



Improving access to insulin: what can be done?



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Practice Points

- International and national barriers to access to insulin need to be addressed in parallel.
- Health system-related factors, such as tendering practices and distribution need to be improved.
- Affordability issues will require government policies and measures to be put in place to ensure that people can afford the insulin they require to survive.
- Most solutions proposed to improve access to medicines focus mainly on availability and price.
- Based on the International Insulin Foundation's findings, the barriers to access to insulin were more to do with problems linked to distribution, tendering and government policies than purely accessibility and affordability issues.
- Three factors are key in addressing the issue of access to diabetes care in resource-poor settings: improve access to medicines, strengthen health systems and ensure that diabetes is on the global health agenda.

SUMMARY A third of the world's population currently has no guaranteed access to essential medicines. Attention has focused on the issue of access to medicines for HIV/AIDS, TB and malaria, but not on access to essential medicines for noncommunicable diseases, including insulin. Insulin has been widely available in the Western world since its discovery in 1921, but in resource-poor settings access to insulin is still problematic due to international and national barriers to access. Solutions proposed have mainly focused on increasing availability and lowering cost. However, insulin alone is not enough for proper diabetes care. In order to improve the lives of people with diabetes, access to medicines needs to be addressed in parallel to creating a health system able to manage all aspects of diabetes care.

A third of the world's population currently has no guaranteed access to essential medicines [1,101]. In the poorest parts of Africa and Asia, this proportion increases to a half [102]. More than 2 billion people in developing countries are therefore unable to fully enjoy their right to health, as outlined in article 12 of the UN's International Covenant on Economic, Social and Cultural Rights [103]. Access to essential medicines is a

prerequisite for the progressive realization of this fundamental human right, and, as such, is an issue of great consequence to the health and well-being of individuals throughout the world [104]. Considerable attention has been paid to the issue of access to medicines for HIV/AIDS, TB and malaria with a particular focus on the issue of patents and prices [2–9]. However, little attention in public health policy debates has been paid

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to questions of access to essential medicines for noncommunicable diseases (NCDs) despite these conditions representing 35 million deaths out of the worldwide total of 58 million, with 80% of these deaths occurring in developing countries where issues of access to medicines are the most prominent [105].

When considering the issues regarding access to medicines, in particular access to insulin, it is important to note that insulin is off-patent and even though its price has significantly dropped over time, with the introduction of industry-sponsored differential pricing initiatives [106], access is still problematic [10–12] despite being viewed by the WHO as an essential medicine [107]. Before the discovery of insulin, children with Type 1 diabetes needed to count calories, weigh their food and sometimes fast. This drastic treatment prevented children from dying of diabetic ketoacidosis and extended their life expectancy by some years before they inevitably died of starvation [13]. This situation changed in 1921 when work carried out by Frederick Banting and Charles Best at the University of Toronto, Canada, led to the discovery of insulin [14,15].

Leonard Thompson was administered with his first injection of insulin on 11 January 1922 in Canada. He was the first patient to be treated with insulin for Type 1 diabetes. Having survived some 2 and a half years from his diagnosis, he had done better than most children with Type 1 diabetes in the preinsulin era. Access to insulin saved Leonard from near certain death [14,15]. Elliott Joslin had spent most of his career seeing his patients with Type 1 diabetes inevitably die. In 1922 he had the opportunity to see this change with his patients being able to access insulin and stated that “a new race of diabetics has come upon the scene” [16].

Despite enormous achievements in the area of care for Type 1 diabetes, an estimated 4 million years of life were lost for people with the disease in the year 2000 [17]. As stated on the cover of issue 9548 of the *Lancet* and the accompanying editorial, from a global perspective, the most common cause of death for a child with Type 1 diabetes is lack of access to insulin [18]. The factors causing this are present both at international and national levels and cannot be addressed in isolation and it is therefore important to understand the wider issues surrounding access to medicines and the path of medicines from the moment they leave the factory until they reach the individual.

The issue of access to medicines

The topic of access to medicines burst into the global public spotlight in 2001 when 39 pharmaceutical companies took the South African government to court over alleged unlawful legislation, which gave the Minister of Health the right to import generic versions of patented drugs and allowed generics to be manufactured locally [19–21]. International policy debates on public health and trade have focused primarily on the relationship between prices and patents and the extent to which they limit access to medicines [5,6,8,22–25].

Key to understanding the issue of access to medicines is price, which is the amount of money needed to purchase goods or services, and affordability, which is being able to meet the expense of goods or services. Prices vary from country to country and affordability is impacted by purchasing power. The other key matter in examining access to medicines is availability. Is the medicine needed actually there when the individual requires it? In examining these two key concepts of affordability and availability, a variety of scenarios are possible, with medicines being available but not affordable, and affordable but not available. The ideal scenario is, of course, for medicines to be freely available to all and affordable, but for this to happen a variety of factors need to be met for the medicine, both before it reaches a given country and once it has entered a given country.

International barriers to access

International barriers are those that affect access to medicines before they arrive at their country of destination. These can be divided into two main categories: patents and prices.

■ Patents

Patents are a set of rights granted to the inventor by a specific country for a limited period of time in exchange for disclosing their invention. Patents act as a barrier as they limit competition and therefore impact on price [26]. Within the framework of the World Trade Organization's Trade-Related Aspects of Intellectual Property Rights (TRIPs), which covers intellectual property for medicines, patent rights are set for a minimum of 20 years. Many medicines that are used in the fight against HIV/AIDS are produced by only one pharmaceutical company that can control its price as they are still under patent protection. For insulin, these patents have

expired except for the newer analog insulins, but the insulin market is controlled by two or three companies.

■ Price

According to DiMasi *et al.* [27] the price of a medicine includes many aspects of research and development and preclinical aspects of the discovery process, manufacturing as well as elements such as the opportunity cost of the funds used in research. For the older formulations of insulin it could be argued that the costs linked to research and development have been recuperated based on the time since they have come to the market. In addition, the initial start-up costs for the manufacturing of insulin are most likely to have been amortized over time. That leaves the raw materials and recurrent costs. Another way that the price of insulin has been seen to increase is the replacement of animal insulin with human insulin, and in some settings the replacement of human insulin by more expensive analogs. In parallel, there has been increased use of prefilled and cartridge devices versus vials, which are also more expensive.

National barriers

Once a given medicine has arrived in a country, national barriers may impede access. Focusing specifically on the affordability and availability of insulin in resource-poor countries, the International Insulin Foundation (IIF) was established by leading academics and clinicians in the field of diabetes and developed the Rapid Assessment Protocol for Insulin Access (RAPIA) in order to assess barriers to diabetes care [28]. The IIF has conducted in-depth assessments in Kyrgyzstan (2009), Mali (2004), Mozambique (2003), Nicaragua (2007), Vietnam (2008) and Zambia (2003) [108–113]. This section builds on this experience to describe the issue of access to insulin at a national level.

■ External factors

Exchange rates can impact medicine purchases as most medicines will be purchased in US dollars. This means that many countries are at the mercy of currency fluctuations. For example, in Nicaragua it was found that between 2005 and 2006 the country purchased 29% more insulin at the same price in US dollars, but the increase in cost of this insulin was equivalent to 35% in the local currency.

■ National policies

Some countries still impose value-added taxes and custom duties on medicines that are imported. This impacts the price later on in the system. In addition to these factors that increase costs, mark-ups throughout the system will also increase the final cost to the end user. For example, in Mali there is a standard mark-up at each level of the health system, which allows for cost recovery. From the central level to facilities this was 18%. In Mozambique, in 2003, the central level charged facilities for storage and transportation costs. These decisions are based on government budgets and priorities. Availability and affordability at facilities is impacted by the organization and effectiveness of the distribution system, which is planned at a central level. With regard to affordability, again government policies and insurance schemes, and so forth, will have an impact. In Mozambique, in 2003, there was a ‘chronic disease law’ that stated that people with chronic diseases, including diabetes, were able to access medicines at an 80% subsidy. During the RAPIA assessment this was found to not be fully implemented. In Nicaragua, access to medicines was provided for free by the government, whereas in Mali cost recovery was in place. Vietnam had insurance schemes, which covered all or a portion of costs related to medicines, but not everyone benefited from this.

■ Health expenditure

Limited budgets and limited resources of individuals, due to high levels of poverty, in resource-poor countries act as barriers to access of insulin, either directly or indirectly: directly if insulin needs to be purchased; indirectly if other costs of treatment and transportation cannot be met due to the poverty of the individual. In countries such as Mali, Mozambique and Zambia, health expenditure by the government is equivalent to US\$28, \$14 and \$36 per person, per year, at average exchange rates, respectively [114]. With the average buyer price for insulin on the International Drug Price Indicator being US\$6.17 and assuming that a person with Type 1 diabetes would need 13 vials of insulin per year this would be equivalent to 2.9, 5.7 and 2.2-times what Mali, Mozambique and Zambia spend per person per year on health [29,115]. As this expenditure is so low, many people will have to pay out-of-pocket for care and medicines. With anywhere from 50 to 90% of

medicines being purchased by people themselves, medicines represent a high proportion of this out-of-pocket expenditure [30].

National purchasing practices

One of the barriers to access to insulin at a national level can be highlighted by the example of findings from the IIF's work in Mali. In August 2004, the Central Medical Store in Mali bought insulin for the first time in 2–3 years. The quantity purchased was extremely small and not sufficient to cover all needs. The reasons given for why insulin had not been ordered previously was that, as Mali promotes the use of generics, it was unable to find a generic supplier of insulin. In addition, when preparing a tender, the Central Medical Store needs to obtain quotes from three potential suppliers, and as there are few suppliers it was unable to do this. The last factor was that insulin is a costly medicine and the limited budget available needs to be prioritized. Poor tendering practices in Zambia meant that insulin needed to be purchased locally through a private wholesaler at an average price per vial of US\$8.33 compared with \$4.62 for insulin purchased during the tender.

National determinants of price

At a national level, prices of medicines will be determined by tendering practices. Based on the experience of the IIF in all the countries surveyed, except for Vietnam, medicines are purchased centrally by the Ministry of Health. In Kyrgyzstan, insulin and oral medicines for diabetes are the only types of medicines procured centrally, with others being sourced through the private sector. The price at which the medicine is sold will be dependent on the tendering practices of these countries, and factors such as the quantities ordered, inclusion of freight and insurance costs. In Vietnam, for example, it was found that the guidance price from the Ministry of Health for metformin 850 mg was six-times higher than prices on the international market. The introduction of special differential prices had an impact on the price at which Mozambique bought its insulin with a drop in price from \$9.00 per vial in 2001 to approximately half this price in 2002. Even though all three countries in sub-Saharan Africa where the RAPIA was implemented should benefit from this initiative, Mali did not. Another factor impacting this cost is the choice of branded versus generic medicines. Most insulin identified during the

different IIF country assessments was from one of the leading manufacturers. An issue identified in Kyrgyzstan was the purchase of insulin in cartridges and also analog insulin, which significantly impacted cost. In examining oral medicines for diabetes, large price differentials were found between branded and nonbranded versions, especially in Vietnam.

No countries had a single price for insulin. Instead, prices were dependent on location of purchase, the complexity of the supply chain and the method by which the medicine was purchased. In addition, price to the end user was determined by government policies both within the health system (e.g., Mozambique's Chronic Disease Law) or outside the health domain (VAT and import duties). Prices in the private sector found during this work were said to be determined on the availability in the public sector and government policies regulating the private sector. For example, in interviews with the private sector in Nicaragua, it was found that insulin was not supplied as it was already widely and freely available. In Mali, Mozambique and Zambia the ratio of the price of insulin in the private sector compared with the public sector was 1.1, 9.0 and 9.1, respectively. This meant, for example, that a person in Zambia unable to get insulin in the public sector would have to pay 9.1-times more for this insulin in the private sector.

Distribution

Distribution of medicines is the responsibility of the Central Medical Store. This organization was based in the capital city with medicines then being distributed to health facilities and regions. The capability of this organization to effectively distribute medicines throughout the country is the first barrier to access. In Mozambique, it was found that 77% of the total quantity of insulin purchased by the country remained in the capital city [31]. In Kyrgyzstan, a similar problem with distribution was identified in addition to some facilities holding large quantities of insulin. In all countries visited there were no observed and reported problems with the cold chain.

Considering the above issues, there is not one issue of national access. The issue is divided between urban and rural areas, and rich and poor. Urban areas have a better supply of medicines and health facilities that are usually closer to the individual. Rich patients can also access medicines in the private sector or by other means, such as getting medicines

from abroad. In addition, the response given to national barriers cannot focus on one aspect, for example tendering and not look at pricing to the individual and distribution, as this may lead to the medicine being available at the central level for a cheap price, but because of cost recovery and poor distribution, not being affordable and available to people throughout the country.

Proposed solutions

To address the issue of access to medicines and insulin in resource-poor countries different means have been proposed or developed. One such example is bulk tendering, which can be performed by a group of countries joining together, as has been carried out in the Caribbean, or for good planning to be developed at a country level to enable large quantities of medicines to be ordered and, therefore, increase bargaining power [32]. Another recommendation has been purchasing medicines from generic producers. Procurement of medicines for HIV/AIDS from generic manufacturers has resulted in savings of over 50% [33].

One of the concerns often raised about generic producers is if the quality of the medicines they produce meets national and international standards. To address this, the WHO has developed a prequalification scheme for medicines for HIV/AIDS, malaria and TB [116]. This scheme allows countries to know that the producer they are buying their medicines from meets the required standards, with regard to good manufacturing practices.

Two other solutions proposed are compulsory licensing, which is the production of generic versions of patented medicines, and local production, as Brazil and India have been capable of doing. Both of these require the necessary infrastructure and capacity to be able to produce these medicines. All these measures address the issue of price, as does differential pricing, which is charging different prices in different markets at a price that is 'fair' for a given market [34].

In theory, these could all be used for insulin, but challenges with regard to the strength of the big manufacturers with, for example, one of the large insulin manufacturers buying a generic manufacturer in Brazil [117]. Furthermore, the start-up costs linked to developing a facility capable of producing insulin are extremely high. Given this situation, differential pricing may be the only option that is feasible in the short term.

UNITAID is another initiative introduced to address access to medicines. UNITAID focuses on HIV/AIDS, TB and malaria, and provides sustainable predictable revenues as well as negotiation of bulk procurement programs for several countries. The Asthma Drug Facility (ADF), established by the International Union against Tuberculosis and Lung Disease, shows how a disease-specific organization was able to develop a program to improve access to medicines for a NCD [35,36]. The ADF uses pooled procurement and purchasing mechanisms in order to get the lowest possible price for asthma medicines.

Looking specifically at insulin and diabetes, two organizations – Insulin for Life and the International Diabetes Federation's (IDF) Life for a Child program – aim to improve access to insulin in the world's poorest countries [118,119]. Insulin for Life collects unused insulin in resource-rich settings and supplies this to countries in resource-poor settings facing either emergency or nonemergency situations. The Life for a Child program aims to meet the children's immediate needs (insulin, syringes, monitoring and education), and tries to build local capacity and influence governments to create sustainable solutions.

These specific examples deal mainly with supply side issues and may impact access to medicines and insulin, but is this enough?

Access to diabetes care: more than just medicines

Based on the IIF's findings, the barriers to access to insulin were more to do with problems linked to distribution, tendering and government policies than purely accessibility and affordability issues [37]. However, these difficulties in accessing insulin were only part of the larger problems of accessing proper diabetes care and treatment. These include access to syringes, tools for diagnosis and follow-up, availability of trained healthcare workers, government policies and the role of diabetes associations.

Insulin alone is not enough. Syringes are required for its delivery. In the countries surveyed, all countries except Nicaragua had VAT on syringes and in all countries they were not readily available in the public sector. The cost and availability of syringes also meant that people reused single-use syringes. Availability of syringes in most countries was found to be problematic with the private sector being the main source where people got their supplies. This was

linked to poor planning in public sector purchases and not linking the purchase of syringes to insulin orders. In the countries studied, the price of a single-use syringe varied from a low of US\$0.03 in Vietnam to US\$1.50 in Zambia.

Affordability and availability of diagnostic tools was also an issue. In Mali, a urine glucose test cost on average of US\$0.89 and a blood glucose test costs US\$2.38. In Mozambique, laboratory tests for inpatients are free and some outpatients needed to pay a fee for blood glucose of US\$0.21. Tests were free for all people with diabetes in Nicaragua. In addition to the possible cost barrier, there is also the actual availability of the testing equipment, which will impact when a person with diabetes goes to the health facility for initial diagnosis or follow-up. In Mozambique in 2003, it was found that only 21% of facilities had a blood glucose meter and only 8% had ketone testing strips.

In looking at overall costs for diabetes in each country, only in Mali is the cost of insulin the most expensive aspect of diabetes care. In two countries (Mozambique and Vietnam) travel costs were actually found to be the highest item of expenditure. In Nicaragua and Zambia syringes represent the largest item of expenditure. Owing to the availability of free insulin, testing and consultations, people with Type 1 diabetes in Nicaragua have the lowest financial burden due to diabetes. However, this still represents 7% of annual income [37]. In the other countries the burden is much higher. Despite a low burden on the individual, the elements of diabetes care provided free still need to be paid for by someone. In Nicaragua, this is the Government health system. For insulin alone, these costs are upwards of US\$90 per person, per year in countries that can spend as little as US\$3 per person, per year on the provision of healthcare.

Access to healthcare facilities is needed in order for patients to receive the necessary care and medicines. One factor that can impact this is the distance people need to travel. In looking at data collected by the IIF in the countries where the Foundation worked, on average transportation costs represented 34.2% of total expenditure of diabetes per year and in Vietnam transportation was the second largest item of expenditure for families with children with Type 1 diabetes after consumables [37,110].

In the sub-Saharan African countries where the IIF has worked, traditional healers and beliefs are an integral part of health provision. People

use traditional healers for financial reasons, easier access and because of their beliefs [38]. This does not constitute a barrier in itself, but causes people to try alternatives or only use them instead of modern medicine. For example, a study in Senegal found that people with diabetes believed that some medicinal plants were effective in the treatment of diabetes [39] and different studies have shown that some of these plants can lower blood glucose in animal models [40,41]. Due to this important role, traditional healers, beliefs and medicines need to be integrated into the response to diabetes.

Through the IIF's work, what has become apparent is that the supply of insulin alone will not improve outcomes for people with diabetes. Insulin, syringes and testing equipment need to be present at the adequate facilities with the right infrastructure and personnel. The IIF has identified 11 points necessary for a 'positive' diabetes environment; these are [42,120]:

1. Organization of the health system
2. Data collection
3. Prevention
4. Diagnostic tools and infrastructure
5. Drug procurement and supply
6. Accessibility and affordability of medicines and care
7. Healthcare workers
8. Adherence issues
9. Patient education and empowerment
10. Community involvement and diabetes associations
11. Positive policy environment

Points 5 and 6 are directly related to the issue of affordability and availability of insulin. However, the issue of improving the lives of people with diabetes needs to look beyond this small part of improving diabetes care in order to create a health system able to manage all aspects of diabetes care. The solutions proposed by donations, purchasing schemes and parallel imports, for example, will impact the price and availability of insulin, but diabetes care is more than just insulin.

As stated by former US President Bill Clinton, "Until we build the human and physical infrastructure needed to deliver effective treatment,

programs will not succeed” [43]. This was in reference to HIV/AIDS, but the same is true for diabetes. The IIF has addressed this, for example, by developing a twinning project in Mozambique, which addressed issues such as healthcare worker training, strengthening of the diabetes association, development of a national NCD policy and preparation of educational materials adapted to Mozambique context [44].

Another example of this strengthening of the health system for better diabetes care is the work of Santé Diabète Mali. This French nongovernmental organization, which has been working in Mali since 2001, has worked closely with the Malian authorities to address the issue of access to insulin and oral medicines for diabetes, but in parallel has developed projects aimed at strengthening diabetes associations, development of culturally adapted education materials and the use of peer educators, healthcare worker training as well as information campaigns for the general public and people with diabetes.

Conclusion

Access to medicines alone cannot improve levels of health for people with diabetes in developing countries. In examining diabetes, it may be argued that the concept of access to medicines needs to be expanded to encompass that of access to treatment [45]. Treatment includes issues such as availability and affordability of diagnostic tools, as well as trained healthcare workers, diabetes education and support provided by a diabetes association.

In addition to this expanded concept it is important for organizations such as the WHO and IDF to address both the international and national barriers to access. At the international level it is ensuring that the best possible price is made available to countries, either through differential pricing, prequalifying generic manufacturers or a purchasing facility, such as the ADF. On a national level the barriers to access to people with diabetes need to be understood and solutions developed based on this clear understanding. RAPIA, developed by the IIF, allows a clear understanding of the barriers to diabetes care to be identified and then targeted actions to take place.

The framework of 11 points proposed by the IIF gives countries a template for action for the increasing burden of diabetes and NCDs. For these conditions the issue of access to medicines and treatment needs to be effectively addressed

by not only providing the medicines needed, but also strengthening health systems and focusing on the wider issue of providing the best possible treatment.

Another key element is to ensure that diabetes and NCDs are placed on the global health agenda as these conditions receive 15-times less funding than for communicable diseases, such as HIV/AIDS, TB and malaria [46]. Improving care for people with diabetes and other NCDs in a resource-poor country has not been addressed by the traditional bilateral and multilateral donors or by the large funds and foundations involved in health, and therefore needs to be brought to their attention. The IDF in collaboration with other international organizations have tried to address this with the launch of a UN General Assembly Special Session on NCDs. Within this call there is mention of funding for essential medicines and also the inclusion of NCD indicators in the Millennium Development Goals [121]. In parallel with this, the IDF was also successful in obtaining a UN Resolution on diabetes, which highlighted the need to strengthen health systems in order to effectively address the challenge of diabetes [122].

These high level meetings and resolutions are key in addressing the increasing burden of diabetes. However, a cornerstone of ensuring that people with diabetes receive the appropriate care they need is to have access to medicines. Much of the discourse for diabetes has sometimes focused on primary prevention or care. In learning from the response to HIV/AIDS, which also started with a UN Assembly Special Session in 2001 [47], both care and primary prevention need to go hand in hand [48]. This can only be achieved with a comprehensive response focused on improving the health system and health-related policies.

Future perspective

Noncommunicable diseases and diabetes are becoming larger and larger health concerns throughout the world, in both resource-rich and resource-poor settings. Access to medicines and care is not only an issue for resource-poor settings and with the increasing burden of diabetes comes increased costs for both the individual and the health system. As diabetes and other NCDs become more widely recognized as public health concerns in resource-poor settings, one would hope that donors will start addressing this issue. In parallel with this, under the TRIPs agreement

countries are able to produce medicines for public health emergencies. The definition of a public health emergency has evolved to include conditions, such as HIV/AIDS, TB and malaria, but as of yet, not NCDs or diabetes. With generic oral medicines widely available, the issue of cost of these medicines, to a certain extent, has been addressed. With regard to insulin, improved access in resource-poor settings will be dependent on, to a certain extent, the goodwill of the large manufacturers to continue differential pricing of insulin. With increasing burdens of diabetes, and therefore need for insulin, it may be expected that in India and China, generic manufacturers will enter the market. In order for these producers to really impact the access to insulin for those people in the world's poorest countries, the WHO and IDF will have to ensure some form of prequalification of manufacturers. With animal insulin now almost having disappeared from the market being replaced by human insulin, one aspect that should be of concern to the diabetes community at large is to ensure that this does not happen with human insulin being replaced by analog insulin.

In looking at the wider issue of improving treatment for diabetes, health systems throughout the world will have to modify their structure, the way they work and also the use of physical and human resources in order to meet the increasing challenge of diabetes. Again, the role of the IDF and WHO in this should be to raise the issue and urgent need for this health system reorientation. Models and tools will need to be developed in order to assist countries in this new health challenge. However, the most urgent task is to get NCDs and diabetes on the global health agenda.

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