Why is insulin and epinephrine more expensive in the United States than in Canada and the U.K?

by

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Submitted to the Department of Economics
School of Natural and Social Sciences
In partial fulfillment of the requirements
For the degree of Bachelor of Arts

Purchase College
State University of New York

December 15, 2022

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Abstract

In the United States insulin and epinephrine injections are known for being more expensive compared to the United Kingdom and Canada. This paper aims to identify the main causes for the price discrepancy. They include higher rate of demand, the differences between healthcare systems, and the differences in pharmaceutical market structure in the U.S. compared to Canada and the U.K. In the U.S. there is a higher rate of individuals who have diabetes and allergies which is likely to increase the demand for insulin and epinephrine. Another factor that leads to the price discrepancy is the difference in healthcare systems in Canada and the U.K. compared to the U.S. Canada and the U.K. markets have institutions that regulate the prices of drugs for pharmaceutical companies unlike in the U.S.

Introduction

In the United States, pharmaceuticals are known for being more expensive compared to other countries around the world such as the United Kingdom and Canada. Insulin and epinephrine are two vital, lifesaving drugs for many individuals with diabetes or allergies. With the rates of these medical conditions rising in the United States, the cost of these pharmaceuticals is increasing at alarming rates when compared to Canada and the United Kingdom. To analyze the price discrepancy between the countries, an evaluation of the rate of demand, the drug market structure as well as the healthcare system in each country was done.

To analyze the price discrepancy between these two drugs in these countries, I reviewed an array of peer revied papers, articles and information provided by government agencies. The first section of my paper will cover the background information and the descriptive statistics of insulin and epinephrine. The second section of my paper will analyze the potential causes of the price difference between insulin and epinephrine in the United States, Canada, and the United Kingdom.

The information collected, allowed me to identify the potential causes of the price difference, one potential cause is the United States has a higher rate of demand for these drugs than in Canada and in the U.K. The second potential cause is how the healthcare system is structured in the U.S. compared to Canada and the U.K. The last potential cause I analyzed is how government policies are implemented towards the market structure of pharmaceuticals.

Insulin and epinephrine are two vital drugs for individuals who are diagnosed with either allergies or diabetes. The cost of these two pharmaceuticals in the U.S. are continuously increasing at prices consumers may not be able to afford. As many individuals today may know of someone who uses either of these two pharmaceuticals, it is important to know why these drugs are potentially offered at a lower cost in another countries.

Background Information

Insulin

Insulin is a life-saving medication for diabetes that has a wide variety and price range depending on the brand and health insurance patient has. Diabetes occurs either when the pancreas does not generate enough insulin (Type 1) or when the body is incapable to process the insulin it does produce (Type 2). According to a study conducted by the Center for Disease and Control and Prevention (CDC), about 34 million Americans have been diagnosed with diabetes and 88 million American adults have been diagnosed with prediabetes which if left untreated will eventually lead to diabetes (CDC, 2022). One vial of insulin contains one shot, depending on the patients' level of severity to control their blood sugar, the number of vials they use varies every day. Insulin has two aspects; the first component is the ingredients whether it is human or analog insulin. Human insulin is derived naturally whereas analog insulin is genetically modified to lower blood sugar levels more rapidly than human insulin. The second aspect is the duration of insulin, there are 5 different

types of insulin: rapid-acting, short-acting, intermediate-acting, long -acting, ultra-long- acting, and sometimes depending on the patients' needs may be mixed together (DCCPGE, 2018). According to the current CDC guidelines, rapid-acting insulin must be injected 15 minutes before eating and short-acting insulin must be injected 30 minutes before eating. Rapid-acting, short-acting, and mixed[1] insulins are injected before meals because it reduces the risk of spikes in blood sugar levels that can be caused during eating or drinking. Intermediate-acting insulin is taken to control blood sugar levels for a half of a day or overnight; long-acting insulin is injected to control blood sugar levels for a full day. Intermediate and long-acting insulin are often used with rapid acting or short acting insulin. Ultra-long-acting insulin doses are injected once every four days (CDC, Types of Insulin, 2021). Depending on the severity of diabetes an individual has they may have to use one vial a day or more.

Table 1 below analyzes the different types of insulin and their prices differentiating on the country as of 2018. The table uses the prices of insulin from 2020 study, the study converted the cost of insulin in these countries to U.S. dollars. In the U.S. all types of insulin are priced at a higher price than the U.K. and Canada.

[1] Premixed insulin or mixed insulin usually combines intermediate and short-acting insulins. Mixed insulins are injected 15 before breakfast and dinner.

TABLE 1: PRICE OF INSULIN IN THE U.S., CANADA, & THE U.K.

	United States	Canada	United Kingdom
STANDARD UNIT[2] (HUMAN INSULIN)	$85.21	$7.11	$5.13
ANALOG	$99.94	$12.99	$8.09
RAPID-ACTING	$119.36	$9.88	$7.22
SHORT-ACTING	$87.20	$7.10	$6.24
INTERMEDIATE-ACTING	$73.56	$7.02	$5.14
LONG-ACTING	$88.10	$15.77	$9.79

(ASPE, 2020)

Epinephrine

Similar price discrepancy can be observed on the epinephrine market. Epinephrine injectors, also well-known as EpiPen, is a medication and hormone that is used to treat severe allergic reactions. Some allergic reactions can be ranging from itching, swelling, and hives of certain body parts. These allergic reactions can occur from food, weather, insects, medications, and other factors. Epinephrine also known as adrenaline, is a hormone that is produced by the adrenal glands. It is estimated that 10.8% of Americans could have life-threatening allergic

[2] A standard unit of insulin is U-100 which means there are a 100 units of insulin per milliliter. There are higher doses such as U-500. Most insulin vials come in 10mL (1000 units).

reactions (Ruchi, 2019). Patients with severe allergies are advised to always have at least one epinephrine injection with them. According to the Food and Drug Administration (FDA), epinephrine injectors can have two dosages, the recommended dose for patients weighing under 66lbs is .15 milliliters and for patients weighing over 66lbs is .30 milliliters (FDA, 2011). Epinephrine autoinjector manufacturing companies produce prefilled autoinjectors that have the recommended dose depending on the patient's weight. The autoinjector dispenses the hormone at the recommended speed, one well-known brand name autoinjector is EpiPen and EpiPen Jr.

In the U.S., the FDA approved that epinephrine injectors are to be supplied in a 2-packs, manufactures have stated that they only sell 2-packs because the first syringe may not properly work, requiring a second dose (CBS, 2018). In the U.K and Canada it is easily accessible to find epinephrine injectors being sold in a 1-pack, many pharmacies carry and distribute 1 and 2-packs which gives a cheaper option to patients.

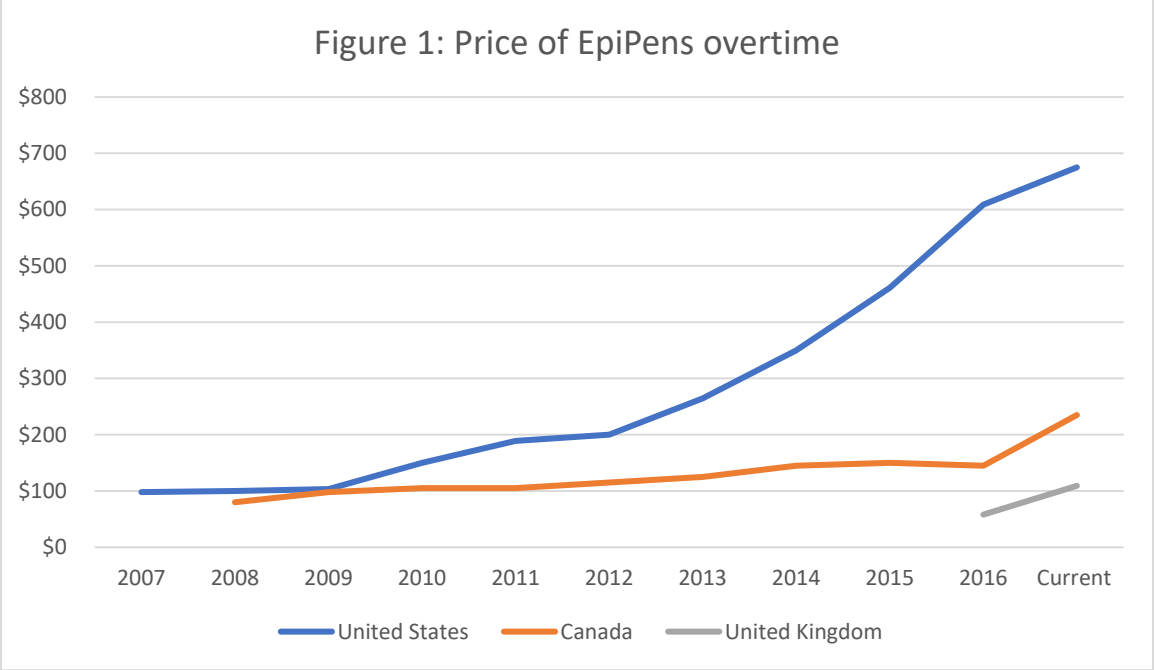


Figure 1 above shows the cost of the brand name autoinjector EpiPen 2 pack from 2007 to 2022 in the U.S., Canada, and the U.K. In 2007, Mylan received the rights to distribute and market

EpiPens, an EpiPen 2-pack had cost less than $100 in the U.S. when they acquired the drug. The cost of epinephrine injectors has not fluctuated greatly over time in Canada but in the U.S. the price has fluctuated substantially. There is data lacking prices of EpiPen cost in the U.K. overtime. Two reliable years regarding this data for the U.K. is 2016 and 2022 (currently).

In 2016, the average wholesale price of 2 EpiPen's in the United States exceeded $700, an increase of 545% from 2007 (Prince, 2018). In Canada, the average wholesale price of EpiPens in 2016 was $350. While the wholesale cost in Canada increased the consumer priced remained below $200 (Canada, Where to Buy EpiPen in the US- Get EpiPen at Canada Prices, 2017). Currently, the price of a 2-pack of EpiPens is $234.99 (Direct, 2022). Currently, a 2 pack of epinephrine injections can cost between $95 to $700 retail for consumers in the U.S. (GoodRx, 2022). This large price range is because consumers can use prescription drug coupons from companies such as GoodRx to decrease the price. In 2016, The National Health Service (NHS), the public healthcare provider in the UK, paid £53 per two pack for EpiPen, then distributed them to consumers who paid only £8.40 (2016) (Miyashiro, 2017).

Potential Causes of the Price Discrepancy

Demand for Insulin

One factor that can possibly cause price imbalance of insulin in the U.S. compared to other countries is higher demand. A main cause that may lead to Type 2 diabetes, which the body cannot process the insulin it produces, is obesity. Someone who is diagnosed with obesity is six times more likely to develop Type 2 diabetes than those who are not obese. Having obesity and Type 2 diabetes increases patients' probability of heart disease. Normally, insulin carries glucose to the muscles to use right away for energy or to the liver, where it is stowed away for later. When someone has obesity, your cells do not allow the insulin to move glucose to either your muscles

or your liver. Where the excess glucose is usually stowed is filled with fat. While the glucose is remains in the bloodstream, the pancreas creates more insulin trying to move the glucose out of your bloodstream (Health, 2022).

In 2018, 26.8% of Canadians were classified as obese and 36.3% of the population was classified as overweight (McDiarmid, 2019). In 2019, the health survey for England classified 28.0% of individuals who lived in the U.K as obese and 36.2% of the population overweight (Baker, 2022). According to the CDC about 42.4% of Americans were classified as obese and 32.5% of the population were classified as overweight (CDC, Adult Obesity Facts, 2021). Figure 2 below analyzes the obesity rate over time in the U.S., Canada, and the U.K. For decades, the obesity rate of the U.S. is substantially higher than the U.K. and Canada. This data was collected from the countries government agencies throughout the years. The most recent reliable data of the obesity rate in the U.S. was recorded in 2018 from the CDC. Over the recent years the CDC did not update their data, making the data from 2018 the most reliable.

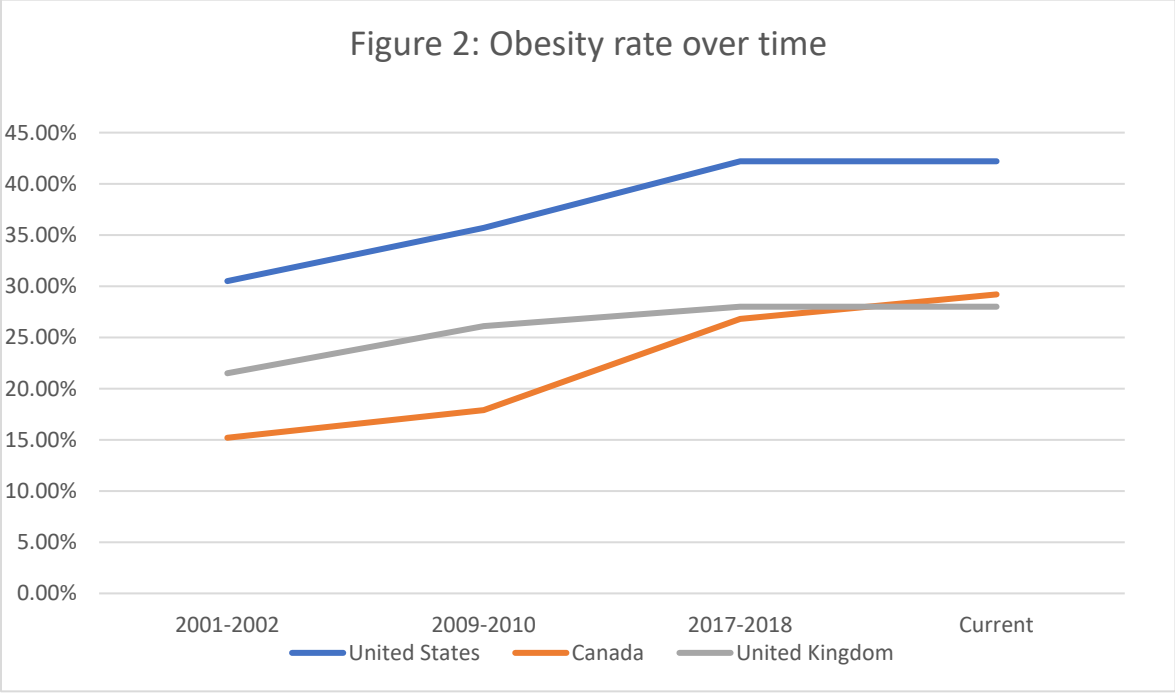
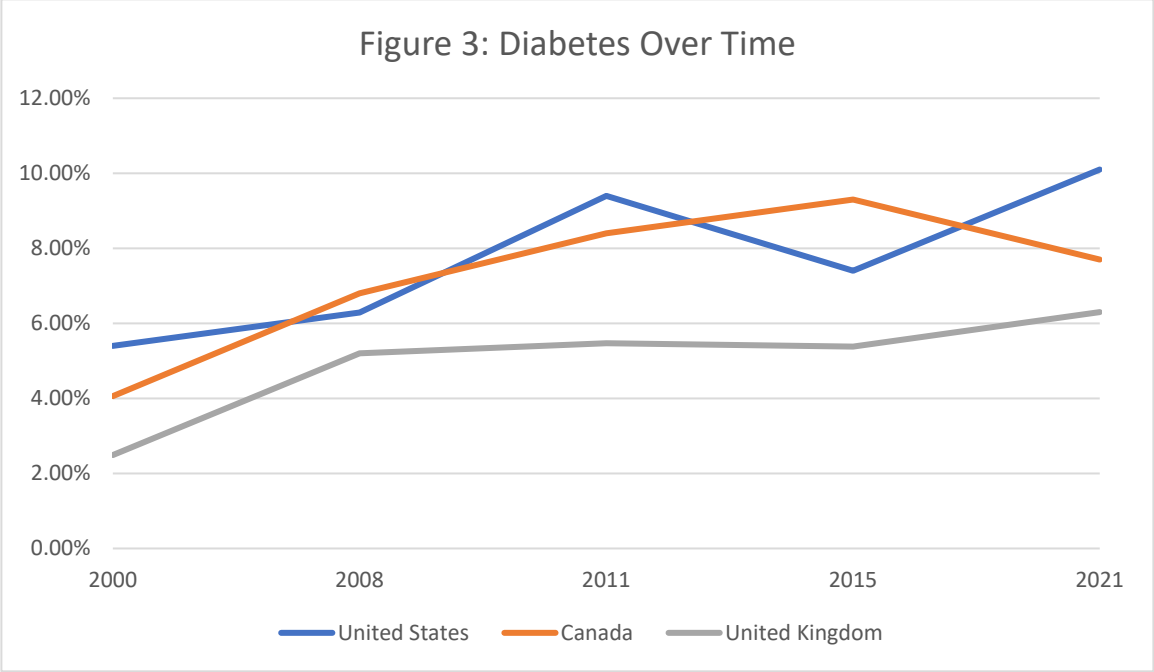


Figure 3 below shows the rate of diabetes over time in the U.S., Canada, and the U.K. I used a government agencies from the U.S. and Canada and reliable article from the U.K. to analyze the diabetes rate over time. In 2015, the rate of diabetes decreased 2 percentage points from 2011. From 2011 to 2021, the rate increased 2.7 percentage points. In the United States approximately 10.1% Americans have been diagnosed with diabetes and 26.2% Americans have prediabetes (CDC, 2022). According to the Diabetes of Canada, in 2020, approximately 28.9% Canadians were either diagnosed with diabetes or have prediabetes (Ottawa, 2020). In 2019, approximately 6.1% of the population in the U.K. were either diagnosed with diabetes (Perraudin, 2019). Other factors that can likely lead to Type 2 diabetes as well family history, stress, and exercise.



Demand for Epinephrine

Anaphylaxis is the result of the body's immune system overreacting to a harmless substance, such as food, insects, and weather conditions. Substances that cause allergic reactions are known as allergens. Individuals who are diagnosed with asthma or eczema have a greater risk of developing anaphylaxis than others (NHS, 2021). Currently, it is estimated that 10.8% of

Americans could have life-threatening allergic reactions (Ruchi, 2019). According to the Food Allergy Canada organization, in 2022 more than 7.9% of Canadians have reported at least having an allergic reaction to one or more food (FCA, 2022). In 2021, 3.3% of the population of the U.K. reported that they live with a food allergy (Wighton, 2021).

The United States has a higher percentage of individuals who have life-threatening allergic reactions than Canada and the U.K. A factor that can possibly cause the United States to have a higher percentage rate of anaphylaxis is lax regulations on the food and drug market. Many countries have banned certain chemicals and additives in their food, drugs, and other products consumers use every day that the U.S. has not. Some chemicals that have been banned or highly regulated in the U.K and Canada are Potassium Bromate, Butylated Hydroxyanisole (BHA), Butylated Hydroxytoluene (BHT), Olestra, Bis(2-ethylhexyl) phthalate (DEHP), Perfluorooctanoic acid and Bisphenol A (BPA). Unlike the U.S. these chemicals, and additives and many more have been banned in many countries due to the risk of leading to life-threatening diseases (Achmadsyahputra, 2017). Several studies have shown, that increased exposure to BPA and DEHP have led individuals to develop asthma and anaphylaxis (Robinson, 2015). The U.S. is constantly behind on regulating toxic substances that may lead to many health risks. In 2008, the U.K. banned the use of manufacturing and marketing goods with the compound, Perfluorooctanoic acid (PFAS also known as forever chemicals) (Industry, 2022). Several studies have concluded, exposure of perfluorooctanoic acid may potentially lead to obesity, asthma, type 2 diabetes, and other life-threatening diseases (Kounang, 2019). In 2016, Canada prohibited the manufacturing, use, marketing, and importation of any goods that were containing PFAS (Gordner, 2022). While, the U.S. has signed a law that will “phase out” PFAS by 2024 products. Many states in the U.S.

have already started prohibiting the use, marketing and manufacturing of goods containing PFAS (Lovells, 2022).

One the main factor that leads to diabetes is obesity. In the United States as there is a higher rate of obesity than in Canada and the United Kingdom. The U.S. also has a higher rate of diabetes than Canada and the U.K. The United States has lax regulations compared to Canada and the United Kingdom on chemicals and additives in products they market. These lax regulations can potentially explain a higher rate of allergies and a higher demand for epinephrine injections in the United States. With everything being equal, higher demand implies higher market price.

Healthcare Systems in the U.S., Canada, and the U.K.

Insurance Systems in the U.S.

Another factor that may contribute to the price discrepancy of insulin and epinephrine is the health insurance systems. In Canada and the U.K. health care is publicly funded unlike the U.S. The U.S. health insurance system is a complicated and intricate system which can be divided into two sections, public and private insurance. Public health insurance is funded by the government, depending on an individual's income, occupation, education, and age they can be covered by public health insurance. Private health insurance is privately funded and is typically accessed through employers or bought by individuals. In all countries, individuals receive access to pharmaceuticals through their health care systems.

Public

Public health care insurance in the United States is divided into three major sectors, Medicare, Medicaid, and CHAMPVA. Medicare is provided to individuals over the age of 65 and in some scenarios to adolescents with disabilities. Medicare is funded by the Social Security

Administration and federal tax revenues (Cubanski, 2019). According to the IRS, individuals who earn a legal salary pay 1.45% of their paycheck to Federal Insurance Contributions Act (FICA) which funds Medicare (IRS, 2021). Medicare can be divided into four parts; the first sector, Medicare Part A is hospital insurance. Most individuals who have Medicare Part A do not have to pay a premium unless they have less than 40 calendar quarters of Medicare-covered employment. In 2022, if an individual has less than 30 calendar quarters of Medicare-covered employment their premium would be $499 per month, if an individual has 30-39 calendar quarters of Medicare-covered employment their premium would be $274 per month (DOI, 2021). Individuals covered by Medicare must pay a deductible. Each sector of Medicare has a separate deductible for the patient to pay. The second portion, Medicare Part B which provides outpatient and medical coverage. In 2022, the premium for Medicare Part B is $170.10 per month, Medicare Part B premiums differentiate depending on their annual income month (DOI, 2021). Another form of receiving insurance is through a Medicare Advantage plan known as Medicare Part C, which allows individuals to access the same plans as Medicare Part A and Part B but with different costs month (DOI, 2021). Medicare's fourth sector specializes in outpatient drug coverage also known as Medicare Part D. Unlike original Medicare, Part D is not directly provided by the government. Part D can only be accessed through private insurance companies which have contracts with the federal government month (DOI, 2021). Many individuals over the age of 65 are dependent on Medicare when they retire.

Medicaid is provided to millions of individuals who have limited resources and income such as low-income adults, children, pregnant women, elderly adults, and people with disabilities. Depending on the individuals' financial situations Medicaid has different coverage options.

Although Medicaid is funded partially by states and the government, it is distributed by states. Each individual state determines what medications can be listed on the formulary.

ACA (Obamacare)

On March 23, 2010, the Affordable Care Act and the Patient Protection Act also known as Obamacare was implemented. These two acts were implemented to expand Medicaid to all individuals earning below 138% of the federal poverty level, expand affordable health insurance to individuals that were not covered, and to reduce the growth rate of health care expenses in the U.S. (Silvers, 2013). Prior to the ACA, dependents were considered individuals that were either 18 years or younger or were in progress of completing their college education were allowed to remain of their parents' insurance policies. After the ACA was implicated dependents were allowed to remain on their parents' policies until the age of 26 (Silvers, 2013). Although the ACA allowed many to receive health insurance, many were required to have health insurance. Individuals who did not have health insurance must claim an exemption or pay a tax penalty on their federal income taxes; these tax penalties are based by the individual's yearly income (HealthCare, 2021). The ACA was successful decreasing the rate of uninsured individuals. According to the U.S. Census Bureau, in 2009 a year prior to the ACA, 16.7% of the U.S. population was uninsured. Throughout time the rate of uninsured individuals decreased. In 2019, 8% of the United States population was not covered by health insurance. In 2020, the number of uninsured individuals increased .6%. Due to the Covid-19 pandemic employment-based insurance decreased 2% from the prior year, this resulted into the .6% decrease (Census, 2010). According to the 2021 Medicaid Enrollment Report 76.7 million people were covered (Medicaid, 2021). Unlike Medicare states have the option to charge premiums and to establish out-of-pocket

spending such as copayments and deductibles (Medicaid, 2021). Certain individuals with certain circumstances can be excused from out-of-pocket costs (Medicaid, 2021).

Civilian Health and Medical Program of the Department of Veteran Affairs (CHAMPVA) is a public health care program provided to veterans or their family members who served in active duty during war, are at least 65 years old or have a disability related to being in the service and have little to no income (VA, 2021).

Private

The majority of the United States population is covered by private health insurance. Private health insurance can be divided into three sectors, Employment-based, Direct- purchase, and TRICARE. Employment- based health insurance is insurance that is purchased by the employers to provide for their employees and their dependents. Employers are typically responsible for choosing which insurance plans and what services they cover for their employees. The cost of the insurance premiums is divided between the employer and the employees. According to the Bureau of Labor Statistics in 2021, employers paid 78% of medical care premiums for single coverage plans and 66% for family coverage plans (BLS, 2021). Employer based health insurance is predominantly the main contributor to private health insurance. Direct-purchase insurance is when individuals pay for their life insurance directly from an insurance company. TRICARE is a regionally managed health care program provided to active and former servicemembers and their families of the U.S. armed forces (MBA, 2021).

In the U.S the healthcare system how pharmaceuticals are distributed is a complicated process. Many shareholders are involved with the pharmaceuticals supply chain such as, manufactures, wholesalers, pharmacy benefit managers (PBMs), pharmacies, insurers, and

employers. The supply chain of pharmaceuticals is heavily affected by government policies implemented.

First, pharmaceutical companies will develop a drug and set a list price then they distribute the pharmaceuticals to wholesalers. Generic drug manufactures will compete with each other for contracts with the three big wholesalers, AmerisourceBergen, Cardinal Health, and McKesson. These three wholesalers dominate the distribution of generic pharmaceuticals, which allows them to set the initial price for the drug. If manufactures do not secure a contract with wholesalers, they can be excluded from the market (Seeley, 2022). Wholesalers will then distribute the product to pharmacies which can have a higher list price (CMS, 2021). Pharmacies may choose to work directly with pharmaceutical manufactures. Pharmacies will then distribute the product to patients and patients will typically have to pay out of pocket costs known as a copayment. After the medication is provided to the patient the pharmacy will bill the patient's insurance company to be reimbursed for the medication (CMS, 2021). If individuals are not covered by insurance or the medication is not covered by the insurance company the individual will tend to pay the full price for the medication (CMS, 2021).

How Governments Negotiate Pharmaceutical Prices in the U.S.

During this process the pharmaceutical companies will pay pharmacy benefit managers. Pharmacy benefit managers also known as PBMs, play a crucial role in the way pharmaceuticals are dispensed. PBMs are known as "middlemen", their main priority is to decrease the price of pharmaceuticals for insurance companies, big employers, and government agencies by negotiating with pharmaceutical manufactures for rebates. Rebates are paid by pharmaceutical manufacturing companies to PBMs in exchange to be placed higher on the insurance formulary sheet (WSJ, 2019). Health Insurance companies use PBMs to manage their pharmacy benefits such as developing the

formulary. A formulary is a list of generic and brand name pharmaceuticals that insurance companies cover. Insurance companies also negotiate prices with drug companies for the pharmaceuticals covered on the formulary. Formularies are divided into tiers, each tier includes either generic, brand-name, preferred generic and brand-name, specialty and/or non-preferred generic and brand-name drugs (Ivey, 2020) . Tier 1 typically lists generic drugs and have the lowest out of pocket cost for patients, insurance companies typically pay the highest portion of the list price. Tier 2 includes non-preferred generic and brand-name pharmaceuticals which have a higher out-of-pocket cost for patients. Tier 3 includes preferred and non-preferred drugs, the out-of-pocket costs for the patients are higher than the first two tiers. Tier 4 includes all types of pharmaceuticals which have the highest out-of-pocket costs for the patient and lowest for the insurance company (Ivey, 2020) . The placement of pharmaceuticals on the formulary sheet is crucial for drug manufactures because more patients will tend to purchase the cheapest drug if possible, generating more profits for the manufactures.

As well as being known for high medication prices, the United States also is known for spending an immense amount of money on their health care. In 2012, the spending of prescription drugs in the U.S. was less than 1%, in 2013 the rate increased to 2% and in 2014 it peaked at 13.5% (AMA, 2021). In 2019, the U.S. healthcare spending reached $3.8 trillion (Martin, 2021). In 2020, the U.S. healthcare spending increased to $4.1 trillion ($12,530 per person). In 2019, prescription drugs accounted for 9.7% of the U.S. healthcare spending (CMS, 2021).

Insurance Systems in the U.K.

The citizens of the United Kingdom have “free”, also known as universal, public health care through the National Health Service. Universal health care is publicly funded by taxes. In 2019, around 79% of the health expenditure was paid mainly through taxation and a small

percentage was funded through other public revenues month (DOI, 2021) (Cooper, 2019). England, Northern Ireland, Scotland, and Whales have their own healthcare systems funded by their own government and parliaments. Universal free health care provides all citizens with health coverage without the cost burden of the expenses. According to the Minister of Health, Anuerin Bevan, free health care allows individuals to experience "freedom from fear" (Cooper, 2019). According to the Minister of Health, many Americans tend to fear and are anxious on whether they have enough money and/or if their insurance will cover their medical needs. The National Health Service stated that the health care system will provide the U.K population with free health care because of the individuals need for help and not on whether or not they can afford it (Light, 2003).

Although the majority of the U. K's population has public health care, a small percentage of individuals pay or receive private health insurance, funded by their employers or themselves. In 2017, a study found that 20.6% of the U. K's population was insured by private care sector (Cooper, 2019). There are different classes of national income rates, depending on the individuals' annual earnings, employment status, and self-earned profits. There are four main classes of national insurance in the U.K. Class 1 is paid by employees and employers, class 2 is paid if an individual is self-employed, class 3 is a voluntary contribution, and class 4 is if an individual is self-employed and have profits over a certain amount.

How Governments Negotiate Pharmaceutical Prices in the U.K.

Compared to the U.S., the U.K. has a less complex understanding of the pharmaceutical supply chain. In the United Kingdom, for a drug to be marketed and retailed the first step after the development is clinical trials (MST, 2021). After a drug manufacture has completed their clinical trials, regulatory authorities will review the clinical trials and analyze whether the drug is safe and effective. If the drug passed the review process, they will be issued a license that will allow them

to be sold and marketed in certain regions on the U.K. After the drug is licensed, the National Institute for Health & Care Excellence (NICE) evaluates the drugs clinical trials and whether it is cost effective to be provided by the NHS. Prices of prescription drugs that are supplied by the NHS are controlled by the Pharmaceutical Price Regulation Scheme (PPRS). PPRS is an agreement between the Department of Health (DoH) and drug manufactures that determine the prices drugs can be marketed for by the NHS, this agreement is renegotiated every 5 years (HOP, 2010). In 2019, the scheme was revised and renamed Voluntary Scheme for Branded Medicinesm (VSBM). This agreement ensures the NHS spending each year on brand name drugs. The scheme works by capping the rate at which the NHS spends on pharmaceuticals (2%). If the NHS spends more than the 2% growth rate that was agreed upon, until the scheme is revised, then companies will automatically pay back the NHS (Sanofi, 2021).

Generic pharmaceutical drugs that are not patent protected are not included in these agreements. The U.K. government relies on market competition to control the prices of pharmaceuticals.

In the U.K. a patent has a lifetime of 20 years similar to the U.S. but the U.K. government set up agreements with pharmaceutical companies to limit the amount of spending on the necessary pharmaceutical drugs. The U.K. government also created new agencies to limit and regulate the cost pharmaceuticals that can be marketed by the public healthcare system. The majority of the U.K. population is covered by universal insurance plans unlike the U.S. as the majority of the population is covered by employer-based insurance plans.

From 2021 to 2022, class 1 individuals earning between the primary threshold and the upper earning limit were deducted 12% of their paycheck from their employers for insurance. Individuals who earned above the limit were deducted 2% of their income from 2021 to 2022.

Recently the government has stated that they will be increasing the rate for 2022 to 2023 by 1.25% (gov.uk, 2022). The increase in national insurance was approved as it allows the government to increase spending on health care. In 2019, the U.K. government spent £225.2 billion on healthcare (£3,371 per person) (Prendergast, 2021). In 2020, government spending increased to £257.6 billion (£3,840 per person) (Prendergast, Healthcare Expenditure, UK Health Accounts 2020, 2022). In 2019/20 the overall drugs cost at list price in the NHS was £20.9 billion (NHS, Prescribing Costs in Hospitals and the Community, 2020).

Insurance Systems in Canada

Similar to the United Kingdom, Canada offers universal health care to their citizens as well as government agencies that help regulate the prices of pharmaceuticals. Each of the 13 provinces in Canada which are publicly funded and administered independently to citizens and is known as Canadian Medicare. Provinces have their own insurance plans which receives financial support from the federal government on a per-capita basis. Depending on an individual's income, a portion of their paycheck will be taxed to fund public health care.

Each province of Canada must comply with the five pillars of the Canada Health Act, which include being publicly administered, comprehensive in coverage conditions, universal, portable across provinces, and accessible. Canadian providence governments are responsible for financing, organizing, and delivering health services to the citizens of the country. Each providence health insurance cover all necessary medical hospital and physician services. Medical services that are not covered under Canadian Medicare, patients must pay out of pocket payments or can be covered by employer based or private insurance. Like most health insurance plans in the United States, some health insurance plans do not cover special health services such as dental,

chiropractic care and physical therapy. Although, Canada offers universal health care, in 2017, 67% of Canadians were also covered by private insurance companies (HealthCanada, 2022) .

How Governments Negotiate Pharmaceutical Prices in Canada

In Canada before a new pharmaceutical drug can be sold, it must be processed and reviewed by scientists in the Health Products and Food Branch (HPFB) which is associated with Health Canada. The HPFB is the national authority that regulates and evaluates drugs that are available to Canadians. When a drug is developed, the manufactures have to administer a variety of preclinical tests to see if the drug is safe on animals. If the drug passes the preclinical test, the manufacturers will apply for the HPFB to conduct a clinical trial in Canada. The clinical trial is to research a recommended drug dose and test if the pharmaceutical drug is safe and effective for humans. If the drug passes the clinical trial, the sponsor of the drug may choose to submit a New Drug Submission with the HPFB. The NDS application states that the benefits of the pharmaceutical drug outweigh the risks and that preclinical and clinical trials were conducted, whether they were conducted in Canada or in other countries. The NDS application must be submitted to Health Canada, the application is analyzed and processed by the HPFB. The HPFB reviews the safety, quality, packaging, and manufacturing. All drugs that are reviewed and allowed to be retailed in Canada are reviewed to ensure that it meets the requirements of the *Food and Drugs Act and its Regulations.* The average time of the drug development to the drug approval in Canada is between 8 and 15 years. If a drug is approved to be sold and marketed by Health Canada, it is the drug manufactures responsibility to seek public funding through the national CDR process (HealthCanada, 2022).

Patented Medicine Prices Review Board (PMPRB) are liable for pricing patented drugs in Canada. The board was launched in 1987 to avoid pharmaceutical companies from price gouging

on drugs. The PMPRB analyzes and compare the prices of similar drugs that are set in seven other countries (France, Germany, Italy, Sweden, the United Kingdom, Japan, Australia, Norway, Spain, Belgium, and the Netherlands). The PMPRB regulate the prices of pharmaceutical drugs, that can be no higher than the median list price in the eleven countries. If there are no reference prices available, the price will be based on the domestic prices of similar drugs. If a drug is believed to be priced too high, they will not allow it on the drug formulary. Since the majority of individuals in Canada are covered by public health insurance, pharmaceutical companies are willing to compromise with the government to gain the most profit (HealthCanada, 2022).

Similar to the United Kingdom, Canada offers universal health insurance to their citizens which heavily impacts the price of pharmaceuticals marketed to consumers. Canada's and the U.K.'s government also implemented agencies to regulate and determine the prices of pharmaceuticals marketed. Unlike Canada and the U.K., big manufacturing companies do not have to rely on the public health care system to maximize their profits in the U.S. Pharmaceutical companies do not feel incentivized to bargain with the U.S. health insurance companies because the majority of the U.S. population, is covered by private health insurers in comparison to other countries. The complicated U.S. healthcare system leads to higher prices of drugs, especially the bargaining power a government has on drug manufacturers.

In Canada, residents pay a health premium if their income is $20,000 or more a year. Usually, the premium is deducted from residents' income or pension. If residents do not have taxes automatically deducted out of their pay, the premium is paid when filing your annual income taxes. If individuals earn $20,000 or less a year, they do not have to pay the health premium. The cost of premiums range depending on income, marital status, and family type. In 2020, an unattached individual earning an average annual income of $44,153, their premium was $4,894 (11.08%) per

year. In 2020, a family of 2 parents and 2 children earning an average of $142,449, their premium cost was $14,474 (10.2%) (Palacios, 2020). In 2021, an unattached individual earning an average income of $49,215, their premium cost was $4,296 (8.7%) per year. In 2021, a family of 2 parents and 2 children earning an average income of $150,177, their premium cost was $15,039 (10%) per year (Li, 2021) (OntarioCa, 2021).

According to the Commonwealth fund in 2016, out-of-pocket payments represented about 15% of the country's health spending, the other 85% was accounted for by long-term care facilities, prescription drugs, and services not covered by public health insurance. Most provinces and territories offer public prescription drug prices for individuals who need social assistance, are over the age of 65, and children (Goldstein, 2021). In 2019, the most recent accurate data available, the national health spending for Canada was $174 billion on healthcare ($4,634 per person) (Li, 2021). In 2020, Canada spent $32.7 billion on total pharmaceutical drugs, which is a 4.3% increase from the prior year (CADTH, 2021).

Market Structure

Research and Development of Insulin and Epinephrine

The process of researching and developing a pharmaceutical drug in the United States takes years before a consumer will see it as a product. It takes about an average of ten to fifteen years in total to process a prescription drug including their clinical trials which can cost up to billions of dollars. Approximately 88% of new pharmaceuticals that enter their clinical trials are not approved by the FDA (CBO, 2021). The market price of pharmaceuticals coincides with the cost of research and development.

In 1922, scientists developed an improved and safer insulin for human use. The developers of insulin sold the patents to the University of Toronto, wanting insulin to be accessible to

individuals who need it. In 1923, Eli Lilly became the first company to acquire an exclusive license to manufacture and produce insulin on a large scale. In 1950, Novo Nordisk began to market and manufacture intermediate acting insulin. In 1953, Sanofi started to produce and market long-acting insulin. Throughout the early 1950s to the early 1980s, chemists were trying to develop and improve insulin to be derived and produced from humans rather than animals. For over a century insulin manufactures have been trying to develop new insulins and new ways insulin can be consumed by patients (Riley, 2022). A study conducted in 2018 estimated that one vial of human insulin costs between $2.28 - $3.42 to produce, and one vial of analog insulin costs between $3.60 - $6.16 to produce (Torres, 2022).

In 1987, the FDA approved the EpiPen, a spring-loaded syringe pre-filled with a dose of adrenaline. For many years EpiPen was consistently changing companies of production, until 2007 when Mylan acquired the patent. Currently, EpiPen is owned and marketed by Mylan but manufactured by Pfizer. For many years EpiPen dominated the market, today there are two brand name epinephrine auto-injectors that dominate the market, EpiPen and Adrenaclick. Each manufacture supplies auto-injectors in two packs, in compliance with FDA recommendations, and have a shelf life between 6-12 months. These auto-injectors must have different components to them as all are under patents (Gordon, 2022). While there are other companies that manufacture auto-injectors, most companies have patents on their products causing a lack of innovation to produce new ways to dispense adrenaline to the body.

Monopolies and Oligopolies

Unregulated monopolies impose a major threat towards government health care costs to many countries in the world. A monopoly is when company has exclusive control over goods and trading to eliminate any other competitors. There are many markets today that are dominated

by a small number of large companies which is known as an oligopoly. Generally, monopolies and oligopolies are supposed to be temporary because "eventually generic competition should emerge as patents expire" (Rajkumar, 2020). Generic drugs can only be released for marketing after the patent of the brand-name drug has expired and is granted approval from the FDA (Meadows, 2003). According to the FDA, the term of a patent in the U.S. is twenty years from when the patent was filed. However, since the FDA takes six to eight years to approve the medication the pharmaceutical company is allowed to request for an extension of five years, which is known as the Hatch-Waxman Act (Kesselheim, 2016). When a patent of a drug is going to expire, the drug company can reformulate their drug which can prolong their patent another twenty years. As a result of the constant manipulation of government protected patents, producing and marketing generic and biosimilar[3] versions of brand name pharmaceuticals become very limited and difficult in the U.S. As well as patent protections, the FDA grants new drugs periods of exclusivity allowing them to be protected from competitors for a certain period of time even if the drug is not patented protected. Depending on the product the length of exclusivity varies. Biological[4] products receive 4 years of filing exclusivity during that period biosimilar manufacturers are prohibited from filing an application; and 12 years of approval exclusivity during which the FDA is prohibited from approving a biosimilar application. Today, many big pharmaceutical companies are abusing the patenting process to withhold the amount of competition developing monopolies and oligopolies. In Canada and the U.K., the patent system is not different from the U.S. but, in the U.S. the patent system effects the general population

[3] Biosimilar: The molecular and biological structure of biosimilar products shows no clinically meaningful difference from the biologic.
[4] Biological product: Biologics are produced from material from a living organism, not chemically synthesized molecules like most other manufactured drugs.

Currently, there are 3 primary insulin manufactures in the U.S. market. Eli Lilly, Sanofi, and Nordisk dominate about 90% of the global insulin market and almost 100% of the U.S. insulin supply. When a company discovers a new or improved way to manufacture or administer insulin or modifies how long it will remain in your system or how quickly it takes effect, it can apply for an extended patent. During the recent years many patents on insulin have expired for Eli Lilly, Sanofi, and Nordisk. These companies have filed extended patents applications years prior allowing them to extend their patent for twenty years more. Pharmaceutical companies are continuously researching and developing new/similar products and adjusting administrative processes in order to extend their patent agreements. Often when big insulin manufactures market new/similar products, the off-patented drug will less likely be prescribed or can possibly be discontinued from the market (Hayes, 2020).

Today, there are six key companies that dominate the global epinephrine market, Mylan Inc, Impax, ALK Abello, Lincoln Medical Ltd, Pfizer, and Sanofi. While the drug itself is not patented the well-known brand-name autoinjector EpiPen used to dispense epinephrine at the recommended speed and dose is patented by Mylan. Epinephrine can be dispensed by normal syringes at a lower cost but requires precision and skill by nurses or technicians (Newsmantra, 2022). EpiPens, are marketed by the pharmaceutical company Mylan which acquired the rights to market the drug in 2007 from the company Merck. This agreement allowed for Mylan to produce certain parts of the autoinjector, but not the drug itself, while owning the brand name and the right to market and distribute the EpiPen. The drug itself was exclusively produced for Mylan by King Pharmaceuticals. In 2010 Pfizer, a company who produced Adrenaclick a similar brand-name product to EpiPen, purchased King Pharmaceuticals. The agreement between Pfizer and Mylan eliminated major competition in the EpiPen market and allowed Pfizer to increase their profits. In

2011, a single pack EpiPen was discontinued in the U.S. and replaced with a twin pack, allowing Mylan to increase the cost. Mylan stated that patients should have two EpiPens at all times because an EpiPen may misfire requiring a second dose. Currently, EpiPens are manufactured by Meridian Medical Technologies a subsidiary for Pfizer and marketed by Mylan (Grim, 2021).

Generics

Currently there are no true generic insulins available to patients because of the strong patents on the drug for consecutive years. Although generic insulins are difficult to produce and market, biosimilar insulins are becoming more accessible and available to patients. A biosimilar drug is a biological product that does not differ clinically from the existing FDA approved product and may be allowed to be interchanged with similar drugs (Rph, 2022). Biosimilar drugs can potentially lower the costs of insulin and increase the accessibility to patients. In July 2021, the FDA approved the first interchangeable biosimilar insulin, Semglee. The biosimilar drug can be used in place of a similar brand name insulin, Lantus. In December 2021, another biosimilar insulin for Lantus was approved by the FDA, Rezvoglar. Many PBMs have either excluded Lantus or have increased their copayment and replaced it with Semglee (Jeremias, 2022).

Epinephrine auto-injector manufactures produce generic versions of their products, which use the same formula, process, and manufacturing facilities used by the brand name manufacture. However, the labeling on the packaging is different from the brand name product. Today, there are three manufactures that produce generic auto-injectors, Mylan, Teva, and Impax (Anderson, 2022). Companies that produce brand-name epinephrine auto-injections such as EpiPen and Adrenaclick, have developed authorized generic version of their own product. In 2016, Mylan and Impax released the first authorized generic auto-injections which are the same drug and devices as the name-brand pharmaceuticals but with a different names and cheaper prices. In 2018, the FDA

approved the first generic version of EpiPen auto-injector not produced and manufactured by the name-brand company, Teva pharmaceuticals was approved to produce epinephrine auto-injectors in the same dose and speed as EpiPens.

In Canada and the U.K. citizens are less effected by monopolies/oligopolies than individuals in the U.S. This leads to competition which is important to regulate the price of goods. Leading the U.K. and Canada to have lower prices than in the U.S.

Pharmacies and Prescription Discount Cards

Pharmacies play a critical role in supplying pharmaceuticals from manufacturers to patients. Pharmacies may work with wholesalers that distribute the drugs at a wholesale rate or they may choose to directly work with the manufacturer (CMS, 2021). Pharmacies will then distribute the drug at a higher price to the consumer. Since, many pharmaceuticals are expensive at the list price in the U.S., many individuals rely heavily on prescription discount cards, copay coupons or pharmaceutical coupons. Prescription discount cards are programs that aid consumers to decrease the price of pharmaceuticals. Pharmacies, doctors' offices, and drug companies partner with prescription discount companies such as GoodRx, who negotiate prices on medications often with the aid of PBMs. Pharmacies try to attract customers into the store by offering discounts on prescription drugs because customers are more likely to buy other items in the pharmacy (Pharmacy, 2021). Every time a prescription discount card is used, the Rx discount companies will receive a small cut of the profit, which may lead to pharmacies losing money on the pharmaceuticals. If an individual uses prescription discount cards they may not be able to use their insurance and have to pay out of pocket (Rossi, 2022). EpiPens have a range of discounts depending on what pharmacy it is purchased at and what brand. As of December 4, 2022, a 2-pack brand name EpiPen retail on average for $733; on GoodRx individuals can find coupons ranging

from 3% to 15% off their purchase. A 2-pack generic epinephrine injector has an average retail of $530; on GoodRx individuals can find up to 74% off their purchase (GoodRx, 2022). Discounts on insulin depends on what type of insulin is prescribed and where it is purchased. Many insulin suppliers work with GoodRx to supply low-cost insulin to individuals, sometimes manufactures will have one-time purchase deals allowing individuals a month's supply of medication (GoodRx, 2022). While prescription discounts relieve many patients of the cost burden of these two critical lifesaving drug, patients still have to pay a heavy cost at the pharmacy.

Limitations

This analysis can be researched further in many aspects to help further my analysis. One aspect that can be researched further, is the number of individuals who purchase insulin and epinephrine in the U.S. compared to the U.K. and Canada. Another aspect that may be further researched is the U.S. healthcare system and the market structure. My analysis covered the prices of these pharmaceuticals in the U.S., Canada, and the U.K. but there were some limitations as some costs of the pharmaceuticals are priced at different units such as pounds (U.K.).

To further my analysis, I would do additional research on the healthcare systems and market structure as well as change the prices of the pharmaceuticals to match the same price unit for the same year. Over the past years, government officials have been discussing implementing government policies to limit the prices of insulin and epinephrine injections. In time there is expected to be further research on this analysis to have a better understanding on why the U.S. has higher price of lifesaving pharmaceuticals as well as analyzing the upgraded policies in the upcoming future.

Conclusion

This paper established that the United States has higher prices for epinephrine and insulin than Canada and the United Kingdom. I reviewed the background of epinephrine and insulin production and analyzed the potential causes of price discrepancies. The main causes I was able to establish are higher rate of demand, the differences between healthcare systems, and the pharmaceutical market structure in the U.S. compared to Canada and the U.K. The main causes that lead to the price discrepancy for these pharmaceuticals is the difference in healthcare system and the market structure in the U.S. compared to the U.K. and Canada.

Currently the U.S. experiences a higher rate of diabetes than the U.K. and Canada, leading to a higher demand for insulin. The same goes for epinephrine, as the U.S. has more citizens with allergies. Unlike the U.S., the U.K. and Canada have government agencies to regulate the prices of pharmaceuticals, restricting companies from price gouging their products. These policies allow the citizens of the U.K. and Canada to be less effected by pharmaceutical monopolies/oligopolies compared to those in the U.S. As a policy implication to help the U.S. decrease the prices of pharmaceuticals would be to implement government agencies similar to the U.K. and Canada to regulate the prices of pharmaceuticals.

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