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ABSTRACT

Recently proposed legislation in Colorado, Connecticut, Florida, Maine, Missouri, Oklahoma, Oregon, Utah, Vermont and West Virginia aims to reduce spending on pharmaceuticals by importing them from Canada. To examine the cost effectiveness of importation, this study analyzes 24 drugs obtained from both an online Canadian supplier and a brick-and-mortar Canadian pharmacy, accounting for the cost savings, the cost of testing, the medical consequences of treatment failure, and the cost of treating an adverse medical event. For a "Representative State", given an adverse medical event, the presumed savings from an online Canadian supplier are exhausted in the treatment of only one patient in the case of Nexium, to 24,318 adverse events for patients in the case of Advair. The analysis shows the cost of testing (99.999% confidence level with 99.999% reliability) exceeds the presumed cost savings in all cases. Pharmaceutical importation plans are politically attractive, but the numbers demonstrate that they fail to deliver cost savings.

KEY WORDS: pharmaceutical importation, drug prices, Canadian pharmacy, cost effectiveness

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EXECUTIVE SUMMARY

Recently proposed legislation in Colorado, Connecticut, Florida, Maine, Missouri, Oklahoma, Oregon, Utah, Vermont and West Virginia aims to reduce spending on pharmaceuticals by importing them from Canada. To examine the cost effectiveness of importation, this study analyzes 24 drugs obtained from both an online Canadian supplier and a brick-and-mortar Canadian pharmacy, accounting for the cost savings, the cost of testing, the medical consequences of treatment failure, and the cost of treating an adverse medical event.

This study analyzes the cost effectiveness of pharmaceutical importation through three lenses.

- Per Patient: calculations for an individual patient, comparing the presumed cost savings to the cost of treating an adverse medical event.
- For a "Representative State" relative to an Adverse Medical Event: calculations for a "Representative State" comparing the presumed costs savings from importation to the cost of treating an adverse medical event.
- For a "Representative State" relative to the Cost of Testing into Safety: calculations for a "Representative State" comparing the presumed cost savings from importation to the expense of testing drugs into safety.

The analysis is based on a number of assumptions. While assumptions are unavoidable in any analysis, the assumptions made in this study are deliberately biased against a finding of the exhaustion of the presumed savings from importation. That is, the study is rigorously structured to estimate the greatest savings possible from pharmaceutical importation. Accordingly, the study's findings – that ***importation is not cost effective*** in the majority of cases – are all the more striking.

For an Individual Patient, regardless of whether one's drugs are obtained from a Canadian online supplier or a brick-and-mortar Canadian pharmacy, in three out of four cases, the annual presumed savings fails to cover the costs of an adverse medical event. For these drugs, patients would need to acquire the cost savings over a period of up to 111 years to cover the costs of one adverse event. Not surprisingly, for the few drugs for which the savings exceed the cost of treating an adverse medical event, the expense of an adverse medical event is modest (less than $50,000). For the majority of drugs, the cost of treating an adverse event will significantly exceed $50,000 and may reach more than $800,000.

For a "Representative State", regardless of whether one's drugs are obtained from a Canadian online supplier or a brick-and-mortar Canadian pharmacy, in three out of four cases, the annual presumed savings for a "Representative State" fails to cover the costs of an adverse medical event. Again, for the few drugs for which the savings exceed the cost of treating an adverse medical event, the expense of an adverse medical event is modest (less than $50,000 per patient), while, for the majority of drugs, the cost of treating an adverse event will significantly exceed $50,000 and may reach more than $800,000. In the analysis of a "Representative State", given an adverse medical event, the presumed savings from an online Canadian supplier are exhausted in the treatment of only one patient in the case of Nexium, and for 24,318 adverse events for patients in the case of Advair. Importantly, for this selection of 24 drugs, the cost savings will

be completely eliminated if a mere 3.2% of imported drugs are counterfeit for a brick-and-mortar pharmacy or 3.5% from a Canadian online supplier.

For a "Representative State", regardless of whether one's drugs are obtained from a Canadian online supplier or a brick-and-mortar Canadian pharmacy, in all cases, the annual presumed savings for a "Representative State" fails to cover the costs of testing a drug into safety with 99.999% confidence and 99.999% reliability. In the case of a lower level of quality assurance, there are a few drugs for which the presumed savings would exceed the cost of testing. If one is willing to accept the risk of a 90% confidence level with 90% reliability, then the presumed savings will (in all but one case) exceed the cost of testing for both online suppliers and brick-and-mortar Canadian pharmacies. Fundamentally, the presumed cost savings may be accrued only when a significant level of risk is present and the dangers of counterfeit drugs is deemed an acceptable gamble.

Quite simply, pharmaceutical importation plans are politically attractive, but the numbers demonstrate that they fail to deliver cost savings and instead may pose a serious threat to patients.

"Given the rapid growth in the prevalence of sophisticated counterfeit drugs, no politician will approve a drug importation scheme without implementing a reasonable measure of regulatory oversight. There are simply too many channels for fake drugs to enter any importation scheme to forgo some meaningful controls. . . Providing a reasonable measure of oversight to reduce the number of counterfeits coming through an importation scheme is complex and costly. It's very hard to 'inspect in' safety after a drug is manufactured. There's no question that a drug importation scheme will increase the flow of counterfeits in the U.S. supply chain. Policy makers would have to weigh that cost against any perceived benefits."

FDA Commissioner Scott Gottlieb
4 March 2016

I. INTRODUCTION

Drug importation schemes are again being propositioned as a remedy to high U.S. drug prices. Recently proposed legislation in Colorado, Connecticut, Florida, Maine, Missouri, Oklahoma, Oregon, Utah, Vermont and West Virginia aim to reduce spending on pharmaceuticals by importing them from Canada. Advocates reason that American patients can lower their drug costs by importing cheaper drugs from countries with lower pharmaceutical prices. What escapes their attention is the need for, and cost of, testing to ensure the safety of those imports. Fundamentally, it has not been established whether it is cost effective to import medicine from a source from which regulatory compliance cannot be assured, and then test it into safety.

In reality, it is very expensive to test suspect medication to the same level of expected safety as FDA-approved medicines made in FDA-monitored factories. The tremendous cost of testing must be taken into account when calculating the cost savings or dissavings associated with buying medicines from a suspicious source. Beyond the costs of testing drugs into safety, it is essential to recognize the cost of potential adverse medical events. Purchasing pharmaceuticals outside of the highly-regulated U.S. supply chain exposes patients to the risks of counterfeit, fraudulent and substandard drugs which may be dangerous or toxic, resulting in serious patient harm.

In order to examine the cost effectiveness of pharmaceutical importation, this study analyzes the cost savings, the cost of testing and the cost of treating an adverse medical event. This entails initially examining 40 drugs, documenting the costs, presumed cost savings from two unregulated suppliers (Canadian online supplier and a brick-and-mortar Canadian pharmacy), the medical consequences of treatment failure, and the expense of treating such adverse events. The results indicate that the true costs of pharmaceutical importation outweigh the anticipated cost savings. When all potential risks and costs are accounted for, it is difficult to justify moving outside of the U.S. supply chain for medicines.

II. DRUGS SELECTED FOR EXAMINATION

This study begins with a list of 40 drugs and due to lack of information and availability ultimately examines approximately two dozen drugs. The initial set of 40 drugs identified for inclusion were selected based on several criteria:

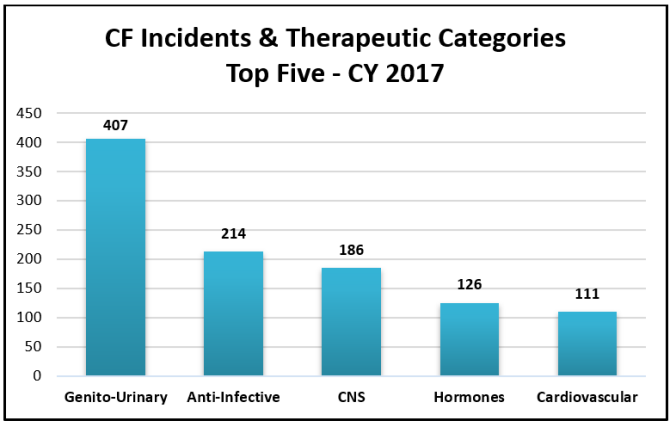
- The selection should include drugs from a wide variety of therapeutic classes, and treatments for a variety of diseases and medical conditions
- The selection should include drugs that are known to be widely counterfeited.
- The selection should include drugs that consumers readily seek to purchase outside the legitimate supply chain.
- The selection should include drugs mentioned in news and media reports that speak to consumers purchasing drugs abroad. Specifically, the Utah Tiajuana Thirteen List (Roe, 2018) (link here), the list promoted by Senator Bernie Sanders (IsraelPharm 2017) (link here), and the list promoted by the National Academy for State Health Policy (NASHP 2017) (link here).
- The selection should draw upon recommendations from experts.

Finally, the specific drugs considered as well as the number of drugs studied was also determined by data availability.

Forty drugs were initially selected for inclusion. The list included the thirteen drugs from the Utah Tijuana Thirteen List, the ten drugs cited by Senator Bernie Sanders, and the ten drugs promoted for importation by the NASHP[1]. In addition, the list reflects drug classes that are known to be widely counterfeited. Drawing on data from the Pharmaceutical Security Institute (PSI), the list includes drugs from each of the top five therapeutic categories. These categories are presented in Figure 1, below. Finally, several drugs were included based on the recommendations of board members of the Partnership for Safe Medicines. The full list of drugs and the source of their inclusion are included in Table 1.

[1] The drug included on the NASHP list was Tracleer. No Canadian sources were found for this drug, so Letairis is listed instead. Letairis is a more popular drug in the same class as Tracleer.

Figure 1: Top Counterfeiting Incidents and Therapeutic Categories



(Pharmaceutical Security Institute, webpost, 2018 (link here))

Combining all of these sources resulted in a list of 40 drugs. Of these, there are six that are not available for online purchase from online Canadian pharmacies. This may be because the drug is a controlled substance (Lyrica) or because the drug is an injectable that requires refrigeration during shipping (Avonex, Copaxone, Forteo, Humira, Stelara). With the elimination of these six drugs, the final list of drugs available from online Canadian pharmacies includes 34 drugs.

In addition to documenting the prices of these drugs from online Canadian pharmacies, the prices were also collected for a local neighborhood (brick-and-mortar) pharmacy in Vancouver, BC, Canada. From the list of 40 drugs, four drugs are not available. These are: Aubagio, Eliquis, Letaris, and Lyrica. The elimination of these four drugs results in a final list of 36 drugs available from a brick-and-mortar Canadian pharmacy.

Finally, there are eight drugs for which no potential adverse event is listed: Augmentin, Celebrex, Cialis, Lyrica, Stendra, Strattera, Synthroid, and Triumeq. For each of these drugs it was either impossible to identify the cost of a worsening condition (infection, rheumatoid arthritis, fibromyalgia, HIV/AIDS, hypothyroidism), or it was impossible to quantify the cost of the potential adverse event (erectile dysfunction, ADHA).

Combining the three lists results in 16 drugs for which all pieces of information are not available: Aubagio, Augmentin, Avonex, Celebrex, Cialis, Copaxone, Eliquis, Forteo, Humira, Letaris, Lyrica, Stelara, Stendra, Strattera, Synthroid, and Triumeq. The remaining 24 drugs were selected for extensive analysis: identification of the drug's indication, description of potential medical adverse events, calculation of cost of treating said adverse events, estimation of the cost of testing the quality, safety and efficacy of the drug. These drugs are highlighted in green Table 1, below.

Table 1: List of Drugs

	Drug	Utah Tiajuana Thirteen List	Bernie Sanders List	NASHP List	PMS Board Member Recommendation	Popular Drug in PSI Drug Class	No Online Canadian Source: controlled	No Online Canadian Source: injectable	No B-&-M Canadian Source	No Quantifiable Adverse Event
1	Abilify		X							
2	Actos				X					
3	Advair		X	X						
4	Albenza					X				
5	Ampyra	X								
6	Aubagio	X							X	
7	Augmentin					X				X
8	Avonex	X						X		
9	Celebrex		X							X
10	Cialis				X					X
11	Copaxone	X						X		
12	Crestor		X		X	X				
13	Eliquis			X		X			X	
14	Enbrel	X								
15	EpiPen		X							
16	Forteo	X						X		
17	Gilenya	X								
18	Harvoni			X	X					
19	Humira	X						X		
20	Januvia		X		X					
21	Letairis			X*					X	
22	Lipitor									
23	Lyrica			X			X		X	X
24	Nexium		X							
25	Orencia	X								
26	Otezla	X								
27	Premarin		X			X				
28	Revatio					X				
29	Sovaldi				X					
30	Stelara	X						X		
31	Stendra					X				X
32	Strattera			X						X
33	Synthroid		X							X
34	Tecfidera	X								
35	Tresiba				X					
36	Triumeq			X	X					X
37	Truvada				X					
38	Xarelto			X						
39	Zetia		X							
40	Zytiga	X								

III. DATA COLLECTION AND METHODOLOGY

Following the selection of the drugs included in this study, several pieces of information were collected for each drug. These included: the US cost of the drug, the cost from a brick-and-mortar Canadian pharmacy, the cost of the drug from an online Canadian supplier, the medical consequences of a treatment failure, the cost of addressing said treatment failure, and the cost of testing the quality of a drug sample.

US cost of the drug through the legitimate supply chain

The lowest available prices were collected for the four most populous cities in the United States: New York, Los Angeles, Chicago, and Houston. In addition to representing the most populous cities in the country, the four cities also represent four distinct geographic regions: East Coast, West Coast, Midwest, and South. These prices were gathered from the GoodRX.com website between January 2, 2019 and January 10, 2019. The average price per unit was then calculated.

Pharmaceutical prices are tremendously variable across regions, pharmacies and individuals. In order to find a U.S. cost that could be used in this analysis, this average US cost is assumed to be a workable proxy for the actual cost paid by patients in the US.

Importantly, the use of the GoodRX.com prices biases the study against a finding of the elimination of all cost savings. It is reasonable to assume that prices negotiated by state entities would be lower than the GoodRX.com prices, reducing the cost savings that are estimated here and more quickly eliminating the cost savings. Moreover, sites such as GoodRX.com offer coupons to consumers that would lower their actual out-of-pocket costs. Failure to include any coupon savings again biases the study against a finding of the elimination of cost savings.

Cost from Brick-and-Mortar Canadian Pharmacy

Canadian pricing data were collected from a "brick and mortar" pharmacy in Vancouver, BC. Marks Marine Pharmacy is located inside Main and Marine Medical Clinic, at 235 SE Marine Dr, Vancouver, BC V5X 2S4, Canada. The pricing data were collected on May 14, 2019. If proponents argue that they will obtain drugs from the Canadian drug supply, from a Canadian pharmacy, these prices provide that information.

Cost from an unregulated Canadian Supplier

The price of each drug was then collected from several (when possible) Canadian online pharmacies. These values were used to calculate the lowest available Canadian price per unit. The following online websites were consulted:

- DiscountDrugsFromCanada.com
- FillerSupplies.com

- CanadianPharmacyWorld.com
- PricePro Pharmacy.com
- InsulinOnline.com
- PlanetDrugsDirect.com
- CanadaDrugsOnline.com

Utilizing the lowest possible Canadian online price available will generate results that provide the largest possible savings. Notably, the study uses the lowest Canadian online price, rather than the average Canadian price. Again, this biases the analysis against a finding of eliminating the cost savings. In essence, this works to understate the extent to which the cost savings is eliminated.

While the online Canadian suppliers deliver the lowest prices, it is important to realize that these suppliers are not safe outlets for U.S. patients. Online suppliers are not regulated and pose significant risks to patients from counterfeit and substandard drugs.

Cost of testing samples

Four laboratories were contacted to obtain this information. Several are unable to provide a quote for the cost of testing samples. The testing cost information utilized in this study was provided by NMS Labs. Four tests are utilized to establish quality, depending on the type of drug, the dosage and the method of administration. These are: Assay, Content Uniformity, Dissolution Rate, and Sterility. For the 24 drugs included in this study, the cost of testing a single sample ranges from $2,500 to $4,100. Table 2, below provides a summary of this information. The full quote may be found in Appendix B.

Table 2: Cost of Testing a Single Sample

Drug	Assay	Dissolution Rate	Content Uniformity	Sterility	Total Cost of Testing
Abilify	$600	$1,200	$1,200	$1,000	$4,000
Actos	$500	$1,000	$1,000		$2,500
Advair	$1,100		$2,000	$1,000	$4,100
Albenza	$500	$1,000	$1,000		$2,500
Ampyra	$500	$1,000	$1,000		$2,500
Crestor	$500	$1,000	$1,000		$2,500
Enbrel	$600		$1,200	$1,000	$2,800
EpiPen	$600		$1,200	$1,000	$2,800
Gilenya	$500	$1,000	$1,000		$2,500
Harvoni	$500	$1,000	$1,000		$2,500
Januvia	$500	$1,000	$1,000		$2,500
Lipitor	$500	$1,000	$1,000		$2,500
Nexium	$600	$1,200	$1,200		$3,000
Orencia	$600		$1,200	$1,000	$2,800
Otezla	$500	$1,000	$1,000		$2,500
Premarin	$600	$1,000	$1,000		$2,600
Revatio	$600	$1,000	$1,000	$1,000	$3,600
Sovaldi	$500	$1,000	$1,000		$2,500
Tecfidera	$500	$1,000	$1,000		$2,500
Tresiba	$600		$1,200	$1,000	$2,800
Truvada	$500	$1,000	$1,000		$2,500
Xarelto	$500	$1,000	$1,000		$2,500
Zetia	$500	$1,000	$1,000		$2,500
Zytiga	$500	$1,000	$1,000		$2,500

Source: NMS Labs.

Determination of Sample Size

The sample size necessary for testing is dependent on the desired confidence level and reliability one would like to have.[2] For example, in order to provide 90% confidence in the quality of the

[2] The number of samples required will depend upon whether one uses Attribute Sampling or Variables Sampling.

- Attribute Sampling: Determine the sample size for a categorical response that classifies each unit as Good or Bad (or, perhaps, In-spec or Out-of-spec).
- Variables Sampling: Determine the sample size for a continuous measurement that follows a Normal distribution.

This endeavor requires the use of Attribute Sampling, a sampling plan that ensures zero defects in the sample, or C=0. The basic formula for sample size based on the desired Confidence level and Reliability is:

$$n = [\ln(1-\text{Confidence})]/[\ln(\text{Reliability})].$$

For example, this formula provides the sample size required to make a 99% confidence statement about the probability an item will be in-spec when your sample of size n has zero defects with 95% confidence. For a test with 99% confidence and 95% reliability, a sample size of 90 would be necessary. Once a sample of a representative drug is collected, each sample will go through a lab test that will determine whether the pill "passes" or "fails". In a

imported drugs, with a 90% reliability, 22 samples must be tested. In order to increase this confidence level to 99.99%, with a 99.99% reliability, 92,099 samples must be tested. In order to increase this confidence level to 99.999%, with a 99.999% reliability, 1,151,287 samples must be tested. Table 3, below, provides the required sample size for combinations of confidence levels (ranging from 0.9 to 0.99999) and reliability (ranging from 0.9 to 0.99999). Accordingly, these testing sample sizes may then be used to estimate the cost of "testing drugs into safety". The table presents the highest ($4,100) and lowest ($2,500) costs of testing the requisite number of samples for each of these combinations of confidence level and reliability.

scenario like this, to demonstrate with confidence level C that at least p% of all pills are of good quality, then there should be n>=ln(1-C)/ln(p) consecutive "passes" for the test. In reliability theory, this is called the "success run theorem". Sources: Westpack.com (link here) and Mintab.com (link here). The author is grateful to Dr. Flavia Sancier-Barbosa for her assistance in determining the appropriate sample size.

Table 3: Sample Size as a Function of Confidence and Reliability

Confidence level (% as decimal)	Reliability (% as decimal)	Sample Size Required: Ln(1-Confidence)/Ln(Reliability)	Cost of Testing Sample at $2500	Cost of Testing Sample at $4100
0.9	0.9	22	$55,000.00	$90,200.00
0.9	0.9	22	$55,000.00	$90,200.00
0.99	0.9	44	$110,000.00	$180,400.00
0.999	0.9	66	$165,000.00	$270,600.00
0.9999	0.9	87	$217,500.00	$356,700.00
0.99999	0.9	109	$272,500.00	$446,900.00
0.9	0.99	229	$572,500.00	$938,900.00
0.99	0.99	458	$1,145,000.00	$1,877,800.00
0.999	0.99	687	$1,717,500.00	$2,816,700.00
0.9999	0.99	916	$2,290,000.00	$3,755,600.00
0.99999	0.99	1146	$2,865,000.00	$4,698,600.00
0.9	0.999	2301	$5,752,500.00	$9,434,100.00
0.99	0.999	4603	$11,507,500.00	$18,872,300.00
0.999	0.999	6904	$17,260,000.00	$28,306,400.00
0.9999	0.999	9206	$23,015,000.00	$37,744,600.00
0.99999	0.999	11507	$28,767,500.00	$47,178,700.00
0.9	0.9999	23025	$57,562,500.00	$94,402,500.00
0.99	0.9999	46049	$115,122,500.00	$188,800,900.00
0.999	0.9999	69074	$172,685,000.00	$283,203,400.00
0.9999	0.9999	92099	$230,247,500.00	$377,605,900.00
0.99999	0.9999	115123	$2,878,217,500.00	$4,720,276,700.00
0.9	0.99999	230257	$575,642,500.00	$944,053,700.00
0.99	0.99999	460515	$1,151,287,500.00	$1,888,111,500.00
0.999	0.99999	690772	$1,726,930,000.00	$2,832,165,200.00
0.9999	0.99999	921029	$2,302,572,500.00	$3,776,218,900.00
0.99999	0.99999	1151287	$2,853,217,500.00	$4,679,276,700.00

Source: Author's calculations.

Determination of Treatment Failure

The author of this study worked with Dr. Peter H. Rheinstein, M.D., J.D., M.S., President, Severn Health Solutions in order to establish the indications for each drug and the consequences of receiving an ineffective dose. The assumption made in compiling this data was that the drug taken was ineffective. In reality, many poor quality medicines are not only ineffective, but they contain dangerous or toxic ingredients that may result in more severe and significant adverse health effects. The complete review of each drug is provided in Appendix A.

Table 4, below, identifies the consequences of ineffective treatment, the potential adverse medical event. While the table includes the complete list of 40 drugs, there are eight drugs for which no potential adverse event is listed: Augmentin, Celebrex, Cialis, Lyrica, Stendra, Strattera, Synthroid, and Triumeq. For each of these drugs it was either impossible to identify the cost of a worsening condition (infection, rheumatoid arthritis, fibromyalgia, HIV/AIDS, hypothyroidism), or it was impossible to quantify the cost of the potential adverse event (erectile dysfunction, ADHA).

Medical consequences of treatment failure

The medical consequences of getting a counterfeit version can vary from no effect to death from a toxic substance.[3] This analysis assumes that the counterfeit version is a placebo, containing no active ingredient, and no harmful ingredients. That is, the treatment is ineffective. Accordingly, the treatment failure is simply the result of taking a drug that does not contain the active pharmaceutical ingredient. Obviously, if a counterfeit drug contains substantial impurities or toxins the adverse effects of ingestion may be significantly more consequential. The consequences of taking a counterfeit drug containing harmful ingredients will be far worse, potentially resulting in death, and more costly to treat. Again, this will bias the analysis against the finding of the elimination of any cost savings.

[3] The Partnership for Safe Medicine (2019) documents the harms of counterfeit drugs and the individuals harmed by them. Dozens of their stories may be found on their website: https://www.safemedicines.org/victim-tragedies

Table 4: Potential Adverse Event

	Drug	Potential Adverse Event
1	Abilify	Suicide attempt
2	Actos	Diabetic ketoacidosis
3	Advair	COPD
4	Albenza	Neurocysticercosis
5	Ampyra	Worsening MS
6	Aubagio	Worsening MS
7	Augmentin	
8	Avonex	Worsening MS
9	Celebrex	
10	Cialis	
11	Copaxone	Worsening MS
12	Crestor	Stroke
13	Eliquis	Stroke
14	Enbrel	Worsening Psoriatic Arthritis
15	EpiPen	Anaphylaxis
16	Forteo	Fracture due to Osteoporosis
17	Gilenya	Worsening MS
18	Harvoni	Liver failure requiring transplant
19	Humira	Worsening Psoriatic Arthritis
20	Januvia	Diabetic Ketoacidosis
21	Letairis	PAH
22	Lipitor	Stroke
23	Lyrica	
24	Nexium	Esophageal Cancer
25	Orencia	Worsening Psoriatic Arthritis
26	Otezla	Worsening Psoriatic Arthritis
27	Premarin	Fracture due to Osteoporosis
28	Revatio	PAH
29	Sovaldi	Liver failure requiring transplant
30	Stelara	Worsening Psoriatic Arthritis
31	Stendra	
32	Strattera	
33	Synthroid	
34	Tecfidera	Worsening MS
35	Tresiba	Diabetic Ketoacidosis
36	Triumeq	
37	Truvada	New HIV-1 infection
38	Xarelto	Stroke
39	Zetia	Stroke
40	Zytiga	Prostate Cancer

Expense of treating such adverse events

Healthcare costs are uniquely difficult to measure. Across the United States costs vary significantly. Moreover, costs may vary significantly across hospitals in the same city or even across patients in the same hospital. Insurance status and the details of a particular plan further complicate measurement of such expenses.

The data on the expense of treating an adverse event was gathered from medical journals and institutional sources. Given the difficulty of specifying medical costs, Appendix C details the sources and methodology used for each calculation used in the analysis. Additional details for each calculation may be found in the original source material.

Table 5 provides the cost of treatment (in 2019 dollars) for the 14 unique adverse medical events found in Table 4. The costs presented here are estimated for the treatment of a patient for one year or a single adverse event. Given that the cost savings from buying Canadian drugs is estimated for a single year, the treatment of an adverse event is also estimated for a single year. Notably, in many cases, the cost of treatment failure will extend over many years and may present a lifelong burden. Again, this assumption biases the results against the finding of eliminating all cost savings.

Table 5: Cost of Treatment for Potential Adverse Medical Events

Potential Adverse Medical Event	Cost in 2019 dollars[4]	Details
Anaphylaxis	$5,958	$4719 annual cost in 2007 dollars
CABG	$165,822	$151,785 in 2014 dollars
COPD	$3,958	$3356 annual cost in 2010 dollars
Diabetic ketoacidosis	$29,023	$26,566 in 2014 dollars
Esophageal Cancer	$93,966	$79,677 initial year in 2010 dollars
New HIV-1 infection	$447,758	$379,668 lifetime cost in 2010 dollars
Liver transplant	$855,022	$812,500 in 2017 dollars
Multiple Sclerosis	$48,893	$42,134 annual cost in 2011 dollars
Neurocysticercosis	$55,085	$48,859 in 2012 dollars
Osteoporosis Fracture	$12,409	$8,600 in 2002 dollars
Prostate Cancer	$23,243	$19,710 initial year in 2010 dollars
Psoriatic Arthritis	$6,699	$6,126 annual cost in 2015 dollars
Pulmonary Arterial Hypertension	$41,617	$32,964 annual cost in 2007 dollars
Schizophrenia: Suicide Attempt	$64,729	$46,024 annual cost in 2003 dollars

Source: Author's calculations using data from medical journals included in Appendix C.

[4] Cost in 2019 dollars was calculated using the Bureau of Labor Statistics' CPI Inflation Calculator (link here).

Number of Patients in a "Representative State"

According to the U.S. Census Bureau (link here), the population of the United State is approximately 328 million and dividing by 50, a representative state would have a population of 6,560,000 people. The Medicaid website (link here) indicates that Medicaid and CHIP now cover nearly 70 million people, or one in every five people in the country. Using 20% of the population as a conservative estimate of the share of people who would utilize a state-importation program, the annual presumed savings may be calculated. Assuming 20% of that population utilizes the state-importation program, this equates to 1,312,000 persons in the representative state. Admittedly, this may be an overestimation of the number of patients. If so, this again biases the analysis against a finding of the elimination of cost savings.

Disease Prevalence

The analysis presented to this point considers only the costs and savings available to an individual patient. Given that the importation programs under consideration would extend to larger populations, by state, it is important to calculate the costs and savings available to a state program, as well as the consequences of such programs.

In the cases of the 14 unique adverse events listed above the calculations have been extended to provide estimates for a "representative state". The disease prevalence was determined for the entire United States. This number was then divided by 50 to calculate the number of patients for a "representative state". Table 6, below, presents the number of patients for each of the 14 unique adverse events. The calculations and sources for these estimates may be found in Appendix D.

Table 6: Number of Patients in a Representative US State for Potential Adverse Medical Events

Potential Adverse Medical Event	Number of Patients in Representative US State
Anaphylaxis	131,200
High Cholesterol: CABG	860,000
COPD	392,400
Diabetic ketoacidosis	606,000
Esophageal Cancer	300
New HIV-1 infection	22,000
Liver transplant	48,000
Multiple Sclerosis	20,000
Neurocysticercosis	41
Osteoporosis Fracture	204,000
Prostate Cancer	3,671
Psoriatic Arthritis	3,490
Pulmonary Arterial Hypertension	4,000
Schizophrenia: Suicide Attempt	29,192

Source: Author's calculations using data from medical journals included in Appendix D.

IV. ANALYSIS

This analysis presents the calculations for an individual patient (Tables 7-9), comparing the presumed cost savings to the cost of treating an adverse medical event. It also presents the calculations for a "Representative State" (Tables 10-13), comparing the presumed cost savings to the costs of treating an adverse medical event and to the costs of testing the imported medicines into safety.

Calculation of presumed cost savings

Utilizing the average US price per unit and the lowest Canadian price per unit (for both the brick-and-mortar pharmacy and the online supplier), the average cost savings per unit was calculated for the 24 drugs for which extensive analysis is possible. For drugs taken for a chronic condition, this number was multiplied by the number of doses prescribed per month to calculate the presumed monthly savings, which was then multiplied by 12 to calculate the presumed annual savings. For drugs taken for an acute condition, the average per unit cost savings was multiplied by the number of doses needed for treatment to calculate the savings per episode per patient. These calculations are presented in Table 7, below.

Table 7: Presumed Cost Savings Per Patient from Online Canadian Supplier and Brick-and-Mortar Canadian Pharmacy

Drugs	Online Canadian savings per patient: yearly	Online Canadian savings per patient: monthly	Online Canadian savings per patient: per episode	US Price less online Canadian Price	B&M Canadian savings per patient: yearly	B&M Canadian savings per patient: monthly	B&M Canadian savings per patient: per episode	US Price less B&M Canadian Price	Average US price per unit♦	Lowest Online Canadian price per unit	Lowest B&M Canadian price per unit
Abilify	$10,270.54	$855.88		$28.53	$9,004.23	$750.35		$25.01	$30.01	$1.48	$5.00
Actos	$6,931.29	$577.61		$19.25	$5,722.84	$476.90		$15.90	$20.08	$0.82	$4.18
Advair	$3,978.57	$331.55		$331.55	$3,438.61	$286.55		$286.55	$396.55	$65.00	$110.00
Albenza			$50,450.40	$209.09			$50,021.87	$208.42	$210.21	$1.13	$1.79
Ampyra	$23,560.40	$1,963.37		$32.72	$23,367.67	$1,947.31		$32.46	$44.95	$12.23	$12.50
Crestor	$1,580.07	$131.67		$4.39	$1,494.40	$124.53		$4.15	$5.82	$1.43	$1.67
Enbrel	$37,823.70	$3,151.98		$787.99	$34,379.70	$2,864.98		$716.24	$1,217.99	$430.00	$501.75
EpiPen			$171.53	$171.53			$168.54	$168.54	$308.53	$137.00	$139.99
Gilenya	$55,650.44	$4,637.54		$154.58	$58,222.00	$4,851.83		$161.73	$261.73	$107.14	$100.00
Harvoni			$34,864.52	$387.38			$17,604.88	$195.61	$1,124.18	$736.80	$928.57
Januvia	$4,777.35	$398.11		$13.27	$3,731.76	$310.98		$10.37	$14.70	$1.43	$4.33
Lipitor	$4,708.92	$392.41		$13.08	$4,808.96	$400.75		$13.36	$14.25	$1.17	$0.89
Nexium	$1,655.49	$137.96		$4.60	$922.76	$76.90		$2.56	$5.60	$1.00	$3.04
Orencia	$32,467.60	$2,705.63		$676.41	$18,260.08	$1,521.67		$380.42	$1,080.41	$404.00	$699.99
Otezla	$24,933.99	$2,077.83		$34.63	$22,343.41	$1,861.95		$31.03	$56.03	$21.40	$25.00
Premarin	$1,540.51	$128.38		$4.28	$1,540.55	$128.38		$4.28	$5.05	$0.77	$0.77
Revatio	$18,707.61	$1,558.97		$17.32	$16,055.72	$1,337.98		$14.87	$23.87	$6.54	$9.00
Sovaldi			$16,843.18	$187.15			$28,662.91	$318.48	$997.05	$809.90	$678.57
Tecfidera	$63,857.73	$5,321.48		$88.69	$65,233.44	$5,436.12		$90.60	$126.10	$37.41	$35.50
Tresiba	$1,852.70	$154.39		$154.39	$1,826.32	$152.19		$152.19	$192.19	$37.80	$40.00
Truvada	$18,702.39	$1,558.53		$51.95	$7,854.39	$654.53		$21.82	$56.12	$4.17	$34.30
Xarelto	$4,495.76	$374.65		$12.49	$3,797.23	$316.44		$10.55	$14.21	$1.73	$3.67
Zetia	$3,382.19	$281.85		$9.39	$3,230.80	$269.23		$8.97	$11.42	$2.02	$2.44
Zytiga	$74,685.00	$6,223.75		$51.86	$72,093.12	$6,007.76		$50.06	$85.19	$33.33	$35.12

Source: Author's calculations, May 2019.

♦Note that the US Price is the average obtained from GoodRX.com.

Ratio of the Expense of Treating an Adverse Event to Presumed Cost Savings <u>Per Patient</u>

Given that cost savings is the primary motivation for pharmaceutical importation, it is essential to consider whether patients actually save money. This section compares the presumed cost savings that will accrue to a patient and compares it to the cost of treating an adverse medical event. Simply stated, if a patient receives a counterfeit version of the imported drug and they suffer the health consequences, will they save any money?

Again, utilizing the average US price per unit and the lowest Canadian price per unit for both online suppliers and brick-and-mortar pharmacies, the average cost savings per unit was calculated. For drugs taken for a chronic condition, this number was multiplied by the number of doses prescribed per month to calculate the presumed monthly savings, which was then multiplied by 12 to calculate the presumed annual savings. For drugs taken for an acute condition, the average per unit cost savings was multiplied by the number of doses needed for treatment to calculate the savings per episode per patient.

As described in Section III above, the data on the expense of treating an adverse event were gathered from medical journals and institutional sources. These expenses are then compared to the presumed cost savings. Tables 8 and 9, below, presents the ratio of treatment expenses to the presumed cost savings for both online Canadian suppliers and brick-and-mortar Canadian pharmacies. The dollar values highlighted in green correspond to the greatest amount of savings across online Canadian suppliers and brick-and-mortar Canadian pharmacies.

Online Suppliers In the case of online suppliers, the annual presumed savings fails to cover the treatment of an adverse event for 18 of the 24 drugs (75%). The calculations indicate that these ratios range from 0.01 for Crestor to 5.65 for Enbrel. That is, for Crestor, the annual savings covers less than 1% of the cost of treating an adverse medical event, such that patients would require 105 years of presumed cost savings to cover the treatment of an adverse medical event. For Enbrel, patients would require 66 days of presumed cost savings to cover the treatment of an adverse medical event. For Crestor, the cost of treating an adverse event is more than 10,500% of the presumed cost savings. Of the 14 adverse medical events considered, the presumed cost savings exceeds the cost of treatment for only 3 conditions (21%). These are: Multiple Sclerosis (Gilenya, Tecfidera), Psoriatic Arthritis (Enbrel, Orencia, Otezla) and Prostate Cancer (Zytiga). For ten of the 24 drugs analyzed, the annual presumed savings is less than 5% the cost of treating an adverse medical event. On average, patients would need to accumulate 24 years of the presumed cost savings to cover the treatment for an adverse medical event.

Brick-and-Mortar Pharmacies In the case of brick-and-mortar suppliers, the annual presumed savings fails to cover the treatment of an adverse event for 18 of the 24 drugs (75%). The calculations indicate that these ratios range from 0.01 for Crestor to 5.13 for Enbrel. That is, for Crestor, the annual savings covers less than 1% of the cost of treating an adverse medical event, such that patients would require 111 years of presumed cost savings to cover the treatment of an adverse medical event. For Crestor, the cost of treating an adverse event is more than 11,100% of the presumed cost savings. For Enbrel, patients would require 71 days of presumed cost savings to cover the treatment of an adverse medical event. Again, of the 14 adverse medical events considered, the presumed cost savings exceeds the cost of treatment for only 3 conditions

(21%): Multiple Sclerosis (Gilenya, Tecfidera), Psoriatic Arthritis (Enbrel, Orencia, Otezla) and Prostate Cancer (Zytiga). For ten of the 24 drugs analyzed, the annual presumed savings is less than 5% the cost of treating an adverse medical event. On average, patients would need to accumulate 20 years of the presumed cost savings to cover the treatment for an adverse medical event.

It is essential to recognize the true danger posed to U.S. patients from drugs that are obtained outside of the highly regulated U.S. supply chain. This is a case in which an attempt to save money ends up leading to even greater expenses in the end. In a relatable situation, at least a dozen U.S. patients have traveled to Mexico for surgical procedures that were less expensive in Tijuana and contracted a rare and potentially deadly strain of bacteria resistant to virtually all antibiotics. Treatment of the deadly superbug has resulted in medical expenses that far outstrip the initial savings (Sun, 2019) (link here). Also, consider two instances in which Canada Drugs, through its subsidiary River East Supplies, distributed counterfeit cancer drugs Avastin and Altuzan (the Turkish version of the drug) in the United States. According to the U.S. FDA, testing of vials of the drugs recovered from these shipments revealed that both contained no active ingredient. In April 2018 the Canadian firm admitted to widespread illegal sales of misbranded and counterfeit prescription drugs in the United States (U.S. FDA, 2018) (link here). Again, the cost savings are eliminated in the face of complete treatment failure.

Per Patient Takeaway Regardless of whether one's drugs are obtained from a Canadian online supplier or a brick-and-mortar Canadian pharmacy, in three out of four cases, the annual presumed savings fails to cover the costs of an adverse medical event. For these drugs, patients would need to acquire the cost savings over a period of up to 111 years to cover the costs of one adverse event. Not surprisingly, for the few drugs for which the savings exceed the cost of treating an adverse medical event, the expense of an adverse medical event is modest (less than $50,000). For the majority of drugs, the cost of treating an adverse event will significantly exceed $50,000 and may reach more than $800,000.

Table 8: Presumed Cost Savings Per Patient from an Online Supplier Relative to the Cost of Treating an Adverse Event

Drugs	Online savings per patient: yearly	Online savings per patient: monthly	Online savings per patient: per episode	US Price less online Canadian Price	Cost of Treating Adverse Event per Patient	Number of Years of Savings needed to cover Adverse Event	Percent of Adverse Event Treatment Covered by Annual Savings
Abilify	$10,270.54	$855.88		$28.53	$64,729	6.30	0.16
Actos	$6,931.29	$577.61		$19.25	$165,822	23.92	0.04
Advair	$3,978.57	$331.55		$331.55	$11,097	2.79	0.36
Albenza			$50,450.40	$209.09	$55,085	1.09	0.92
Ampyra	$23,560.40	$1,963.37		$32.72	$48,893	2.08	0.48
Crestor	$1,580.07	$131.67		$4.39	$165,822	104.95	0.01
Enbrel	$37,823.70	$3,151.98		$787.99	$6,699	0.18	5.65
EpiPen			$171.53	$171.53	$4,719	27.51	0.04
Gilenya	$55,650.44	$4,637.54		$154.58	$48,893	0.88	1.14
Harvoni			$34,864.52	$387.38	$812,500	23.30	0.04
Januvia	$4,777.35	$398.11		$13.27	$29,023	6.08	0.16
Lipitor	$4,708.92	$392.41		$13.08	$165,822	35.21	0.03
Nexium	$1,655.49	$137.96		$4.60	$93,966	56.76	0.02
Orencia	$32,467.60	$2,705.63		$676.41	$6,699	0.21	4.85
Otezla	$24,933.99	$2,077.83		$34.63	$6,699	0.27	3.72
Premarin	$1,540.51	$128.38		$4.28	$12,409	8.06	0.12
Revatio	$18,707.61	$1,558.97		$17.32	$41,617	2.22	0.45
Sovaldi			$16,843.18	$187.15	$812,500	48.24	0.02
Tecfidera	$63,857.73	$5,321.48		$88.69	$48,893	0.77	1.31
Tresiba	$1,852.70	$154.39		$154.39	$29,023	15.67	0.06
Truvada	$18,702.39	$1,558.53		$51.95	$447,758	23.94	0.04
Xarelto	$4,495.76	$374.65		$12.49	$165,822	36.88	0.03
Zetia	$3,382.19	$281.85		$9.39	$165,822	49.03	0.02
Zytiga	$74,685.00	$6,223.75		$51.86	$23,243	0.31	3.21

Source: Author's calculations.

Table 9: Presumed Cost Per Patient Savings from a Brick-and-Mortar Canadian Pharmacy Relative to the Cost of Treating an Adverse Event

Drugs	B&M savings per patient: yearly	B&M savings per patient: monthly	B&M savings per patient: per episode	US Price less B&M Canadian Price (per unit)	Cost of Treating Adverse Event per Patient	Number of Years of Savings needed to cover Adverse Event	Percent of Adverse Event Treatment Covered by Annual Savings
Abilify	$9,004.23	$750.35		$25.01	$64,729	7.19	0.14
Actos	$5,722.84	$476.90		$15.90	$165,822	28.98	0.03
Advair	$3,438.61	$286.55		$286.55	$11,097	3.23	0.31
Albenza			$50,021.87	$208.42	$55,085	1.10	0.91
Ampyra	$23,367.67	$1,947.31		$32.46	$42,134	2.09	0.48
Crestor	$1,494.40	$124.53		$4.15	$165,822	110.96	0.01
Enbrel	$34,379.70	$2,864.98		$716.24	$6,699	0.19	5.13
EpiPen			$168.54	$168.54	$4719	28.00	0.04
Gilenya	$58,222.00	$4,851.83		$161.73	$42,134	0.84	1.19
Harvoni			$17,604.88	$195.61	$812,500	46.15	0.02
Januvia	$3,731.76	$310.98		$10.37	$29,023	7.78	0.13
Lipitor	$4,808.96	$400.75		$13.36	$165,822	34.48	0.03
Nexium	$922.76	$76.90		$2.56	$93,966	101.83	0.01
Orencia	$18,260.08	$1,521.67		$380.42	$6,699	0.37	2.73
Otezla	$22,343.41	$1,861.95		$31.03	$6,699	0.30	3.34
Premarin	$1,540.55	$128.38		$4.28	$12,409	8.05	0.12
Revatio	$16,055.72	$1,337.98		$14.87	$41,617	2.59	0.39
Sovaldi			$28,662.91	$318.48	$812,500	28.35	0.04
Tecfidera	$65,233.44	$5,436.12		$90.60	$42,134	0.75	1.33
Tresiba	$1,826.32	$152.19		$152.19	$29,023	15.89	0.06
Truvada	$7,854.39	$654.53		$21.82	$447,758	57.01	0.02
Xarelto	$3,797.23	$316.44		$10.55	$165,822	43.67	0.02
Zetia	$3,230.80	$269.23		$8.97	$165,822	51.33	0.02
Zytiga	$72,093.12	$6,007.76		$50.06	$23,243	0.32	3.10

Source: Author's calculations.

Presumed Cost Savings for a "Representative State"

Given that the majority of importation proposals are presented at the state level, it is worthwhile to consider the financial implications for a "Representative State". Recognizing that this "Representative State" correlates to 1/50th of the population of the United States and that some states will be larger and others smaller, it is still illustrative to consider the implications. The cost-versus-savings calculations for a "Representative State" are presented in Tables 10 and 11, below. Table 10 depicts the presumed savings from Online Suppliers, while Table 11 depicts the presumed savings from a Brick-and-Mortar Pharmacy.

Number of Patients The population of a "representative state" is assumed to be 1/50th of the population of the United States, approximately 6,540,000 people. The number of patients for each condition considered here is assumed to be 1/50th of the U.S. patient population suffering from the named condition.

Covered Patients In order to estimate the number of "covered patients" in a "representative state", it is assumed that 20% of the impacted patient population will enroll in the state program. This fraction was utilized because approximately one in five individuals in the U.S. is currently covered by Medicaid.[5]

Total Presumed Cost Savings The total amount of presumed cost savings is calculated by multiplying the number of covered patients by the presumed cost savings (either per year or per episode). Again, this number may be an overestimation which again biases the analysis against a finding of the elimination of all cost savings.

Cost of Treating an Adverse Medical Event Estimates of the cost of treating an adverse medical event were gleaned from medical journals and government sources. These are presented and detailed in Appendix C.

Number of Adverse Events Covered by Presumed Savings This number corresponds to the maximum number of adverse events that could be covered through by the expenditure of the presumed cost savings. It is calculated by dividing the total presumed savings by the cost of treating an adverse event. That is, this number represents the number of patients that would be covered by the State's presumed savings, in the case of an adverse event. These numbers range from a low of 0.59 adverse events for patients in the case of Nexium, to 24,318 adverse events for patients in the case of Advair. That is, the State's cost savings would be exhausted before treating one adverse medical event in the case of Nexium, and after more than 24,000 patients in the case of Advair.

Adverse Events would exhaust presumed savings after covering this share of Covered Patients If the presumed cost savings were exhausted covering adverse events, it is important to know not only how many patients could be covered, but the share of patients enrolled in the plan taking a particular drug. This share is calculated by dividing the number of adverse events covered by presumed savings by the number of covered patients. In the case of Online Suppliers, this

[5] This fraction can easily be changed if other assumptions are more defensible or appropriate for this calculation. In addition, if needed, it should be possible to make the calculations for a specific state.

number ranges from 0.95% (Crestor) to 564% (Enbrel). In the case of a Brick-and-Mortar Pharmacy, this number ranges from 0.90% (Crestor) to 513% (Enbrel). From both sources, if an adverse medical event affected less than 1% of all patients taking Crestor, the entire presumed cost savings would be wiped out. Alternatively, one can think of this as the share of counterfeit drugs that would wipe out all cost savings from an importation program.

Cost of treating an Adverse Event in 100% of Covered Patients The cost of treating an adverse medical event in 100% of covered patients taking a particular drug is calculated by multiplying the cost of treating an adverse event by the total number of covered patients. This number ranges from approximately $452,000 to more than $28.5 billion dollars.

Losses from treating adverse events in 100% of Covered Patients less Presumed Cost Savings Finally, the extent to which the cost of treating an adverse event in 100% of covered patients exceeds the presumed cost savings is calculated. The overage between the cost of treating an adverse medical event in 100% of the covered population and the presumed cost savings comes from subtracting the presumed cost savings from the cost of treating an adverse event in 100% of covered patients. In all but six cases (for three conditions) the cost of treatment far exceeds the presumed cost savings. The presumed savings is dwarfed by the potential cost of treating adverse medical events. These estimates range from savings of $60 million to losses of $28 billion.

Losses from treating adverse events in 10% of Covered Patients beyond Presumed Cost Savings Fortunately, it is highly unlikely that 100% of covered patients will experience an adverse medical event. Assuming that only 10% of drugs are counterfeit and result in an adverse event, approximately half of the 24 drugs will result in a situation in which the presumed savings is eliminated by the cost of treating an adverse event. However, these are the drugs in which the losses greatly exceed the potential savings.

All of these calculations are presented in Table 10 (online suppliers) and Table 11 (brick-and-mortar), below. The calculations are included for the subset of 24 drugs for which all information is available.

Online Suppliers In the case of online suppliers, the annual presumed savings fails to cover the treatment of an adverse event for 18 of the 24 drugs (75%). The calculations indicate that these ratios range from 0.01 for Crestor to 5.65 for Enbrel.

Brick-and-Mortar Pharmacies In the case of online suppliers, the annual presumed savings fails to cover the treatment of an adverse event for 18 of the 24 drugs (75%). The calculations indicate that these ratios range from 0.01 for Crestor to 5.13 for Enbrel.

"Representative State" Adverse Medical Events Takeaway Regardless of whether one's drugs are obtained from a Canadian online supplier or a brick-and-mortar Canadian pharmacy, in three out of four cases, the annual presumed savings for a "Representative State" fails to cover the costs of an adverse medical event. Again, for the few drugs for which the savings exceed the cost of treating an adverse medical event, the expense of an adverse medical event is modest (less than $50,000 per patient), while, for the majority of drugs, the cost of treating an adverse

event will significantly exceed $50,000 and may reach more than $800,000. Importantly, for this selection of 24 drugs, the cost savings will be completely eliminated if a mere 3.2% of imported drugs are counterfeit for a brick-and-mortar pharmacy or 3.5% from a Canadian online supplier.

Table 10: Presumed Online Cost Savings for a "Representative State" relative to Cost of an Adverse Medical Event

Drugs	Savings per year	Savings per episode	Number of Patients *	Covered Patients ♠	Total Presumed Savings ♦	Cost of Treating an Adverse Event per patient	Number of Adverse Events Covered by Presumed Savings⅀	Adverse Events would exhaust presumed savings after covering this share of Covered Patients ⏚	Cost of treating an Adverse Event in 100% of Covered Patients Δ	Losses from treating adverse events in 100% of Covered Patients beyond Presumed Cost Savings ☋	Losses from treating adverse events in 10% of Covered Patients beyond Presumed Cost Savings
Abilify	$10,270.54		29,192	5838	$59,963,520.74	$64,729	926.38	15.87%	$377,913,793.60	($317,950,272.86)	$22,172,141.38
Actos	$6,931.29		606,000	121200	$840,072,348.00	$165,822	5066.11	4.18%	$20,097,626,400.00	($19,257,554,052.00)	($1,169,690,292.00)
Advair	$3,978.57		392,400	78480	$312,238,173.60	$11,097	28137.17	35.85%	$870,892,560.00	($558,654,386.40)	$225,148,917.60
Albenza		$50,450.40	41	8	$413,693.28	$55,085	7.51	91.59%	$451,697.00	($38,003.72)	$368,523.58
Ampyra	$23,560.40		20,000	4000	$94,241,600.00	$48,893	1927.51	48.19%	$195,572,000.00	($101,330,400.00)	$74,684,400.00
Crestor	$1,580.07		860,000	172000	$271,772,040.00	$165,822	1638.94	0.95%	$28,521,384,000.00	($28,249,611,960.00)	($2,580,366,360.00)
Enbrel	$37,823.70		3,490	698	$26,400,942.60	$6,699	3941.03	564.62%	$4,675,902.00	$21,725,040.60	$25,933,352.40
EpiPen		$171.53	131,200	26240	$4,500,947.20	$4,719	953.79	3.63%	$123,826,560.00	($119,325,612.80)	($7,881,708.80)
Gilenya	$55,650.44		20,000	4000	$222,601,760.00	$48,893	4552.83	113.82%	$195,572,000.00	$27,029,760.00	$203,044,560.00
Harvoni		$34,864.52	48,000	9600	$334,699,392.00	$812,500	411.94	4.29%	$7,800,000,000.00	($7,465,300,608.00)	($445,300,608.00)
Januvia	$4,777.35		606,000	121200	$579,014,820.00	$29,023	19950.21	16.46%	$3,517,587,600.00	($2,938,572,780.00)	$227,256,060.00
Lipitor	$4,708.92		860,000	172000	$809,934,240.00	$165,822	4884.36	2.84%	$28,521,384,000.00	($27,711,449,760.00)	($2,042,204,160.00)
Nexium	$1,655.49		300	60	$99,329.40	$93,966	1.06	1.76%	$5,637,960.00	($5,538,630.60)	($464,466.60)
Orencia	$32,467.60		3,490	698	$22,662,384.80	$6,699	3382.95	484.66%	$4,675,902.00	$17,986,482.80	$22,194,794.60
Otezla	$24,933.99		3,490	698	$17,403,925.02	$6,699	2597.99	372.20%	$4,675,902.00	$12,728,023.02	$16,936,334.82
Premarin	$1,540.51		204,000	40800	$62,852,808.00	$12,409	5065.10	12.41%	$506,287,200.00	($443,434,392.00)	$12,224,088.00
Revatio	$18,707.61		4,000	800	$14,966,088.00	$41,617	359.61	44.95%	$33,293,600.00	($18,327,512.00)	$11,636,728.00
Sovaldi		$16,843.18	48,000	9600	$161,694,528.00	$812,500	199.01	2.07%	$7,800,000,000.00	($7,638,305,472.00)	($618,305,472.00)
Tecfidera	$63,857.73		20,000	4000	$255,430,920.00	$48,893	5224.28	130.61%	$195,572,000.00	$59,858,920.00	$235,873,720.00
Tresiba	$1,852.70		606,000	121200	$224,547,240.00	$29,023	7736.87	6.38%	$3,517,587,600.00	($3,293,040,360.00)	($127,211,520.00)
Truvada	$18,702.39		22,000	4400	$82,290,516.00	$447,758	183.78	4.18%	$1,970,135,200.00	($1,887,844,684.00)	($114,723,004.00)
Xarelto	$4,495.76		860,000	172000	$773,270,720.00	$165,822	4663.26	2.71%	$28,521,384,000.00	($27,748,113,280.00)	($2,078,867,680.00)
Zetia	$3,382.19		860,000	172000	$581,736,680.00	$165,822	3508.20	2.04%	$28,521,384,000.00	($27,939,647,320.00)	($2,270,401,720.00)
Zytiga	$74,685.00		3,671	734	$54,833,727.00	$23,243	2359.15	321.32%	$17,065,010.60	$37,768,716.40	$53,127,225.94

* The population of a "representative state" is assumed to be 1/50th of the population of the United States, approximately 6,540,000 people. The number of patients for each condition considered here is assumed to be 1/50th of the U.S. patient population.

♠ The number of "covered patients" is assumed to be 20% of the patient population in a "representative state". This fraction was utilized because approximately one in five individuals in the U.S. is covered by Medicaid.

♦ This number comes from multiplying the number of covered patients by the savings (either per year or per episode).

⅀ This number comes from dividing the total presumed savings by the cost of treating an adverse event.

⏚ This number comes from dividing the number of adverse events covered by presumed savings by the number of covered patients.

Δ This number comes from multiplying the cost of treating an adverse event by the total number of covered patients.

☋ This number comes from subtracting the presumed cost savings from the cost of treating an adverse event in 100% of covered patients.

Source: Author's calculations.

Table 11: Presumed Brick-&-Mortar Cost Savings for a "Representative State" relative to Cost of an Adverse Medical Event

Drugs	Savings per year	Savings per episode	Number of Patients *	Covered Patients ♠	Total Presumed Savings ♦	Cost of Treating an Adverse Event	Number of Adverse Events Covered by Presumed Savings⇟	Adverse Events would exhaust presumed savings after covering this share of Covered Patients⇣	Cost of treating an Adverse Event in 100% of Covered Patients Δ	Losses from treating adverse events in 100% of Covered Patients beyond Presumed Cost Savings ☋	Losses from treating adverse events in 10% of Covered Patients beyond Presumed Cost Savings
Abilify	$9,004.23		29,192	5838	$52,570,296.43	$64,729	812.16	13.91%	$377,913,793.60	($325,343,497.17)	$14,778,917.07
Actos	$5,722.84		606,000	121200	$693,608,208.00	$165,822	4182.85	3.45%	$20,097,626,400.00	($19,404,018,192.00)	($1,316,154,432.00)
Advair	$3,438.61		392,400	78480	$269,862,112.80	$11,097	24318.47	30.99%	$870,892,560.00	($601,030,447.20)	$182,772,856.80
Albenza		$50,021.87	41	8	$410,179.33	$55,085	7.45	90.81%	$451,697.00	($41,517.67)	$365,009.63
Ampyra	$23,367.67		20,000	4000	$93,470,680.00	$48,893	1911.74	47.79%	$195,572,000.00	($102,101,320.00)	$73,913,480.00
Crestor	$1,494.40		860,000	172000	$257,036,800.00	$165,822	1550.08	0.90%	$28,521,384,000.00	($28,264,347,200.00)	($2,595,101,600.00)
Enbrel	$34,379.70		3,490	698	$23,997,030.60	$6,699	3582.18	513.21%	$4,675,902.00	$19,321,128.60	$23,529,440.40
EpiPen		$168.54	131,200	26240	$4,422,489.60	$4,719	937.17	3.57%	$123,826,560.00	($119,404,070.40)	($7,960,166.40)
Gilenya	$58,222.00		20,000	4000	$232,888,000.00	$48,893	4763.22	119.08%	$195,572,000.00	$37,316,000.00	$213,330,800.00
Harvoni		$17,604.88	48,000	9600	$169,006,848.00	$812,500	208.01	2.17%	$7,800,000,000.00	($7,630,993,152.00)	($610,993,152.00)
Januvia	$3,731.76		606,000	121200	$452,289,312.00	$29,023	15583.82	12.86%	$3,517,587,600.00	($3,065,298,288.00)	$100,530,552.00
Lipitor	$4,808.96		860,000	172000	$827,141,120.00	$165,822	4988.13	2.90%	$28,521,384,000.00	($27,694,242,880.00)	($2,024,997,280.00)
Nexium	$922.76		300	60	$55,365.60	$93,966	0.59	0.98%	$5,637,960.00	($5,582,594.40)	($508,430.40)
Orencia	$18,260.08		3,490	698	$12,745,535.84	$6,699	1902.60	272.58%	$4,675,902.00	$8,069,633.84	$12,277,945.64
Otezla	$22,343.41		3,490	698	$15,595,700.18	$6,699	2328.06	333.53%	$4,675,902.00	$10,919,798.18	$15,128,109.98
Premarin	$1,540.55		204,000	40800	$62,854,440.00	$12,409	5065.23	12.41%	$506,287,200.00	($443,432,760.00)	$12,225,720.00
Revatio	$16,055.72		4,000	800	$12,844,576.00	$41,617	308.64	38.58%	$33,293,600.00	($20,449,024.00)	$9,515,216.00
Sovaldi		$28,662.91	48,000	9600	$275,163,936.00	$812,500	338.66	3.53%	$7,800,000,000.00	($7,524,836,064.00)	($504,836,064.00)
Tecfidera	$65,233.44		20,000	4000	$260,933,760.00	$48,893	5336.83	133.42%	$195,572,000.00	$65,361,760.00	$241,376,560.00
Tresiba	$1,826.32		606,000	121200	$221,349,984.00	$29,023	7626.71	6.29%	$3,517,587,600.00	($3,296,237,616.00)	($130,408,776.00)
Truvada	$7,854.39		22,000	4400	$34,559,316.00	$447,758	77.18	1.75%	$1,970,135,200.00	($1,935,575,884.00)	($162,454,204.00)
Xarelto	$3,797.23		860,000	172000	$653,123,560.00	$165,822	3938.70	2.29%	$28,521,384,000.00	($27,868,260,440.00)	($2,199,014,840.00)
Zetia	$3,230.80		860,000	172000	$555,697,600.00	$165,822	3351.17	1.95%	$28,521,384,000.00	($27,965,686,400.00)	($2,296,440,800.00)
Zytiga	$72,093.12		3,671	734	$52,930,768.70	$23,243	2277.28	310.17%	$17,065,010.60	$35,865,758.10	$51,224,267.64

* The population of a "representative state" is assumed to be 1/50th of the population of the United States, approximately 6,540,000 people. The number of patients for each condition considered here is assumed to be 1/50th of the U.S. patient population.

♠ The number of "covered patients" is assumed to be 20% of the patient population in a "representative state". This fraction was utilized because approximately one in five individuals in the U.S. is covered by Medicaid.

♦ This number comes from multiplying the number of covered patients by the savings (either per year or per episode).

⇟ This number comes from dividing the total presumed savings by the cost of treating an adverse event.

⇣ This number comes from dividing the number of adverse events covered by presumed savings by the number of covered patients.

Δ This number comes from multiplying the cost of treating an adverse event by the total number of covered patients.

☋ This number comes from subtracting the presumed cost savings from the cost of treating an adverse event in 100% of covered patients.

Source: Author's calculations.

Presumed Cost Savings for a "Representative State" relative to the Cost of "Testing into Safety"

The cost of testing the authenticity and quality of the imported medicine is based on the estimated cost provided by NMS Labs. As described earlier, Table 2 provides the cost of the different types of testing a single sample to ensure the quality of each drug. Utilizing this information to determine the savings or dissavings available to a "Representative State", the calculations are presented for 24 drugs in Tables 12 and 13, below, representing the online and brick-and-mortar estimates respectively.

It is important to recognize that the testing estimates provided here only include the cost of the tests. The cost of purchasing the requisite number of samples needed for testing is not included in these cost estimates. Again, this assumption biases the results against a finding of the elimination of the presumed cost savings.

Number of Samples that could be Tested, Exhausting the Presumed Savings The maximum number of doses that could be tested while exhausting the presumed cost savings is calculated by dividing the total presumed savings by the cost of testing a specific drug.

Presumed Savings Less the Cost of Testing with a 90% Confidence Level and 90% Reliability In order to ensure the quality of a particular drug with a 90% confidence level and 90% reliability, 22 samples must be tested. The difference in the cost of testing 22 samples of the imported drugs and the presumed cost savings available from importation is calculated by subtracting the presumed cost savings from the cost of testing all imported doses.

Presumed Savings Less the Cost of Testing with a 99.99% Confidence Level and 99.99% Reliability In order to ensure the quality of a particular drug with a 99.99% confidence level and 99.99% reliability, 92,099 samples must be tested. The difference in the cost of testing 92,099 samples of the imported drugs and the presumed cost savings available from importation is calculated by subtracting the presumed cost savings from the cost of testing all imported doses.

Presumed Savings Less the Cost of Testing with a 99.999% Confidence Level and 99.999% Reliability In order to ensure the quality of a particular drug with a 99.999% confidence level and 99.999% reliability, 1,151,287 samples must be tested. The difference in the cost of testing 1,151,287 samples of the imported drugs and the presumed cost savings available from importation is calculated by subtracting the presumed cost savings from the cost of testing all imported doses.

Online Suppliers In the case of online suppliers, to ensure the quality of a particular drug with a 90% confidence level and 90% reliability, 22 samples must be tested and the savings exceed the cost of testing for all 24 drugs. In order to ensure the quality of a particular drug with a 99.99% confidence level and 99.99% reliability, 92,099 samples must be tested and the savings exceeds the cost of testing for 8 drugs. In order to ensure the quality of a particular drug with a 99.999% confidence level and 99.999% reliability, 1,151,287 samples must be tested and presumed savings are dwarfed by the cost of testing for all drugs. The cost of testing ranges

from 2.43 times the presumed savings for Advair to 34,770 times the presumed savings for Orencia. That is, the cost of testing ranges from 243% the presumed savings (Advair) to 3,477,079% the presumed savings (Orencia).

Brick-and-Mortar Pharmacies In the case of brick-and-mortar pharmacies, to ensure the quality of a particular drug with a 90% confidence level and 90% reliability, 22 samples must be tested and the savings exceed the cost of testing for 23 of the 24 drugs. In order to ensure the quality of a particular drug with a 99.99% confidence level and 99.99% reliability, 92,099 samples must be tested and the savings exceeds the cost of testing for 9 drugs. In order to ensure the quality of a particular drug with a 99.999% confidence level and 99.999% reliability, 1,151,287 samples must be tested and presumed savings are dwarfed by the cost of testing for all drugs. The cost of testing ranges from 2.48 times the presumed savings for Nexium to 62,382 times the presumed savings for Orencia.

"Representative State" Testing into Safety Takeaway Regardless of whether one's drugs are obtained from a Canadian online supplier or a brick-and-mortar Canadian pharmacy, in all cases, the annual presumed savings for a "Representative State" fails to cover the costs of testing a drug into safety with 99.999% confidence and 99.999% reliability. In the case of a lower level of quality assurance, there are a few drugs for which the presumed savings would exceed the cost of testing. If one is willing to accept the risk of a 90% confidence level with 90% reliability, then the presumed savings will (in all but one case) exceed the cost of testing for both online suppliers and brick-and-mortar Canadian pharmacies.

Table 12: Presumed Online Cost Savings for a "Representative State" relative to the Cost of Testing

Drugs	Savings per year	Savings per episode	Number of Patients *	Covered Patients ♠	Total Presumed Savings ♦	Cost of Quality Testing (per sample)	Number of samples that could be tested, exhausting the Presumed Savings⁜	Online Presumed Savings Less Cost of Testing with 90% confidence and 90% reliability (22 samples)	Online Presumed Savings Less Cost of Testing with 99.99% confidence and 99.99% reliability (92,099 samples)	Online Presumed Savings Less Cost of Testing with 99.999% confidence and 99.999% reliability (1,151,287 samples)
Abilify	$9,004.23		29,192	5838	$59,963,520.74	$4,000	14991	$59,875,520.74	($308,432,479.26)	($4,545,184,479.26)
Actos	$5,722.84		606,000	121200	$840,072,348.00	$2,500	336029	$840,017,348.00	$609,824,848.00	($2,038,145,152.00)
Advair	$3,438.61		392,400	78480	$312,238,173.60	$4,100	76156	$312,147,973.60	($65,367,726.40)	($4,408,038,526.40)
Albenza		$50,021.87	41	8	$413,693.28	$2,500	165	$358,693.28	($229,833,806.72)	($2,877,803,806.72)
Ampyra	$23,367.67		20,000	4000	$94,241,600.00	$2,500	37697	$94,186,600.00	($136,005,900.00)	($2,783,975,900.00)
Crestor	$1,494.40		860,000	172000	$271,772,040.00	$2,500	108709	$271,717,040.00	$41,524,540.00	($2,606,445,460.00)
Enbrel	$34,379.70		3,490	698	$26,400,942.60	$2,800	9429	$26,339,342.60	($231,476,257.40)	($3,197,202,657.40)
EpiPen		$168.54	131,200	26240	$4,500,947.20	$2,800	1607	$4,439,347.20	($253,376,252.80)	($3,219,102,652.80)
Gilenya	$58,222.00		20,000	4000	$222,601,760.00	$2,500	89041	$222,546,760.00	($7,645,740.00)	($2,655,615,740.00)
Harvoni		$17,604.88	48,000	9600	$334,699,392.00	$2,500	133880	$334,644,392.00	$104,451,892.00	($2,543,518,108.00)
Januvia	$3,731.76		606,000	121200	$579,014,820.00	$2,500	231606	$578,959,820.00	$348,767,320.00	($2,299,202,680.00)
Lipitor	$4,808.96		860,000	172000	$809,934,240.00	$2,500	323974	$809,879,240.00	$579,686,740.00	($2,068,283,260.00)
Nexium	$922.76		300	60	$99,329.40	$3,000	33	$33,329.40	($276,197,670.60)	($3,453,761,670.60)
Orencia	$18,260.08		3,490	698	$22,662,384.80	$2,800	8094	$22,600,784.80	($235,214,815.20)	($3,200,941,215.20)
Otezla	$22,343.41		3,490	698	$17,403,925.02	$2,500	6962	$17,348,925.02	($212,843,574.98)	($2,860,813,574.98)
Premarin	$1,540.55		204,000	40800	$62,852,808.00	$2,600	24174	$62,795,608.00	($176,604,592.00)	($2,930,493,392.00)
Revatio	$16,055.72		4,000	800	$14,966,088.00	$3,600	4157	$14,886,888.00	($316,590,312.00)	($4,129,667,112.00)
Sovaldi		$28,662.91	48,000	9600	$161,694,528.00	$2,500	64678	$161,639,528.00	($68,552,972.00)	($2,716,522,972.00)
Tecfidera	$65,233.44		20,000	4000	$255,430,920.00	$2,500	102172	$255,375,920.00	$25,183,420.00	($2,622,786,580.00)
Tresiba	$1,826.32		606,000	121200	$224,547,240.00	$2,800	80195	$224,485,640.00	($33,329,960.00)	($2,999,056,360.00)
Truvada	$7,854.39		22,000	4400	$82,290,516.00	$2,500	32916	$82,235,516.00	($147,956,984.00)	($2,795,926,984.00)
Xarelto	$3,797.23		860,000	172000	$773,270,720.00	$2,500	309308	$773,215,720.00	$543,023,220.00	($2,104,946,780.00)
Zetia	$3,230.80		860,000	172000	$581,736,680.00	$2,500	232695	$581,681,680.00	$351,489,180.00	($2,296,480,820.00)
Zytiga	$72,093.12		3,671	734	$54,833,727.00	$2,500	21933	$54,778,727.00	($175,413,773.00)	($2,823,383,773.00)

⁜ This number is calculated by dividing the total presumed savings by the cost of testing.
⸸ This number is calculated by dividing the number of doses that could be tested (exhausting the presumed cost savings) by the total number of imported doses.
ↀ This number is calculated by multiplying the cost of testing by the total number of imported doses.
♦ This number is calculated by subtracting the presumed cost savings from the cost of testing all imported doses.
Source: Author's calculations.

Table 13: Presumed Brick-&-Mortar Cost Savings for a "Representative State" relative to the Cost of Testing

Drugs	Savings per year	Savings per episode	Number of Patients *	Covered Patients ♠	Total Presumed Savings ♦	Cost of Quality Testing (per sample)	Number of units (samples) that could be tested, exhausting the Presumed Savings⸸	B&M Presumed Savings Less Cost of Testing with 90% confidence and 90% reliability (22 samples)	B&M Presumed Savings Less Cost of Testing with 99.99% confidence and 99.99% reliability (92,099 samples)	B&M Presumed Savings Less Cost of Testing with 99.999% confidence and 99.999% reliability (1,151,287 samples)
Abilify	$10,270.54		29,192	5838	$59,963,520.74	$4,000	13143	$52,482,296.43	($315,825,703.57)	($4,552,577,703.57)
Actos	$6,931.29		606,000	121200	$840,072,348.00	$2,500	277443	$693,553,208.00	$463,360,708.00	($2,184,609,292.00)
Advair	$3,978.57		392,400	78480	$312,238,173.60	$4,100	65820	$269,771,912.80	($107,743,787.20)	($4,450,414,587.20)
Albenza		$50,450.40	41	8	$413,693.28	$2,500	164	$355,179.33	($229,837,320.67)	($2,877,807,320.67)
Ampyra	$23,560.40		20,000	4000	$94,241,600.00	$2,500	37388	$93,415,680.00	($136,776,820.00)	($2,784,746,820.00)
Crestor	$1,580.07		860,000	172000	$271,772,040.00	$2,500	102815	$256,981,800.00	$26,789,300.00	($2,621,180,700.00)
Enbrel	$37,823.70		3,490	698	$26,400,942.60	$2,800	8570	$23,935,430.60	($233,880,169.40)	($3,199,606,569.40)
EpiPen		$171.53	131,200	26240	$4,500,947.20	$2,800	1579	$4,360,889.60	($253,454,710.40)	($3,219,181,110.40)
Gilenya	$55,650.44		20,000	4000	$222,601,760.00	$2,500	93155	$232,833,000.00	$2,640,500.00	($2,645,329,500.00)
Harvoni		$34,864.52	48,000	9600	$334,699,392.00	$2,500	67603	$168,951,848.00	($61,240,652.00)	($2,709,210,652.00)
Januvia	$4,777.35		606,000	121200	$579,014,820.00	$2,500	180916	$452,234,312.00	$222,041,812.00	($2,425,928,188.00)
Lipitor	$4,708.92		860,000	172000	$809,934,240.00	$2,500	330856	$827,086,120.00	$596,893,620.00	($2,051,076,380.00)
Nexium	$1,655.49		300	60	$99,329.40	$3,000	18	($10,634.40)	($276,241,634.40)	($3,453,805,634.40)
Orencia	$32,467.60		3,490	698	$22,662,384.80	$2,800	4552	$12,683,935.84	($245,131,664.16)	($3,210,858,064.16)
Otezla	$24,933.99		3,490	698	$17,403,925.02	$2,500	6238	$15,540,700.18	($214,651,799.82)	($2,862,621,799.82)
Premarin	$1,540.51		204,000	40800	$62,852,808.00	$2,600	24175	$62,797,240.00	($176,602,960.00)	($2,930,491,760.00)
Revatio	$18,707.61		4,000	800	$14,966,088.00	$3,600	3568	$12,765,376.00	($318,711,824.00)	($4,131,788,624.00)
Sovaldi		$16,843.18	48,000	9600	$161,694,528.00	$2,500	110066	$275,108,936.00	$44,916,436.00	($2,603,053,564.00)
Tecfidera	$63,857.73		20,000	4000	$255,430,920.00	$2,500	104374	$260,878,760.00	$30,686,260.00	($2,617,283,740.00)
Tresiba	$1,852.70		606,000	121200	$224,547,240.00	$2,800	79054	$221,288,384.00	($36,527,216.00)	($3,002,253,616.00)
Truvada	$18,702.39		22,000	4400	$82,290,516.00	$2,500	13824	$34,504,316.00	($195,688,184.00)	($2,843,658,184.00)
Xarelto	$4,495.76		860,000	172000	$773,270,720.00	$2,500	261249	$653,068,560.00	$422,876,060.00	($2,225,093,940.00)
Zetia	$3,382.19		860,000	172000	$581,736,680.00	$2,500	222279	$555,642,600.00	$325,450,100.00	($2,322,519,900.00)
Zytiga	$74,685.00		3,671	734	$54,833,727.00	$2,500	21172	$52,875,768.70	($177,316,731.30)	($2,825,286,731.30)

⸸ This number is calculated by dividing the total presumed savings by the cost of testing.
⸸ This number is calculated by dividing the number of doses that could be tested (exhausting the presumed cost savings) by the total number of imported doses.
ᔓ This number is calculated by multiplying the cost of testing by the total number of imported doses.
♦ This number is calculated by subtracting the presumed cost savings from the cost of testing all imported doses.
Source: Author's calculations.

V. ISSUES AFFECTING COST NOT STUDIED

There are several issues that will certainly impact the cost of an importation program that are not included in this study. These issues are beyond the scope of this work, but will undoubtedly reduce the estimated cost savings. These include: shortages, quality controls, legal liability, post-sale pharmacovigilance, and the implementation cost. Each is briefly addressed here in turn.

Shortages

Importation schemes will be unable to supply the quantities of drugs demanded by U.S. consumers and shortages are virtually guaranteed to occur. Fundamentally, Canada does not have a sufficient supply of drugs to satisfy American demand. Canada's population is just one-ninth of the US population. That is, 37 million people, compared to 318 million in the United States. Annually, 627 million prescriptions are dispensed in Canada, while 4.4 billion are dispensed in the US. If 100% of US prescriptions were filled in Canada, the annual Canadian drug supply would be exhausted in just 52 days. (Shepherd, 2018) (link here)

In addition, it is important to recognize that drug shortages are already a significant problem in Canada (DrugShortagesCanada, 2019) (link here). Drug shortages have become a chronic problem for the Canadian healthcare system. In a single week in September 2018, 25 drugs were added to the drug shortage list (Crowe, 2018). "As Canada continues to grapple with a relentless stream of drug shortages, one in four adults in the country has either personally been affected in the last three years or knows someone who has, according to a survey commissioned by the Canadian Pharmacists Association." (Ireland, 2018) (link here)

The Canadian market receives a supply of medicines designed to meet the needs of Canada. There will not be sufficient quantities to export to the United States. Moreover, one can imagine backlash against such efforts as Canadians begin to experience shortages of drugs because the supply went to the U.S.

Quality Controls in a Foreign Country

The U.S. Food and Drug Administration expends tremendous resources in their efforts to maintain the safety and security of the pharmaceutical supply chain. It would be impossible for them, or a state entity, to enforce quality controls in Canada. They do not have the resources or the jurisdiction to do so. Moreover, given the global nature of the international pharmaceutical market, enforcing quality controls in Canada would be insufficient. The efforts would need to be global, extending to every country producing or transshipping drugs.

Legal Liability

Given the risks of obtaining a counterfeit drug and the associated medical consequences, states must consider their legal liability. Since the medicines are obtained outside of the regulated supply chain, the pharmaceutical manufacturer is unable to guarantee the quality of their products. Arguably, they may not be held responsible for the quality of imported drugs. If the legal liability rests with the state, the expense of insuring against adverse events must be incorporated into the cost of an importation program.

Post-Sale Pharmacovigilance

Post-sale pharmacovigilance is a critical element of safeguarding the pharmaceutical supply chain and ensuring that medicines are safe and effective. Given that the drugs are purchased outside of the legitimate supply chain the manufacturer has lost the ability to guarantee the quality or the responsibility for pharmacovigilance. The question remains "who is responsible for post-sale pharmacovigilance?" The costs associated with establishing such a program must be accounted for, and again, will reduce the estimated cost savings.

Implementation cost

The implementation costs of an importation program will increase the cost of the program and reduce the estimated savings. According to George Karavetsos, the former head of the FDA's Office of Criminal Investigation, the implementation costs of a state importation program will be significant. He notes that "our drug supply is safe because of efforts in the area of licensing and enforcement of the FDA. Just the enforcement division alone, which [he] ran, has an annual budget of over $75 million dollars. The division of the FDA that conducts inspections and quality initiatives has a budget of at least three times that." (Karavetsos, 2019) Granted, these figures finance a national program. Nevertheless, a state program will necessarily have to duplicate many of the federal functions and the costs will be in accordance with that.

VII. CONCLUSIONS

This study evaluates the cost savings generated by pharmaceutical importation programs. The focus here is on the potential savings resulting from the purchase of drugs from both an online Canadian supplier and a brick-and-mortar Canadian pharmacy. This analysis is done for a typical patient and also for a "Representative State". Importantly, the analysis incorporates the cost of an adverse medical event as well as the cost of "testing drugs into safety". These data establish that pharmaceutical importation does not ultimately result in cost savings when the expense of treatment failure and quality testing are included in the calculus.

In the case of an online Canadian supplier, for the 24 drugs analyzed, patients would need to acquire the cost savings over a period of up to 111 years to cover the costs of one adverse event. Not surprisingly, for the few drugs for which the savings exceed the cost of treating an adverse

medical event, the expense of an adverse medical event is modest (less than $50,000). For the majority of drugs, the cost of treating an adverse event will significantly exceed $50,000 and may reach more than $800,000. For a "Representative State", in the presence of an adverse medical event, the presumed savings from an online Canadian supplier are exhausted in the treatment of only one patient in the case of Nexium, to 24,318 adverse events for patients in the case of Advair. Further, the analysis shows that the cost of testing (99.999% confidence level with 99.999% reliability) exceeds the presumed cost savings in all cases, from more than two times the presumed costs savings to more than 34,000 times. Importantly, the assumptions underlying this analysis were biased against this finding, resulting in a likely underestimation of the true cost of pharmaceutical importation programs.

The analysis presented for a brick-and-mortar Canadian pharmacy mirrors the results for an online Canadian supplier. Again, the true savings of pharmaceutical importation is evaluated in multiple contexts: relative to the occurrence of an adverse medical event, relative to the cost of testing, on a per-patient basis and for a "Representative State". These data establish that pharmaceutical importation does not ultimately result in cost savings when the expense of treatment failure and quality testing are included in the calculus. For a "Representative State", in the presence of an adverse medical event, the presumed savings from a brick-and-mortar Canadian pharmacy are exhausted in the treatment of only one patient in the case of Nexium and after 28,137 adverse medical events in the case of Advair . Further, the analysis shows that the cost of testing (99.999% confidence level with 99.999% reliability) exceeds the presumed cost savings: testing costs range from 248% the presumed cost savings (Nexium) to 6,238,180% the presumed cost savings (Orencia).

Pharmaceutical importation plans are politically attractive, but realistically dangerous and expensive if implemented safely. The risks seem too great to justify the presumed cost savings that would quickly evaporate in the face of adverse medical events or a serious attempt to truly test the quality of the imported drugs. While purchasing price-controlled medicines from a Canadian supplier does deliver some cost savings, it also involves significant risk. Instead of lowering prices for patients these pharmaceutical importation schemes can be expected to both harm patients and cost them more than the presumed importation savings. Ultimately, the numbers demonstrate that pharmaceutical importation fails to deliver cost savings.

BIBLIOGRAPHY

American College of Rheumatology. "Statistics: Prevalence Statistics," webpost, 2019. Available at: https://www.rheumatology.org/Learning-Center/Statistics/Prevalence-Statistics

American Thoracic Society. "Pulmonary Hypertension," chapter 17 in Breathing in America: Diseases, Progress and Hope, online post, 2010. Available at: https://www.thoracic.org/patients/patient-resources/breathing-in-america/resources/chapter-17-pulmonary-hypertension.pdf

Bentley, T. Scott and Steven J. Phillips. "Milliman Research Report: 2017 U.S. organ and tissue transplant cost estimates and discussion," Milliman, August 2017. Available at: http://www.milliman.com/uploadedFiles/insight/2017/2017-Transplant-Report.pdf

Blume, S.W. and J.R. Curtis. "Medical costs of osteoporosis in the elderly Medicare population," Osteoporosis International, June 2011, vol.22, no 6, pp. 1835-1844. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21165602

Burgos-Pol, R., J.M. Martinex-Sesmero, J.M. Ventura-Cerda, I.Elias, M.T. Caloto, and M.A. Casado. "The Cost of Psoriasis and Psoriatic Arthritis in 5 European countries: A Systematic Review, Actas dermo-sifiliográficas, September 2016, vol. 107, no.7, pp.577-590. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27316590

Center for Disease Control and Prevention (CDC). "Atrial Fibrillation Fact Sheet," webpost, August 22, 2017. Available at: https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_atrial_fibrillation.htm

Centers for Disease Control and Prevention, (CDC). "Attention-Deficit/Hyperactivity Disorder," webpost, September 21, 2018. Available at: https://www.cdc.gov/ncbddd/adhd/data.html

Centers for Disease Control and Prevention (CDC). "Chronic Obstructive Pulmonary Disease (COPD)," webpost, June 5, 2018. Available at: https://www.cdc.gov/copd/data.html

Center for Disease Control and Prevention (CDC). "High Cholesterol Facts," webpost, December 6, 2018. Available at: https://www.cdc.gov/cholesterol/facts.htm

Center for Disease Control and Prevention (CDC). "HIV/AIDS," webpost, November 16, 2018. Available at: https://www.cdc.gov/hiv/statistics/overview/index.html

Center for Disease Control and Prevention (CDC). "HIV Cost-effectiveness," webpost, March 8, 2018. Available at: https://www.cdc.gov/hiv/programresources/guidance/costeffectiveness/index.html

Centers for Disease Control and Prevention. (CDC, National Center for Chronic Disease Prevention and Health Promotion, Division of Diabetes Translation). "National Diabetes Statistics Report, 2017: Estimates of Diabetes and Its Burden in the United States," webpost,

2017. Available at: https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

Center for Disease Control and Prevention (CDC). "United States Cancer Statistics: Data Visualizations," webpost, 2019. Available at: https://gis.cdc.gov/Cancer/USCS/DataViz.html

Center for Disease Control and Prevention (CDC). "Viral Hepatitis," webpost, April 30, 2018. Available at: https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm

Crowe, Kelly. "It's not just the EpiPen. Canada had 25 new drug shortages this week alone," CBC News, September 18, 2018. Available at: https://www.cbc.ca/news/health/second-opinion-drug-shortages180908-1.4815355

Desai, Dimpi, Dhruv Mehta, Priyanka Mathias, Gopal Menon, and Ulrich K. Schubart. "Health Care Utilization and Burden of Diabetic Ketoacidosis in the U.S. Over the Past Decade: A Nationwide Analysis," Diabetes Care, August 2018, no.41, no.8, pp.1631-1638. Available at: http://care.diabetesjournals.org/content/41/8/1631.long

DrugShortagesCanada.ca. Available at: https://www.drugshortagescanada.ca/

Ernstsson, Olivia, Hanna Gyllensten, Kristina Alexanderson, Petter Tinghog, Emille Friberg, and Anders Norfund. "Cost of Illness of Multiple Sclerosis – A Systematic Review," PLOS One, July 13, 2016. Available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0159129

Endocrine Society. "Endocrine Facts and Figures," webpost, 2019. Available at: http://endocrinefacts.org/health-conditions/thyroid/4-hyperthyroidism/

Fair Health Consumer. "Estimate your healthcare expenses," webpost, 2019. Available at: https://www.fairhealthconsumer.org/

Giacomino, Bria, Peter Cram, Mary Vaughan-Sarrazin and Saket Girotra. "Abstract 208: Association of Hospital Prices for Coronary Artery Bypass Graft Surgery with Hospital Quality and Reimbursement," Circulation: Cardiovascular Quality and Outcomes, May 1, 2015, vol.8, no. supplement 2, pg.8. Available at: https://www.ahajournals.org/doi/abs/10.1161/circoutcomes.8.suppl_2.208

GoodRX. Website providing drug pricing information, 2019. Available at: https://www.goodrx.com/

Gottlieb, Scott. "What Trump Should Have Said on Drug Prices," Forbes, webpost, March 4, 2016. Available at: https://www.forbes.com/sites/scottgottlieb/2016/03/04/why-trump-is-wrong-on-drug-prices/#a11a1d72e747

Guarascio, Anthony J., Shauntá M. Ray, Christopher K. Finch and Timothy H. Self. "The Clinical and Economic Burden of Chronic Obstructive Pulmonary Disease in the USA,"

ClinicoEconomics and Outcomes Research, 17 June 2013, vol. 5, pp.235-245. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3694800/

Harding, Anne. "A type of drug used by 50 million Americans has been linked to an increased risk of death," Business Insider, Reuters, webpost, July 5, 2017. Available at: https://www.businessinsider.com/r-heartburn-drugs-tied-to-greater-mortality-2017-7

Ireland, Nicole. "'Unprecedented' drug shortages affecting many Canadians, new survey suggests," webpost, CBC News, December 10, 2018. Available at: https://www.cbc.ca/news/health/canadian-pharmacists-association-drug-shortage-survey-1.4938557

IsraelPharm. "USA vs Canada vs Israel Drug Prices," webpost, 2017. Available at: http://www.israelpharm.com/blog/canada-vs-israel-drug-price-comparison/

Karavetsos, George. Testimony to the Colorado House of Representatives, Denver, Colorado, April 17, 2019.

Kirson, Noam Y., Howard G. Birnbaum, Jasmina I. Ivanova, Tracy Waldman, Matt Schiller, N. Joish Vijay, and Todd Williamson. "Pulmonary Arterial Hypertension (PAH): Direct Cost of Illness in the US Privately Insured Population, Chest Journal, October 2010, vol.138, no.4, Supplement, pp.376A. Available at: https://journal.chestnet.org/article/S0012-3692(16)42051-9/fulltext

Louie, Grant. "Psoriatic Arthritis," Johns Hopkins Arthritis Center, webpost, August 28, 2017. Available at: https://www.hopkinsarthritis.org/arthritis-info/psoriatic-arthritis/

Mariotto, A.B., K.R. Yabroff, Y. Shao, E.J. Feuer, and M.L. Brown. "Projections of the Cost of Cancer Care in the United States: 2010-2020," Journal of the National Cancer Institute, January 19, 2011, vol.103, no.2, pp.117-128. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21228314

Marks Marine Pharmacy. Available at: https://rxcanada4less.com/

Medicaid.gov. "October 2018 Medicaid & CHIP Enrollment Data Highlights," webpost, 2019. Available at: https://www.medicaid.gov/medicaid/program-information/medicaid-and-chip-enrollment-data/report-highlights/index.html

Melly, Ludovic, Gianluca Torregrossa, Timothy Lee, Jean-Luc Jansens, and John D. Puskas. "Fifty years of coronary artery bypass grafting," Journal of Thoracic Disease, March 2018, vol.10, no.3, pp.1960-1967. Available here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5906252/

Minitab. "How Many Samples Do You Need to Be Confident Your Product Is Good?" webpost, July 12, 2017. Available at: https://blog.minitab.com/blog/the-statistical-mentor/how-many-samples-do-you-need-to-be-confident-your-product-is-good

National Academy for State Health Policy (NASHP). "Will States Save by Importing Drugs from Canada? Yes, Here's How," webpost, 2017. Available at: https://nashp.org/wp-content/uploads/2017/11/drug-infographic-2.pdf

National Cancer Institute. "Cancer Prevalence and Cost of Care Projections: Annualized Mean Net Costs of Care per Patient," 2011. Available at: https://costprojections.cancer.gov/annual.costs.html

National Institute of Mental Health. "Schizophrenia," webpost, May 2018. Available at: https://www.nimh.nih.gov/health/statistics/schizophrenia.shtml#part_154880

National Multiple Sclerosis Society. "MS Prevalence," webpost, 2019. Available at: https://www.nationalmssociety.org/About-the-Society/MS-Prevalence

National Osteoporosis Foundation. "NOF Releases Updated Data Detailing the Prevalence of Osteoporosis and Low Bone Mass in the U.S." webpost, June 2, 2014. Available at: https://www.nof.org/news/54-million-americans-affected-by-osteoporosis-and-low-bone-mass/

National Psoriasis Foundation "Statistics," webpost, 2018. Available at: https://www.psoriasis.org/content/statistics

NMS Labs. Available at: https://www.nmslabs.com/

O'Neal, Seth E. and Robert H. Flecker. "Hospitalization Frequency and Charges for Neurocysticercosis, United States, 2003-2012," Emerging Infectious Diseases, June 2015, vol.21, no.6. Available at: https://wwwnc.cdc.gov/eid/article/21/6/14-1324_article

Partnership for Safe Medicines. "Counterfeit Drugs Harm Real People. We're Collecting Their Stories," webpost, May 2019. Available at: https://www.safemedicines.org/victim-tragedies

Patel, D.A., D.A. Holdford, E. Edwards, and N.V. Carroll. "Estimating the Economic Burden of Food-Induced Allergic Reactions and Anaphylaxis in the United States," Journal of Allergy and Clinical Immunology, vol.128, no.1, July 2011, pp.110-115.e5. Available at: https://www.jacionline.org/article/S0091-6749(11)00431-3/pdf

Pharmaceutical Security Institute (PSI). "Counterfeiting Situation: Therapeutic Categories," webpost, 2019. Available at: http://www.psi-inc.org/therapeuticcategories.cfm

Reveille, John D. "Epidemiology of Spondyloarthritis in North America," American Journal of Medical Sciences, April 2011, vol.341, no.4, pp. 284–286. Available at: https://www.sciencedirect.com/science/article/abs/pii/S0002962915313197?via%3Dihub

Rheinstein, Peter H. M.D., J.D., M.S., President, Severn Health Solutions, personal communication with author, February 2019.

Roe, Gina. "Utah insurer plans to send patients to Mexico for cheaper medicine," KUTV.com, webpost, October 29, 2018. Available at: https://kutv.com/news/local/utah-insurer-plans-to-send-patients-to-mexico-for-cheaper-medicine

Selvin, E., A.L. Burnett, and E.A. Platz. "Prevalence and risk factors for erectile dysfunction in the US," American Journal of Medicine, February 2007, vol.120, no.2, pp.151-157. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17275456

Shepherd, Marv "U.S. Drug Importation: Impact on Canada's Prescription Drug Supply," Health Economics and Outcome Research: Open Access, vol.4, no.1, 2018. Available at: http://www.safemedicines.org/wp-content/uploads/2017/08/us-drug-importation-impact-on-canadas-prescription-drug-supply-2471-268X-1000146.pdf

Sun, Lena H. " They went to Mexico for surgery. They came back with a deadly superbug," The Seattle Times, January 23, 2019. Available at: https://www.seattletimes.com/nation-world/they-went-to-mexico-for-surgery-they-came-back-with-a-deadly-superbug/

U.S. Bureau of Labor Statistics. "CPI Inflation Calculator," webpost. Available at: https://www.bls.gov/data/inflation_calculator.htm

U.S. Census Bureau. U.S. and World Population Clock, website. Accessed March 2019. Available at: https://www.census.gov/popclock/

U.S. Food and Drug Administration Office of Criminal Investigations. "April 13, 2018: Canadian Drug Firm Admits Selling Counterfeit and Misbranded Prescription Drugs Throughout the United States," webpost, April 13, 2018. Available here: https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/criminal-investigations/april-13-2018-canadian-drug-firm-admits-selling-counterfeit-and-misbranded-prescription-drugs

Westpak. "Sample Size for Attributes When C=0," webpost. Accessed on May 28, 2019. Available at: https://www.westpak.com/page/resources/calculator/sample-size-for-attributes-when-c-is-zero

Whitehead, Nadia. "Why A Pill That's 4 Cents In Tanzania Costs Up To $400 In The U.S.," NPR.org, webpost, December 11, 2017. Available at: https://www.npr.org/sections/goatsandsoda/2017/12/11/567753423/why-a-pill-thats-4-cents-in-tanzania-costs-up-to-400-in-the-u-s

Wright, Nicole C., Anne C. Looker, Kenneth G. Saag, Jeffrey R. Curtis, Elizabeth S. Delzell, Susan Randall, and Bess Dawson-Hughes. "The Recent Prevalence of Osteoporosis and Low Bone Mass in the United States Based on Bone Mineral Density at the Femoral Neck or Lumbar Spine," Journal of Bone and Mineral Research, November 2014, vol.29, no.11, pp.2520-2526. Available at: https://onlinelibrary.wiley.com/doi/full/10.1002/jbmr.2269

Zhu, Baojin, Haya Ascher-Svanum, Doublas E. Faries, Xiaomei Peng, David Salkever, and Eric P. Slade. "Costs of treating patients with schizophrenia who have illness-related crisis events,"

BMC Psychiatry, 2008, vol.8, p.72. Available at:
https://bmcpsychiatry.biomedcentral.com/articles/10.1186/1471-244X-8-72

APPENDIX A

Description of the indications for each drug and the consequences of receiving an ineffective dose. Compiled by Dr. Peter H. Rheinstein, M.D., J.D., M.S., President, Severn Health Solutions.

	Drug	Generic Name	Dosage Form	Generic Available?	BLACK BOX	Indications	Consequences if Ineffective	Remarks
1	Abilify Oral Long Acting	aripiprazole	 Tablets Deep IM	 Yes No	Yes	Schizophrenia, Bipolar I	Recurrence of Symptoms, Rehospitalization, Suicide attempts in severely depressed	Abilify Maintena is once a month deep IM injection that allows some patients to be released from and stay out of institutions; Labeling states Deep IM injection s to be given by health care provide only.
2	Actos	pioglitazone	Tablets	Yes	Yes	Type 2 Diabetes Mellitus	Increased Blood Sugar may result in end organ damage without warning, Diabetic ketoacidosis may require hospitalization.	
3	Advair	fluticasone/ salmeterol inhalation	Metered aerosol Powder	 No One Only	No	Asthma, COPD	Increased shortness of breath may result in Emergency Room visits; Adrenal Insufficiency may be fatal	See warnings in Advair Patient Info regarding sudden discontinuation. First generic (Mylan) approved 1/30/2019
4	Albenza	albendazole	Oral Tablets	Yes	No	Neurocysticercosis (pork tapeworm) Cystic echinocccosis (Hydatid Disease, dog tapeworm)	Epilepsy (neurocysticercosis) Cysts in Liver and Lungs – Sometimes Fatal (hydatid disease)	Requires monthly blood test during treatment. Untreated tapeworm infestation also can be spread through human feces (https://www.who.int/taeniasis/transmission/en)
5	Ampyra	dalfampridine	Tablets	Yes	No	Improves walking speed in multiple sclerosis	Patients may be more disabled requiring more personal care	
6	Augmentin	amoxicillin/ clavulanate	Tablets Suspension	Yes	No	Antibacterial (lower respiratory tract, acute otitis media. sinus, skin, urinary)	Infection worsens – May lead to hospitalizations	One of the most frequently prescribed antibacterial agents.
7	Aubagio	teriflunomide	Tablets	No	Yes	Relapsing Multiple Sclerosis	Faster progression of multiple sclerosis and disability	
8	Avonex	interferon beta-1a	IM injection	No	No	Relapsing Multiple Sclerosis	More relapses with faster progression of disability	IM injection once weekly x 4, then once monthly
9	Celebrex	celecoxib	Oral capsules	Yes	Yes	OA, RA, JRA, ankylosing spondylitis, acute pain, primary dysmenorrhea	Symptoms not relieved	
10	Cialis	tadalafil	Tablets	No	No	Erectile Dysfunction benign prostatic hypertrophy	Erectile Failure, Anxiety Possible Acute Urinary Retention with ER visits and catheterization	Pharmacologic treatment of BPH has greatly reduced the need for prostate surgery
11	Copaxone	glatiramer	SQ Injection	Two only	No	Relapsing Multiple Sclerosis	Faster progression of multiple sclerosis and disability	Dose is 20 mg daily or 40 mg three times per weeks
12	Crestor	rosuvastatin	Tablets	Yes	No	Reduce high triglycerides and high cholesterol; slow progression of atherosclerosis; reduce risk of stroke, myocardial infarction, arterial revascularization procedures	Faster progression of atherosclerosis with increased incidence of stroke, myocardial infarction and revascularization surgery	Progression of disease may be insidious until irreversible damage has occurred.
13	Eliquis	apixaban	tablets	No	Yes	reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation;	Increased risk of thrombotic events (stroke, pulmonary embolus, systemic emboli); Recurrence of Deep Vein Thrombosis	Package insert explicitly states risk of sudden discontinuation (which would be the result of taking an ineffective

						prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery; treatment of DVT and PE, and for the reduction in the risk of recurrent DVT and PE following initial therapy		counterfeit product). Permanent injury and disability could occur without warning
14	Enbrel	etanercept	SQ Injection	One biosimilar	Yes	Rheumatoid Arthritis (RA); Polyarticular Juvenile Idiopathic Arthritis (JIA); Psoriatic Arthritis (PsA); Ankylosing Spondylitis (AS); Plaque Psoriasis (PsO) in patients 4 years or older	Worsening of symptoms and disease progression.	SQ injection once weekly for most indications Enbrel is disease modifying so that an ineffective counterfeit medication may lead to actual; disease progression in addition to increased symptoms.
15	EpiPen	epinephrine	Autoinjector (SQ and/or IM)	One Only	No	Emergency treatment of anaphylaxis	Worsening tachycardia with fall in blood pressure, convulsions, wheezing, dyspnea, angioedema possibly fatal	Defective autoinjector may result in delay of administering lifesaving medication even if effective drug is present in counterfeit injector
16	Forteo	teriparatide	SQ injection	No	Yes	Postmenopausal osteoporosis in women; increase of bone mass in men with primary or hypogonadal osteoporosis; osteoporosis due to glucocorticoid therapy	Fractures of Hips, Back, Other Bones resulting in hospitalization and surgery; Irreversible progression of osteoporosis	Once daily injection from 28-day device; Progression of osteoporosis may not be apparent until fracture occurs. Hip fractures in older women are followed by death within one year in a significant percentage of patients.
17	Gilenya	fingolimod	Capsules	No	No	Relapsing Multiple Sclerosis	Faster progression of multiple sclerosis and disability	Label states "first dose of GILENYA in a setting in which resources to appropriately manage symptomatic bradycardia are available. Monitor all patients for 6 hours after the first dose for signs and symptoms of bradycardia with hourly pulse and blood pressure measurement."
18	Harvoni	ledipasvir/ sofosbuvir	Tablets	No	Yes	Treatment of Certain Patients with Hepatitis C	Progression of hepatitis C with need for liver transplant; may be fatal; primary (hepatocellular) liver cancer	Ineffective treatment may result in persistence of infection and spread of Hepatitis C to other individuals
19	Humira	adalimumab	SQ Injection	One biosimilar (not approved for all uses)	Yes	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Adult Crohn's Disease, Pediatric Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa, Uveitis	Worsening of symptoms with faster progression of underlying disease.	SQ injection every other week in most patients, SQ injection once weekly in some RA patients. Humira is disease modifying so that an ineffective counterfeit medication may lead to actual; disease progression in addition to increased symptoms.
20	Januvia	sitagliptin	Tablets	No	No	Type 2 Diabetes Mellitus	Increased Blood Sugar may result in end organ damage without warning, Diabetic ketoacidosis may require hospitalization.	Also sold in combination with ertugliflozin (Steglujan) and metformin (Janumet)
21	Letairis	ambrisentan	Tablets	No	No	Pulmonary Arterial Hypertension (PAH)	Reduced exercise ability; Disease progression and hospitalization	Labeled indication is "reduce the risks of disease progression and

								hospitalization for worsening PAH, and to improve exercise ability."
22	Lipitor	atorvastatin	Tablets	Yes	No	Reduce the risk of MI, stroke, revascularization procedures in adult patients and in some patients age 10-17; Reduces elevated total-C, LDL Cholesterol, apo-B, and triglyceride levels	Increased risk of MI, stroke, revascularization procedures; progression of atherosclerosis; Patients with very high triglycerides may be at increased risk of pancreatitis	Prescribing information actually states that Lipitor reduces risk of MI, stroke, and revascularization procedures in addition to lowering cholesterol and triglycerides. These conditions may result in hospitalizations, permanent disability and/or death. Atorvastatin is also sold in combination with amlodipine (Caduet) and ezetimibe (formerly Liptruzet, now only generics).
23	Lyrica	pregabalin	Capsules; Controlled Release Tablets, Solution	No	No	Diabetic Peripheral Neuropathy; Post Herpetic Neuralgia; Partial Onset Seizures; Fibromyalgia; Neuropathic pain from Spinal Cord Injury	Return of pain from DPH, PHN, fibromyalgia, and spinal cord injury with disability and absence from work. Loss of control of partial onset seizures.	Unexpected recurrence of seizures may lead to motor vehicle and on-the-job accidents with injuries to the patient and to others.
24	Nexium	omeprazole	Tablets, Capsules, Suspension, IV	Yes No No No	No	GI Reflux Disease, Risk reduction of NSAID-associated gastric ulcer, H. pylori eradication to reduce risk of duodenal ulcer recurrence, pathological hypersecretory conditions including Zollinger-Ellison Syndrome; Nexium IV is used to reduce risk of rebleeding after endoscopic treatment for acute bleed gastric or duodenal ulcers	Formation or recurrence of gastric and duodenal ulcers with blood loss – sometimes requiring surgery and hospitalization. Untreated esophagitis can lead to changes in the structure of the esophagus increasing the risk of cancer. (https://www.mayoclinic.org/diseases-conditions/esophagitis/symptoms-causes/syc-20361224)	Tablets are also available OTC
25	Orencia	abatacept	IV injection SQ injection	No	No	Adult Rheumatoid Arthritis (RA); Juvenile Idiopathic Arthritis; Adult Psoriatic Arthritis (PsA)	Worsening of symptoms and disease progression.	Lyophilized powder for IV Prefilled syringes and autoinjector SQ Orencia is disease modifying so that an ineffective counterfeit medication may lead to actual; disease progression in addition to increased symptoms.
26	Otezla	apremilast	Tablets	No	No	Psoriatic Arthritis, Plaque Psoriasis	Worsening of tender and swollen joint counts; worsening or return of skin lesions	Twice daily with dosage titration in first week
27	Premarin	conjugated estrogens	Tablets IV Injection IM Injection Vaginal Cream	No	Yes	Tablets are used for Vasomotor Symptoms due to Menopause; Hypoestrogenism due to Hypogonadism, Castration or Primary Ovarian Failure; Palliation of Metastatic Disease; Prevention of Postmenopausal Osteoporosis IV is used for short term treatment of abnormal uterine bleeding Cream is used for symptoms of vulvar and vaginal atrophy due to menopause	Failure to relieve symptoms, progression of osteoporosis with fractures, hospitalization, surgery and disability; IV – failure to control uterine bleeding	Lyophilized powder is for injection Also sold in combination with medroxyprogesterone Progression of osteoporosis may be insidious until irreversible damage has occurred.
28	Revatio	sildenafil	Tablets Suspension	Yes No	No	Pulmonary Arterial Hypertension (PAH)	Reduced exercise ability; Disease progression and hospitalization	Labeled indication is "improve exercise ability and delay clinical worsening"

			IV Injection	One Only				IV injection is for patients "temporarily unable to take oral medication" Same active ingredient as Viagra.
29	Sovaldi	sofosbuvir	tablets	No	Yes	Treatment of Certain Patients with Hepatitis C	Progression of hepatitis C with need for liver transplant; may be fatal; primary (hepatocellular) liver cancer	Ineffective treatment may result in persistence of infection and spread of Hepatitis C to other individuals. Also sold in combination with ledipasvir Harvoni – see above), velpatasvir (Epclusa) and velpatasvir + voxilaprevir (vosevi).
30	Stelara	ustekinumab	IV Injection SQ Injection	No	No	Psoriasis (Ps), Psoriatic Arthritis (PsA); Crohn's Disease (CD)	Worsening of symptoms and disease progression.	Dosing: Psoriasis SQ to start, at 4 weeks, then q 12 weeks; Crohn's IV to start, then SQ q 8 weeks X
31	Stendra	avanafil	tablets	No	No	Erectile Dysfunction	Erectile Failure, Anxiety	
32	Strattera	atomoxetine	Capsules	Yes	No	ADHD	Behavioral Problems; Difficulties in School	
33	Synthroid	levothyroxine	tablets	Yes	Yes	Hypothyroidism; Adjunct in treatment of TSH dependent thyroid cancer	Recurrence of symptoms of hypothyroidism including depression, weight gain, infertility, heart failure; Progression of thyroid cancer	
34	Tecfidera	dimethyl fumarate	capsules	No	No	Relapsing multiple sclerosis	Faster progression of multiple sclerosis and disability	Delayed-release capsules are important for efficacy because half-life of active ingredient is short.
35	Tresiba	insulin degludec	SQ injection	No	No	Diabetes Mellitus (Type 1 or Type 2)	Increased Blood Sugar may result in end organ damage without warning, Diabetic ketoacidosis may require hospitalization	FlexTouch pen delivers prescribed amount Also sold in multiple-dose vial
36	Triumeq	abacavir/ dolutegravir/ lamivudine	tablets	No	Yes	Treatment of HIV-1 Infection	Progressions of AIDS with disability and death	Ineffective treatment may result in persistence of infection and spread of Human Immunodeficiency Virus to other individuals. Individual ingredient are sold separately, but there is no generic form of dolutegravir.
37	Truvada	Emtricitabine/ tenofovir disoproxil fumarate	Tablets	No – Only approved generic discontinued	Yes	Treatment of HIV-1 infection; HIV-1 Pre-Exposure Prophylaxis	Progressions of AIDS with disability and death; New HIV-1 infection in patients who believed themselves to be protected	Ineffective treatment may result in persistence of infection and spread of Human Immunodeficiency Virus to other individuals. Ineffective prophylaxis may result in patients who believed themselves protected contracting HIV,
38	Xarelto	rivaroxaban	tablets	No	Yes	reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation; prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery; treatment of DVT and PE, and for the reduction in the risk of recurrent DVT and PE following initial therapy; Reduction of Risk of Major	Increased risk of thrombotic events (stroke, pulmonary embolus, systemic emboli); Recurrence of Deep Vein Thrombosis	Package insert explicitly states risk of sudden discontinuation (which would be the result of taking an ineffective counterfeit product). Permanent injury and disability could occur without warning.

						Cardiovascular Events in Patients with Chronic Coronary Artery Disease (CAD) or Peripheral Artery Disease (PAD)		
39	Zetia	ezetimibe	Tablets	Yes	No	Reduction of elevated cholesterol and lipids	Label states, "The effect of ZETIA on cardiovascular morbidity and mortality has not been determined." However, patients with elevated cholesterol and lipid are at increased risk of MI, stroke, revascularization procedures; progression of atherosclerosis; Patients with very high triglycerides may be at increased risk of pancreatitis	Permanent injury and disability could occur without warning. Also sold in combination with simvastatin.(Vytorin) and atorvastatin (formerly Liptruzet, now only generics)
40	Zytiga	abiraterone	Tablets	Yes 250 No 500	No	Metastatic prostate cancer	Earlier disease progression and shorter patient survival	

APPENDIX B

Quote for the cost of testing drug quality: Assay, Dissolution Rate, Content Uniformity, Sterility. Provided by NMS Labs.

Quote for Testing Drug Quality

Products				COSTS for testing by test for a single batch (multiple batches reduce price by -0.5% each additional batch)					
	Product Type/Delivery System	Dosages	Total # of all dosages	Assay	Dissolution Rate	Content Uniformity	Sterility	Price for Testing Each Dose	Price for all Doses Once
Abilify	Tablets and Oral Solution	2, 5, 10, 15, 20, 30mg +30mg/ml	7	$600	$1,200	$1,200	$1,000	$4,000	$28,000
Actos	Tablets	15, 30, 45mg	3	$500	$1,000	$1,000		$2,500	$7,500
Advair	Inhaled powder and aerosol	50, 100, 115, 125, 150, 200, 230,250, 500 mcg	9	$1,100		$2,000	$1,000	$4,100	$36,900
Albenza	Tablets	200, 400mg	2	$500	$1,000	$1,000		$2,500	$5,000
Augmentin	Tablets and Oral Solution	500, 875, 1000, 100, 150, 200mg	6	$600	$1,200	$1,200		$3,000	$18,000
Ampyra	Tablets	10mg	1	$500	$1,000	$1,000		$2,500	$2,500
Aubagio	Tablets	7, 14mg	2	$500	$1,000	$1,000		$2,500	$5,000
Celebrex	Tablets	50, 100, 200, 400mg	4	$500	$1,000	$1,000		$2,500	$10,000
Cialis	Tablets	2.5, 5, 10, 20, 40, 60mg	6	$500	$1,000	$1,000		$2,500	$15,000
Crestor	Tablets	5, 10, 20, 40mg	4	$500	$1,000	$1,000		$2,500	$10,000

Eliquis	Tablets	2.5, 5mg	2	$500	$1,000	$1,000		$2,500	$5,000
Enbrel	Injection Syrine	50mg/ml	1	$600		$1,200	$1,000	$2,800	$2,800
EpiPen	Injection Syringe	0.3, 0.15mg	2	$600		$1,200	$1,000	$2,800	$5,600
Gilenya	Tablets	0.5mg	1	$500	$1,000	$1,000		$2,500	$2,500
Harvoni	Tablets	400mg	1	$500	$1,000	$1,000		$2,500	$2,500
Januvia	Tablets	25, 50, 100mg	3	$500	$1,000	$1,000		$2,500	$7,500
Letairis	Tablets	5, 10, 20, 40mg	4	$500	$1,000	$1,000		$2,500	$10,000
Lipitor	Tablets	10, 20, 40, 80mg	4	$500	$1,000	$1,000		$2,500	$10,000
Nexium	Tablets and Oral Suspension	2.5, 5, 10, 20, 40mg	5	$600	$1,200	$1,200		$3,000	$15,000
Orencia	Injection Syringe	125mg/ml	1	$600		$1,200	$1,000	$2,800	$2,800
Otezla	Tablets	10, 20 30mg	2	$500	$1,000	$1,000		$2,500	$5,000
Premarin	Oral Tablet and Vaginal Cream	0.3, 0.625, 0.9, 1.25mg	4	$600	$1,000	$1,000		$2,600	$10,400
Revatio	Tablets and Injection Syringe	20, 50, 100mg	3	$600	$1,000	$1,000	$1,000	$3,600	$10,800
Sovaldi	Tablets	400mg	1	$500	$1,000	$1,000		$2,500	$2,500
Stendra	Tablets	100, 200mg	2	$500	$1,000	$1,000		$2,500	$5,000
Strattera	Tablets	10, 18, 25, 40, 60mg	5	$500	$1,000	$1,000		$2,500	$12,500
Synthroid	Tablets	25-200mcg	12	$500	$1,000	$1,000		$2,500	$30,000
Tecfidera	Tablets	120, 240mg	2	$500	$1,000	$1,000		$2,500	$5,000

Tresiba	Auto-injector	100u/ml	1	$600		$1,200	$1,000	$2,800	$2,800
Triumeq	Tablets	50, 300, 600mg	3	$500	$1,000	$1,000		$2,500	$7,500
Truvada	Tablets	150, 200, 300mg	3	$500	$1,000	$1,000		$2,500	$7,500
Xarelto	Tablets	15, 20mg	2	$500	$1,000	$1,000		$2,500	$5,000
Zetia	Tablets	10mg	1	$500	$1,000	$1,000		$2,500	$2,500
Zytiga	Tablets	250, 500mg	2	$500	$1,000	$1,000		$2,500	$5,000
							Totals	**$91,500**	**$313,100**

APPENDIX C

This Appendix details the sources and methodology used to calculate the expense of treating adverse events. Additional details for each calculation may be found in the original source material.

The costs presented here are estimated for the treatment of a patient for one year or a single adverse event. Given that the cost savings from buying Canadian drugs is estimated for a single year, the treatment of an adverse event is also estimated for a single year. Notably, in many cases, the cost of treatment failure will extend over many years and may present a lifelong burden. Again, this assumption biases the results against the desired finding of eliminating all cost savings.

Anaphylaxis The direct cost of anaphylaxis is estimated by Patel, et.al. (2011) in an article in the Journal of Allergy and Clinical Immunology (link here). The mean cost per patient is estimated to be $4719 (in 2007 dollars).

Care to treat Chronic Obstructive Pulmonary Disease (COPD) Failure to treat COPD, a common lung disease, results in difficulty breathing, further damage to the lungs, and disease progression. According to a 2013 study by Guarascio et al. (link here), "data indicate that with each progressive stage of COPD, as defined in a previous GOLD guideline, patients with stage I COPD experienced the lowest direct cost of $1681 per patient per year, stage II patients $5037 per patient per year, and those in stage III had the highest cost of $10,812 per patient per year." Assuming disease progression moves patients from stage I to stage II, the annual difference in direct cost is $3356 (in 2010 dollars). [Hospitalization for COPD, Healthcare Bluebook's Fair Price: $6,646 on 22 May 2019]

Coronary artery bypass grafting (CABG), Valve Repair, Complex Heart Surgery Stroke and heart attack are typical medical adverse events associated with untreated high cholesterol and heart disease. According to a recent article in the Journal Circulation by Giacomino et al. (link here), the mean price for CABG obtained from the hospitals was $151,784.64, and ranged from $44,824 - $448,039 (in 2014 dollars).

Neurocysticercosis Failure to effectively treat a pork tapeworm may result in Neurocysticercosis. A 2015 study by O'Neal and Flecker (link here) found an estimated 18,584 hospitalizations for neurocysticercosis and associated hospital charges totaling >US $908 million (between 2003 and 2012). This correlates to an average cost of treatment of $48,859 in 2012 dollars.

Diabetic ketoacidosis Failure to effectively treat diabetes may result in diabetic ketoacidosis. As described in a 2018 study by Desai et al. (link here), "[a]lthough our ability to treat diabetes and its associated complications has significantly improved, presentation with uncontrolled diabetes leading to ketoacidosis remains a significant problem." The study reviewed the National Inpatient Sample database for all hospitalizations in which DKA was the principal discharge diagnosis during 2003–2014 and calculated the population incidence by using U.S. census data. The mean hospital charges were $26,566 per admission in 2014.

Esophageal Cancer Failure to treat GI Reflux Disease may result in esophageal cancer. According to the National Cancer Institute (link here) drawing on a study by Mariotto et al. (2011) (link here), the annualized mean net costs of care per patient for esophageal cancer were $79,822 (male, $79,532 female) for the initial year and $6,450 (male, $6,853 female) annually continuing.

HIV/AIDS Failure to prevent a new HIV-1 infection may result in the contraction of HIV-1. According to the CDC (link here), the lifetime treatment cost of an HIV infection can be used as a conservative threshold value for the cost of averting one infection. Currently, the lifetime treatment cost of an HIV infection is estimated at $379,668 (in 2010 dollars).

Liver Transplant Failure to treat Hepatitis C may result in liver failure and the necessity of a liver transplant. According to a 2017 Milliman Research Report (Bentley & Phillips, 2017) (link here), the estimated US average 2017 transplant cost, the amount of billed charges for a liver transplant, was $812,500. [Healthcare Bluebook's Fair Price: $59,301]

Multiple Sclerosis Failure to effectively treat MS may result in a worsening of the disease. The cost estimates used here are based on a systematic review. The article by Ernstsson et.al. (2016) (link here) draws on the results of 1,326 publications from January 1969 to January 2014. The cost estimates were compared across 29 studies. The EDSS Classification of the disease includes groups I, II, and III. The article provides the annual cost per patient according to 2011 US dollar Purchasing Power Parity (USDPPP). The mean annual cost for group I is $22,719, for group II is $40,153, and for group III is $64,853. The difference between group I and group II is $17,434. The difference between group II and group III is $24,700. The difference between group I and group III is $42,134.

Neurocysticerocosis According to a recent CDC article (link here), between 2003 and 2012 there were an estimated 18,584 hospitalizations for neurocysticercosis with associated hospital charges totaling >US $908 million. This equates to approximately $48,859 per hospitalization in 2012 dollars.

Osteoporosis Resulting in Fracture Failure to treat Osteoporosis may result in a fracture. According to a 2011 study by Blume and Curtis (link here), "Of 30.2 million elderly Medicare recipients in 2002. . . [the] estimated mean impact of fractures on annual medical cost was $8,600 (95% confidence interval, $6,400 to $10,800), implying a US cost of $14 billion ($10 to $17 billion)." [Healthcare Bluebook's Fair Price for a femur fracture: $8,554]

Prostate Cancer Failure to treat prostate cancer will result in earlier disease progression and shorter patient survival. According to the National Cancer Institute (link here), the cost of treating prostate cancer in the initial year is $19,710, with an additional cost of $3,201 in subsequent years. [Healthcare Bluebook's Fair Price for prostate removal: $14,075]

Psoriatic Arthritis (PsA) Treatment failure may result in worsening of symptoms and disease progression. A 2016 study by Burgos-Pol et al. (link here) aimed to assess the burden of PsA in five European countries. The authors considered both direct costs (medical and nonmedical) and indirect costs, adjusted for country-specific inflation and converted to international dollars using purchasing power parity exchange rates for 2015 ($US PPP). The study found the total annual cost per patient ranged from $10,924 to $17,050 for psoriatic arthritis. Direct costs were the largest component of total expenditure and the severity of the disease was associated with higher costs. Accordingly, the differential between the lowest cost estimate and the highest is $6126.

Pulmonary Arterial Hypertension (PAH) Failure to treat Pulmonary Arterial Hypertension (PAH) will result in the progression of the disease and worsening symptoms. According to a 2010 article in the Chest Journal (the Official Publication of the American College of Chest Physicians) (link here), mean direct patient costs in 2007 dollars were $2,023 per month. In addition, circulatory/respiratory system-related patient costs were $724 per month.

Schizophrenia Treatment failure may result in the recurrence of symptoms, rehospitalization, and suicide attempts. In a 2008 BMC Psychiatry article by Zhu et al. (link here), direct mental health treatment costs for patients who had experienced 1 or more of 5 recent crisis events were compared to propensity-matched samples of persons who had not experienced a crisis event. "Across all 5 categories of crisis events, patients who had a recent crisis had higher average annual mental health treatment costs than patients in propensity-score matched comparison samples. Average annual mental health treatment costs were significantly higher for persons who attempted suicide ($46,024), followed by persons with psychiatric hospitalization in the past 6 months ($37,329), persons with prior arrests ($31,081), and persons with violent behaviors ($18,778)." The data utilized in the study dated from 1997 to 2003. Given that no information was provided about inflation-adjustment of the costs, it is assumed that the costs are represented in 2003 dollars.

APPENDIX D

This Appendix details the sources and methodology used to calculate the disease prevalence in a representative US state. Additional details for each calculation may be found in the original source material.

Disease Prevalence

In the cases of the 14 unique adverse events listed above the calculations have been extended to provide estimates for a "representative state". The disease prevalence was determined for the entire United States. This number was then divided by 50 to calculate the number of patients for a "representative state".

Anaphylaxis According to an Asthma and Allergy Foundation of America (AAFA) study published in the Journal of Allergy and Clinical Immunology (link here), anaphylaxis, a life-threatening allergic reaction, occurs in approximately one in 50 Americans. Many believe the rate is higher, probably closer to one in 20. Dividing the population of a "representative state" by 50, this amounts to approximately 131,200 patients per state.

COPD The CDC (link here) notes that the "prevalence of COPD varies considerably by state, from <4% in Hawaii, Colorado, and Utah to >9% in Alabama, Tennessee, Kentucky, and West Virginia. States with the highest COPD prevalence are clustered along the Ohio and lower Mississippi Rivers." A conservative estimate is 6% nationally. This equates to 19,620,000 individuals nationally or approximately 392,400 patients in each US state.

Diabetes According to a recent report by the CDC (link here), an estimated 30.3 million people of all ages—or 9.4% of the U.S. population—had diabetes in 2015. Dividing this number by 50, a representative state would have 606,000 patients.

Esophageal Cancer According to the CDC (link here), each year in the United States, about 15,000 people in the United States are diagnosed with esophageal cancer. Dividing by 50, this amounts to 300 patients in each US state.

High Cholesterol necessitating CABG The CDC (link here) estimates that 55% of US adults who need cholesterol medicine are currently taking it. This amounts to 43 million people. Dividing by 50, this amounts to approximately 860,000 patients in each US state.[6]

Hepatitis C The CDC (link here) estimates that 2.4 million people in the United States are living with hepatitis C virus infection. Dividing by 50, this amounts to approximately 48,000 patients in each US state.

HIV The CDC (link here) estimates that at the end of 2015, 1.1 million persons aged 13 and older were living with HIV infection in the United States. Dividing by 50, this amounts to approximately 22,000 patients in each US state.

[6] CABG According a recent article in the Journal of Thoracic Disease (link here), Coronary artery bypass grafting (CABG) is the most commonly performed cardiac surgery procedure worldwide, representing annual volumes of approximately 200,000 isolated cases in the US. Dividing the population of a "representative state" by 50, this amounts to approximately 4,000 patients per state.

Multiple Sclerosis The National Multiple Sclerosis Society (link here) estimates that approximately one million people are living with MS in the United States. Dividing by 50, this amounts to approximately 20,000 patients in each US state.

Neurocysticerocosis According to a recent CDC article by O'Neal and Flecker (2015) (link here), between 2003 and 2012 there were an estimated 18,584 hospitalizations for neurocysticercosis. This equates to approximately 2065 per year. Dividing by 50, this is approximately 41 patients in each US state.

Osteoporosis Citing a recent article in the Journal of Bone and Mineral Research by Wright et al. (2014) (link here), the National Osteoporosis Foundation (NOF) (link here) reports that 10.2 million adults have osteoporosis. Dividing by 50, this amounts to approximately 204,000 patients in each US state.

Prostate Cancer The CDC (link here) reports that 183,529 new cases of Prostate Cancer were reported in 2015, the last year for which incidence data are available. Dividing by 50, this amounts to approximately 3,671 new cases per state.

Psoriatic Arthritis According to Louie (2017) of the Johns Hopkins Arthritis Center (link here), the prevalence of psoriatic arthritis is approximately 0.04-0.1% of the U.S. adult population. The mean value of this estimate is 0.07%. In the 2010 U.S. Census, the number of people under age 18 was 24.0% of the total population. Accordingly, the current adult population in the U.S. is 249280000 people. Given this, psoriatic arthritis effects 174,496 individuals in the U.S. This equates to approximately 3490 people in a "representative state".

Pulmonary Arterial Hypertension (PAH) According to the American Thoracic Society (link here), approximately 200,000 hospitalizations occur annually in the United States with pulmonary hypertension as the primary or secondary diagnosis. For a "representative state" this equates to 4,000 individuals.

Schizophrenia According to the National Institute of Mental Health (link here), across studies that use household-based survey samples, clinical diagnostic interviews, and medical records, estimates of the prevalence of schizophrenia and related psychotic disorders in the U.S. range between 0.25% and 0.64%. This provides a mean value of 0.445%. Assuming that the population of the United States is approximately 328 million, and dividing by 50, a representative state would have a population of 6,560,000 people. Accordingly, a representative state would have 29,192 patients.