A Global Comparison of Insulin Prices

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Executive Summary

The affordability and accessibility of insulin is a topic of broad public interest for several factors, not the least of which is the absolute need for insulin in persons with diabetes who might otherwise die without treatment. The relative number of patients with diabetes globally, and the amount of money government programs, commercial plan sponsors, and patients expend on diabetic medicines such as insulin has also generated significant interest in insulin prices. To date, research has broadly found that insulin prices vary considerably within the global market, with some countries paying significantly more per unit of insulin than others, sometimes for the same medication.¹ This finding has led to public healthcare policy discussions that include, but are not limited to, government-subsidized healthcare and/or international reference-based pricing for pharmaceutical products.² ³

This study expands on prior research into insulin prices by providing detailed insulin price comparisons across the globe. It presents insulin price variability on a per-insulin-package basis and measures insulin affordability relative to a country's individual measures of economic wealth – namely, median annual income, average annual income, and gross domestic product (GDP) per capita. This research examined insulin prices at retail pharmacies, the total package price of insulin as well as the patient cost to obtain the package, in 20 countries of varying economic status. In so doing, the goal of this research is to provide greater context and transparency into insulin pricing and affordability.

This study found that when comparing retail insulin product prices between countries, there was considerable variability in cost, with the United States and other Westernized democracies having the highest insulin prices.



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Unweighted Average Insulin Product Cost, by Country Economic Status plus US and Insulin Type (Fig. 14, pg. 22)

These findings are largely in line with prior insulin pricing research, which includes recognizing that the high U.S. prices at pharmacies may not reflect net prices after rebates or other price concessions. However, when comparing insulin prices against average or median annual incomes, the insulin prices in the United States and other Western countries were more affordable than their costs would suggest. In fact, the high-income countries, which had the highest insulin package prices, were some of the most affordable places to obtain insulin, as measured against the economic factors of individuals within those same countries. For example, the United States ranks in the middle of the pack for the 20 countries included in this study based upon the percentage of median annual income dedicated to purchasing insulin.



Annualized Measure of Insulin Affordability by Country and Economic Status Based on Median Annual Income (Fig. 27, pg 31)

Overall, this study found that while individual insulins had wide ranges in prices for the same insulin product, an even broader range was observed when comparing annualized insulin package prices as a percentage of median annual income, where the range was 3% [Canada] to 108% [Burkina Faso].

This research highlights the broad affordability challenges with insulin prices, where even countries with low insulin prices may still struggle to afford their insulin, and suggests that additional policy may be needed to ensure adequate access to insulin is achieved globally.

This study was requested by, and fully funded from, the McPike-Zima Foundation.

Availability of the Web Tool

To provide transparency regarding the measures within this study, as well as others not directly assessed in this paper, 3 Axis Advisors, in conjunction with the McPike-Zima Foundation, has made available a web-based tool, **The World Insulin Price Comparison Map**, on <u>www.3axisadvisors.com</u>, for interested parties to explore. Furthermore, the website contains a text file (Insulin_Prices.txt) of the underlying data available for download free of charge so that anyone can further research the topic of insulin affordability.

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Background

Since its discovery, the life-saving nature of injected insulin was evident. Before the 1920s, there were no effective pharmacological agents for the management of diabetes. Rather, treatment options were limited to dietary measures, which were of limited efficacy. As such, a person diagnosed with diabetes at that time had a lifespan of a few years at best.^{4 5} Because of this, type 1 diabetes was a fatal condition, with people dying within months of developing the condition. This changed on January 11, 1922, when Leonard Thompson became the first person with diabetes to receive injections of insulin. Having been close to death, the dose of insulin, which at the time was derived from animal sources, brought Mr. Thompson out from a near-comatose state. The continued insulin injections enabled Mr. Thompson to live for another 13 years.⁶ The inventors of insulin sold the patent for their discovery to the University of Toronto for \$1 each, in part because they recognized the importance of their discovery and the need to make it available to as many persons with diabetes as possible.⁷ The University of Toronto would go on and license drugmaker Eli Lilly to commercialize the product, which quickly brought it to market in the United States and beyond. By October 1923, just over a year after the first dose was given, it was estimated that 7,500 physicians were treating 25,000 patients with diabetes using Eli Lilly's insulin - a testament to the built-up demand for treatment at the time as well as its rapid commercialization.⁸

In the years that followed, several advancements would be made to insulin (Figure 1). Insulin advancements included efforts to increase the purity of the product (i.e., crystallization), extend the duration of action (i.e., neutral protamine Hagedorn [NPH] insulin), and ultimately produce insulin without reliance upon animal sources (i.e., recombinant insulin).^{9 10} Today, there are no fewer than seven different types of insulin available in dozens of formulations globally.¹¹ The variety of formulations of insulin is necessary to effectively treat the growing number of people with diabetes, as each advancement, or analog of insulin, are designed to mimic the body's natural pattern of insulin release.¹²



Figure 1: Timeline of Insulin's Development

Today, more than 420 million people worldwide have diabetes. As the history of insulin development demonstrates, insulin is essential for survival for persons with diabetes who need

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it. A person with type 1 diabetes, whose diabetes is a result of too little insulin production by the pancreas, can die in days or hours without insulin.¹³ For many people with type 2 diabetes, whose diabetes is a result of their blood cells not responding to insulin as well, insulin is also necessary.¹⁴ Without insulin, persons with type 2 diabetes can suffer painful complications. Unfortunately, high prices and a lack of available insulin are currently a significant barrier to treatment for many diabetics, especially in low- and middle-income countries. Insulin production is concentrated in a small number of manufacturing facilities, and three manufacturers - Eli Lilly, Novo Nordisk, and Sanofi - control most of the global market. This lack of more robust competition results in prices that are prohibitively high for many people and health systems.¹⁵ To contextualize this, we know from information available in the United States that competition for equally interchangeable generic drug products can result in significant price reductions when just three manufacturers are competing for market share. In an analysis conducted involving data from 2015 and 2017, the U.S. Food and Drug Administration (FDA) found that prices can be 50% cheaper when three manufacturers are competing to produce the same generic product relative to the single brand product (Figure **2**).¹⁶



Figure 2: FDA Research on Generic Competition Relative to Number of Manufacturers

While this FDA study is not directly attributable to insulin prices (as patents and interchangeability rules prevent direct substitution between most insulin products), it does highlight one of the concerns related to insulin therapies - that despite three manufacturers

competing for market share with what many *insurers* may consider interchangeable products, insulin prices have not become significantly more affordable as we may see other competitive pharmaceutical markets. That said, it is possible that the growing development of biosimilars for insulin may change some of these dynamics going forward.¹⁷

For people living with diabetes, access to affordable treatment is critical to their survival, as the development of insulin highlights.¹⁸ Nonetheless, concerns related to the affordability, and therefore accessibility, of insulin are well documented. Several studies have investigated insulin affordability, generally from the perspective of the United States, where it is recognized that insulin list prices are significantly higher than the rest of the world.^{19 20} Since 1977, the World Health Organization's (WHO's) Model List of Essential Medicines has included soluble and intermediate-acting insulin. However, as of 2021, the WHO list now includes the long-acting insulin analogues (i.e., insulin degludec, detemir, and glargine) as well as human insulin. Inclusion in the WHO list may result in more countries putting long-acting analogues on their national medicines lists, and negotiating with manufacturers for lower prices. It can result in more products entering the international market, which typically creates competition to bring prices down. This competition also usually gives countries a greater choice of drug products and in this instance, demonstrates the global focus on controlling insulin prices.²¹

Despite the focus on insulin affordability over the years, there remains a lack of comparison data between global insulin prices and affordability within the public domain. Existing literature has generally grouped insulin products by type and does not provide detailed comparable data between each country's price for a given formulation of insulin. The lack of data may limit the proper assessment of the scope of the insulin affordability issue. With this in mind, 3 Axis Advisors, in collaboration with T1International and the Sonia Nabeta Foundation, undertook a study to gather and make available insulin availability and price information from 20 countries. Pricing information was collected from retail pharmacies and wholesalers and differentiated by any government program(s) within the country which may influence pricing. These prices were then aggregated and compared by not only the type of insulin product, but individual economic measures within each country, for a view into the range of insulin prices and affordability presently available.

This study presents findings on comparable insulin product availability, pricing, and affordability between 20 countries of varying economic status. Unlike prior studies, individual product pricing (i.e., price per vial or box of pens) is available for direct comparison on an online tool freely available at <u>www.3AxisAdvisors.com</u>. Additionally, the underlying database for this analysis is available on the same website to support other research endeavors into this issue.

This study was requested by, and fully funded from, the McPike-Zima Foundation.²²

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Methods

Our study relied upon a variety of data sources to compare global insulin prices. Our preference was for electronic databases of pricing information (i.e., government websites); however, those were not readily available for all the countries in our study. As a result, individual pharmacies, and wholesalers within select countries, were surveyed for insulin prices with the goal of obtaining a sampling of low-, middle-, and high-income countries. When necessary, the surveys of insulin prices within a country were conducted in a standardized format by the Sonia Nabeta Foundation to assess overall price per product and the price to a person with diabetes to obtain the product, inclusive of any government programs that may offer cost assistance.

All prices were collected in local currencies and converted into U.S. dollars based on October 1, 2021, exchange rates. All insulin prices from multiple pharmacies within a country were aggregated and then standardized based on the active ingredient, strength, dosage form, and package size for each insulin product (i.e., the cost per one vial or one box of pens) with consideration given to any government health system differences within the country for insulin delivery.¹ These differences are identified in data based upon the "Program" field within the web tool and text file. Aggregation of the data enables direct comparison among insulin products across countries regardless of individual product names, which may be unique to that country.

There were two principal pricing characteristics we wanted to quantify in this study. The first was the total price for the package at retail pharmacies (i.e., full product value recognized at the pharmacy), and the second was the price a person with diabetes could be anticipated to incur to obtain the package of insulin at retail pharmacies (i.e., patient cost share). To start with the first price, the total price for the package at retail pharmacy would be inclusive of any government or insurance subsidy, as well as any patient pay obligations. For example, in the Pharmacy Benefit Schedule (PBS) in Australia, the cost for a package of Fiasp® was recorded as 211.58 AUD based upon the information collected online. Note that although a patient in Australia would only be exposed to a maximum of 41.30 AUD, the total package price is higher because the government, and indeed all people in Australia, are subsidizing the cost (**Figure 3**):

Figure 3: Example 1- Insulin Package Price Cost Example in Australia



ⁱ For example, payment under government-subsidized programs were identified and separated from retail insulin prices.

However, not all products have only one formulation as is the case with the Fiasp[®] example above, nor do all countries standardize prices across equally interchangeable formulations of a product like Australia does within the PBS. To address this, we aggregated prices across like formulations by assigning all of the products to a base name - representative of the active ingredient, strength, and dosage form of the product. This enables us to compare products directly country to country regardless of product name. An example of this performed calculation is presented below based upon data gathered from Burkina Faso (**Figure 4**).:

Retail Pharmacy 1				
Insulin Brand/ Product name	Product Size	Туре	Total cost for	Patient cost for product
Lantus Solostar pen 100UI/ml	1 pen/3ml	long acting analog	12000FCFA	12000FCFA
Retail Pharmacy 2				
Insulin Brand/ Product name	Product Size	Туре	Total cost for	Patient cost for product
Lantus Solostar pen 100UI/ml	5 x 3 ml	long acting analog	50425 FCFA	50425 FCFA
Lantus Solostar pen 100UI/ml	1 x 3 ml	long acting analog	13825 FCFA	13825 FCFA

Figure 4: Example of Insulir	Price Calculation,	Multiple Prices,	Burkina Faso ⁱⁱ
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The **first step** in **Figure 4** was to aggregate all rows into equivalent base name terminology. In the above instance, all products were identified as insulin glargine 100U pens. The second step was to determine the average insulin glargine 100U pen price based upon the reported cost and size. This was done by first calculating a per mL unit price based upon the average of the package sizes gathered. This was accomplished by first averaging the reported 3 mL pen size prices together (12,000 FCFA + 13825 FCFA = 25,825 FCFA; 25,825 divided by 2 = 12,912.5 FCFA). The 15 mL package (5 x 3 mL) was then calculated to 3 mL pen size (50,425 FCFA divided by 5 = 10,085 FCFA). The results of the two package sizes were then averaged (12,912.5 FCFA + 10,085 FCFA = 22,997.5 FCFA; 22,997.5 divided by 2 = 11,498.75 FCFA). The resulting amount was divided by 3 (the total mL in the pen) to record the per mL price (11,498.75 FCFA divided by 3 = 3832.92 FCFA). This per mL price was recorded in our text file and was done to ensure that all product sizes could be standardized. Note that in collecting prices, our goal was to standardize all products to the same package size regardless of which sizes may be available in each country (See **Table 4** later in report for the complete list of unique insulin types and their standardized sizes).

With the gathered data, comparisons were made based on the number of insulin products available per country, the per-product prices between products, and the anticipated annual cost of each insulin product relative to the individual economic measures of median annual income, average annual income, and gross domestic product (GDP) per capita.

The **Supplementary Materials** section of this report contains additional details on the survey methods, data sources for each country, and data aggregation process.

ⁱⁱ Individual pharmacy names were collected but are blinded in consideration of their desire for anonymity

Results

Insulin Product Availability by Country

The first assessment conducted as part of the study was the availability of insulin products. Availability of insulin is perhaps the most important consideration in regard to diabetes treatment. As the history of diabetes demonstrates, failure to have appropriate treatment options available can lead to worse healthcare outcomes, up to and including death for patients who cannot access needed treatments. Additionally, as insulin product development has evolved over time, newer insulins are generally recommended by treatment guidelines over older formulations because of improvements to blood glucose control, which in turn can lead to improved healthcare outcomes.²³ ²⁴ Three assessments of product availability were made in this study: the number of insulin products by country, the types of insulin available by country, and the specific active ingredient formulations of insulin available by country.

Number of Insulin Products by Country

The first assessment performed was the availability of unique products by country. **Figure 5** (on the next page) summarizes these results where a unique product is defined as a product with the same active ingredient, strength, and formulation (e.g., insulin aspart 100 unit/mL *vial* would be a single unique product; insulin aspart 100 unit/mL *pens* would be a second unique product; see **Table 4** later in the report):



As can be seen in **Figure 5**, the number of available unique insulin products ranges from a low of two (Malawi) to a high of 41 (United States). The unweighted average across the 20 countries

with available data is 13.9 unique insulin products per nation. The median number of unique insulin products is 10. The average number of unique products available weighted based on the total population size of each country is 22.3.

The number of unique products in **Figure 5** is highest in the United States, in part due to it being the only country where the inhaled insulin product is available. The inhaled insulin product Afrezza[®] accounts for six unique products based upon the available strengths for that product and our definition of unique product.²⁵ To help better contextualize product availability, **Figure 6** (on the next page) displays the same information as **Figure 5**, but only counts product availability based upon the active ingredient within the product (i.e., insulin aspart is counted only once).



Full Name	Income Status	Number of Unique Active Ingredients
Algeria	Middle-income	4
Australia	High-income	10
Bahamas	High-income	7
Benin	Middle-income	6
Burkina Faso	Low-income	7
Canada	High-income	11
Denmark	High-income	11
Gambia	Low-income	8
Kenya	Middle-income	10
Malawi	Low-income	2
Morocco	Middle-income	5
New Zealand	High-income	9
Nigeria	Middle-income	10
Senegal	Middle-income	8
South Africa	Middle-income	7
Sudan	Low-income	5
Tanzania	Middle-income	7
Тодо	Low-income	3
Uganda	Low-income	6
United States	High-income	12
Low-income	Middle-income	High-income

Figure 6: Number of Unique Active Ingredients for Insulin by Country

The availability of different unique insulin products appears generally related to the income status of the country, with higher income countries having a greater number of available products, as identified in **Figure 7** (below):



Figure 7: Number of Unique Insulin Products by Economic Status, Country

The availability of different types of insulin can also be expressed based upon the active ingredient of the insulin product, as demonstrated previously in **Figure 6**. When assessing the availability of different types of active ingredients of insulin products by country and economic status we again observe that the higher-income countries are associated with a greater number of options; however, the differences are less extreme. As seen in **Figure 8** (on the next page), the number of available products by active ingredient ranges from a low of two (Malawi) to a high of 12 (United States). The unweighted average across the 20 countries with available data is 7.5. The median number of insulin products by active ingredient is 7.5. The average number of unique products available weighted based on the total population size of each country is 9.3.



Figure 8: Number of Insulin Products based upon Active Ingredient by Economic Status, Country

Types of Insulins Available by Country

The second assessment performed was the availability of products by insulin type; specifically, rapid-acting, short-acting, intermediate-acting, long-acting, and mixed insulins. **Figure 9**, **Figure 10**, and **Figure 11** (on the next few pages) summarizes these results:



Figure 9: Number of Unique Insulins by Type and Country, Low-income

Figure 10: Number of Unique Insulins by Type and Country, Middle-income





Figure 11: Number of Unique Insulins by Type and Country, High-income

Note that under current diabetes treatment guidelines, insulin is the primary treatment option in all patients with type 1 diabetes and may be used as an option for those with type 2.^{26 27 28} Typically, patients on insulin require multiple daily injections. People needing insulin usually use short-acting insulin or rapid-acting insulin analogue given before meals together with one or more daily separate injections of intermediate or long-acting insulin.²⁹ Although each type of insulin may produce the desired blood glucose results when appropriately dosed and monitored, there is evidence to suggest that rapid-acting insulins should be used preferentially to short-acting insulins, and long-acting insulins are preferred to intermediate-acting insulins because of their ability to provide greater blood glucose management and improved quality of life.^{30 31} Note that in both instances, these results are more readily observed in people with type 1 diabetes than in those with type 2 diabetes. Malawi and Togo have neither a single rapid-acting nor a long-acting insulin product available at the pharmacies and wholesalers included in our study. This lack of options may lead to poorer health outcomes for patients with diabetes (particularly type 1) within those countries because of the lack of access to generally preferred therapeutic options.

Active Ingredients Available by Country's Economic Status

Within each insulin type, a variety of insulin formulations are generally available. For example, within the long-acting insulin type are the formulations of insulin degludec, insulin detemir, and insulin glargine. The availability of these formulations varies significantly between each economic status. In **Figure 12** (on the next page), we examine the availability of specific formulations of insulin by counting the countries within each economic status that have the product available. The most commonly available formulations across our study within each insulin type (i.e., rapid-acting, short-acting, etc.) are insulin aspart, regular insulin, insulin NPH, insulin glargine, and insulin aspart and insulin aspart protamine mixture as well as insulin NPH and insulin regular.



Figure 12: Availability of Active Ingredients within Economic Status of Countries

Insulin Prices by Country

The study next made price comparisons between insulin products by country and insulin type. This view is similar to prior research work studying insulin pricing variability across countries.³² ³³ Our goal in performing this assessment was to address the variability in insulin pricing structure given the consolidated nature of insulin manufacturing (see **Background** earlier in the report). It has been observed that despite having similar manufacturing origins, pricing differences between countries for the same product, such as a Humalog[®] pen (Eli Lilly and Company), can vary significantly.³⁴

As identified in our methods, there were two principal pricing characteristics we wanted to quantify in this study. The first was the total price for the package at retail pharmacies (i.e., full product value recognized at the pharmacy), and the second was the price a person with diabetes could be anticipated to incur to obtain the package of insulin at retail pharmacies (i.e., patient cost share) [See **Example 1** in **Detailed Methodology**, page 59].

To calculate these costs, we took the prices for each package, and to each patient, we were able to gather in each country – regardless of whether insurance or government program was involved – and compared the prices for the same unique product. While we did collect wholesaler prices, they were not a focus of the analysis presented in this report. Standardized pricing comparisons in our report are made as all values are presented in U.S. dollar, based upon the October 1, 2021, currency conversion rates between each country's local currency and the U.S. dollar. (See **Detailed Methodology** for additional details).

Three assessments of insulin pricing were conducted in this study. The first was an assessment on insulin type pricing by economic status; the second was an assessment of insulin pricing based on the active ingredient, or base formulation, of the insulin product (e.g., insulin aspart); and the third examined price trends for the most common insulin products reviewed in our study.

Insulin Prices by Type and Country's Economic Status

In our first view (**Figure 13** on the next page), we compare the broad economic statuses via an unweighted average of the country and insulin types. We are unable to weight these figures as this study lacks access to utilization data of insulin products within each country studied. Prices are averaged across the type of insulin based on the underlying cost for 1 package size value of each product (i.e., one 10 mL vial or a box of insulin pens [15 mL]). Because of our reliance on package prices, we ensured that all captured prices were standardized to the same quantity (i.e., all vials were presented in costs equivalent to 10 mL vials) [See **Example 2** in **Detailed Methodology**, page 60].

We present average per-package prices because they are representative of how an individual would most likely purchase insulin (i.e., in whole product sizes). It is important to recognize in **Figure 13** that we are calculating the total package price and not the patient's cost to obtain the package of insulin. Within several of the countries in our study, it is common for healthcare goods and services to be paid for with insurance, which can include government programs. These government programs can include special access to low- or no-cost insulin for low-income patients (i.e., Medicaid in the U.S., reduced copayments in Australia's PBS, etc.). The presence of cost-assistance for insulin can significantly vary country-to-country. This first view

does not consider the impact of any government or insurance program(s) impact on patient cost, because even when those programs are present, they must be funded (which generally means that costs are being shared collectively). Stated differently, focusing on total retail package prices first enables us to assess the total cost to the country for the insulin products available within it, even if those costs are being shared collectively or within large groups.

As can be seen in **Figure 13**, there are significant differences in U.S. dollar-equivalent pricing between each economic grouping, although there are some general trends, such as long-acting products being more expensive than intermediate-acting insulin products, which may represent a cheaper alternative to the newer long-acting formulations.



Figure 13: Unweighted Average Insulin Product Cost, by Country Economic Status and Insulin Type

In examining **Figure 13**, pricing differences are evident when comparing high-income countries to the other economic groupings. However, **Figure 13** is influenced by the inability to weight the pricing based upon utilization within each country. To demonstrate, in **Figure 14** (on the next page) we present the same information as **Figure 13** but break out the United States from the other high-income countries due to the confounding impact U.S. drug prices are having within the high-income grouping.



Figure 14: Unweighted Average Insulin Product Cost, by Country Economic Status plus US and Insulin Type

In reviewing **Figure 14**, the high-income group excluding the U.S. is still more expensive within insulin types compared to the low- and middle-income groups. While there are still differences between each economic group, there is less extreme variability between each economic grouping (absent the U.S.). However, the United States group, which is now clearly visible, has significantly higher comparable insulin prices than would have been assumed based upon its status as a high-income country in Figure 13. The reason for this is due in part to the phenomenon of prescription drug rebates and discounts in the U.S. A rebate is "the return of part of the purchase price by the seller to the buyer".³⁵ In the case of the prescription drugs within the United States, insulin rebates are generally paid by drug manufacturers to a pharmacy benefit manager (PBM), who then shares a portion with the health insurer, or in some cases, directly with a U.S. government program.³⁶ The value of these rebates for insulin within the United States can be difficult to quantify, as demonstrated by a recent two-year investigation conducted by the U.S. Senate Finance Committee.³⁷ This report found significant variability in the ability of insurers to secure rebates, but noted they could be upwards of 75% of the drug's typical Wholesale Acquisition Cost (WAC) [a measure of retail pharmacy price in the U.S.]. Of note is that this level of rebating is precisely the amount necessary to bring the pricing experience within the U.S. into alignment with the other high-income countries for long-acting insulins. In Figure 15 (on the next page), we demonstrate this by identifying the level of rebate pricing concession necessary for each insulin type to bring a hypothetical net U.S. price into alignment with the other high-income countries. Again, these hypothetical values in our model are actually consistent with the amount of rebates reportedly offered in select instances according to the U.S. Senate Finance Committee report.



Figure 15: Model US Rebates Necessary to Achieve Parity with Other High-income Countries

Figure 15 provides valuable insights into the dynamics of U.S. drug pricing, where rebates can play a significant role in determining net price. However, these are not the focus of this report as the rebate is rarely recognized at the retail pharmacy in the U.S.

In examining each of the economic statuses closer via breaking out the individual countries (**Figures 16 through 18**), we can see more variability in average aggregate pricing within each country based on insulin type. Again, we are presenting unweighted averages for each categorization of insulin in these figures. Of particular note, some of the least expensive insulin products are available in the lower income countries.



Figure 16: Unweighted Average Insulin Product Cost, by Insulin Type, Low-Income Countries







Figure 18: : Unweighted Average Insulin Product Cost, by Insulin Type, High-Income Countries

As already observed in **Figures 13 & 14**, there are differences between the economic statuses of countries and the average insulin pricing across insulin types. The most obvious is that, outside the United States, the highest average insulin price does not exceed approximately U.S. \$150 equivalent per package. Furthermore, when examining insulin type pricing trends, it is generally true that the older products (i.e., short- and intermediate-acting insulins) are cheaper on average than the newer products (i.e., rapid- and long-acting insulins).

Insulin Prices by Active Ingredient, Insulin Type, and Economic Status

The next insulin pricing analysis conducted examined insulin prices across the specific formulations of insulin within an insulin type – for example, comparing insulin aspart formulation pricing within the rapid-acting insulins group. Because not all countries had prices available for each unique product, such as an insulin aspart 10 mL vial or a pack of insulin aspart pens, this is the most detailed comparison of per-product insulin pricing broadly possible. As before, values presented here are an unweighted average across the various package costs of insulin products in each economic status grouping for the 20 countries in this study. **Figures 19 through 23** demonstrate that the higher income countries are exposed to significantly higher prices for the same active ingredient relative to their lower income counterparts.



Figure 19: Rapid-Acting Insulin Pricing by Country Economic Status







Figure 22: Long-Acting Insulin Pricing by Country Economic Status



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Figure 23: Mixtures of Insulin Pricing by Country Economic Status

Insulin Prices by Active Ingredient

One of the ongoing policy debates within the United States has been benchmarking drug prices to international markets, a practice often referred to as international reference pricing.³⁸ Of note, some countries already make comparisons across foreign markets part of determining reimbursement for drugs within their country.³⁹ In this section, we compare the unweighted average package prices of the most common formulations of insulin products within our study within the rapid-acting, short-acting, and long-acting types of insulin. These categories were chosen as they are broadly consistent with the insulins on the WHO's Model List of Essential Medicines. As can be seen from Figures 24 through 26, there is variability in pricing both within a formulation across countries broadly and within countries of similar economic status.





Figure 25: Short-Acting Insulin Pricing for Insulin Regular Formulations by Country and Economic Status





Figure 26: Long-Acting Insulin Pricing for Insulin Glargine by Country and Economic Status

Insulin Affordability by Country

The final analysis conducted as part of this study measured the relative affordability of insulin products across the globe. For this analysis, we compared aggregate insulin pricing information gathered to the median and average annual income, as well as the GDP per capita of each country in our study. In this section, the average insulin prices per product from the prior section are annualized by multiplying the value by 12 to represent the cost to acquire 1 package of product once per month during the year. This figure was then divided by the median annual income, average annual income, or GDP per capita value within each country.ⁱⁱⁱ Although people with diabetes likely require multiple types of insulin (i.e., a rapid-/short-acting agent for meals plus a basal long-acting insulin) and may require more than 1 package of insulin product per month, this view provides some insights into the overall affordability of insulin based on patients who have to pay the full cost to acquire insulin (such as is the case in countries without national coverage programs for insulin or for countries that have deductible requirements before assistance on insulin pricing is offered). We therefore felt this was the most equitable way to make broad global comparisons of insulin affordability within the disparate countries in our study.

To be clear, many of the countries in our study have financial support programs for patients, which may be state-sponsored or private insurance, sharing a portion, or all, of insulin costs. The prevalence and accessibility of these programs is hard to capture in this analysis, and the information was not readily available in each country. Nevertheless, we attempt to make some comparisons on a patient's cost to acquire insulin across the retail sector based upon the gathered data via a similar approach (i.e., annualizing the per-package average patient cost and dividing by the economic measures). The webtool launched alongside this report available at <u>www.3AxisAdvisors.com</u> captures and presents the information regarding insulin package prices, patient cost share, government programs, etc., and is available for further research.

Affordability as Measured by Median Annual Income

The first measure of insulin affordability presented is a comparison of the aggregate annualized package payment rate for each insulin product relative to the median annual income of each country. As shown in **Figure 27**, the high-income countries, with the exception of the United States, have a lower total percentage of their median income dedicated to purchasing the average insulin product within their country each month relative to the low- and middle-income countries. The United States ranks in the middle of the pack in terms of the percentage of median income dedicated to insulin purchases according to **Table 1**. This is likely due to the fact that rebates and other price concessions are not recognized at the retail pharmacy in the U.S.

ⁱⁱⁱ Please note that the Bahamas and New Zealand did not have an available median income for comparison



Figure 27: Annualized Measure of Insulin Affordability by Country and Economic Status Based on Median Annual Income

Table 1: Ranked Order Measure of Insulin Affordability Relative to Median Annual Income by Country

Full Name		Percentage of Annual Median Income for Annualized Average Price of Insulin Product in Country			
CANADA	4	3%			
DENMAR	K	4%			
AUSTRALI	A	8%			
SUDAN		11%			
TOGO		14%			
UGANDA	Ą	15%			
ALGERIA	A Contraction of the second seco	23%			
TANZANI	A	26%			
UNITED STA	TES	28%			
MOROCC	0	33%			
SOUTH AFR	ICA	36%			
SENEGA	L	41%			
MALAW	l	43%			
GAMBIA	\	51%			
BENIN		55%			
KENYA		67%			
NIGERIA	N	73%			
BURKINA FASO		108%			
Low-income	Middle-income	High-income			

Figure 28 further examines affordability relative to median income based upon the previously discussed insulin types. This view provides an assessment of affordability and suggest that older formulations (i.e., short- and intermediate-acting insulin) are more affordable relative to the newer formulations. This view also demonstrates that there are some countries whose average insulin product in a given type is more than the median income available to most residents in that country.





The final view into insulin affordability we measured based upon the median annual income was based upon the gathered data on patient cost share for insulin. In **Figure 29** (on the next page), we see that the people with diabetes in low- and middle-income countries may face more direct pressures on affordability than people in high-income countries. Again, this view assumes universal access to government programs within the countries for which we obtained government program data; however, this is almost certainly an over-estimation of affordability in those countries.



Figure 29: Insulin Affordability Measured by Average Patient Cost Share Relative to Median Annual Income of Each Country

Affordability as Measured by Average Annual Income

The next measure of insulin affordability is similar to the one prior. Rather than compare aggregate annualized insulin prices with median income, this section compares insulin prices with average income within a country. Universally, the use of average income relative to median income makes insulin appear more affordable, as each country's percentage to the average is lower than the median measure, which is to be expected. Possibly related to income inequality being greater in other countries, the United States is further up the list (**Figure 30**, **Table 2**) when rank-ordering affordability in this assessment.





 Table 2: Ranked Order Measure of Insulin Affordability Relative to Annual Income by Country

Full Name		Percentage of Annual Average Income for Annualized Average Price of Insulin Product in Country			
CANADA	4	2%			
DENMAR	K	3%			
AUSTRAL	IA	7%			
SUDAN		9%			
TOGO		10%			
UGAND	Д	10%			
SOUTH AFF	RICA	14%			
TANZANI	A	19%			
ALGERIA	Ą	20%			
UNITED STA	ATES	21%			
MOROCC	0	24%			
MALAW	1	28%			
SENEGA	L	31%			
BENIN		39%			
GAMBIA	Ą	39%			
KENYA		49%			
NIGERIA	A	59%			
BURKINA FASO		80%			
Low-income	Middle-income	High-income			



Figure 31: Insulin Affordability by Insulin Type Relative to Average Annual Income of Each Country

Figure 32: Insulin Affordability Measured by Average Patient Cost Share Relative to Average Annual Income of Each Country



Note that in either measure – median annual income from the prior section or average annual income in this section – a single package of insulin product purchased monthly equates to, at the very least, 2% or more of annual income. The majority of countries (at least 14 out of 18 measured; Bahamas and New Zealand unassessed) have annualized package prices of insulin that equate to 10% or more of annual income. These calculations exclude the likely need for more than one type of insulin for a given insulin-dependent person with diabetes, nor does it factor in the cost for diabetic supplies to properly administer the insulin (e.g., syringes, needles, blood glucose meter, etc.). Ultimately, these measures suggest that there is a broad insulin affordability challenge globally, as other reports have demonstrated that even in what appear to be the most affordable countries for insulin, such as Canada, individuals still report struggles in affording their medication.⁴⁰

Affordability as Measured by GDP per Capita

The final measure of insulin affordability conducted in this study was annualized average insulin prices relative to the GDP per capita of each country. This measure was selected because it was the most widely available for each country in our study. Similar to the prior section, this measure presents insulin as more affordable than either the median or average annual income (**Figures 33, Table 3, Figure 34, Figure 35**).

Figure 33: Annualized Measure of Insulin Affordability by Country and Economic Status Based on GDP per Capita



Full Name		Percentage of GDP per Capita for Annualized Average Price of Insulin Product in Country				
NEW ZEALA	ND	1%				
CANADA		1%				
DENMAR	<	1%				
BAHAMAS	S	2%				
AUSTRALI	Д	3%				
SUDAN		4%				
SOUTH AFRI	CA	5%				
ALGERIA		5%				
UGANDA	、	5%				
TOGO		6%				
TANZANIA	4	7%				
UNITED STA	TES	8%				
SENEGAL	-	10%				
NIGERIA		11%				
BENIN		11%				
MOROCC	C	12%				
KENYA		13%				
MALAWI		19%				
GAMBIA		30%				
BURKINA FA	SO	35%				
Low-income	Middle-income	High-income				

Table 3: Ranked Order Measure of Insulin Affordability Relative to GDP per Capita by Country



Figure 34: Insulin Affordability by Insulin Type Relative to the GDP per Capita of Each Country

Figure 35: Insulin Affordability Measured by Average Patient Cost Share Relative to GDP per Capita of Each Country



Discussions

Conversations about insulin affordability have been ongoing across the globe, likely since the development of insulin as a therapeutic option. From the initial development of insulin price was an important consideration, as the patents for its original discovery were sold for \$1. The importance of insulin pricing can hardly be understated for people with diabetes, given that the history of insulin development also demonstrates that failure to adequately treat and control diabetes can lead to significant morbidity and mortality. Despite this history, millions of people with diabetes still suffer complications from their disease annually. As recently as 2019, it was estimated that diabetes was the direct cause of 1.5 million deaths across the globe.⁴¹ Often, the focus of insulin pricing conversations is on the per-unit price differences that may exist between the various healthcare systems across the globe. Although this research is important, and has demonstrated that some of the wealthiest countries, such as the United States, pay significantly more for the same or similar insulin product, such conversations may overlook some of the broader affordability challenges people with diabetes face.

This study confirms prior research into insulin prices demonstrating that higher income countries are paying more for similar insulin products relative to lower-income countries. For example, a 2020 study by T1International found that 25% of people living with type 1 diabetes globally underused insulin at least once within the previous year due to cost, including individuals in high-income countries like the U.S.⁴² However, when measuring insulin affordability relative to a country's income (i.e., median or average annual income) or productivity (GDP per capita), the wealthier countries generally have lower percentages of annual incomes dedicated to purchasing one product of insulin per month than the lowerincome countries, even before factoring in government and/or private party insurance subsidies. This observation is made despite those high-income countries paying higher insulin prices than their lower-income counterparts. To be clear, the measures in this study focus on package prices of insulin which may not be reflected of insulin prices net of all discounts. The importance of these unknown price discounts is hard to understate given that the assessment made of hypothetical net U.S. insulin prices, in this study relative to other high-income countries. While the amount of discounting necessary to match these foreign markets is significant (i.e., 75% or more), they are likely occurring, as noted in the aforementioned U.S. Senate Finance Committee's insulin investigation.⁴³ However, it is highly unlikely that the full value of U.S. rebates or other price concessions ultimately reach all end consumers. This is because when the study attempted to measure the affordability of insulin based upon average patient costs to obtain a package, the U.S. was still higher than the other high-income countries. Ultimately, even in countries where cost assistance for insulin is available, the availability of these programs may not be uniform, and the impact of insulin affordability is likely still best measured on the package price total cost value (and not just what a patient may pay), as those costs must be shared collectively in whatever program may be present.

The findings of this study may help explain the growing trend of medical tourism as it relates to purchasing healthcare services like insulin. Medical tourism occurs when individuals – often those within wealthy countries – travel abroad to obtain healthcare services.⁴⁴ This is done because the services are cheaper abroad than in their country of residence. However, the findings of this study also reveal that that is not an option for all people with diabetes. There is

not necessarily always going to exist a country whose prices are more affordable than your own. Furthermore, it is likely not a practical solution either, as the smaller countries may not have adequate stock of insulin for both their own citizens as well as travelers from abroad. Ultimately, insulin affordability today is perhaps best characterized in relative terms, that varies based upon who is answering the affordability question.

In financial terms, the behavior of insulin pricing observed within this study is perhaps best described as price discrimination. Price discrimination is defined as "the practice of charging a different price for the same good or service."45 A variety of price discrimination practices are recognized in microeconomics. Third-degree price discrimination occurs when a company charges a different price to individual consumer groups, largely on the perceived ability to pay of each group. For example, a theater may divide moviegoers into seniors, adults, and children, with each paying a different price to see the same movie. Though the underlying service in this example is the same, the movie being seen, the theater may give kids and seniors a lower price than it charges adults for the same service. This analogy best seems to describe the observations within our study related to insulin prices globally. The underlying insulin product in our study may be the same, but the charge for that product can vary significantly depending upon where a person is located. We spent considerable time checking our sources to confirm prices relative to some of the observations in our data. For example, a Lantus (insulin glargine; Sanofi-Aventis) product has a considerable range of pricing behavior across the countries in our study; ranging from approximately US \$10 (Kenya) to US \$300 (United States) per vial, despite all formulations of Lantus being traced back to the same manufacturer. It should be noted that one of the key limitations of this study was its focus on retail pricing. As already discussed, the study does not account for the net price of a product after any rebate or chargeback that may occur following the sale of the product to an individual. However, whether rebates exist or not does not necessarily mean that their value is directly passed along to the end consumer, nor does their presence ensure that insulin is more accessible.

Despite the wide range of insulin prices observed across all types and formulations in this study, insulin remains out of reach for many individuals, as seen in the economic measure of this study. In most cases, namely 14 out of 18 measured, large percentages (approximately 10% or more) of each individual's annual incomes may need to be dedicated to purchase a single insulin product they need to survive. This appears to be a significant challenge given the estimated growth in the number of people with diabetes globally in the coming years.⁴⁶ Insulin affordability is a global challenge and likely requires global initiatives and cooperation to address and ensure everyone has access to high-quality and affordable products. While insulin has existed as a therapeutic option for 100 years, the inability to address its affordability globally may suggest an unpromising outlook in combating the accessibility and affordability of treatment options for other disease states, such as cancer.

Availability of the Web Tool

As this paper demonstrates, a variety of measures can be used to assess insulin affordability in a global market. Insulin is a necessary therapeutic component of many diabetic regimens for individuals of all socioeconomic statuses. To provide transparency regarding the measures within this study as well as others not directly assessed in this paper, 3 Axis Advisors, in conjunction with the McPike-Zima Foundation, has made available a web-based tool on

<u>www.3AxisAdvisors.com</u> for interested parties to explore. Furthermore, the website contains a text file of the underlying data available for download free of charge so that anyone can further research the topic of insulin affordability.

Acknowledgements

This report would not have been possible without the McPike-Zima Foundation, which requested and provided the full funding for the research. Additionally, this report was made possible thanks to collaboration with the organizations of T1International and the Sonia Nabeta Foundation. T1International provided research support and critical review while the Sonia Nabeta Foundation coordinated the collection of insulin pricing data from Africa and critical review.

Sonia Nabeta Foundation

The Sonia Nabeta Foundation is a tax-exempt organization under section 501(c)(3) of the United States Internal Revenue Code founded in honor of Sonia Stephanie Nabeta, who fought a valiant fight against type 1 diabetes until her death on August 5, 2015. Through a variety of programs, the Foundation advocates for improved access to healthcare for patients with type 1 diabetes within Africa.⁴⁷

T1International

T1International (T1I) is a non-profit led by people with, and impacted by, type 1 diabetes. T1I believes in a world where everyone with type 1 diabetes – no matter where they live – has everything they need to survive and achieve their dreams. They support local communities by giving them the tools they need to stand up for their rights so that access to insulin and diabetes supplies becomes a reality for all. T1I accepts no funding from pharmaceutical companies in order maintain their independence and advocate for change.⁴⁸

The McPike-Zima Foundation

The McPike-Zima Foundation is dedicated improving people's lives globally by fostering sustainable change across the areas of education, the environment, and health (with the focus on type 1 diabetes). They aim to bring a business mindset to their funding decisions, evaluating an organization's potential impact and ability to attain long-term effectiveness. The McPike-Zima Foundation has a preference on funding local and grassroots organizations, which are best positioned to make a difference in their respective communities.

About 3 Axis Advisors

3 Axis Advisors LLC is an elite, highly specialized consultancy that partners with private and government sector organizations to solve complex, systemic problems and propel industry reform through data-driven advocacy. With a primary focus on identifying and analyzing US drug supply chain inefficiencies and cost drivers, 3 Axis Advisors LLC offers unparalleled expertise in project design, data aggregation and analysis, government affairs, and media relations. 3 Axis Advisors LLC arms clients with independent data analysis needed to spur change and innovation within their respective industries. The cofounders of 3 Axis Advisors LLC were instrumental in exposing the drug pricing distortions and supply chain inefficiencies embedded in Ohio's Medicaid managed care program. They are also the cofounders of 46brooklyn Research, a nonprofit organization dedicated to improving the transparency and accessibility of drug pricing data for the American public. To learn more about 3 Axis Advisors LLC, visit www.3axisadvisors.com.





Supplementary Materials

Detailed Methodology

Data Sources

All analytics performed in this study were based on the combination of the following raw data sources:

- 1. Currency Conversion Database
- 2. Country Economic Database
- 3. Australia Pharmacy Benefit Scheme (PBS) database
- 4. Canadian Provinces Formulary Search (Alberta, British Columbia, New Brunswick, Novo Scotia, Ontario) database
- 5. Danish Medicines Agency database
- 6. The Center for Medicare & Medicaid Services (CMS) National Average Drug Acquisition Cost (NADAC) database
- 7. CMS Medicare Part D Dashboard database
- 8. Medi-Span PriceRx by Wolters Kluwer Clinical Drug Information Inc. (WKCDI)
- 9. Small Chain and Independent US Pharmacy Reimbursement Data
- 10. Surveys of Wholesale and Retail Pharmacy Reimbursements within the African Continent
- 11. Surveys of Wholesale and Retail Pharmacy Reimbursements within the Bahamas
- 12. Global Currency Conversions

Details regarding these sources and the transformations made to the base data are provided within this section.

Currency Conversion Database

We relied upon currency conversion information from OANDA Corporation.⁴⁹ OANDA is a financial services provider that offers internet-based foreign exchange trading and currency information.

OANDA was founded in 1995 and was the first to offer online access to a variety of currency exchange-rate information free of charge.⁵⁰

This data was accessed for the purpose of this report on October 1, 2021.

Country Economic Database

Our work relied on the 2021 compiled country economic data of mean, median, and GDP per capita data available at World Population Review for all countries in our study but the Bahamas and New Zealand.⁵¹ The World Population Review aggregates several data sources for their figures but represented one of the few centralized sources of data we could find that had the economic indicators of interest for this study. For the Bahamas and New Zealand, we used WorldoMeter⁵² data for GDP per capita.

We also relied on The World Bank's definitions of low-, middle- and high-income countries based on the current fiscal year (2022) data.⁵³ According to The World Bank, these classifications are made as follows:

"For the current 2022 fiscal year, low-income economies are defined as those with a GNI per capita, calculated using the World Bank Atlas method, of \$1,045 or less in 2020; lower middle-income economies are those with a GNI per capita between \$1,046 and \$4,095; upper middle-income economies are those with a GNI per capita between \$4,096 and \$12,695; high-income economies are those with a GNI per capita of \$12,696 or more."

This data was accessed for the purpose of this report on October 1, 2021.

Australia Pharmacy Benefit Scheme (PBS) database

The Australian Government provides select medications at a subsidized rate to its residents via the Pharmaceutical Benefit Scheme (PBS). The PBS began as a limited scheme in 1948, with free medicines for pensioners and a list of 139 'life-saving and disease preventing' medicines free of charge for others in the community. Today, the PBS provides timely, reliable and affordable access to necessary medicines for Australians. The PBS is part of the Australian Government's broader National Medicines Policy. The maximum patient charge to obtain a medication through the PBS is 43.10 AUD.⁵⁴

The PBS makes available on its website downloadable data regarding the pricing and maximum copay obligations for medications the PBS covers.

This data was accessed for the purpose of this report on July 12, 2021.

Canadian Provinces Formulary Search (Alberta, British Columbia, New Brunswick, Nova Scotia, Ontario) database

Governments in Canada have instituted mechanisms to control drug prices. At the provincial level, these mechanisms include the development of drug formularies, which are lists of medications available for coverage within the drug benefits offered within the province, reference-based prices for products, and limits on pricing markups. The Patented Medicine Review Board (PMPRB), an independent quasi-judicial body, regulates the prices of medicines sold in Canada.⁵⁵

While the maximum average potential price (MAPP) set by the PMPRB is a valuable insight into drug prices within Canada, each province's approach to drug pricing is helpful in that it also establishes the patient cost share for accessing medications. As a result, we relied upon the electronic data available within the provinces of Alberta⁵⁶, British Columbia⁵⁷, New Brunswick⁵⁸, Nova Scotia⁵⁹, and Ontario⁶⁰ to establish insulin prices within Canada. Note that there was no pricing information listed within the New Brunswick formulary for insulin products and so they do not appear in this report. Average copayments were based upon the following for each province:

- Alberta: 30% of the package price up to a maximum of \$25.61
- British Columbia: 100% of the package price as no single insulin will result in greater than \$10,000 in annual expenditures.⁶²

- Nova Scotia: 20% of the package price.⁶³
- Ontario: \$6.11 per prescription.⁶⁴

This data was accessed for the purpose of this report on July 12, 2021.

Danish Medicines Agency database

The Danish Medicines Agency (DKMA), known locally as Lægemiddelstyrelsen, is the supreme pharmaceutical authority in Denmark. The purpose of the agency is to ensure that medicinal products used in Denmark are safe and effective. The DKMA also identifies the sale price of pharmaceuticals within the country. This is accomplished via required pricing disclosures by pharmaceutical companies. Prices of medicines are fixed by pharmaceutical companies and sold at the same prices from all pharmacies in Denmark. The pharmaceutical companies report changes in prices every fortnight to the DKMA, which subsequently informs pharmacies and their citizens of the applicable prices.⁶⁵ Since January 1, 2006, a fixed annual maximum copayment was introduced on expenses for reimbursable medicine stated at reimbursement prices. The maximum patient's co-payment amounts to DKK 4,270 per year (in 2021). This means that all citizens automatically receive 100% of the reimbursement price on reimbursable medicine if the citizen's annual co-payment for reimbursable medicine (stated at reimbursement prices) exceeded DKK 4,270 (in 2021).

This data was accessed for the purpose of this report on July 12, 2021.

New Zealand Online Pharmaceutical Schedule

The Pharmaceutical Schedule is a list of all government funded medicines and related products in New Zealand. The Ministry of Health and elected Government set policies. These include who is eligible for publicly funded treatment and who pays patient co-payments. The typical copayment by a patient for a medicine on the Schedule is \$5 NZD and was the basis of estimated copayments for insulin in our study.⁶⁶

This data was accessed for the purpose of this report on November 1, 2021.

CMS' National Average Drug Acquisition Cost (NADAC) database

NADAC was developed by the Centers for Medicare and Medicaid Services (CMS), "to provide a national reference file to assist State Medicaid programs in the pricing of Covered Outpatient Drug claims to reflect the actual acquisition cost (AAC) of drugs."⁶⁷ As such, NADAC's goal is to be the most comprehensive public measurement of market-based retail pharmacy acquisition cost.

NADAC is compiled by Myers and Stauffer on behalf of CMS. It is generated from a voluntary monthly invoice cost survey of 2,500 randomly selected retail pharmacies (with 450-600 respondents). After Myers and Stauffer completes its data processing and clean-up activities, it publishes the survey results at the National Drug Code (NDC) level on Medicaid.gov. As state Medicaid fee-for-service programs have shifted to an actual acquisition cost (AAC) basis to comply with the Covered Outpatient Drug Rule (CMS-2345-FC), many states have utilized NADAC as the primary proxy for acquisition cost. As such, **we believe NADAC is the best publicly available pricing benchmark to approximate average pharmacy invoice costs**. We relied on the NADAC database extensively throughout this report as the best estimate for a drug's actual acquisition cost.

This data was accessed for the purpose of this report on July 12, 2021.

CMS' State Drug Utilization Database

State agencies responsible for Medicaid operations are responsible for reporting drug utilization for covered outpatient drug expenditures incurred by their programs to CMS. Utilization is reported on a quarterly basis and published on Medicaid.gov approximately four months after the close of each quarter. The database includes total dollars spent, units reimbursed, and prescriptions for each 11-digit National Drug Code (NDC) per quarter, by state and program type (i.e., Managed Care or Fee-for-Service).⁶⁸ The data does not include patient cost share; however, as assumed \$4 per prescription based upon the maximum allowable copayments for eligible populations in Medicaid.⁶⁹

The data for 2021 was downloaded on October 1, 2021 and included in the study as representative of Medicaid program reimbursements for insulin products in the U.S.

CMS' Medicare Database

CMS makes available formulary, pharmacy network, and pricing data for Medicare Prescription Drug Plans and Medicare Advantage (MA) Prescription Drug Plans (with the exception of employer and Program of All-Inclusive Care for the Elderly plans). These non-identifiable files are available on a monthly and a quarterly basis. This pricing data was relied upon to establish average aggregate insulin pricing information within the Medicare program including patient cost share. Patient cost share was calculated as an unweighted average based upon the fixed copay amounts. This means it does not include plans that have a percentage based copay in calculating the average.

The most recent data for 2021 was downloaded on October 1, 2021 and included in the study as representative of Medicaid program reimbursements for insulin products in the U.S.

Medi-Span PriceRx by Wolters Kluwer Clinical Drug Information, Inc.

Medi-Span PriceRx is an online pricing and drug information portal developed by Wolters Kluwer Clinical Drug Information, Inc. (WKCDI). PriceRx offers one of the most extensive histories of drug manufacturer pricing, with NDC-level drug pricing dating back to the 1980s.⁷⁰ PriceRx was the source of the raw AWP and wholesale acquisition cost (WAC) data that we used to calculate aggregated quarterly AWPs for our analyses.

PriceRx also contains clinical information, enabling identification of drug products by a hierarchical therapeutic classification system. This classification helps standardize drug lists and is the basis for all therapeutic category investigations. This classification system was used to identify brand vs. generic status, prescription drug status, and therapeutic drug classes among other clinical information.

This data was accessed for the purpose of this report on July 12, 2021.

Small Chain and Independent Pharmacy Reimbursement database

3 Axis Advisors has access to de-identified pharmacy claims data of hundreds of independent/small chain community pharmacies across the U.S. This data is in the standard, NCPDP Telecommunication format, enabling easy identification of drug product,

reimbursement, and patient cost share. This data was used to represent typical U.S. retail pharmacy pricing and cost share for patients.

This data was accessed for the purpose of this report on July 12, 2021.

Survey of Retail and Wholesale Pharmacy Pricing within Africa (Algeria, Benin, Burkina Faso, Gambia, Kenya, Malawi, Morocco, Nigeria, Senegal, South Africa, Tanzania, Togo, and Uganda) 3 Axis Advisors, in conjunction with T1International and Sonia Nabeta Foundation, developed a standard collection form to assess insulin pricing. The format of that form, along with the provided instructions for use, are available within the Supplementary Materials section of this report. The Sonia Nabeta Foundation interviewed retail and wholesale pharmacies within the countries of Algeria, Benin, Burkina Faso, Gambia, Kenya, Malawi, Morocco, Nigeria, Senegal, South Africa, Tanzania, Togo, and Uganda to obtain insulin pricing information for each.

The Sonia Nabeta Foundation provided context for each country's health system in the price surveys they conducted.

This data was collected over July, August, and September 2021.

Algeria Price Survey

Algeria manufactures insulin through joint ventures with Sanofi, Eli Lilly, and Novo Nordisk. Pfizer has manufacturing rights in Algeria. All manufacturing is done at state-owned Saidal Plants. Retail and wholesalers deal directly with the Pharmaboard of Algeria. The price of insulin is controlled by the government.

Three retail pharmacies and no wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Prices of insulin were the same at all three surveyed pharmacies.

Medicines are reimbursed at 80% of the reference price. All patients who are employed in the formal sector and have chronic diseases (including diabetes) are reimbursed 100% of the costs of care and medicines (patients receive medicines free-of-charge, as they are covered by health insurers which pay pharmacies a fixed price). Low-income formal sector workers (i.e. with health insurance) are identified by the Algerian Ministry of National Solidarity and Family and local authorities (districts and sub-districts). Individuals belonging to this patient group are provided a card which grants them access to free medication and care. The ministry and local authorities pay for their health care costs.

Benin Price Survey

The prices of pharmaceutical products in the Benin private sector are regulated by the government.⁷¹ Limited national programs exist to combat non-communicable disease treatment, which can help people with diabetes access care at lower costs.

Four retail pharmacies and four wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. With the exception of the OMS/Programme Nationale De Lutte Contre Les Maladies Non Transmissibles Du Benin, prices were uniform across wholesalers and pharmacies.

Burkina Faso

There is no Universal Health Insurance available for insulin in Burkina Faso. Select private insurances exist and require 20% of the insulin product cost as the out-of-pocket co-payment for insulin (in addition to premium payments).

Four retail pharmacies and their wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies and wholesalers. The prices used in this study reflect the average price per unique product across the surveyed groups.

Gambia Price Survey

The majority of people with diabetes in Gambia reportedly get their insulin from a government hospital, because it is provided free of charge. However, hospitals can run out of insulin, requiring patients to obtain their insulin from other sources. Private pharmacies generally run very low on stock of insulin, as it is not a priority drug for those pharmacies given the low demand due to typical patient reliance on government hospitals for sourcing. Private insurance is available to patients that pay premiums, and some companies provide health insurance.

Three retail pharmacies and one wholesaler were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies, and the prices used in this study reflect the average price per unique product across the three surveyed pharmacies.

Kenya Price Survey

Four retail pharmacies and three wholesalers in Kenya were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies and wholesalers. The prices used in this study reflect the average price per unique product across the surveyed groups.

Malawi Price Survey

Health insurance companies only cover insulin costs in Malawi when accessed at recognized private hospitals and clinics. All purchases made by patients at retail pharmacies are made at full patient cost. Patients are able to access free health services at government hospitals.

Four retail pharmacies and three wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies and wholesalers. The prices used in this study reflect the average price per unique product across the surveyed groups.

Morocco Price Survey

In Morocco, government policy regulates insulin mark-ups to 10% for wholesalers and 30% for retail pharmacies. A value-added tax (VAT) of 7% is applied to some locally produced and imported medicines.

Three retail pharmacies and three wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies and wholesalers. The prices used in this study reflect the average price per unique product across the surveyed groups.

The survey did not specify patient cost share information, and so it was assumed to be 100% of the package cost.

Nigeria Price Survey

Insulin is available for free at public hospitals in Nigeria; however, supply can be an issue. As a result, most people with diabetes reportedly purchase their medicines from private retail pharmacies that generally do not accept insurance or other government subsidies.

Four retail pharmacies and two wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies and wholesalers. The prices used in this study reflect the average price per unique product across the surveyed groups.

Senegal Price Survey

Insulin pricing in retail pharmacies is set and approved by the Senegal government. It is believed that some insulin prices are subsidized by the government.

Four retail pharmacies and four wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. No pricing variability for the same product was observed between the surveyed locations.

South Africa Price Survey

Government hospitals and government clinics provide insulin for free to those in South Africa who cannot afford medicines. Insulin package prices maybe be subsidized by other parties, such as charitable foundations or insurers, reducing the out-of-pocket costs for persons with diabetes in South Africa.

Four retail pharmacies and three wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies and wholesalers. The prices used in this study reflect the average price per unique product across the surveyed groups.

Sudan Price Survey

Prices of medicines in Sudan are controlled by the National Medicine and Poisons Board (NMPB). Prices are pre-decided during the registration process. Registration prices are expressed as cost of goods, plus shipping insurance and freight by air to Khartoum (CIF). Importers (i.e., wholesalers) are given 23% calculated from the CIF (Registration price) as profit. Importers (wholesalers) are allowed to sell in bulk to pharmacies. Pharmacies (retailers) are selling medicines at a 20% markup from wholesale to patients.⁷²

One retail pharmacy and one wholesaler were surveyed by the Sonia Nabeta Foundation to establish the prices in this study.

There are two national and state-owned health insurances available for Sudan nationals namely: National Health Insurance Fund and Shawamikh Health insurance Company. Nationals have to pay a premium to enroll, and that insurance covers 75% of the cost of medicine.

Tanzania Price Survey

All retail pharmacies in Tanzania accept either Strategis Insurance and/or the National Health Insurance Fund (NHIF).

Four retail pharmacies and four wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies and wholesalers. The prices used in this study reflect the average price per unique product across the surveyed groups.

Togo Price Survey

Four retail pharmacies and four wholesalers in Togo were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. No pricing variability for the same product was observed between the surveyed locations.

Uganda Price Survey

There are multi-partner programs within Uganda that enable children to get access to insulin and supplies for free. Limited insurance options appear to exist, as reported prices for patients are 100% of the package size at the pharmacies surveyed.

Three retail pharmacies and three wholesalers were surveyed by the Sonia Nabeta Foundation to establish the prices in this study. Pricing variability by product was observed between retail pharmacies and wholesalers. The prices used in this study reflect the average price per unique product across the surveyed groups.

Survey of Retail and Wholesale Pharmacy Pricing within the Bahamas

3 Axis Advisors, in conjunction with T1International and Sonia Nabeta Foundation, developed a standard collection form to assess insulin pricing. The format of that form, along with the provided instructions for use, are available within the **Supplementary Materials** section of this report. The Diabetic Research Institute interviewed retail and wholesale pharmacies within The Bahamas to obtain insulin pricing information for each.

This data was collected over July 2021.

Insulin Pricing Survey Methods

For those countries where electronic sources of insulin prices were unable to be identified, the Sonia Nabeta Foundation surveyed local pharmacies for pricing information. Data was collected in the following format:

Insulin Brand/ Product	Product Size	Туре	Total cost for Product Size	Patient cost for product	With Insurance Co	Special government healthcare	Comments
Name				size	payment	programs	
The name of the product as it appears on the packaging	The total volume (in mL) being provided by the product	The classification of the insulin (e.g., rapid- acting)	The local currency monetary value of the package	The local currency monetary charge to obtain the package	The local currency monetary charge to obtain the package via an insurance program	The local currency monetary charge to obtain the package via a government program	For each line, detail any specifics of the way the medication was obtained (i.e., which insurance or government program)

Data Aggregation and Standardization

Identification of Products by Active Ingredient, Strength, Dosage Form and Package Sizes

In order to make equivalent comparisons between the various insulin products within the countries studied, we relied upon the active ingredient, strength, dosage form, and package size for each insulin product. Each unique combination is identified as a unique product for the purposes of this study. This was done because although each country may have an insulin product that is comprised of the same active ingredient, strength, dosage form and package size, the naming convention may differ country to country. The following table summarizes the relationships relied upon for this study:

Insulin Type	Active Ingredient	Strength	Dosage Form	Package Size	Product Name(s)
	Insulin aspart	100 unit per mL	Vial	10 mL	Insulin aspart, Novolog, Novolog ReliOn, NovoRapid
			Pen	15 mL (5 x 3 mL)	Insulin aspart FlexPen, Novolog FlexPen, Novolog ReliOn FlexPen, NovoRapid FlexPen
			Cartridge	15 mL (5 x 3 mL)	Insulin aspart Penfill, Novolog Penfill, NovoRapid Penfill
Rapid-Acting	Insulin aspart (with Niacinamide)	100 unit per mL	Vial	10 mL	Fiasp
			Pen	15 mL (5 x 3 mL)	Fiasp FlexPen
			Cartridge	15 mL (5 x 3 mL)	Fiasp PenFill
	Inculin	100 unit	Vial	10 mL	Apidra
	glulisine per mL		Pen	15 mL (5 x 3 mL)	Apidra SoloStar
	Insulin lispro	100 unit	Vial	10 mL	Admelog, Humalog, Insulin lispro, Lyumjev
		permL	Pen	15 mL (5 x 3 mL)	Admelog SoloStar Humalog Junior Kwik Pen,

Table 4: Unique Insulin Types Available Globally⁷³

Insulin Type	Active Ingredient	Strength	Dosage Form	Package Size	Product Name(s)
					Humalog Kwik Pen, Insulin Lispro Junior KwikPen, Insulin Lispro Pen, Lyumjev KwikPen
			Cartridge	15 mL (5 x 3 mL)	Humalog
		200 unit per mL	Pen	15 mL (5 x 3 mL)	Humalog KwikPen, Lyumjev KwikPen
		4 & 8 & 12 Unit	Cartridge	180 count	Afreeza Inhalation Powder
		8 & 12 Unit	Cartridge	90 count	Afreeza Inhalation Powder
		8 & 12 Unit	Cartridge	180 count	Afreeza Inhalation Powder
	Insulin Regular	4 & 8 Unit	Cartridge	90 count	Afreeza Inhalation Powder
	(Human)	4 & 8 Unit	Cartridge	180 count	Afreeza Inhalation Powder
		4 Unit	Cartridge	90 count	Afreeza Inhalation Powder
		8 Unit	Cartridge	90 count	Afreeza Inhalation Powder
		12 Unit	Cartridge	90 count	Afreeza Inhalation Powder
Short-Acting	Insulin Regular (Human)	100 unit per mL	Vial	10 mL	Actrapid, Actraphane, Humulin R, Novolin R, Novolin R ReliOn
			Pen	15 mL (5 x 3 mL)	Actrapid Pen, Actraphane FlexPen, Novolin R FlexPen, Novolin R ReliOn FlexPen
		500 unit	Vial	10 mL	Humulin R U-500
		per mL	Pen	3 mL	Humulin R U-500 KwikPen
Intermediate- Acting	Insulin NPH (Human) (Isophane)	100 unit per mL	Vial	10 mL	Humulin N, Insulatard, Insulet Rapid, Novolin N, Novolin N ReliOn, Protaphane

Insulin Type	Active Ingredient	Strength	Dosage Form	Package Size	Product Name(s)
			Pen	15 mL (5 x 3 mL)	Humulin N KwikPen, Insulatard FlexPen, Insulet Rapid Pen, Novolin N FlexPen, Novolin N ReliOn FlexPen, Protaphane Pen
		100 unit	Vial	10 mL	Tresiba
	Insulin	per mL	Pen	15 mL (5 x 3 mL)	Tresiba FlexTouch
	degludec	200 unit per mL	Pen	9 mL (3 x 3 mL)	Tresiba FlexTouch
	Insulin	100 unit	Vial	10 mL	Levemir
	detemir	permL	Pen	15 mL (5 x 3 mL)	Levemir FlexTouch
		100 unit per mL	Vial	10 mL	Basaglar Lantus, Optisulin, Semglee
Long-Acting			Pen	15 mL (5 x 3 mL)	Basaglar KwikPen, Lantus SoloStar, Optisulin SoloStar Semglee Pen
				1.5 mL	Toujeo SoloStar
	Insulin glargine			4.5 mL (3 x 1.5 mL)	Toujeo SoloStar
				3 mL	Toujeo Max SoloStar
		300 unit per mL	Pen	6 mL (2 x 3 mL)	Toujeo Max SoloStar
Mixtures	Insulin aspart protamine & aspart (human) (70- 30)	100 unit per mL	Vial	10 mL	Insulin aspart prot & aspart 70-30, Novolog Mix 70- 30, NovoMix 30

Insulin Type	Active Ingredient	Strength	Dosage Form	Package Size	Product Name(s)
			Pen	15 mL (5 x 3 mL)	Insulin aspart prot & aspart 70-30 FlexPen, Novolog Mix 70-30 FlexPen, NovoMix 30 FlexPen
			Vial	10 mL	Humalog Mix 75- 25
	Insulin lispro protamine & lispro (75-25)	100 unit per mL	Pen	15 mL (5 x 3 mL)	Humalog Mix 75- 25 KwikPen, Insulin Lispro Protamine & Lispro 75-25 Pen
	Insulin lispro protamine & lispro (50-50)	100 unit per mL	Vial	10 mL	Humalog Mix 50- 50
			Pen	15 mL (5 x 3 mL)	Humalog Mix 50- 50 KwikPen
	Insulin NPH & Regular (60- 40)	100 unit per mL	Vial	10 mL	Novolin GE
	Insulin NPH & Regular (70- 30)	100 unit per mL	Vial	10 mL	Humulin 70-30, Novolin 70-30, Novolin ReliOn 70- 30, Mixtard 30
			Pen	15 mL (5 x 3 mL)	Humulin 70-30 KwikPen, Novolin 70-30 FlexPen, Novolin ReliOn 70- 30 FlexPen

Currency Conversion into USD

The study relied upon exchange rate information as of October 1, 2021, to convert local currencies into USD equivalents. The following table identifies our assumptions for currency exchange:

Country	Exchange rate for 1 USD on 10/1/2021 ⁷⁴
Low-income Co	untries
Burkina Faso	566.037 XOF
Gambia	51.3300 GMD
Malawi	803.674 MWK
Sudan	438.000 SDG
Тодо	566.037 XOF
Uganda	3532.13 UGX
Middle-income	Countries
Algeria	137.073 DZD
Benin	566.037 XOF
Kenya	109.604 KES
Morocco	8.9575 MAD
Nigeria	410.711 NGN
Senegal	566.037 XAF
South Africa	14.9705 ZAR
Tanzania	2304.59 TZS
High-income Co	ountries
Australia	1.3802 AUD
Bahamas	1.0000 BSD
Canada	1.2678 CAD
Denmark	0.8629 EUR
New Zealand	1.4454 NZD
United States	1.0000 USD

Table 5: October 1, 2021 Exchange Rate

Aggregating Pricing by Unique Product

A given country may report several prices for a given insulin product. These could vary between regions of the country (e.g., the provinces of Canada), within individual pharmacies surveyed (e.g., retail pharmacies surveyed in Africa), or within the aggregation of products to their active ingredient and dosage form (e.g., Basaglar and Lantus insulin pens). To account for this variability, each price of insulin collected for each product were first assigned a unique product identifier (see Identification of Products by Active Ingredient, Strength, Dosage Form and Package Sizes from prior section). All equivalent packages in a country were first averaged together. Those prices were then converted to unit prices per mL and then averaged across each program that data was collected for in that country by the unique product identifier. Calculated average package size prices were then calculated off of these averages by standardizing each dosage form into fixed mL sizes. Specifically, all vials are presented as a 10 mL size for this study, all pens are standardized 15 mL unless their specific packaging only comes in lower quantities (i.e. 9 mL), and all cartridges are standardized to 15 mL (again,

consistent with the sizes identified previously in **Identification of Products by Active Ingredient, Strength, Dosage Form and Package Sizes**).

Below is an example of how these calculations were performed based upon a surveyed response received. All prices with the same identified base name products within a country were aggregated to form an average experience:

Insulin Brand/ Product name Pro		Product Size	Туре	f	Total cost or Product Size	Patient cost for product size	Witł Co	h Insurance payment	
1 Lantus 10ml vial Long-act		Long-acting		4750 SDG		10 n	0-25% of et value		
_					2			3	
	 Based upon the product name provided, this line was recorded as insulin_glargine_100U_vial (base name), and insulin_glargine (active ingredient) for the purposes of this study. Any products with different names in the pricing source for the country, such as Basaglar, Optisulin, Semglee, etc., were aggregated within the same base name and active ingredient identifier. [See Table 4 in report for complete list of unique insulin types and recorded sizes] 				Based u reported the per f was first (e.g., 47 divided This per recorde and was ensure t sizes col standard vials wo presente	pon the d cost and size, mL unit price calculated 50 SDG 10 = 475 SDG) mL price was d in our raw file done to hat all product uld be dized (i.e., all uld be ed as10 mL)). 2	A similar to the tot the prod was take calculate copayme amounts In instand the abov range of were pro higher va taken (e.s 4750 SD 1187.5 S	approach al cost for uct size n to ent ces like e where a options vided the alue was g., 25% of G = DG)
					[See fat for com unique i and reco	plete list of plete list of nsulin types orded sizes]			

Figure 36: Example Insulin Price Calculation - Sudan

The above calculation was an actual response we received from Sudan and you can see that information reflected in the raw file available online.

2021	Year
SD	Country
SUDAN	COUNTRY_NAME
Low-income	COUNTRY_INCOME_STA TUS
1277	medianIncome
1592	meanIncome
4122	gdpPerCapitaPPP
44909.35	pop2021
438	20211001_1USD_EQUIV ALENT
Retail	Program
INSULIN_GL ARGINE_10 0U_VIAL	BASE_PRODUCT_NAME
INSULIN_GL ARGINE	ACTIVE_INGREDIENT
Long-Acting Insulins	INSULIN TYPE
10	PACKAGE_SIZE_TOTAL
475	Avg Unit Price Paid
1187.50	Avg Patient Copayment per Rx

The following represents a country where multiple package prices were received and represents how aggregation was handled across multiple products.

Figure 37: Example of Insulin Price Calculation, Multiple Prices, Burkina Faso^{iv} RETAIL PHARMACIES

Retail Pharmacy 1					
Insulin Brand/ Product name	Product Size	Туре	Total cost for	Patient cost for product	
Lantus Solostar pen 100UI/ml	1 pen/3ml	long acting analog	12000FCFA	12000FCFA	
Retail Pharmacy 2					
Insulin Brand/ Product name	Product Size	Туре	Total cost for	Patient cost for product	
Lantus Solostar pen 100UI/ml	I/ml 5 x 3 ml long acting analog 50425 FC		50425 FCFA	50425 FCFA	
Lantus Solostar pen 100UI/ml	1 x 3 ml	long acting analog	13825 FCFA	13825 FCFA	
0			2		
Based upon the product name provided, this line was recorded as insulin_glargine_100U_pen (base name), and insulin_glargine (active ingredient) for the purposes of this study. [See Table 4 in report for complete list of unique insulin tupos and recorded sizes]	Based upon the reported cost and size, a per mL unit price was calculated based upon the average of the package sizes gathered. This means that the 3 mL pen size were averaged together (12,000 FCFA + 13825 FCFA = 25,825 FCFA; 25,825 divided by 2 = 12,912.5 FCFA). The 15 mL package (5 x 3 mL) was calculated to 3 mL pen size (50,425 FCFA divided by 5 = 10,085 FCFA). The results of the two package sizes were then averaged (12,912.5 FCFA + 10,085 FCFA = 22,997.5 FCFA; 22,997.5 divided by 2 = 11,498.75 FCFA). The resulting amount was divided by 3 a 3832.92				
	J FCFA). This per mL price was recorded in our raw file and was done to ensure that all product sizes could be standardized (i.e., all pens would be presented as 15 mL)				
	[See Table 4 in report for complete list of unique insulin types and recorded sizes]				

Because of the focus on package prices, it was felt appropriate to first aggregate prices by package size in each country and then convert into a per mL unit price which was then standardized across packages. While the figure above does not present the patient cost share calculation, it was performed to the same degree as the total cost for the product. This can be easily confirmed given the total cost and patient cost were the same for all packages.

^{iv} Retail pharmacy names were provided but are kept anonymous at the request of reporting pharmacies.

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