Why Are We Failing to Address the Issue of Access to Insulin? A National and Global Perspective

David Beran,[1] Irl B. Hirsch,[2] and John S. Yudkin[3]

Diabetes Care 2018;41:1125–1131 | https://doi.org/10.2337/dc17-2123

Insulin was discovered in 1921 and soon became widely available in high-income countries. However, many people currently in need of this life-saving medicine are unable to access it. This is a global phenomenon, impacting not only populations of low- and middle-income countries but low-income populations in the U.S. In the U.S., the rate of diabetic ketoacidosis remains high in certain subpopulations, the cost of insulin being the main precipitating factor. On a global level the main cause of mortality for a child with type 1 diabetes is a lack of access to insulin, and in sub-Saharan Africa the life expectancy of a child with type 1 diabetes can be as low as 1 year. One lens for considering the issue of access to health and medicines is to consider society as a three-legged stool. In this paradigm, the role of the public sector is to provide "protections" to the population it serves; the private sector is made up of "responsible businesses" that supply many of the goods and services people need; and the plural sector comprises communities and not-for-profits providing the "social affiliations" that are needed. For HIV/AIDS, each of these "legs" played a role in improving access. Civil society raised awareness of the issue and advocated for access to treatment. Governments provided funding and responses both nationally and globally. Finally, the private sector played its role, under pressure from civil society and governments, in lowering the price of medicines and developing programs to expand access. Here, we use this framework to describe the shortcomings in access to insulin from a U.S. and global perspective.

Insulin was discovered in 1921 and soon became widely available in high-income countries (HICs). However, many people currently in need of this life-saving medicine are unable to access it (1). This is a global phenomenon, impacting not only populations of low- and middle-income countries (LMICs) but low-income populations in HICs as well. In the U.S., the rate of diabetic ketoacidosis remains high in certain subpopulations, the cost of insulin being the main precipitating factor (2,3). On a global level, the main cause of mortality for a child with type 1 diabetes is a lack of access to insulin (4), and in sub-Saharan Africa the life expectancy of a child with type 1 diabetes can be as low as 1 year (5).

Access to medicines relates to issues of affordability and availability. A study of health spending in the U.S. between 1996 and 2013 found that diabetes had the highest expenditure of 155 conditions in 2013, at US$ 101.4 billion (6). For insured adults in the U.S., out-of-pocket expenditures for insulin increased significantly by 89% between 2000 and 2010 (7). Medicaid reimbursement for insulin on a per-unit basis increased by 7.9% per year between 1991 and 2004 (8). More recently, the increased cost for diabetes to Medicare was 19.5%, primarily through increases in unit costs (9).

In LMICs the issue is not only whether people can afford their insulin but also whether they can find it within the health system. In countries where insulin had to be paid for by the individual, the average cost was US$ 35.40 per year (range US$ 2.60–US$ 141.44)

[1]*Division of Tropical and Humanitarian Medicine, University of Geneva and Geneva University Hospitals, Geneva, Switzerland*
[2]*University of Washington, Seattle, WA*
[3]*University College London, London, U.K.*

Corresponding author: David Beran, david.beran@unige.ch.

Received 10 October 2017 and accepted 19 March 2018.

See accompanying article, p. 1299.

in the public sector and US$ 95.71 (US$ 6.89–US$ 218.40) in the private sector (1). On average, insulin was available in 56% of facilities in the public sector but in only 39% in the private sector.

One lens for considering the issue of access to health and medicines is to consider society as a three-legged stool (10). In this paradigm, the role of the public sector is to provide "protections" to the population it serves, the private sector is made up of "responsible businesses" that supply many of the goods and services people need, and the plural sector comprises communities and not-for-profits providing the "social affiliations" that are needed. For HIV/AIDS, each of these "legs" played a role in improving access to care and medication. Civil society raised awareness on the issue and advocated for access to treatment. Governments provided funding and responses both nationally and globally. Finally, the private sector played its role, under pressure from civil society and governments, in lowering the price of medicines and developing programs to expand access (11–13). Here, we use this framework to describe the shortcomings in access to insulin from a U.S. and global perspective.

THE ROLE OF GOVERNMENTS

The role of the government is to protect its citizens. When it fails in this role there is an impact on society as a whole (14). As such, it has moral, legal, and regulatory responsibilities toward its citizens, improving their health while fulfilling global commitments to health. The World Health Organization (WHO) estimates that countries need to spend a minimum of US$ 44 per person per year to provide basic health-related services to their populations (15). In 2011, 26 LMICs spent less than that amount, largely because of limited government resources. The situation in HICs is less about the total amount spent but rather its unequal distribution in the population. Total U.S. health expenditure is 214 times the minimum amount specified by WHO, but the U.S. has lower health outcomes in comparison with other HICs (16,17), which might be explained by inequalities in the distribution of resources to certain groups (18,19).

International declarations and covenants mandate "the creation of conditions which would assure to all medical service and medical attention in the event of sickness" (20,21). Included in this principle is the issue of access to medicines. From these global obligations more than 100 countries have incorporated this "Right to Health" in their national constitutions (22). To translate these overarching statements into practical realities requires an alignment of different policies as well as consideration of how health care is organized, financed, and provided (23). Although the U.S. does not ensure coverage for all of its population, the government has intervened in the past to improve access to medicines (24).

Government regulations, such as intellectual property laws and imposition of tariffs and taxes on medicines, also impact access to medicines. In various LMICs, hidden costs can increase the price of a medicine by as much as 17-fold (25), thus representing a supplementary burden on the individual or health system. Regulation of the approval of pharmaceutical products is another responsibility of governments. One area relevant to insulin is the regulation of biosimilars (follow-on biologics). This requires regulatory capacity, a legal basis (26), and guidelines for health professionals and information for the public. To date, regulation of biosimilars globally is not standardized and continues to evolve (27), meaning that the potential savings to health systems and individuals have not yet materialized (28,29).

These elements are part of the larger role that governments can have in improving the health of their populations. This includes the role of the government as a funder of research (30). The government is also a purchaser and/or provider of health care and thus is incentivized to bring novel, and preferably cost-effective, products to market. Most HICs, including the U.S. through federally funded programs, have some form of direct or indirect price control on medicines (31). Besides price controls, purchasing mechanisms such as tenders, which are widely used in LMICs, can enable countries to save money on the medicines they purchase, as this process shifts the power to the purchaser. Mexico and Canadian provinces have succeeded in this approach (31). Many of these mechanisms lead to lower prices for medicines in most HICs in comparison with the U.S. (Fig. 1).

In HICs, access to services will be dependent on a variety of factors, including population density and socioeconomic factors of different populations. In LMICs, urban-rural imbalances in care provision (32,33) are further exacerbated by weak health systems. Also of importance is the financial burden of care, including medicines, on the individual and the health system.

Besides national obligations, governments also have global commitments either through global "goals" or as donors. These global goals have shown some success, for example, with the Millennium Development Goals leading to improvements in maternal and child mortality and the numbers receiving antiretroviral treatment (34). The Sustainable Development Goals include health-related

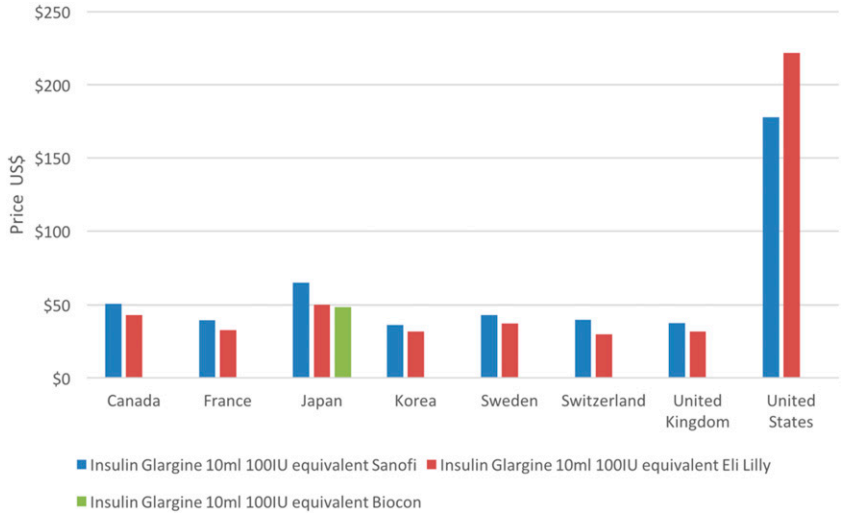

Figure 1—Comparison between originator and biosimilar insulin glargine prices per 10 mL 100 international units (IU)/mL insulin equivalent (US$). References: Canada (101), France (price excluding dispensing fee) (102), Japan (58), Korea (103), Sweden (104), Switzerland (ex factory price) (105), U.K., (106), and U.S. (user price CVS Boston, MA) (107).

indictors, access to medicines, universal health coverage, and specific mention of noncommunicable diseases (NCDs) (35,36). Specifically, following a United Nations (UN) High-level Meeting on NCDs in 2011 (37), WHO, the UN agency responsible for global health, developed a Global Action Plan on NCDs (38). This plan includes targets relative to access to medicines. Through their participation in these organizations and meetings, countries make commitments both to the global community and to their populations to address these issues. However, these commitments have not been translated into funding: between 1990 and 2014, only 1.5% of the US$ 458 billion development assistance for health (one-third from the U.S.) was allocated to NCDs (39). This translates into a lack of focus and adequate response for diabetes and access to insulin.

A "RESPONSIBLE" PRIVATE SECTOR (?)

The main responsibility of the private sector is to provide a return on investment (14). In the case of several industries, this may impact adversely on health, with front groups, lobbyists, and research funding and donations employed to represent the industries as positive "corporate citizens" (40). Unlike Big Food, Big Soda, or Big Tobacco, Big Pharma provides commodities that are needed in order to improve health. In 2014, the 15 largest global pharmaceutical companies had sales of approximately US$ 527 billion (41). The U.S. represented 58% of the total market for new medicines, and Europe and Japan a further 31% (42). Thus, the rest of the world and the majority of the global population account for only 11% of the market for new medicines. The global market for insulin was valued at US$ 20.8 billion in 2012 (43). In the U.S. the value of insulin sales in 2011 totaled US$ 8.3 billion, a 14.9% increase compared with 2010 (44).

The insulin market is unique in that although insulin was discovered in 1921, three multinational pharmaceutical companies (the "Big Three") control 99% of the insulin market value (96% of volume) (45). This domination of the market has led to both the disappearance of animal insulin and the rapid upturn in the use of analog insulin (1). Greene and Riggs (46) describe how older insulins disappear from the market without generating any generic competition. In contrast to most other medicines, the price of insulin in the U.S. has increased, while in LMICs it has remained stable (7,8,25,47,48). Although intellectual property is not an issue for human insulin, and many of the current analogs are already or will shortly be off patent (49), an increase in the patents on delivery devices is a concern (50).

Kessel (51) argues that the roles of the pharmaceutical industry comprise improving health as well as generating profits for shareholders. Increasingly, a shift has been seen to a focus more on profits and less on patient care and outcomes. New developments in insulin have led to marginal changes, but there have nevertheless been significant increases in price (46). These price increases cannot be justified by higher production costs as the processes for human and analog insulin are the same once the changes to the insulin molecule have been made for the analogs (52).

The Big Three do have various corporate social responsibility activities both in the U.S. and globally, with differential pricing in LMICs and patient assistance programs in the U.S. Some donation programs are supported by these companies, but policy analyses suggest that such initiatives are neither sustainable nor transparent and impact negatively on improving access to medicines (53,54). One way the pharmaceutical industry is assessed as a "corporate citizen" is through the Access to Medicine Index, which looks at "how the top 20 research-based pharmaceutical companies make medicines, vaccines and diagnostics more accessible" in LMICs (55). The Big Three are ranked 6th (Sanofi), 10th (Novo Nordisk), and 17th (Eli Lilly) on this index.

The Big Three are not the only private-sector actors who have an impact on the issue of access to insulin. Biosimilar companies are also for-profit enterprises and can have a role to play in improving access to insulin if they sell their products at an affordable price (29,56). One of the Big Three has launched its own biosimilar insulin glargine, which has been approved in the U.S. and Europe (57). To date the only biosimilar insulin from other producers to have received regulatory approval by a highly stringent authority (Japan) is a glargine biosimilar from an Indian company (58). In general, the increased competition from generic medicines results in lower prices (59), but it is still too early to tell the impact of biosimilars on the affordability of insulin (Fig. 1).

There are several intermediaries between producer and user that impact the final price of insulin. In the U.S., pharmacy benefit managers (PBMs) are responsible for managing the prescriptions for private health insurance (commercial and individual), Medicare recipients, and federal and state government employees (30), and have contributed to increasing medicine costs in the U.S. (60). PBMs are able to get rebates which can account for as much as 50% of the list price for insulin, but it is not clear if these savings are passed on to patients (61,62). These organizations are also big businesses, with the top three PBMs generating over US$200 billion in revenue and controlling 80% of the PBM market. In LMICs, wholesalers and other intermediaries increase the price at different levels of the supply chain. Data for insulin from the private sector of five LMICs show a 13.0% to 59.0% mark-up between wholesaler and patient prices (33). In many LMICs, private pharmacies play an important role in the provision of medicines (63), but with variable quality of service (63) and substantially higher prices than in the public sector (64).

Shareholder expectations and the strategies of investors may also impact the overall strategy of the pharmaceutical industry, but these factors have not been assessed (65). They can nevertheless clearly have an impact on management structure and vision of companies (66,67).

IS THERE REALLY A PLURAL SECTOR FOR DIABETES?

The role of the plural sector is to maintain a balance as well as to redress imbalances and challenge the status quo. To be able to do this, it needs to be free from the influence of governments and the private sector (10). Mintzberg (10) states that the plural sector should "be owned by no one."

In diabetes the plural sector comprises various national and international associations. Many of these associations receive funding from the pharmaceutical industry and also the food sector, raising the issue of their independence (68–70). To date, the International Diabetes Federation (IDF), whose mission is to "promote diabetes care, prevention and a cure worldwide" (71) and which claims to be the global diabetes advocate, has failed to take action on the issue of access to insulin. Although the question of access is mentioned in the IDF Strategic Implementation

Plan 2016–17 (72), the focus is solely on an insulin donation program (the Life for a Child Program), an approach which raises many issues of generalizability and sustainability. To its credit, the American Diabetes Association (ADA) has taken the lead in addressing access to insulin with the launch of a petition and campaign on affordable insulin (73). To the authors' knowledge, this is the first time that a diabetes-related civil-society organization has played its role in holding a government and the private sector to account.

Foundations in the area of diabetes research also play an important role. For example, JDRF (formerly known as the Juvenile Diabetes Research Foundation) focuses on the discovery and development of advances in the care of people with type 1 diabetes until a cure can be discovered (74). JDRF has been extremely effective in raising the profile of type 1 diabetes through highly motivated parents, not without some criticism for its focus on a cure (75). Like ADA, JDRF has come out with a statement on the issue of access to insulin (76), but research and projects on the issue of access to insulin are not included in its remit.

Social media also provides an opportunity for people with diabetes to regain a voice or share messages, as was done by ADA for its campaign. With their global reach, tools such as Facebook and Twitter would be ideal ways to develop communities around the issue of access to insulin. Many examples of social media and diabetes focus on peer groups where individuals can share experiences (77,78). A review of the use of social media in diabetes found that most posts were related to clinical management advice as well as promotional activities for various treatments, raising issues of safety (79). Social media is a relatively new tool for advocacy, but it is one of many tools that is needed, and organizations need to allocate the appropriate resources in order to use it to its full potential (80).

Academia, another component of the plural sector, has two roles. First, as with this article, it has a role in highlighting the issue of access to insulin. The other role is in research and development (R&D) of diabetes medicines. When they discovered insulin, Banting and Best were based at an academic institution, and, clearly, universities have a key role to play in R&D as places of discovery (81). However, seeing that much funding for diabetes research comes from governments and the private sector, independence is also the challenge for academics, as it is for diabetes associations.

The elements described above are summarized in Fig. 2.

RECOMMENDATIONS FOR MOVING THE ISSUE FORWARD

Governments need to ensure that universal health coverage includes insulin and diabetes care and that the health system is adapted to the delivery of care for people with diabetes. When addressing the issue of the price of medicines, all the drivers of price need to be looked at, including increasing competition and government intervention to reduce prices, as well as focusing on factors at the provider and patient levels (30). Increasing competition will require ensuring better access to biosimilar products produced by more companies than just the Big Three. The U.S. Food and Drug Administration has recently announced that it will include insulin on a list of priority medicines with the aim of lowering its price (82). Governments have a variety of means to control prices, including price setting, regulating mark-ups within the supply chain, and ensuring rational choices are made based on the use of essential medicines lists and health technology assessments. Although many of these proposals seem unlikely to be introduced in the U.S., it is important to note that regulations with regard to price exist for federally funded programs (83).

All countries in the world spend some of their health resources on diabetes. One of us has proposed that 5% of this funding be allocated to innovation in the delivery of care and insulin (1). Such funds could be made available nationally and internationally for operational research to ensure that diabetes-related funding is used effectively and efficiently. IDF has estimated that diabetes-related expenditure was US$ 727 billion in 2017 (84). Optimizing the use of these funds, and earmarking 5% (US$ 36 billion) for expanding diabetes care, would address many of the challenges presented in this article.

The role of the private sector is to provide goods and services and a return on investment. In addition, it is also a funder of research and should play a role as a corporate citizen. At present, the private sector is failing with regard to diabetes. Other companies have been able to develop models for becoming better corporate citizens, setting targets beyond those traditionally related to their core business and linking their business to sustainability (85). This does not come without criticism from traditional business circles (86). In other areas, such as mobile phones, companies have been able to expand coverage, even in poor settings in Africa, by leapfrogging traditional approaches and segmenting their market (87). To date the pharmaceutical market focuses on HICs (mainly the U.S., Europe, and Japan) with a high value and "low" volume view. If pharmaceutical companies were to take a long-term view and invest in segmenting the market as other companies have done, they could potentially "open" their markets to millions of people

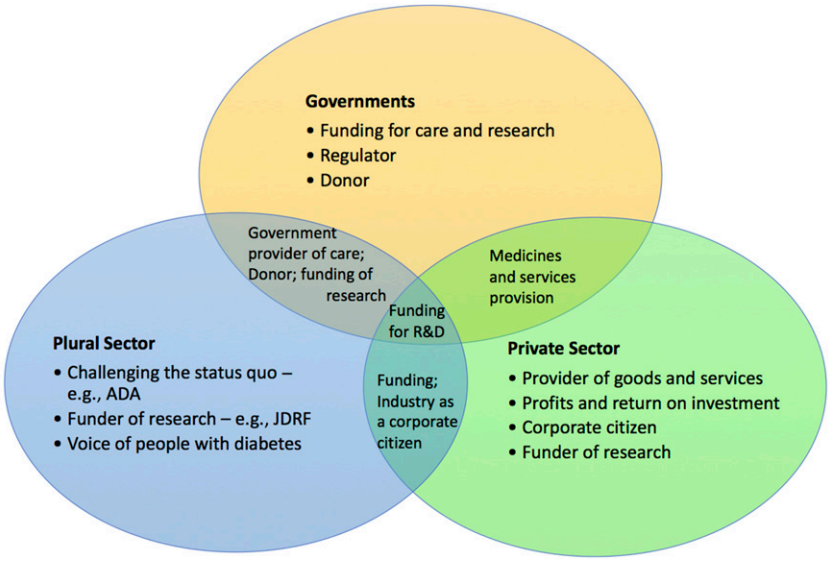

Figure 2—Areas of focus of the three different sectors.

who currently fail to access their products (88). Another approach that moves away from the for-profit model would be a social enterprise that could either be part of one of the multinational corporations or a new start-up venture (89,90).

A key driver in any business decision is the impact it will have on investors and shareholders. These key players in the private sector might wish to consider the difference in investing in pharmaceutical companies versus in other areas. This difference in view needs to include a longer time perspective, truly assessing corporate social responsibility, in part because of the need to consider ranking systems such as the Access to Medicine Index (55).

For all these changes to happen, there needs to be an independent and effective diabetes civil society that holds governments and the private sector to account. The concept of civil society is that of individuals who come together for a specific cause. These individuals are also voters, employees, customers, and benefactors and can also use their power to change business as usual. Different social media tools amplify this voice, but a rallying goal is needed. One such goal or target could be the upcoming insulin centenary in 2021 (91). This could provide the diabetes community with an opportunity to rally around a global cause and truly try to make a difference.

CONCLUSIONS

Access to insulin needs to be framed within the wider health system and all the elements needed to provide appropriate diabetes care. However, what changed the course of diabetes management in 1922 was access to insulin and, as Elliott Joslin stated, "a new race of diabetics has come upon the scene" (92).

Mintzberg's presentation of society as a three-legged stool (10) provides an interesting framework for analysis of the issue of access to insulin. Figure 2 shows how the common link between the different sectors is funding for R&D. This R&D is possibly skewed in that the aim is for innovative medicines, means of delivery, and models of care versus the issue of access to insulin.

In the U.S. the "plural sector" is regaining some power on the issue of access to insulin through the initial work of the ADA (73) and citizens bringing class action lawsuits against insulin manufacturers (93). Social media is also a tool that might assist in raising awareness about this issue at different levels. There is also a push in the U.S. by some in government for more price transparency, which is already present in many HICs (94) (Fig. 1).

Globally, though, the power remains in the hands of the private sector, with little involvement and action from either the IDF, individual governments, or WHO. Given that currently the plural sector receives a large portion of its funding from the private sector, can it truly be active in addressing the issue of access to insulin? Each leg of the stool that Mintzberg describes exists as a group of individuals, but as shown in Fig. 2 there are areas of overlap between these three sectors, versus them being stand-alone "legs." For example, the leadership of many diabetes organizations is predominantly composed of clinicians and not individuals with diabetes. IDF has had four clinicians in its last five presidents (95). The Board of Directors of the ADA includes fourteen members, of whom three are medical doctors, three others are researchers or other health professionals, and two are working in the area of health care or the pharmaceutical industry (96). These key opinion leaders serve as links between the different sectors, for example, by being national experts on the issue of diabetes and receiving funding from governments and/or the private sector.

Academics and clinicians stand on the front lines in terms of the research they do and as witnesses to the challenges their patients encounter. Both these constituencies have in the past raised their voices to address a variety of societal issues. Specifically, we argue that clinicians need to view their roles as encompassing the best care both for the individual patient in front of them and for the collective of people with diabetes in a health system and society with many health needs. The issue concerns the interaction between the individual and populations. For the individual with diabetes, we of course want what is best for them. This, however, has an impact on overall diabetes management and the health of populations. At the heart of this discussion is the use of human insulin versus more expensive analog insulins (97). It has been argued that less effective interventions can be justified if they are more affordable, as from an ethical perspective it is preferable to provide a larger number of people with treatment as opposed to the more expensive alternative for fewer people (98). The former WHO Director-General Dr. Gro Harlem Brundtland stated, ". . .if services are to be provided for all then not all services can be provided. The most cost-effective services should be provided first" (99).

We live in a globalized world. A presentation at the ADA can impact diabetes management throughout the world. A scientific article published on results in Boston can be accessed and read, and can impact practice, throughout LMICs. In the U.S. and other HICs, the issue for type 1 diabetes seems to have evolved from insulin to that of access to the latest technology or even a cure for diabetes. In diabetes, progress is often measured by novelty: new insulin, new medicines, and new technology. These clearly have a positive impact on many individuals, but not on the majority of people living with diabetes globally. Franklin D. Roosevelt said, "The test of our progress is not whether we add more to the abundance of those who have much, it is whether we provide enough for those who have little" (100). If a cure or the artificial pancreas becomes a reality, will someone with type 1 diabetes in Mozambique benefit? As a diabetes community, we need to continue to push for innovation and developments in the field of diabetes, and these should be welcomed. However, we must not forget that many people with diabetes in this day and age still are unable to access an innovation from 1921, and there is no debate: this is unacceptable.

Duality of Interest. D.B. has received funding in the past from IDF and ADA to attend their scientific conferences. His current research funding comes from the Swiss Government and Health Action International as part of the Addressing the Challenge and Constraints of Insulin Sources and Supply (ACCISS) study, which is cofunded by The Leona M. and Harry B. Helmsley Charitable Trust and Stichting International Christian Fellowship. None of these sources had any involvement in the analysis included in this review. He has also worked with WHO (paid and unpaid consultancies) on issues relevant to access to medicines for diabetes care, primary health care, and noncommunicable diseases in general. He also is an advisor to the Board of Trustees of the International Insulin Foundation and on the Board of Directors of Santé Diabète. Both organizations are independent nongovernmental organizations working in the area of diabetes. For this work D.B. does not receive any compensation but has been reimbursed travel-related expenses to attend meetings. I.B.H. has received funding from ADA, JDRF, The Leona M. and Harry B. Helmsley Charitable Trust, the National Institutes of Health, and Medtronic Diabetes. He has consulted with

Abbott Diabetes Care, Adocia, Bigfoot Biomedical, and Roche. Since 2002, J.S.Y. has acted as chairman and trustee of the International Insulin Foundation, a U.K.-based charity advocating on affordable diabetes care. He has served on several committees for WHO and has been reimbursed for travel to their meetings. He has also been reimbursed for travel to educational meetings and received an honorarium for a lecture at the Danish Diabetes Academy Winter School in March 2017. No other potential conflicts of interest relevant to this article were reported.

References

1. Beran D, Ewen M, Laing R. Constraints and challenges in access to insulin: a global perspective. Lancet Diabetes Endocrinol 2016;4:275–285
2. Seyoum B, Berhanu P. Profile of diabetic ketoacidosis in a predominantly African American urban patient population. Ethn Dis 2007;17:234–237
3. Randall L, Begovic J, Hudson M, et al. Recurrent diabetic ketoacidosis in inner-city minority patients: behavioral, socioeconomic, and psychosocial factors. Diabetes Care 2011;34:1891–1896
4. Gale EA. Dying of diabetes. Lancet 2006;368:1626–1628
5. Beran D, Yudkin JS. Diabetes care in sub-Saharan Africa. Lancet 2006;368:1689–1695
6. Dieleman JL, Baral R, Birger M, et al. US spending on personal health care and public health, 1996–2013. JAMA 2016;316:2627–2646
7. Lipska KJ, Ross JS, Van Houten HK, Beran D, Yudkin JS, Shah ND. Use and out-of-pocket costs of insulin for type 2 diabetes mellitus from 2000 through 2010. JAMA 2014;311:2331–2333
8. Luo J, Avorn J, Kesselheim AS. Trends in Medicaid reimbursements for insulin from 1991 through 2014. JAMA Intern Med 2015;175:1681–1686
9. The Express Scripts Lab. *Express Scripts 2015 Drug Trend Report*. St. Louis, MO, Express Scripts, 2016
10. Mintzberg H. *Rebalancing Society*. Oakland, CA, Berrett-Koehler Publishers, Inc., 2015
11. Ramiah I, Reich MR. Building effective public-private partnerships: experiences and lessons from the African Comprehensive HIV/AIDS Partnerships (ACHAP). Soc Sci Med 2006;63:397–408
12. Katz IT, Bassett IV, Wright AA. PEPFAR in transition—implications for HIV care in South Africa. N Engl J Med 2013;369:1385–1387
13. Bendavid E, Holmes CB, Bhattacharya J, Miller G. HIV development assistance and adult mortality in Africa. JAMA 2012;307:2060–2067
14. Frieden TR. Government's role in protecting health and safety. N Engl J Med 2013;368:1857–1859
15. World Health Organization. *WHO Global Health Expenditure Atlas*. Geneva, World Health Organization, 2014
16. Meisler L. Americans die younger despite spending the most on health care [article online]. Bloomberg, 2 August 2017. Available from https://www.bloomberg.com/graphics/2017-health-care-spending/. Accessed 2 January 2018
17. Organisation for Economic Cooperation and Development (OECD). *Society at a Glance 2011*. Paris, OECD Publishing, 2011
18. Braveman PA, Cubbin C, Egerter S, Williams DR, Pamuk E. Socioeconomic disparities in health in the United States: what the patterns tell us. Am J Public Health 2010;100(Suppl. 1):S186–S196
19. Organisation for Economic Cooperation and Development (OECD). *United States: Tackling High Inequalities. Creating Opportunities For All*. Paris, OECD Publishing, 2014
20. United Nations General Assembly. Universal declaration of human rights. Paris, United Nations, 1948 (Part A of General Assembly resolution 217 [III])
21. Seuba X. A human rights approach to the WHO Model List of Essential Medicines. Bull World Health Organ 2006;84:405–407; discussion 408–411
22. Hogerzeil HV, Samson M, Casanovas JV, Rahmani-Ocora L. Is access to essential medicines as part of the fulfilment of the right to health enforceable through the courts? Lancet 2006;368:305–311
23. Nygren-Krug H, Hogerzeil HV. Human rights: a potentially powerful force for essential medicines. Bull World Health Organ 2006;84:410
24. Ross JS, Kesselheim AS. Prescription-drug coupons—no such thing as a free lunch. N Engl J Med 2013;369:1188–1189
25. Ewen M, Joose HJ, Ashigbie P, Beran D, Laing R. *Insulin Prices Profile*. Amsterdam, Health Action International, 2016
26. Burstein HJ, Schrag D. Biosimilar therapy for ERBB2 (HER2)-positive breast cancer: close enough? JAMA 2017;317:30–32
27. Lapteva M, Singhal M, Kalia Y. *Biosimilar Insulin Regulatory Profile*. Amsterdam, Health Action International, 2017
28. Aronson JK, Ferner RE. How similar are biosimilars? BMJ 2016;353:i2721
29. Bauchner H, Fontanarosa PB, Golub RM. Scientific evidence and financial obligations to ensure access to biosimilars for cancer treatment. JAMA 2017;317:33–34
30. Kesselheim AS, Avorn J, Sarpatwari A. The high cost of prescription drugs in the United States: origins and prospects for reform. JAMA 2016;316:858–871
31. Organisation for Economic Cooperation and Development (OECD). *Pharmaceutical Pricing Policies in a Global Market*. Paris, OECD Publishing, 2008
32. Boerma JT, Bryce J, Kinfu Y, Axelson H, Victora CG; Countdown 2008 Equity Analysis Group. Mind the gap: equity and trends in coverage of maternal, newborn, and child health services in 54 Countdown countries. Lancet 2008;371:1259–1267
33. Beran D, Yudkin JS. Looking beyond the issue of access to insulin: what is needed for proper diabetes care in resource poor settings. Diabetes Res Clin Pract 2010;88:217–221
34. United Nations. *The Millennium Development Goals Report 2015*. New York, United Nations, 2015
35. Fuster V, Voûte J. MDGs: chronic diseases are not on the agenda. Lancet 2005;366:1512–1514
36. United Nations. Sustainable development goals [Internet], 2016. Available from http://www.un.org/sustainabledevelopment/sustainable-development-goals/. Accessed 15 December 2016
37. UN General Assembly. Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. New York, United Nations General Assembly, 2012 (Annex to Resolution A/RES/66/2 adopted 19 September 2011)
38. World Health Organization. *Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013–2020*. Geneva, World Health Organization, 2013
39. Dieleman JL, Graves C, Johnson E, et al. Sources and focus of health development assistance, 1990–2014. JAMA 2015;313:2359–2368
40. World Health Organization. WHO Director-General addresses health promotion conference [article online], 2013. Available from http://www.who.int/dg/speeches/2013/health_promotion_20130610/en/. Accessed 22 February 2016
41. Staton T. The top 15 pharma companies by 2014 revenue [article online]. FiercePharma, 2015. Available from http://www.fiercepharma.com/special-report/top-15-pharma-companies-by-2014-revenue. Accessed 22 December 2016
42. European Federation of Pharmaceutical Industries and Associations (EFPIA). *The Pharmaceutical Industry in Figures*. Brussels, EFPIA, 2016
43. Wirtz V. *Insulin Market Profile*. Amsterdam, Health Action International, 2016
44. Rotenstein LS, Ran N, Shivers JP, Yarchoan M, Close KL. Opportunities and challenges for biosimilars: what's on the horizon in the global insulin market? Clin Diabetes 2012;30:138–150
45. Schultz K. *The global diabetes care market*. Novo Nordisk, 2011. Available from https://www.yumpu.com/en/document/view/3266542/the-global-diabetes-care-market-kare-schultz-novo-nordisk. Accessed 12 September 2017
46. Greene JA, Riggs KR. Why is there no generic insulin? Historical origins of a modern problem. N Engl J Med 2015;372:1171–1175
47. Hua X, Carvalho N, Tew M, Huang ES, Herman WH, Clarke P. Expenditures and prices of antihyperglycemic medications in the United States: 2002–2013. JAMA 2016;315:1400–1402
48. Tylee T, Hirsch IB. Costs associated with using different insulin preparations. JAMA 2015;314:665–666
49. Kaplan W, Beall R. *Insulin Patent Profile*. Amsterdam, Health Action International, 2016
50. Luo J, Kesselheim AS. Evolution of insulin patents and market exclusivities in the USA. Lancet Diabetes Endocrinol 2015;3:835–837
51. Kessel M. Restoring the pharmaceutical industry's reputation. Nat Biotechnol 2014;32:983–990
52. Ferrer-Miralles N, Domingo-Espín J, Corchero JL, Vázquez E, Villaverde A. Microbial factories for recombinant pharmaceuticals. Microb Cell Fact 2009;8:17
53. Cone J. There is no such a thing as "free" vaccines: Why MSF rejected Pfizer's donation offer of pneumonia vaccines [article online]. The BMJ Opinion, 19 October 2016. Available from http://blogs.bmj.com/bmj/2016/10/19/jason-cone-there-is-no-such-a-thing-as-free-vaccines-why-msf-rejected-pfizers-donation-offer-of-pneumonia-vaccines/. Accessed 21 October 2016
54. Choudhry NK, Lee JL, Agnew-Blais J, Corcoran C, Shrank WH. Drug company-sponsored patient assistance programs: a viable safety net? Health Aff (Millwood) 2009;28:827–834
55. Access to Medicine Foundation. *Access to Medicine Index 2016*. Haarlem, the Netherlands, Access to Medicine Foundation, 2016
56. Perrin C, Ewen M, Beran D. The role of biosimilar manufacturers in improving access to insulin globally. Lancet Diabetes Endocrinol 2017;5:578
57. U.S. Food and Drug Administration. FDA approves Basaglar, the first "follow-on" insulin glargine product to treat diabetes [article online], 16 December 2015. Silver Spring, MD, U.S. Food and Drug Administration. Available from https://wayback.archive-it.org/7993/20170722061458/http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm477734.htm. Accessed 17 December 2016

58. Biocon. Biocon's insulin glargine launched in Japan [article online], 15 July 2016. Bangalore, India. Available from http://www.biocon.com/biocon_press_releases_150716.asp. Accessed 22 December 2016
59. U.S. Food and Drug Adminstration. Generic competition and drug prices [article online], 2015. Silver Spring, MD, U.S. Food and Drug Administration. Available from http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm. Accessed 22 December 2016
60. Is there a cure for high drug prices? [article online]. *Consumer Reports*, August 2016. Available from http://www.consumerreports.org/drugs/cure-for-high-drug-prices/. Accessed 22 December 2016
61. Lipska K. Break up the insulin racket. *New York Times*, 21 February 2016, p. SR5
62. Robbins R. The insulin market is heading for a shakeup. But patients may not benefit [article online]. Stat, 14 October 2016. Available from https://www.statnews.com/2016/10/14/insulin-prices-generics/. Accessed 15 October 2016
63. Smith F. The quality of private pharmacy services in low and middle-income countries: a systematic review. Pharm World Sci 2009;31:351–361
64. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet 2009;373:240–249
65. Hill S, Kieny MP. Towards access 2030. Lancet 2017;389:341–343
66. Reuters. U.S. headwinds force change of CEO at Novo Nordisk [article online]. *Fortune*, 1 September 2016. Available from http://fortune.com/2016/09/01/novo-nordisk-ceo-retire-insulin/. Accessed 17 December 2016
67. Torsoli A. Sanofi U.S. sales executive leaves after insulin forecast [article online]. Bloomberg, 4 December 2014. Available from https://www.bloomberg.com/news/articles/2014-12-04/sanofi-diabetes-chief-said-to-leave-after-insulin-forecast. Accessed 17 December 2016
68. American Diabetes Association. Our corporate supporters [Internet], 2017. Alexandria, VA, American Diabetes Association. Available from http://www.diabetes.org/about-us/corporate-support/our-corporate-supporters.html. Accessed 7 January 2017
69. International Diabetes Federation. Our partners [Internet], 2015. Brussels, International Diabetes Federation. Available from http://www.idf.org/partners/meet-our-partners. Accessed 7 January 2017
70. Beran D, Capewell S, de Courten M, et al. The International Diabetes Federation: losing its credibility by partnering with Nestlé? Lancet 2012;380:805
71. International Diabetes Federation. Mission & strategy [Internet], 2015. Available from https://www.idf.org/who-we-are/mission-strategy.html. Brussels, International Diabetes Federation. Accessed 7 January 2017
72. International Diabetes Federation. *Strategic Implementation Plan 2016-17*. Brussels, International Diabetes Federation, 2015
73. American Diabetes Association. Accessibility and affordability of diabetes medications [article online], 23 February 2016. Alexandria, VA, American Diabetes Association. Available from https://makeinsulinaffordable.org/statement/. Accessed 10 January 2017
74. JDRF. Research funding facts [article online], 2017. Available from http://jdrf.org/about-jdrf/fact-sheets/research-funding-facts/. Accessed 10 July 2017
75. Pérez-Peña R. Beyond 'I'm a diabetic,' little common ground. *New York Times*, 17 May 2006, p. A1
76. JDRF. Achieving insulin access and innovation [article online], 2017. Available from http://www.jdrf.org/get-involved/jdrf-advocacy/insulin-access/. Accessed 17 July 2017
77. Petrovski G, Zivkovic M, Stratrova SS. Social media and diabetes: can Facebook and Skype improve glucose control in patients with type 1 diabetes on pump therapy? One-year experience. Diabetes Care 2015;38:e51–e52
78. Hernandez M. Diabetes and social media: a prescription for patient engagement. Diabetes Management 2013;3:203–205
79. Greene JA, Choudhry NK, Kilabuk E, Shrank WH. Online social networking by patients with diabetes: a qualitative evaluation of communication with Facebook. J Gen Intern Med 2011;26:287–292
80. Ariza-Montes JA, Lucia-Casademunt AM. *ICT Management in Non-Profit Organizations*. Hershey, PA, IGI Global, 2014
81. Chokshi DA. Improving access to medicines in poor countries: the role of universities. PLoS Med 2006;3:e136
82. Edney A. FDA targets insulin for increased competition to lower prices [article online]. Bloomberg, 15 December 2017. Available from https://www.bloomberg.com/news/articles/2017-12-15/fda-targets-insulin-for-increased-competition-to-lower-prices. Accessed 2 January 2018
83. Song Z. Using Medicare prices—toward equity and affordability in the ACA marketplace. N Engl J Med 2017;377:2309–2311
84. International Diabetes Federation. *IDF Diabetes Atlas*. 8th ed. Brussels, International Diabetes Federation, 2017
85. Confino J. Unilever's Paul Polman: challenging the corporate status quo [article online]. *The Guardian*, 24 April 2012. Available from https://www.theguardian.com/sustainable-business/paul-polman-unilever-sustainable-living-plan. Accessed 18 December 2017
86. Borelli T. Unilever and the failure of corporate social responsibility [article online]. *Forbes*, 15 March 2017. Available from https://www.forbes.com/sites/econostats/2017/03/15/unilever-and-the-failure-of-corporate-social-responsibility/. Accessed 18 December 2017
87. Manson K. Africa takes lead in mobile revolution [article online]. *Financial Times*, 14 March 2013. Available from https://www.ft.com/content/0846ab76-8c8d-11e2-8ee0-00144feabdc0. Accessed 18 December 2017
88. Prahalad CK, Hammond A. Serving the world's poor, profitably. Harv Bus Rev 2002;80:48–57, 124
89. Smith PA. A do-it-yourself revolution in diabetes care [article online]. *New York Times*, 22 February 2016. Available from https://www.nytimes.com/2016/02/23/health/a-do-it-yourself-revolution-in-diabetes-care.html. Accessed 18 December 2017
90. Achrol R, Kotler P. Marketing's lost frontier: the poor. Markets Globalization Dev Rev 2016;1:3
91. Beran D, Basey M, Wirtz V, Kaplan W, Atkinson M, Yudkin JS. On the road to the insulin centenary. Lancet 2012;380:1648
92. Feudtner C. *Bittersweet: Diabetes, Insulin, and the Transformation of Illness*. Chapel Hill, The University of North Carolina Press, 2003
93. Hagens Berman Sobol Shapiro LLP. Insulin manufacturers hit with class-action lawsuit over drug price inflation scheme and RICO violations – time to break up the insulin racket [article online], 30 January 2017. Available from https://www.hbsslaw.com/cases/insulin-overpricing/pressrelease/insulin-overpricing-insulin-manufacturers-hit-with-class-action-lawsuit-over-drug-price-inflation-scheme-and-rico-violations-time-to-break-up-the-insulin-racket. Accessed 10 July 2017
94. Noon A. Nevada senate passes insulin-price bill tough on drugmakers [article online]. *U.S. News & World Report*, 19 May 2017. Available from https://www.usnews.com/news/best-states/nevada/articles/2017-05-19/nevada-senate-passes-insulin-price-bill-tough-on-drugmakers. Accessed 10 July 2017
95. Hirst M. Keep the fire burning. Diabetes Voice 2013;58:4
96. American Diabetes Association. American Diabetes Association thanks the 2016 Principal Officers and welcomes 2017 officers to national Board of Directors [article online], 2017. Alexandria, VA, American Diabetes Association. Available from http://www.diabetes.org/newsroom/press-releases/2017/american-diabetes-2017-board-of-directors.html. Accessed 7 January 2017
97. Lipska KJ, Hirsch IB, Riddle MC. Human insulin for type 2 diabetes: an effective, less-expensive option. JAMA 2017;318:23–24
98. Persad GC, Emanuel EJ. The ethics of expanding access to cheaper, less effective treatments. Lancet 2016;388:932–934
99. World Health Organization. *The World Health Report 1999: Making a Difference*. Geneva, World Health Organization, 1999
100. FDR Four Freedoms Park. FDR's Second Inaugural Address, January 20, 1937 [article online], 20 January 2014. Available from http://www.fdrfourfreedomspark.org/blog/2015/2/17/fdrs-second-inaugural-address-january-20-1937. Accessed 20 September 2017
101. Diabetes Canada. Approximate cost reference list for antihyperglycemic agents [Internet], March 2016. Available from http://guidelines.diabetes.ca/browse/appendices/appendix5_2016. Accessed 31 May 2017
102. National Agency for the Safety of Medicines and Health Products. Base de données publique des médicaments [Internet], 2017. Available from http://base-donnees-publique.medicaments.gouv.fr/index.php-result [in French]. Accessed 31 May 2017
103. Ji-young S. Basaglar challenges Sanofi's insulin drug Lantus [article online]. The Investor, 17 April 2017. Available from http://m.theinvestor.co.kr/view.php?ud=20170414000728. Accessed 31 May 2017
104. Dental and Pharmaceutical Benefits Agency (TLV). Welcome to the TLV [article online], 2017. Available from https://www.tlv.se/beslut/sok/lakemedel/ [in Swedish]. Accessed 31 May 2017
105. Spezialitätenliste [Internet], 2017. Available from http://www.spezialitätenliste.ch [in German]. Accessed 31 May 2017
106. Taylor P. Lilly and Boehringer launch Lantus biosimilar in UK [article online]. PMLive, 26 August 2015. Available from http://www.pmlive.com/pharma_news/lilly_and_boehringer_launch_lantus_biosimilar_in_uk_806879. Accessed 31 May 2017
107. Good Rx. Insulins [article online], 2017. Available from https://www.goodrx.com/insulins. Accessed 31 May 2017