with the diagnosis and treatment of type 1 diabetes in LMICs.

Service delivery and quality of care

1. National diabetes programmes should develop evidence-based clinical guidelines for the diagnosis and treatment of type 1 diabetes.
2. National diabetes programmes should develop or strengthen a person-centred approach to care, with integrated services for diabetes, nutrition advice, and treatment of other non-communicable and/or chronic diseases.
3. National diabetes programmes should continue to train large numbers of general doctors and paramedical staff in the prevention, diagnosis and treatment of type 1 diabetes and its complications.

Health system performance and financing

4. The national government should establish and implement a national diabetes policy, covering financing and service delivery of diabetes care.
5. The national government should ensure that services for the prevention, diagnosis and treatment of type 1 diabetes and its complications are available, accessible, acceptable and of good quality, and linked to a national patient register. Free diagnosis and treatment of type 1 diabetes should be included in all national health insurance schemes.

6. Donor agencies should ensure that all donations of medicines, diagnostics and equipment follow the World Health Organization Guidelines for Medicine Donations.
7. National diabetes programmes should report regularly on programme targets, the number of people living with diabetes covered, health outcomes, key health system data, the role of partners, and project financing.

Sustainability

8. National diabetes programmes and donors should plan the transition to programme support of recipients of donated insulin beyond their eligibility well in advance. This transition should be supported with specific investments and programme activities; links with existing insulin discount programmes should be strengthened.
9. Donor-supported programmes—such as LFAC and CDiC—should be continued and expanded in countries in need for as long as diagnosis and treatment of type 1 diabetes and its complications are not yet included in national health insurance schemes.

Recommendations for donor agencies: ten steps to phase out an insulin donation programme

- 1) Support a programme with a free basic package of diagnosis and treatment for as many children with type 1 diabetes as possible, and patient education, thereby preventing the almost certain death these children would otherwise face; and create a national patient register for follow-up and reporting;
- 2) Collaborate with the national diabetes programme and other donors to create a national continuum of care for type 1 diabetes from childhood to early adulthood by, for example, combining in every eligible country the CDiC donation programme (up to age 18), the LFAC donation programme (up to age 25) and the Base of the Pyramid (BoP) and other insulin discount programmes (for adults);
- 3) Assist national authorities in creating systems to prevent, diagnose and treat acute and chronic complications of type 1 diabetes;
- 4) Provide detailed information on key aspects of the support programme, such as the number and basic characteristics of recipients; the number, type and value of diagnostic tests and medicines donated; the nature and cost of other programme activities supported; and basic health outcomes such as mortality, weight gain, mean HbA_{1c} levels, and frequency of complications;
- 5) Deliver to national authorities, donor organisations, and national health insurance systems, the proof of concept that type 1 diabetes can be diagnosed and treated successfully and cost-effectively in LMICs;
- 6) Encourage national authorities to develop and implement a national diabetes policy as a commitment and guide for action to achieve universal access to decentralised health services for the prevention, diagnosis and treatment of diabetes, as part of the progressive realisation of the right to health;
- 7) Encourage national authorities to create systems whereby young adults living with diabetes are empowered to access affordable standard diabetes care after their eligibility for the donation programme ends;
- 8) Work with the national government towards inclusion of standard diagnosis, care and treatment of diabetes in social health insurance programmes;
- 9) Encourage the national government to integrate the prevention, diagnosis and treatment of diabetes and its complications with the delivery of nutritional advice and other services for the prevention and treatment of other chronic conditions such as HIV, tuberculosis, leprosy, and hypertension;
- 10) Phase out donor involvement as soon as these objectives have been achieved.

1. Introduction

About 100 million people worldwide need insulin to manage their diabetes. However, more than half of these people cannot afford and/or access this much-needed medicine (1). To address inequities and inefficiencies in the global insulin market, identification of causes of barriers to insulin access is needed. The Addressing the Challenge and Constraints of Insulin Sources and Supply (ACCISS) Study sets out to do this.

In the first phase of the ACCISS study, the global insulin market is mapped from different angles, to determine which pharmaceutical companies manufacture and distribute insulin; current formulations, prices, production scale, distribution channels, trade issues; and regulatory issues related to market authorisation for biosimilars.

The ACCISS study of insulin in low- and middle-income countries (LMIC) is not complete without consideration of the supply of insulin through corporate social responsibility (CSR) and other programmes by the three main insulin-producing companies (Eli Lilly and Company [hereafter Eli Lilly], Novo Nordisk, and Sanofi), as well as the World Diabetes Foundation (WDF), the International Diabetes Federation's (IDF), Life for a Child (LFAC)] programme, and the Sanofi Espoir Foundation (SEF). This is the subject of the current study.

The main insulin manufacturers have established or support programmes to promote access to insulin for poor and disadvantaged patients, often in least-developed—and some lower-middle income—countries. These initiatives vary between donations or price discounts of insulin, diagnostic materials and/or equipment, to comprehensive multi-year programmes of building and equipping specialised diabetes clinics, holding diabetes camps, training patients and health workers, and supporting advocacy, screening, diagnosis, treatment and follow-up.

Some of these programmes are supported directly by pharmaceutical companies and are easily identified as such. An example is the Novo Nordisk Changing Diabetes® in Children (CDiC) programme. Other initiatives are funded and implemented through separate foundations, such as the WDF, which was founded and is largely supported by Novo Nordisk, or the IDF, which partners with Novo Nordisk, Sanofi, AstraZeneca and Eli Lilly. In the current study, these foundations are included as separate organisations. Most of these foundations present themselves as fully independent, although it should be noted that some remain largely dependent on company donations. The influence of the companies on foundation management and oversight is not always clear.

The current study attempts to identify, describe and estimate the magnitude of insulin donation programmes; the type of insulin provided through these initiatives (human insulin or insulin analogues); the public health impact of these programmes; future challenges; and practical recommendations. The ultimate goal of the study is to further improve the contributions of the large manufacturers and other organisations towards equitable global access to insulin.

2. Methods

The first source of data was publicly available information from reports, websites and documents of the three main insulin-producing companies and the relevant diabetes organisations. Systematic web searches were performed to check that no important programmes and initiatives had been overlooked. Additional information, especially related to the public health impact of the programmes and future challenges, was obtained from peer-reviewed literature, conference presentations, and discussions with programme managers from a number of country programmes from sub-Saharan Africa. The companies and foundations also provided comments on earlier drafts of the report.

Insulin-Producing Companies

Novo Nordisk, Eli Lilly and Sanofi produce and supply over 90 percent of insulin in the world (2). Their websites, annual reports and other reports were screened for information on insulin donation or price discount programmes. The most recent information was sought, focusing on the years 2010–2015, with information on 2016 not available at the time of report publication. As a first step, all diabetes programmes with components of advocacy, prevention, screening, training and treatment were identified. Within these programmes, projects with a component of insulin donation or insulin pricing policies were identified and further considered. Finally, programmes with a component of directly or indirectly supplying insulin to people living with type 1 diabetes (children, adolescents and adults) and to pregnant women with gestational diabetes mellitus (GDM) were identified for further analysis.

Each of the three companies was reviewed separately. For each project with an insulin donation or pricing policy component, information was collected, where available, on the number of patients treated, the type (human or analogue) and amount of insulin supplied, the price of the insulin (full donation or supply at reduced cost), the type of health facility (public, private not-for-profit, or private for-profit), the stated duration of the commitment, any conditions attached to the project, and any recorded health outcomes of the programme (e.g., the number of patients stabilised on insulin, or survival rates).

All three companies present information on their social initiatives in a ‘sustainability’ or ‘CSR section of their websites. However, the three companies have different approaches to reporting. Novo Nordisk has an integrated report, and their CSR report is included in the annual report. The annual reports of 2011–2015 were reviewed (3). Sanofi has separate annual, financial and CSR reports. We included CSR reports from 2011–2016 (4). Eli Lilly has separate annual and CSR reports. CSR reports 2010, 2011/12, 2012/13, 2014, 2015 and 2016 were reviewed (5).

Besides the annual and CSR reports, companies issue additional publications. Examples are Sanofi’s *Access to Healthcare: Programs developed by our affiliates*, or Eli Lilly’s *Global Health Programs Report*. A preliminary search on the previously identified key words was performed in these publications. Company press releases were also reviewed (see below).

Foundations

The websites and annual reports of the foundations, federations and their various related support programmes, often specified by recipient country, were consulted. Novo Nordisk previously had a programme website for their Changing Diabetes

initiative, but this site has now been integrated into their main website (6). Eli Lilly has dedicated programme websites for the Lilly Non-communicable Diseases (NCD) Partnership and LillyPad (7,8). The SEF publishes annual reports. The annual reports of 2011, 2012–13, 2013–14, and 2014–15 were reviewed (9). The WDF publishes an annual review on its website. Moreover, they report on every single project (398 ongoing projects in 2015). Programme websites were also reviewed. The annual reports for 2011–2015 of the IDF were retrieved and analysed. The annual reports from 2011 to 2015 of LFAC and several published papers on the health impact of LFAC programmes were also analysed. IDF works with member associations in various regions worldwide and publishes the general achievements of these associations on their website. These achievements were included in our analysis if they were related to the supply of insulin. More information on these member associations and their projects is available on the IDF website (10).

Access to Medicine Index

Publicly available information from the three companies was compared and supplemented with information submitted by the companies to the Access to Medicine (ATM) Foundation as part of the ATM Index. The ATM Foundation is an independent, international not-for-profit organisation dedicated to addressing the challenges of access to medicine, with a focus on LMICs. Besides focused reports, one of the foundation's key outputs is their biennial Access to Medicine Index. This index ranks 20 of the world's largest pharmaceutical companies according to their efforts to improve access to medicine in developing countries. The Index publicly recognises companies for their investments in access to medicine, raising awareness of relevant issues within pharmaceutical companies and providing them with a transparent means by which they can assess, monitor and improve their own performance, as well as their public and investment profiles. Consistent iterations of the Index highlight industry trends and provide a basis for multi-stakeholder dialogue and solution building (11).

The ATM Index 2014 is based on a framework of seven technical areas: General Access to Medicine Management; Public Policy and Market Influence; Research and Development; Equitable Pricing, Manufacturing and Distribution; Patents and Licencing; Capability Advancement in Product Development and Distribution; and Product Donations and Philanthropic Activities. In 2016, these categories were changed slightly. Relevant information on company programmes and activities from Novo Nordisk, Eli Lilly and Sanofi was retrieved. Some of this information was made available to the ATM Foundation under a non-disclosure agreement. In our study, this information is marked as 'undisclosed' and not used for the analysis.

Other Websites and Google® Search

The website of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) was also reviewed. Some of its information on diabetes is included in our report, although most information overlaps with company publications (12). Finally, our search for company initiatives was completed by Google® searches and a review of press releases from each of the organisations' websites as a final check to identify any remaining projects that had not been identified by the systematic searches described above.

Keywords and Search Terms

Sub-headings, ‘sustainability’ and ‘corporate social responsibility’, were the first point of focus. Subsequent search words were: ‘insulin’, ‘donation’, ‘tiered pricing’, ‘differential pricing’, ‘philanthropic’, ‘human insulin’, ‘human insulin’ in combination with previously identified brand names, and previously identified programme names. Key words were also combined, such as ‘Eli Lilly’ + ‘Novo Nordisk insulin donation’. Project names documented in the annual/CSR reports were also used as key words to find additional news publications.

Information on Public Health Impact and Future Challenges

In the course of the review of earlier drafts of the report, an increasing number of conference presentations and recently published articles were made available through the various support programmes. New presentations on the public health impact of the programmes in Cameroon, Guinea, Mali and Tanzania were made at the Third African Diabetes Conference in Yaoundé in April 2017. During this conference, programme managers from Ghana, Kenya, Nigeria, Senegal, Rwanda, and South Africa provided additional information on progress in their programmes, the challenges they are facing, and their suggested solutions.

Exclusion Criteria

The following programme components are not included in this study: health care professional (HCP) training programmes, donation programmes for testing strips and syringes, diabetes foot or eye care programmes, diabetes leadership forums, diabetes research programmes, building diabetes clinics, and diabetes awareness campaigns.

3. Results

3.1 Programmes in Support of Prevention, Diagnosis and Treatment of Diabetes

The number and range of projects in support of various aspects of type 1 and 2 diabetes education, prevention, diagnosis, treatment and care, is very large. For example, the WDF website lists 398 different support projects in 112 countries between 2002 and 2015, with a total budget of US\$109.7 million (13). Many of these projects focus on advocacy, prevention, screening, training of patients and health workers, establishment of treatment centres, supply of equipment and mobile clinics (Table 1).

Table 1. Initiatives in support of diabetes diagnosis, care and treatment

<p><u>Eli Lilly</u>: Connecting Hearts Abroad, Lily NCD Partnership, Academic Model Providing Access to Health Care (AMPATH), Lily TruAssist, Diabetes Conversations, Diabetes Camps, Diabetes and Disney</p>

<p><u>Novo Nordisk</u>: Blueprint for Change, Changing Diabetes in Children, Changing Diabetes in Pregnancy, Cities Changing Diabetes, Changing Diabetes Leadership Forum, Changing Diabetes Barometer, Base of the Pyramid, Diabetes Attitudes Wishes and Needs (DAWN2), Steno Diabetes Centre</p>

Sanofi: Be He@lthy Be Mobile, Healthy Children Happy Children, Reaching Rural Populations, StarBem/Alcance, E-diabete, International Diabetes Practices Management Study, Access to Health Care programmes, Act for Diabetes, Sanofi Espoir Foundation

IDF: Collaboration with 230 national diabetes organisations in 170 countries; Life for a Child, World Diabetes Day, Young Leaders in Diabetes Programme, IDF Diabetes Atlas, Bringing Research in Diabetes to Global Environments and Systems (BRIDGES), Kids and Diabetes in Schools (KiDS), Women in India with GDM Strategy (WINGS), Diabetes Africa Foot Initiative (DAFI), Diabetes Education Consultative Section (DECS)

WDF: 398 partnerships projects in 117 countries (2002– 2015); WDF/East Africa, WDF/West Africa, WDF/Sub Saharan Africa, WDF/Type 1 diabetes programmes, WDF/Diabetes in Pregnancy, WDF/Type-2 Diabetes

3.2 Company-supported Programmes with a Component of Donated or Discounted Insulin

3.2.1 Eli Lilly and Company

Product Donations

With regard to donations, Eli Lilly states that they try to help people at different income levels to get access to medicines (14). In 2014, Eli Lilly reported US\$550 million in product donations, including insulin donations. Insulin donations are given to different programmes including to LFAC (see below), disaster relief, and the Academic Model Providing Access to Healthcare (AMPATH) project in Kenya. Eli Lilly also responds to disasters with cash and products to help affected people in response to specific requests by relief agencies. In 2014, Eli Lilly gave \$1.9 million in cash and products in the wake of natural disasters (14).

AMPATH is a collaborative health improvement project in Kenya with the Moi Teaching and Referral Hospital in Eldoret. It was created in 2001 and initially focused on HIV. Diabetes, hypertension and cancer were included at a later date. Since 2002, Eli Lilly has donated nearly \$60 million in medicines to AMPATH for the treatment of diabetes, mental illness and cancer (15). Lilly TruAssist is a patient assistance programme for people living in the United States (16). This latter programme falls outside the scope of our study.

Differential Pricing

Eli Lilly states that it supports efforts by other parties to decrease the final price of medicine to patients through, for example, minimising value-added taxes and mark-ups applied in the supply chain (17). Information on the level of discounting given to a number of middle-income countries, and the number of patients benefitting, is not disclosed by the company.

3.2.2 Novo Nordisk

Novo Nordisk has set a long-term target to reach 40 million people with Novo Nordisk diabetes care products by 2020 (Changing Diabetes 40by20). Novo Nordisk launched the following programmes to reach their target: Changing Diabetes® is the main initiative, and comprises CDiC, Changing Diabetes® in Pregnancy (CDiP), Cities Changing Diabetes®, Changing Diabetes® Leadership Forum, and Changing Diabetes® Barometer. Novo Nordisk also runs the BoP project, which targets the working poor in certain LMIC with price discounts. Novo Nordisk complements their efforts by providing financial support to the WDF (see below) and a differential pricing policy for least-developed countries (LDC).

Insulin Donations

Novo Nordisk issued the following statement on donations:

“While we believe that product donations are not a sustainable way of improving access to healthcare, we maintain an active policy on emergency relief in disaster-struck areas. When appropriate, we donate products, in-kind services and sometimes cash to partner organisations that are equipped and experienced for operations under these circumstances. We always work in adherence with WHO’s Interagency Guidelines for Drug Donations.” (18)

Novo Nordisk supported disaster relief in 2010 with US\$177,000 for flood victims in Pakistan, of which US\$88,000 was given to the Danish Red Cross and the rest spent on insulin and medical supplies. Fifty thousand vials of insulin were donated for the victims of the earthquake in Haiti (18).

The CDiC programme was launched in 2009 in collaboration with the WDF, the International Society for Pediatric and Adolescent Diabetes (ISPAD), and Roche. The objective of the programme is to improve delivery of care to children with type 1 diabetes in resource-poor settings. The project is running in Cameroon, Democratic Republic of Congo, Ethiopia, Guinea, Kenya, Tanzania, Uganda, Bangladesh and India. In 2017, it expanded into Senegal, Ivory Coast, Sudan, Myanmar and Cambodia (19). For each country, a different approach is implemented, including improvement of infrastructure, training and education of HCPs, provision of insulin and blood glucose monitoring equipment, patient education material, patient registry systems, and best practice sharing (20, 21, 22, 23). The initial aim was to reach 10,000 children; at the end of 2014, 13,199 children were reached, 5,479 HCPs were trained and 108 clinics were established (24). Novo Nordisk committed to investing US\$25 million in the first five years. According to Novo Nordisk, all children enrolled in the programme have access to free insulin. Although it is not explicitly stated in the documents, country programme representatives have confirmed that human insulin is supplied.

The CDiP programme was established in 2009, running in Colombia, India and Nicaragua. These countries were chosen based on their high rates of GDM. The objectives of this project are to improve diabetes-related maternal health during pregnancy and ensure healthy pregnancy outcomes, promote awareness and improve access to screening (25). In 2014, 28,385 women were screened for GDM and 2,837 women with GDM were diagnosed, treated and educated. In addition, 3,700 health care workers were trained in GDM screening and management (26). Insulin donations do not seem to be a key feature of the programme, but not all related information is fully disclosed. These programmes are not considered further here.

Differential Pricing

Novo Nordisk has formulated a differential pricing policy for LDC, as defined by the United Nations. This policy was launched in 2001 and reviewed in 2012. Novo Nordisk offers human insulin in vials to all LDC at or below a market price of 20 percent of the average prices for human insulin in vials in the western world. The western world is defined as Europe (European Union, Switzerland, Norway), the United States, Canada and Japan. In 2012, the mean price was US\$4.80 per vial and in 2013 and 2014 it was US\$5.10 per vial; in 2015 it was US\$5 per vial. In 2014, Novo Nordisk reported sales according to the differential pricing policy in 32 countries, overall. The list of countries is undisclosed, types, quantities and prices of insulin supplied at the reduced rate are not published (27). For 2017, the price was set at US\$4 per vial of human insulin (28).

The BoP project was initiated in 2010 and is running in Nigeria, Ghana, Kenya and India. Novo Nordisk states that, with different business models, the project targets the working poor (earning less than \$1,500–\$3,000 per annum) by developing scalable, sustainable and profitable solutions to increase access to diabetes care, as well as to provide value to the business of Novo Nordisk. In every participating country, Novo Nordisk has a different approach. In 2015, a price reduction of 75 percent was given on human insulin, with 6,000 recipients in Kenya, 1,548 in Ghana, and 900 in Nigeria.

3.2.3 Sanofi

The Sanofi approach to improving healthcare is reported in their annual CSR Report. In addition, Sanofi publishes a report, *Access to Healthcare: Programs developed by our affiliates*, on a yearly basis. In this document, all CSR activities and programmes are reported.

Insulin Donations

No information was found on insulin donation programmes by Sanofi.

Differential Pricing

Differential pricing is applied for medicines for a range of diseases within Sanofi's Access to Medicine Programme, which does not include diabetes (29). Yet Sanofi has several projects running in Egypt targeting acute infections, childhood diseases, hypertension and diabetes. Through these projects, Sanofi reports to have reached 14,000 physicians in 2013. Approximately 30,000 patients are reported to benefit from appropriate treatment and affordable prices. Sanofi provides branded originator products of several medicines, including glimepiride, at a cost of E£1 (US\$0.13) (30). It also gave a 35–50 percent discount on Lantus® to 24,000 people in Egypt in 2010–2015 (31). Tiered pricing schemes for 2,000–6,000 beneficiaries are reported from the Philippines in 2011–13, and six treatment centres in Ghana in 2015 (32, 33).

Sanofi launched StarBem in 2013 in Brazil as a continuation of the previous Alcance programme. The project aims to support people living with diabetes with their treatment through a comprehensive approach. This includes a tiered pricing programme to people who cannot afford diabetes treatment products, including insulin, hypertension and cholesterol medicines, and glucose meters and strips. The discount is based on patient income. In 2013, more than 18,000 people benefited

from the tiered pricing programme. In total, more than 40,000 people had benefited from the overall programme that included information, education, support and access (31, 34).

For the Sanofi Espoir Foundation, the search queries did not result in any hits on insulin donation or differential pricing programmes. Therefore, this foundation is not considered further in this report.

3.3 Foundation Programmes with a Component of Donated or Discounted Insulin

3.3.1 International Diabetes Federation

The IDF is an umbrella organisation of over 230 national diabetes associations in 170 countries and territories. All IDF's projects are reported on the IDF website, including the IDF's donation programme, LFAC, which is discussed separately below. Other IDF projects involve education, awareness and advocacy.

3.3.2 World Diabetes Foundation

The WDF was founded by Novo Nordisk in 2002, which remains its main financial contributor. WDF is a non-commercial foundation, governed by an independent board of six experts in the field of diabetes and access to health care in developing countries. The WDF states that it is set up outside and completely independent of the company (35). The stated aim of the WDF is to promote access to prevention and care of diabetes through training and capacity building of health care workers, patient education and self-management, diagnostic materials and equipment, and preventive programmes of advocacy, awareness, and school projects. Through its activities, the WDF attempts to contribute to the World Health Organisation (WHO) Global Action Plan for the Prevention and Control of NCDs (36).

From 2002 to September 2015, the WDF provided US\$109 million for 398 partnership projects in 117 countries (37). WDF states that its support programmes do not include insulin donations or differential pricing. Insulin is provided by local health authorities, Novo Nordisk, or funded by third parties. Yet, some earlier WDF programmes have reported a free insulin component. Examples are the WDF programme in sub-Saharan Africa from 2008–2012 (Ethiopia, Kenya, Nigeria, Tanzania and Uganda) and later programmes from 2012–2016 in a number of countries in East and West Africa (38, 39, 40). With regard to patient numbers, most of these latter programmes overlap with those reported by LFAC and CDiC. However, some WDF countries are not included in LFAC and CDiC (Benin, Gambia, Ivory Coast, Niger and Sierra Leone). There is no specific mention of free treatment in these countries and it is therefore assumed that these five programmes do not include insulin donations.

Most other WDF country programmes with a treatment component for type 1 diabetes also overlap with LFAC and CDiC. However, the programmes in China (2011–2015), Pakistan (2010–2013) and Sudan (2009–2012) specifically mention people with diabetes treated with free insulin (1,681, 1,957 and 2,000, respectively). These numbers do not overlap with other programmes and are therefore included in our estimates.

3.3.3 Life For a Child

In 2001, the IDF launched the LFAC programme to support children with diabetes in the developing world. The programme contributes insulin, syringes, blood glucose monitoring equipment, education materials, training, treatment guidelines, research, infrastructure and capacity building, and vocational training. The programme also tries to raise more awareness for diabetes. The programme supports children and adolescents until the age of 26.

Eli Lilly is one of the main suppliers of insulin for the project. Eli Lilly's commitment to LFAC was 800,000 vials of insulin between 2008–2015. This is estimated to help around 24,000 children in sub-Saharan Africa, Asia and South America. In 2014, US\$157,542 was spent on insulin products and insulin was made available in 29 of the 46 countries involved in the programme. In 2014, the LFAC programme helped 17,000 children; this number has risen to 18,320 in 2016 (41). Eli Lilly is donating another 780,000 vials for 2016–2018 (42). LFAC also partners with Insulin for Life to provide insulin to two countries. This insulin comes from unused supplies from pharmacies and insulin users.

In 2014, LFAC's largest donor—The Leona M. and Harry B. Helmsley Charitable Trust—commissioned the London School of Hygiene and Tropical Medicine (LSHTM) to conduct a comprehensive formal evaluation of the work of LFAC (43). The work was conducted by a team led by Professor Martin McKee and Dr Sue Atkinson. Site visits were conducted in five countries: Rwanda, India, Jamaica, Mexico, and Philippines. The evaluation was completed in 2015. The review covered five themes: the IDF-LFAC structure and organisation; optimal strategic framework for high impact sustainable results; changes to policies that could improve quality, quantity, efficiency and effectiveness; impacts on countries, systems and children; and impact on long-term sustainability in type 1 diabetes care delivery systems. The authors conclude:

“LFAC is a strong programme that is delivered well and is highly valued by the countries and the children, young people and their families that are supported by it. It is clear that LFAC enables children and young people with type 1 diabetes to survive and, as the programme and country policies strengthen, enables them also to thrive. (The review) identifies a need for developing country leadership and building local capacity, implementing approaches that catalyse systemic improvements in type 1 diabetes care delivery systems. (...) There is a need for a higher priority to be given to the medium and long term sustainability of the support provided for children with type 1 diabetes, making full use of the experiences gathered by LFAC and the information that it has collected on burden of disease, health needs, and barriers to be overcome in obtaining effective care by people with type 1 diabetes.”

The evaluation report presents valuable information on the financial side of the programme. In 2014, LFAC spent US\$ 1,412,134 in cash, of which 70.3 percent on direct country support. US\$157,542 (16 percent of country support funds) was spent on insulin, US\$406,237 (41 percent) on strips and meters, and US\$211,941 (21 percent) on HbA_{1c} measurement. The rest of the country budget was spent on education (5 percent), training (3 percent), research (5 percent), and other support (9 percent). The report mentions that in-kind insulin was also received for a stated value of \$3,156,230. It is not clear from the report how this value is determined (e.g., OECD retail price or international non-profit wholesale price).

3.4 Estimated Number of People Receiving Donated Insulin

Excluding support programmes in the United States (which are outside the scope of this study) and humanitarian emergency donations (which are very incidental in nature), the estimated numbers of people with type 1 diabetes benefitting from multi-year LFAC, CDiC and WDF programmes with a component of free insulin in 43 low- and middle income countries are listed in Table 2. The estimated number of patients receiving free insulin is summarised in Table 3 and graphically represented in Figure 1.

Table 2. Company-supported country programmes for patients with type 1 diabetes with a component of donated insulin in LMIC (2009–2015)

LFAC	WDF	CDiC
Africa		
Burkina Faso		
Burundi		
	Cameroon	Cameroon
Congo		
Congo DR	Congo DR	Congo DR
Eritrea		
Ethiopia	Ethiopia	Ethiopia
Ghana		
		Guinea
Kenya	Kenya	Kenya
Mali		
Mauritania		
Nigeria	Nigeria	
Rwanda		
Sudan	Sudan	
Tanzania		Tanzania
Togo		
	Uganda	Uganda
Zimbabwe		
Americas		
Bolivia		
Cayman Islands		
Dominican Republic		
Ecuador		
Guatemala		
Guyana		
Haiti		
Jamaica		
Mexico		
Asia/Oceania		
Azerbaijan		
Bangladesh		Bangladesh
Cambodia		
	China	
Fiji		
		India
Maldives		

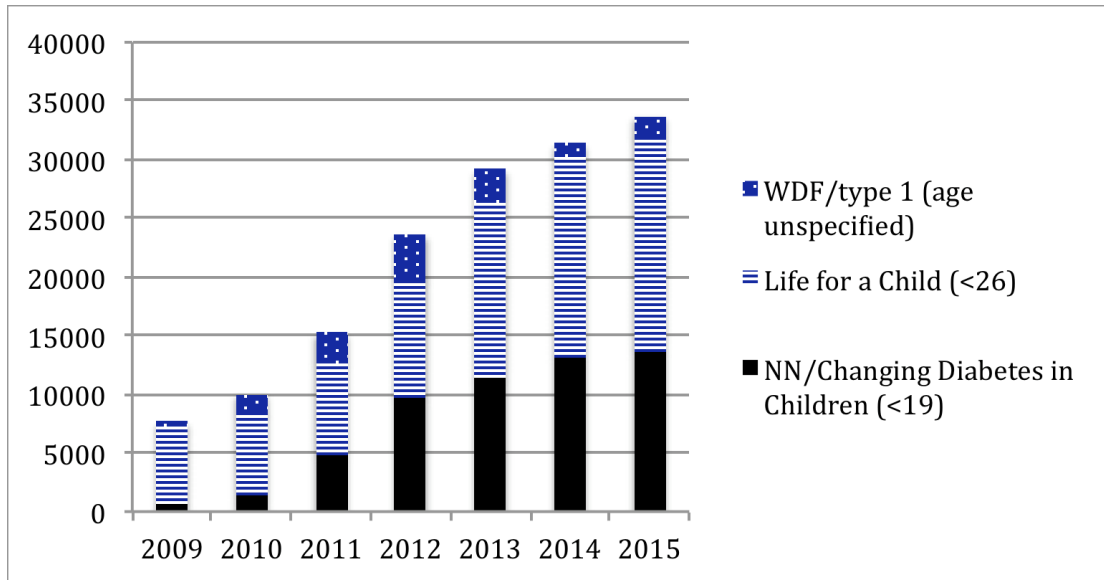
LFAC	WDF	CDiC
Nepal		
Pakistan	Pakistan	
Papua New Guinea		
Philippines		
Solomon Islands		
Tajikistan		
Uzbekistan		
Vietnam		

Table 3. Estimated number of patients with type 1 diabetes, benefitting from company or company-supported programmes with a component of donated insulin, in 43 LMICs (2009–2015)

	2009	2010	2011	2012	2013	2014	2015
CDiC (<19-21)	713	1328	4748	9710	11403	13199	13700
LFAC (<26)	<i>6480</i>	<i>7200</i>	8000	10000	15000	17000	18320
WDF (type 1)	<i>500</i>	<i>1500</i>	<i>2500</i>	<i>3900</i>	<i>2757</i>	<i>1200</i>	1681
Total	8193	11528	17748	27510	31917	32599	35382

Note: Numbers in italics are author's estimates based on published multi-year figures.

Figure 1. Estimated number of patients with type 1 diabetes, benefitting from company-supported programmes with a component of free insulin in 43 LMICs



3.5 Health Impact of Donation Programmes

Health impact has been evaluated in an increasing number of national support programmes with a component of free insulin. Thirteen studies from 10 country programmes include data on health impact. These are the programmes in Bolivia, Cameroon, Ghana, Guinea, Haiti, Northern India, Mali, Nepal, Rwanda, and Tanzania (44-56). The data presented in the following sections are from these studies, unless otherwise specified.

3.5.1 Increase in Body Weight

The programmes in Tanzania, India and Rwanda report on increased in body weight. In Cameroon, the average body weight increased from 53 kg at the start to 61 kg after nine months of treatment (45, 46). In India, the mean body mass index (BMI) of 48 patients increased from 15.4 to 19 kg/m² in three years (50). In Rwanda, the mean BMI of 500 patients increased from 19.8 to 20.7 kg/m² over three years (53, 54).

3.5.2 Reduction in Mortality

The programmes in Cameroon, Guinea, Tanzania and Uzbekistan report on reductions in diabetes-related mortality in the course of the programme. The study in Uzbekistan is the largest and most systematic study to date, reporting on mortality figures from 1998 to 2014 (57). In this period, diabetes-related mortality fell from 24.5/1000 patient years to 2/1000 patient years. With 31/88 (35.2 percent) of recorded cause of deaths, renal failure was the most common cause, followed by acute complications such as pneumonia, diabetic keto-acidosis, tuberculosis and hypoglycaemia. In Cameroon, mortality over five years was around 10 percent, down from an estimated 80 percent before the programme started; with keto-acidosis, infections, renal insufficiency and severe hypoglycaemia as causes (in descending order of frequency) (45, 46). In Tanzania, mortality fell from 9/300 people in 2011 to 0/750 people in 2014, and in Guinea, from 35 children in 2010 to nine children in 2013 (48, 55, 56). In Rwanda, mortality was 6.2 percent after five years and 17.5 percent after 10 years (53, 54).

3.5.3 Reduction in HbA1c

Five country studies have reported data after one to three years, and five after six to eight years. The median of the reported mean HbA1c values of patients entering the programme was 11.5 percent (range: 10.3–14 percent). The median of the reported mean end values was 8.4 percent (range 7.9–10.43). The largest reduction in mean HbA1c values was usually achieved within one year.

Two studies report a reduction in the proportion of patients with elevated HbA1c values. In Tanzania, the proportion of patients with HbA1c values between 11 and 14 percent decreased from 72 percent in 2008 to 50 percent in 2012–13 (53). In Rwanda, the proportion of patients with HbA1c values above 14 percent decreased from 30.8 percent to 9 percent after two years (52).

3.5.4 Reduction in Frequency of Complications

Programmes in Bolivia, Cameroon, Haiti, India, Nepal, Rwanda, and Tanzania report on the frequency of acute and chronic complications among their patients. However, only three studies report changes over time. In Cameroon, the annual frequency of serious hypoglycaemia reduced from 27/104 (26 percent) to 15/104 (14.4 percent) over five years. In the same period, the annual frequency of serious keto-acidosis decreased from 31/104 (29.8 percent) to 7/104 (6.7 percent) (45, 46). In Tanzania, serious ketoacidosis decreased from 30/300 (10 percent) in 2011 to 5/750 (0.6 percent) in 2014 (55, 56). In Rwanda, over a two-year period, no significant changes were seen in the frequency of micro-albuminuria (from 21 to 19.6 percent) and nephropathy (from 4.7 to 5.4 percent). However, the frequency of hypertension increased from 31.8 percent to 40 percent (53, 54).

No longitudinal data are available from other countries. The programme in Haiti reports 6/32 (18.8 percent) cases of severe hypoglycaemia and 5/32 (15.6 percent)

cases of serious keto-acidosis (49). In one hospital in Nepal, 43 percent of the patients enlisted in the programme were admitted for complications; 87 percent of patients suffered from at least one episode of hypoglycaemia although serious hypoglycaemia was rare at 6 percent (52). In Tanzania, 56 percent of patients suffered from at least one episode of hypoglycaemia, but serious episodes were also rare at 0.6 percent (55, 56). In Bolivia, there were several people with serious nephropathy (44).

3.5.5 School Performance and Social Development

Programmes in Bolivia, Ghana, Guinea, Haiti, India, Nepal, and Tanzania reported on the school performance of children. The Bolivia and Nepal programmes report that over 90 percent of children attend school normally; in the India project, 31/47 children attend school, 12/47 have finished school, and 3/47 have married (44, 50, 52). The programme in Guinea reports that delayed puberty and delayed growth have decreased (48). Other programmes are less positive. In both Haiti⁴⁹ and in Tanzania,^{55 56} only half the children attend school; in Ghana diabetes was limiting school attendance for 46 percent of children, with 19 percent not in the appropriate grade (47, 49, 55, 56). In Haiti, 92 percent of the children attending school receive inappropriate grades for their level; in Tanzania 33 percent missed school and three quarters showed poor performance.

3.6 Public Health Impact of Donation Programmes

3.6.1 Increase in the Number of Facilities and Patients

Table 3 and Figure 1 describe the rapid increase in the number of patients benefitting from the programmes with a component of donated insulin. For example, in Rwanda, the programme started with 25 people in 2004 and included 699 people in 2014. Tanzania started with 50 people in 2003; in 2016 the programme included 2116 people. Mali rose from seven patients in 2007 to 453 in 2016; Guinea from 44 patients in 2009 to 448 people in 2013.

Most programmes report similar increases in the number of treatment centres or participating health facilities. Rwanda grew from 10 facilities in 2009 to 40 hospitals in 2014. The programme in Tanzania started with one diabetes clinic in 2003 and has recently rolled out to 187 district hospitals. In Guinea, the programme grew from nine hospitals in 2009 to 64 hospitals in 2013; in Cameroon, from two centres in 2010 to nine centres in 2015, covering all but two provinces. The LFAC 2016 fact sheet mentions that 20 LFAC country programmes now claim near-universal national coverage of children with type 1 diabetes (58).

Globally, there are about 542,000 children below the age of 15 living with type 1 diabetes (according to 2015 IDF Atlas numbers). LFAC estimates that 112,000 of these children are in need of support (56). Our estimates therefore indicate that about one-third of these children are now covered by programmes with a component of insulin donation.

3.6.2 Policy Impact of Donation Programmes

The impact of the donation programmes on national health policy is, of course, not easy to prove or quantify. The LFAC evaluation of 2013 concluded that the programmes led to better training, more free care, and health systems that are better

able to deal with diabetes (43). They also report from Jamaica that awareness of type 2 diabetes has increased, and that a patient register has been established. In 2017, the programme in Tanzania reported that the government is taking over the procurement and supply of insulin; that an NCD unit has been established in the Ministry of Health with six staff; and that diabetes care is increasingly being integrated with clinics for HIV, tuberculosis, leprosy, dental care and nutrition (55).

Several programmes report that the donation programmes have delivered a very important proof of concept: they have shown that it is possible that children with type 1 diabetes can successfully be diagnosed and treated in LMIC, and that most (up to 80–90 percent) can survive into young adulthood. The programmes have also proven that it is possible to arrange for regular HbA1c testing (usually in a few designated centres in the country) and that exit strategies for patients reaching the maximum age of the programme are possible (see below, Section 3.7.3).

In several countries, especially those where the programme is able to diagnose and treat most new cases of type 1 diabetes, the diabetes programmes have become a visible and recognised part of the national health system. On the other hand, the LFAC evaluation report mentions that in most of the large countries where the LFAC programme only covers a small proportion of the need (e.g., Mexico, India, Nigeria and Philippines), a national policy dialogue has usually not taken place.

3.7 Challenges

Despite the considerable progress that has been made in the diagnosis, treatment and survival of children with type 1 diabetes, several challenges remain as identified in the literature and by national programme staff. These can be divided into challenges in quality of care, health system performance and financing, and sustainability, and are presented below.

3.7.1 Service Delivery and Quality of Care

As stated by the programme manager in Mali: “We are able to keep the children alive, but from now on we must also work on their quality of life.” For example, in Cameroon, only 25 percent of children are well controlled. In Tanzania, 98 percent of children are poorly controlled, usually because of inadequate dosing to save on the cost of insulin and frequency of clinic visits, lack of parental support, irregular diet and hence fear of taking insulin, insulin cool storage, and stigma at school (55). Other programmes mention the frequency of acute complications, such as ketoacidosis (16–18 percent), serious hypoglycaemia (7.5–19 percent) and infections (11 percent); and chronic conditions such as cataracts (19 percent), retinopathy (20 percent), neuropathy (9.2 percent) and nephropathy (9–9.4 percent). Few programmes, except Tanzania, have started routine screening for chronic complications, such as diabetic foot disease and eye diseases. Tanzania seems the only programme so far with integrated diabetes care and nutritional services.

In Tanzania, rapid staff turnover of trained staff necessitates a continuing education programme for new health workers. In Guinea, only 12 percent of health workers are medical doctors and much emphasis is, therefore, placed on task-shifting to paramedical workers, as in many industrialised countries (48).

3.7.2 Health System Performance and Financing

Achieving universal access to diagnosis and care of type 1 diabetes remains a challenge to any health system; not least because of the life-long treatment costs

involved. The median cost of a basket of basic treatment of type 1 diabetes in 15 LMIC was US\$553 per year (range: US\$ 255–1,185) representing 56 percent (range: 12–370 percent) of the mean gross domestic product and 153 percent (range: 20–1,535 percent) of the mean family income. The mean cost of insulin was 26 percent, syringes five percent, test strips for two measurements per day 62 percent, and HbA1c testing four times per year was eight percent. It is clear that most people living with diabetes and their families are unable to finance these costs themselves and will remain dependent on external support. Even in Tanzania, where a government commitment has been made to supply insulin free of charge, the supply does not reach all regions and is sometimes erratic.

In Rwanda, every additional glucose test per week reduced the mortality risk by seven percent (54). In the study on the cost of standard diabetes care mentioned above, the cost of test strips is around two to three times that of human insulin, representing 62 percent of the total cost of the package. With insulin free of charge, or supplied at an affordable price, the cost of glucose monitoring is therefore becoming an important limiting factor.

Some countries report specific supply problems. The programme in Tanzania has experienced problems with customs clearance of donated insulin, when insulin was shipped by donors not following the WHO guidelines on medicine donations (e.g., when donated products were not registered in the recipient country). Some donated products arriving in Kenya had a short remaining shelf-life and expired while still under customs clearance. Nigeria is struggling with different types of syringes for 10, 50 and 100 IU.

Many families face serious challenges in receiving optimal diabetes care. In Tanzania, 24 percent of patients mentioned lack of time, 61 percent transport costs, 48 percent medication costs, 41 percent lack of medication, and 21 percent the cost of diagnostics as main problems. On average, they spent 53 percent of family income on one child with diabetes (55). In Guinea, a marked increase in mortality after five years of treatment suggests that, in the end, some parents may have given up (48).

3.7.3 Sustainability

In general, the rising number of surviving people living with type 1 diabetes is seen as a threat to the continued viability of donation programmes. In fact, there are two aspects to this: the sustainability of diabetes care for those surviving out of the programmes (19/21 years of age for CDiC or 26 years for LFAC), called “transition”, and the continuation of financial support, including insulin donations, to the donation programmes in general, called “sustainability of donation programmes”.

In the LFAC evaluation, 31 (78 percent) country programmes indicated that they cannot support individuals through the transition. Several solutions are being tried in different countries with some success. In Tanzania, children under 18 are registered in the CDiC programme and covered until age 22; the LFAC programme accepts them between 19 and 22 years and covers them up to 26 years (55). In other words, the two programmes complement each other.

Several programmes include activities to train the adolescents to earn a living and ultimately pay for their own treatment. In Rwanda and Tanzania, vocational training is offered. In Tanzania and Haiti, the young adults are being trained and recruited to become counsellors for other children with diabetes. In Tanzania, microcredits are made available to start a small business. In Bangladesh, the young adults are trained in mobile phone repairs. In India, 12/47 children have finished school are now

working; 3/47 have married. In conclusion, some countries have shown that a successful transition is possible, but it must be planned in advance and needs additional investments. Such transition programmes need to be started in other countries, and some of the good experiences mentioned above could be used as a model.

The general sustainability of donation programmes is another challenge. Recently, the CDiC programme was extended beyond its original target date of 2015, to cover 20,000 children by 2020 (the latest figure was 13,700 children in 2015). Insulin donations to the LFAC programme seem to be assured until 2018. There are no signals that the major donors are considering withdrawing their support; the CDiC recently expanded into five new countries (Cambodia, Ivory Coast, Myanmar, Senegal, and Sudan). Yet, it should be recognised that donation programmes, essential as they can be in certain situations, can never offer a final and sustainable solution.

4. Discussion

4.1 Range and Quality of Available Information

Public reporting on the programmes is widely scattered, largely incomplete and sometimes inconsistent. Most information provided to the ATM Index 2014 was covered by confidentiality agreements. It is hopeful to note that the information submitted for the 2016 Index was more complete and included references to health impact of the donation programmes. However, information on the type, quantities and values of the donations and discount programmes remained confidential in 2016, as well.

The level of detail varies greatly between programmes, countries and years. When medicine donations are mentioned on the websites or in reports, the types and quantities of the different products are rarely specified. When financial amounts are disclosed it is not clear whether these amounts are based on retail sale prices in OECD countries, or on international not-for-profit wholesale prices, as required under the WHO *Interagency Guidelines for Medicine Donations* (60). Using the former would generally lead to a much higher reported value of the donation than a value based on the prices for which the recipient organisation would have been able to purchase generic versions of the same products at world market prices.

For most donation programmes, whether the patients receive human or analogue insulin is not officially published. Only direct contacts with several programmes have revealed that most donations (especially those through LFAC and CDiC) concern human insulin. There is even less information available for the various differential pricing programmes, as information on the relevant countries, type of products, quantities per country, and any conditions, restrictions and sustainability provisions is rarely provided as public information. Whenever such information is submitted by the companies to the ATM Index, it is covered by confidentiality agreements.

It is only in recent years that an increasing number of papers presented at scientific meetings and/or published in peer-reviewed journals describe the health impact of the support programmes. These papers are the main source of the future challenges and suggested solutions presented in the next section.

The scientific quality of these papers, and therefore the strength of the evidence they present on the health impact of donation programmes, is not very high. None of the

papers had a control group, about two-thirds were simple “pre-post” studies (reporting some health statistics before and after a certain period), and the rest were “post-only” (reporting on current health indicators). This lack of scientific rigour in reporting on the impact of donation programmes is in line with the findings of a recent systematic review of company reports on the impact of access programmes, which found that nearly all evaluations were of low quality (62 percent), or very low (32 percent) quality (60).

4.2 Impact of the Donation Programmes

Although information on the inputs and outcomes of the programmes is scattered, incomplete and of low quality, some conclusions can be drawn.

The most important country programmes with a component of donated insulin are part of IDF’s LFAC programme, which is supported by insulin donations from Eli Lilly. Altogether, programmes with a component of donated insulin in the period 2009–2015 were identified in 43 LMICs (Table 2).

The number of people, mostly children, benefitting from the donated insulin rose from an estimated 8,193 in 2009 to 35,382 in 2016. Most country programmes witnessed a large and steady increase in people being treated (e.g., from 25 patients in 2004 to 699 patients in 2014 in Rwanda), and an equal rise in the number of treatment centres (e.g., from one diabetes clinic in 2003 to 187 district hospitals in 2016, in Tanzania). Several countries (e.g., Tanzania, Mali, Cameroon and Guinea) claim they now cover most newly diagnosed children and adolescents with type 1 diabetes.

In 2015, there were about 542,000 children below the age of 15 globally with type 1 diabetes. LFAC estimates that 112,000 of these children are in need of support (56). Our estimates therefore indicate that about one-third of these children are now covered by programmes with a component of insulin donation.

Thirteen recent studies from 10 country programmes include data on the health impact of the programmes. Three countries report an increase in body weight or BMI. The increase in BMI was most marked in India, probably reflecting the poverty and/or that most patients were initially underweight. In Africa, the rise in bodyweight was much less, at around five percent. Four countries report a reduction in mortality. The most detailed study, from Uzbekistan, reports a reduction from 24.5/1000 patient years in 1998 to 2/1000 in 2014, when the programme had achieved full coverage. In two African countries, Cameroon and Rwanda, mortality was six–10 percent after five years and 17–20 percent after 10 years.

The continuing mortality of people living with type 1 diabetes while under treatment may be an indication that the continued financial, emotional and time investment burden to families and parents may be too much in the end. In Tanzania, the mean financial burden of one child with diabetes consumed 53 percent of family income. This implies huge economic opportunity costs to the family, including the other children. There is a suspicion that some families simply give up in the end. If this is indeed true, there is yet another reason to include diagnosis and treatment of type 1 diabetes in any national health insurance package, as part of universal health coverage and included in the Sustainable Development Goals.

Most studies report a decrease in the mean HbA1c value, which is often reached within the first years of the programme. Most programmes reach a median value of 8.5 percent (range 7.9–10.43), which is still above the target value in most high-

income countries. This finding is in line with the observation that a large proportion of children are not fully stabilised (e.g., in Cameroon and Tanzania) and continue to suffer from acute and chronic complications, although the overall frequency of complications has decreased over time. Particularly serious complications, such as severe hypoglycaemia and diabetic keto-acidosis, have become less frequent.

The impact of the donation programmes on national health policy is not easy to prove or quantify. Most reports say that the programmes have led to better training, more free care, and health systems that are better able to deal with diabetes. The government of Tanzania is taking over the procurement and supply of insulin and has established a NCD unit in the Ministry of Health. Several programmes report that the donation programmes have shown that it is possible that children with type 1 diabetes can successfully be diagnosed and treated in LMICs, and that most (up to 80–90 percent) can survive to young adulthood. The programmes have also proven that it is possible to arrange for frequent HbA_{1c} testing (usually in a few designated centres in the country) and that transition strategies for young people reaching the maximum age of the programme are indeed possible. In countries where the programme is able to diagnose and treat most new cases of type 1 diabetes, the diabetes programmes have become a visible and recognised part of the national health system.

Overall, we can conclude that the support programmes with a component of donated insulin, such as LFAC and CDiC, have made a considerable impact on the lives of over 35,000 children with type 1 diabetes—who owe their lives to these programmes—and to their families. The huge rise in the number of people living with diabetes under treatment in 43 LMICs and the parallel increase in the number of treatment centres would probably not have taken place—at least yet—without the external support from these programmes. Yet, these programmes currently only cover one-third of children with type 1 diabetes in need globally and their overall health outcomes are still far from ideal. In that sense, the programmes have not yet reached their maximum potential.

For people living with diabetes and their families, free insulin is probably the most visible aspect of the programme as it is clear that patients simply do not come to the clinics when the medicine is not available or too expensive. Yet the cost of insulin represents only one quarter of total supply costs (alongside syringes, glucose meters and strips, and HbA_{1c} testing). In addition to supplies, the programmes have also invested much in other essential activities, such as advocacy, awareness building, patient and health worker training, and other health system support (59). Therefore, free insulin has been an essential condition for success, but is not sufficient on its own and must be placed alongside many other essential programme components.

4.3 Sustainability

The “transition”, the continuation of diabetes care for those surviving out of the programmes (19/21 years of age for CDiC or 26 years for LFAC), is the first aspect of sustainability. Several countries have begun specific activities aimed at empowering the young adults to gain a living and look after themselves (section 3.6.3). These activities seem to be successful—at least in part—but they are not yet part of all country programmes.

The continuation of donor support for LFAC, CDiC and WDF programmes is another challenge. In this respect, it should be noted that there is no indefinite growth in the number of children with type 1 diabetes in need of support. When a country programme has reached the stage that nearly all children are covered (e.g., in

Tanzania), the number of beneficiaries will gradually become stable, with a similar number of children coming in and transitioning out (except for a slow increase from general population growth). The need for external support therefore also becomes relatively stable with regard to the population of children (unless surviving children remain eligible as adults). This fact should reassure donors.

The ultimate sustainable solution is the inclusion of standard diabetes care in national social health insurance programmes in all LMIC. It is generally accepted that chronic care of life-threatening diseases, such as diabetes, are of highest priority when social health insurance schemes are established. In the interim, the donation programmes perform a very important role, leading to great health benefits to individuals and their families.

Focusing on insulin and other essential supplies, recent studies allow us to make a careful estimate of the total cost of the necessary insulin, tests strips, and HbA1c testing for all 80–120,000 children with type 1 diabetes in need of support. The median cost—in 15 LFAC countries—of a package of 18x10ml insulin, 1/3 glucometer, two strips per day, two syringes per week, and four HbA1c tests per year, came to US\$553 per year (57). If we apply these median cost estimates to all patients in need, the amount for all 80–120,000 patients would be around US\$44.2–66.3 million per year. Of this total, an estimated US\$12.4 million (28 percent) would be needed for insulin, and US\$27.4 million (62 percent) for glucose tests; the rest for syringes (five percent) and HbA1c tests (eight percent).

In another approach, we could estimate that these 80,000–120,000 people living with type 1 diabetes would need 1.44–2.16 million vials of insulin per year. At Novo Nordisk's mean reduced price for LMIC of US\$4 per vial (2017), the total amount needed would be US\$5.8–8.7 million per year (the real cost for manufacturing companies would be less). On this basis, it should be relatively easy to fund free insulin for all children with type 1 diabetes in need of support. This figure compares well with an earlier estimate, by John Yudkin in 2000, of US\$3–5 million per year for insulin for people living with type 1 diabetes in least-developed countries (62).

The cost of diagnostics is much more of a barrier. In the cost estimate mentioned above, the mean cost for twice daily glucose testing and HbA1c testing four times per year amounted to nearly three times the cost of insulin. This is the most important area in which programme costs must urgently be reduced, either through donations, long-term price discounts, or more (biosimilar) competition in the market. The latter could perhaps be achieved through the targeted development of a generic glucometer and strips, as suggested in the LFAC evaluation (43).

5. Recommendations

In the following section, some practical recommendations are presented, based on the technical challenges identified in national diabetes programmes with a component of donated insulin. It is acknowledged that many challenges identified in the published literature—and by the national programme staff consulted—relate to diabetes programmes, in general, and often go far beyond the aspect of insulin donations only.

The fact that national governments, and not donors, are ultimately responsible for national health systems is fully acknowledged. However, there are two reasons why this wide range of practical recommendations is presented, nevertheless. Firstly, donation programmes cannot and should not be seen in isolation from national

diabetes programmes. Secondly, programmes with a component of donated insulin have often filled a void in national health systems and have thereby generated, often for the first time, valuable experiences with the diagnosis, and treatment of type 1 diabetes in LMIC. These recommendations may help maximising the potential of donation programmes towards the ultimate goal of equitable and sustainable systems of diagnosis and treatment of type 1 diabetes.

5.1 Quality of Care

1: National diabetes programmes should develop evidence-based clinical guidelines for the diagnosis and treatment of type 1 diabetes.

Justification and explanation: Evidence-based clinical guidelines are an essential basis for training, financing, supply and supervision. The guidelines will promote the standardisation of insulin type and strength, and size of syringes. They should form the basis for the relevant section of the national list of essential medicines, and/or the national reimbursement list. They will also support the establishment of new treatment centres, and task-shifting to paramedical staff and integrated NCD or chronic care clinics.

Practical implications: Clinical guidelines can be developed in collaboration with the national government and international organisations, such as WHO. Ideally, they should be part of general national standard treatment guidelines for other common diseases, but this is not an absolute requirement. They can be published electronically and in hard copy. They should also include guidelines on the recommended type and frequency of diagnostic tests (e.g., glucose testing at least twice daily and HbA1c testing four times per year).

2: National diabetes programmes should develop or strengthen a person-centred approach to care, with integrated services for diabetes, nutrition advice, and treatment of other non-communicable and/or chronic diseases .

Justification and explanation: Many people living with diabetes experience problems with attending regular diabetes care services, due to lack of time and transport costs. Children with type 1 diabetes often do not take the second dose of insulin due to food insecurity or stigma at school, or in an effort to save costs.

Practical implications: These services should be delivered by paramedical staff, and close to the home, at schools, or in community pharmacies, and should include routine screening for common complications. Diabetes services could be integrated with nutritional advice, and services for the continuous treatment of HIV, tuberculosis, leprosy, and cardiovascular diseases. The links between donor-supported programmes, national associations and the national health system must be strengthened, with the latter taking the lead on culturally appropriate community-based training.

3: National diabetes programmes should continue training large numbers of general doctors and paramedical staff in the prevention, diagnosis and treatment of type 1 diabetes and its complications.

Justification and explanation: Rapid turn-over of trained staff, and the need to further expand and decentralise diabetes care and treatment services mean that high numbers of new staff need to be trained.

Practical implications: Training should be based on the national clinical guidelines for diabetes, and should be combined with integrated care for chronic diseases.

5.2 Health System Performance and Financing

4: The national government should establish and implement a national diabetes policy, covering financing and service delivery of diabetes care.

Justification and explanation: A national diabetes policy is a commitment to a goal and a guide to action. Many different policy decisions, investments, regulations and activities are needed in order to achieve universal access to prevention, diagnosis and treatment of type 1 diabetes. Some objectives may be contradictory (e.g. existing laws may prohibit prescribing by paramedical workers; heavy import duties may be levied on donated insulin). A national policy can identify and resolve such obstacles.

Practical implications: There are international reference materials that can be used as a model. However, the value of an imported policy text is very limited. The analytical and consultative process of developing a national diabetes policy is an essential mechanism to bring national stakeholders together, to create awareness for the issue, and to promote ownership of the problem by all parties involved.

5: The national government should ensure that services for the prevention, diagnosis and treatment of type 1 diabetes and its complications are available, accessible, acceptable, and of good quality, and linked to a national patient register. Free diagnosis and treatment of type 1 diabetes should be included in all national health insurance schemes.

Justification and explanation: The cost of standard care for type 1 diabetes is too high for out-of-pocket payment by most families, leading to bankruptcy and death. Some health insurance schemes have included glucose strips in the package, but not in sufficient numbers (e.g., only two strips per week). Chronic care for common life-threatening diseases, such as type 1 diabetes, is therefore of highest priority for health insurance schemes. A national patient register will facilitate patient follow up, payment of benefits, and screening for complications.

Practical implications: Most existing health insurance systems include chronic treatment for life-threatening diseases in their basic benefit package; these can be used as an example. With rapidly increasing use of mobile telephones and electronic connectivity, clinical follow-up and direct payment of vouchers, subsidies or reimbursements to patients are increasingly feasible.

6: Donor agencies should ensure that all donations of medicines, diagnostics and equipment follow the WHO Guidelines for Medicine Donations.

Justification and explanation: Not all insulin donations follow the WHO guidelines. Some non-governmental organisations, such as Insulin for Life, send products collected from patients or pharmacies, or products that are not registered for use in the recipient country, and sometimes close to expiry. The sale and use of such medicines is illegal in many donor countries; as donations, they undermine national quality regulations, national clinical guidelines, and national standardisation efforts.

Practical implications: Most recurrent problems are identified and addressed in the WHO guidelines (Annex 1). The type of donated insulin should follow national

clinical guidelines, the national list of essential medicines, and national quality standards. Insulin donations should always be planned in close collaboration with the recipients, and should respect and support national health systems and programmes. The cost of diagnostic tools, such as glucose strips and HbA1c testing, has become the main barrier to good quality care; programme efforts should now also focus on long-term donations or price discounts of such diagnostic materials.

7: National diabetes programmes should report regularly on programme targets, the number of people living with diabetes covered, health outcomes, key health system data, the role of partners, and project financing.

Justification and explanation: Current experiences prove that cost-effective diagnosis and treatment of type 1 diabetes in LMIC is very much possible and can yield great health benefits, at moderate costs. However, most programme reporting is scattered and largely incomplete. Good reporting will create the necessary data to support the case for inclusion of diabetes care in national health and health insurance schemes.

Practical implications: Key data to be collected and published on a routine basis include: programme aims and targets; number of treatment centres; number and basic characteristics of patients; number and type of diagnostic tests and treatments supplied; health outcomes, such as mortality and cause of death, mean body weight, mean level of HbA1c, type and frequency of morbidity and mortality per year and over time; the roles and expectations of programme partners; transition strategies for people living with type 1 diabetes after the end of the eligibility; and programme financing mechanisms such as insurance schemes, direct subsidies and donations, and out of pocket payments.

5.3 Sustainability

8: National diabetes programmes and donor agencies should plan the transition of recipients of donated insulin beyond their eligibility to programme support well in advance. This transition should be supported with specific investments and programme activities; links with existing insulin discount programmes should be strengthened.

Justification and explanation: Eligibility for the two most important donor-supported programmes ends at age 19–21 (CDiC) or age 26 (LFAC). Many country programmes cannot offer support in managing this transition, although some promising examples of vocational training have been reported from Bangladesh, Haiti, India, Rwanda, and Tanzania. The long-term solution is to include standard diabetes diagnosis and treatment in national health insurance packages. In the interim, practical support to all people living with type 1 diabetes, not just children and adolescents, remains very much needed.

Practical implications: Solutions must work in two directions: creating a situation of gainful employment and functioning normally in society on the one hand, for example, by offering vocational training, and improving access to affordable good quality adult diabetes care on the other hand. The first is often seen as part of the support programme for patients with type 1 diabetes in collaboration with local diabetes associations; the latter is a matter of national health policy and, ultimately, national health insurance. In the interim, programmes should strengthen their links with insulin discount programmes for adults, such as Novo Nordisk's BoP programme, or its general insulin discount programme for least developed countries.

9: Donor-supported programmes, such as LFAC and CDiC, should be continued and expanded in countries in need for as long as the diagnosis and treatment of type 1 diabetes and its complications are not yet included in national health insurance schemes.

Justification and explanation: Several national programmes with a component of donated insulin have delivered the proof of concept that diagnosis and treatment of type 1 diabetes in LMIC is very much possible, with large improvements in survival, mean body weight, mean HbA1c values, and frequency of complications; and various possibilities for transitioning out of the support programme. The programmes have also made contributions to the health system in participating countries, especially in those countries where most children with type 1 diabetes are now diagnosed and treated. Continued donor support is justified by the health benefits listed above; by the fact that patient numbers are stabilising in countries with full coverage, so that the level of donor support will stabilise; and by the fact that further valuable health system experience can be gained from the screening, early diagnosis and treatment of complications, and from integration with national comprehensive NCD services.

Practical implications: The discussion with the national government on the development of a national diabetes policy, and the inclusion of standard diabetes care in national health insurance schemes, needs to continue. The proof of concept, the increasing practical experience, the proven cost-effective treatment, and pressure by surviving patients, will all help in this regard. Ten steps to phase out an insulin donation programme are presented below.

5.4 Phasing Out Donor Support

While the recommendations in the previous sections concern the general impact and health systems aspects of the support programmes, this report would not be complete without a set of recommendations specially aimed at the donor programmes concerned.

A donor-supported programme for the diagnosis and treatment of type 1 diabetes in LMIC could have the following trajectory towards a fully independent and sustainable national programme. The order in which these steps are presented below could reflect a natural course of events in a country, starting with free diagnosis and treatment for an increasing number of children and adolescents with type 1 diabetes (as is currently the case in many countries) and ending with a full-fledged national system (the ultimate goal). The assumption is that donor-supported programmes, after successful achievement of steps 1-5, would be in a strong position to convince and encourage national diabetes associations and government authorities to take the subsequent steps towards a national programme.

Donor agencies should:

- 1) Support, in selected LMICs in need, a programme with a free basic package of education, diagnosis and treatment for as many children with type 1 diabetes as possible, thereby preventing the almost certain death these children would otherwise face; and create a national patient register for follow-up and reporting;
- 2) Collaborate with the national government, diabetes associations, and other diabetes-centred groups and donors to create a national continuum of care for type 1 diabetes from childhood to early adulthood, for example, by combining in every eligible country the CDiC donation programme (up to age 18-21), the

IDF/LFAC donation programme (up to age 25) and the Base of the Pyramid and other insulin discount programmes for adults;

- 3) Assist national authorities in creating systems to prevent, diagnose and treat acute and chronic complications of type 1 diabetes in children and adults;
- 4) Provide detailed information on key aspects of the support programme, such as the number and basic characteristics of recipients; the number, type and value of diagnostic tests and medicines donated; the nature and cost of other programme activities supported; and basic health outcomes such as mortality, weight gain, mean HbA1c levels, and frequency of complications;
- 5) Deliver to national authorities, donor organisations, and national health insurance systems, the proof of concept that type 1 diabetes can successfully and cost-effectively be diagnosed and treated in LMICs;
- 6) Encourage national authorities to develop and implement a national diabetes policy, as a public commitment and a guide for action to achieve universal access to decentralised health services for the prevention, diagnosis and treatment of diabetes, as part of the progressive realisation of the right to health;
- 7) Encourage national authorities to create systems, whereby young adults are empowered to procure affordable standard diabetes care after their eligibility for the donation programme ends;
- 8) Work with the national government towards inclusion of standard diagnosis, care and treatment of diabetes in national health insurance programmes;
- 9) Encourage the national government to integrate the prevention, diagnosis and treatment of diabetes and its complications with the delivery of nutritional advice and other services for the prevention and treatment of other chronic conditions such as HIV, tuberculosis, leprosy, and hypertension;
- 10) Phase out donor involvement as soon as these objectives have been achieved.

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