PRESCRIPTION INSULIN DRUG PRICING REPORT

COLORADO DEPARTMENT OF LAW
NOVEMBER 2020

Letter from Attorney General Phil Weiser

The Honorable Jared Polis
Governor
State Capitol
200 E. Colfax Ave.
Denver, Colorado 80203

The Honorable Mike Conway
Commissioner of Insurance
Division of Insurance
1560 Broadway, #110
Denver, Colorado 80202

The Honorable Mike Weissman
Chair, Committee on the Judiciary
Colorado House of Representatives
State Capitol
200 E. Colfax Ave.
Denver, Colorado 80203

The Honorable Pete Lee
Chair, Committee on the Judiciary
Colorado Senate
State Capitol
200 E. Colfax Ave.
Denver, Colorado 80203

Dear Governor Polis, Senator Lee, Representative Weissman, and Commissioner Conway:

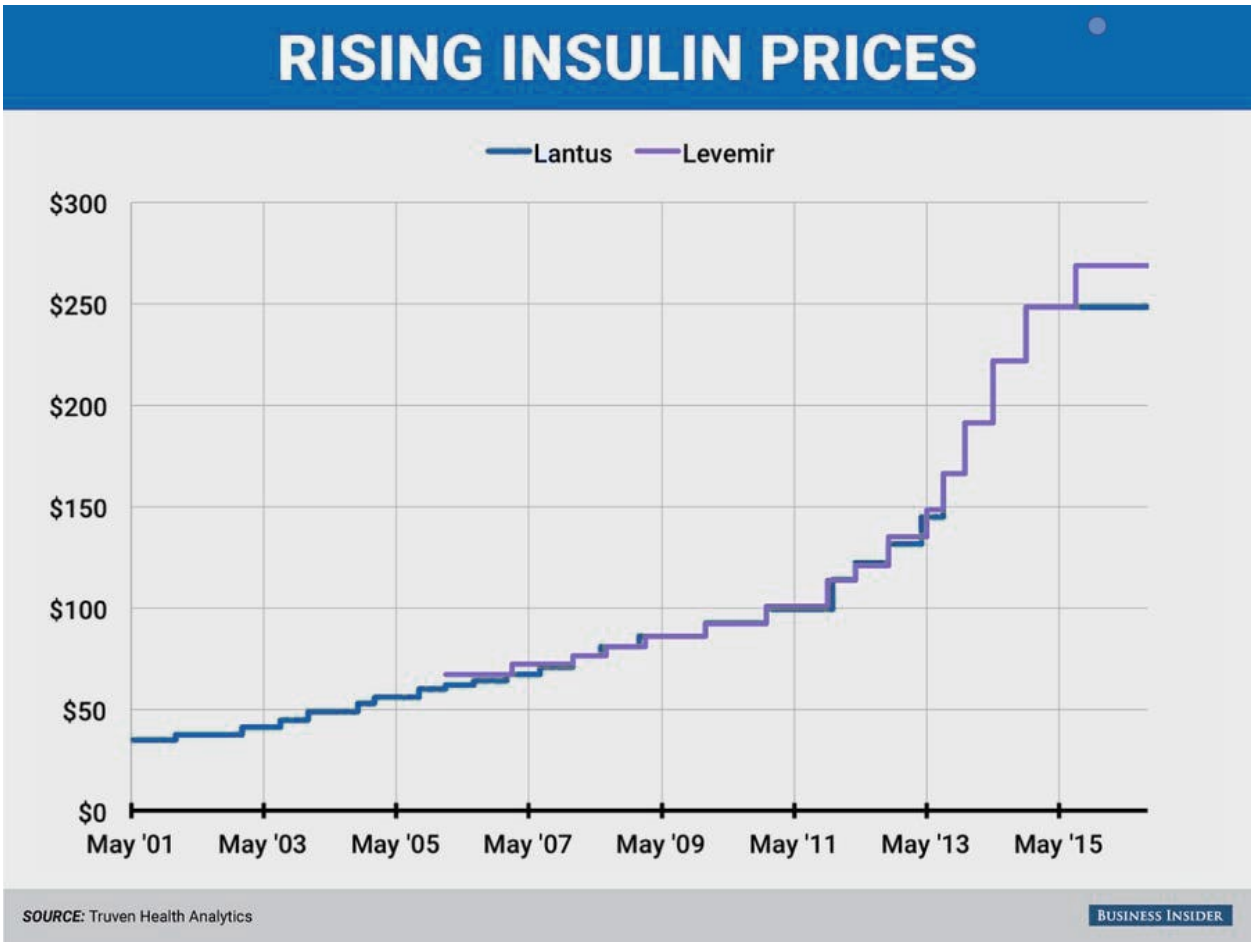
House Bill 19-1216 ("Concerning Measures to Reduce a Patient's Costs of Prescription Insulin Drugs, and, in Connection Therewith, Making an Appropriation"), directed the Department of Law ("Department") to study the cost of insulin to Colorado consumers, with specific focus on evaluating adequate consumer protections in insulin drug pricing. As required by Section 24-31-110, C.R.S., the Department investigated and studied the manufacture and sale of prescription insulin drugs in Colorado, including drivers of insulin prescription costs, and now submits this report of the Department's study and investigation.

As captured in this report, the rising prices of insulin in Colorado—by an inflation-adjusted 262 percent between 2007 to 2018,[1]—painfully impacts people's lives. This increase in insulin pricing, at an annual mean change of 12.6 percent, is nearly four times the rate of inflation during this same period. For Colorado Medicaid, insulin prices have increased some 66.5 percent for some formulations in just the last six years. The burden is even higher for our residents who are uninsured or underinsured (many with high deductibles) and who end up paying full price for needed insulin and other supplies.

The stories and surveys captured by the Department staff reveal the painful consequences felt by many Coloradans and their families, including that approximately 40 percent of all survey respondents reported using insulin are forced to ration their use of this life-saving product at least once a year. In some cases where individuals lack access to insulin, respondents even reported choosing to fast as a means of managing their blood sugar levels.

[1] Inmaculada Hernandez et al., *Changes in List Prices, Net Prices, and Discounts for Branded Drugs in the US*, 2007-2018, 323 JAMA 854, 856 (Mar. 3, 2020).

The reasons behind the rising price of insulin are both straightforward and complex. The straightforward reason is that there is limited competition both (1) at the manufacturer level, with only one recently approved generic or "biosimilar" insulin; and (2) at the distribution level, with secret and disconcerting practices on the part of pharmacy benefit managers ("PBMs"). The limited competition at the manufacturer level has produced a predictable pricing system, with increases matched by two major brands of long-acting insulin in lockstep:[2]



As one study put it, "if it seems odd that prices would rise like this in a competitive market, it highlights the hold that drug brands have over doctors who prescribe medicines, and the patients who pay for them."[3] In short, the lack of competition is a major reason why insulin is not affordable.

The complexity that enters the picture relates to underlying market dynamics as well as how our patent system works. One explanation offered by the pharmaceutical companies for rising insulin prices is the practices and incentives raised by PBMs.

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[2] Lydia Ramsey Pflanzer, *There's Something Odd About the Way Insulin Prices Change*, BUSINESS INSIDER, Sept. 17, 2016, https://www.businessinsider.com/rising-insulin-prices-track-competitors-closely-2016-9.

[3] *Id.*

PBMs purportedly act to reduce prescription drug expenditures and to help patients achieve better health outcomes. Part of the expenditure reductions supposedly come through rebates secured by PBMs, though PBMs do not consistently pass these rebates on to insurance carriers or consumers. With insulin, and perhaps many other drugs, this system presents a challenge. As Professor Robin Feldman, Professor of Law and Director of the University of California Hastings Center for Innovation,[4] put it, drug companies "raise[] prices so that the PBM can demonstrate a greater 'spread' between the original price and the post-rebate price."[5] Or, as one analysis related, "[g]iven the current lack of transparency related to who gets to keep the discounts negotiated by [PBMs], they may have an incentive to put costlier, branded drugs into their plans and pocket the difference between the negotiated rebate and the net price to the consumer."[6] In short, the incentives of PBMs threaten to act as a driver to raise costs to consumers, enabling those firms to increase profit margins.[7] Moreover, as Professor Feldman concludes, the role of PBMs and the rebate system "make it difficult for an entrant to gain a foothold in the market."[8]

On the patent front, a significant concern is that the major manufacturers have successfully extended their patent protection—well beyond the prescribed period of exclusion—through the practice of obtaining a "new" patent on a different delivery method or other feature. The companies then remove the legacy product and only sell the new product with the newly patented delivery method or feature, including slight variations in formulation. This practice, sometimes called product hopping or "evergreening," has attracted increasing criticism. As Professor Robin Feldman put it, "78 percent of the drugs associated with new patents were not new drugs, but existing ones." [9] The major three producers of insulin, she explains, "have employed extensive evergreening techniques to extend their protections in the insulin market."[10] Unfortunately, we have taken steps backwards from when the original inventors of insulin sold the patent for $1 to ensure that it would be affordable to those who need it.

In this report, we offer a series of policy recommendations to address concerns about the rising price of insulin. Many of them relate to federal policy, including patent reform, regulation of PBMs, and options to encourage entry of generic drug makers (including U.S. Food and Drug Administration action in this area). This report also offers state policy recommendations, including the option for Colorado to join a bulk purchasing cooperative and explore possible regulation of PBMs.

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[4] Professor Feldman also holds the title of Arthur J. Goldberg Distinguished Professor Law and the Albert Abramson '54 Distinguished Professor of Law Chair at UC Hastings Law.

[5] Robin Feldman, *Insulin Costs in the State of Colorado* at 23 (Oct. 7, 2020) ("Feldman Report").

[6] Duane Schulthess, *Insulin Prices and Pharmacy Benefit Manager Rebates: Pin the Tail on The Patient*, STAT NEWS, Mar. 19, 2020, https://www.statnews.com/2020/03/19/insulin-prices-pbm-rebates/

[7] *Id.* (In theory, the PBMs could be providing saving to the employers who offer health care plans, but the concern is that, in practice, "there is growing concern that these companies may be hanging onto rebates and offering coverage on their formularies only to those companies providing the biggest, fattest margins.").

[8] Feldman Report, *supra* note 5 at 23.

[9] *Id.* at 5.

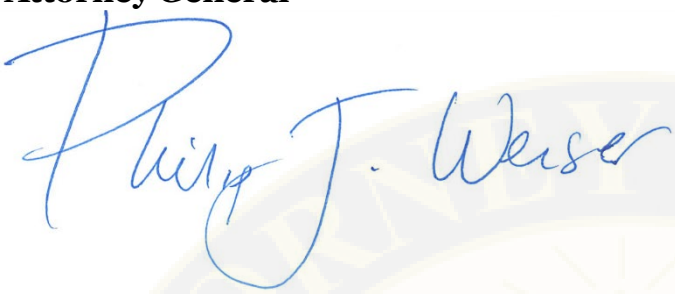
[10] *Id.* at 7.

Finally, I want to acknowledge the important leadership and work that went into producing this report. The Department of Law is grateful for the leadership of Representative Dylan Roberts, Senator Kerry Donovan, and Senator Kevin Priola in sponsoring House Bill 19-1216. Furthermore, I am particularly appreciative for our Office-wide team that committed themselves to compiling this report for the General Assembly. This team invested considerable time, thought, and effort to pull together a range of information into a clear narrative. I also extend the Department's gratitude to Professor Robin Feldman, whose pro bono contributions to this effort were most valuable and are provided in Appendix B. We also were aided greatly by the almost 400 Coloradans who came forward and provided stories and facts related to their personal experience with insulin.

Sincerely,

Phil Weiser

Attorney General



cc: Members, Committee on the Judiciary, Colorado House of Representatives

Members, Committee on the Judiciary, Colorado Senate

Table of Contents

Executive Summary

In HB 19-1216, the Colorado General Assembly directed the Colorado Department of Law ("Department") to "[i]nvestigate pricing of prescription insulin drugs . . . made available to Colorado consumers to ensure adequate consumer protections in pricing of prescription insulin drugs and whether additional consumer protections are needed." After the Department completed the investigation, the General Assembly directed the Department to "issue and make available to the public a report detailing its findings from the investigation," including a summary of insulin pricing practices and legislative and other policy recommendations.[11]

During the period of this investigation and study, the Department found, based on publicly available data, an unjustifiable increase in price on all insulin products long after original patent protections had expired. Department staff examined a number of factors that contributed to the price increases, including the unique regulatory environment surrounding biologic medicines like insulin, secret rebates paid by drug manufacturers that may or may not be passed on in full to insurance companies and ultimately patients, the role of drug formularies and preferential tiering within those formularies, and the manipulation of various other barriers to entry of competition in the insulin market.

In particular, the Department's investigation found:

01 Drug pricing in general, and insulin pricing in particular, is driven by a complex web of interrelated prices, fees, discounts, and rebates without attendant transparency to allow a full exposition of that structure or its impacts;

02 The United States pays the highest drug prices of any developed country—more than 200 percent higher than in some countries—and insulin prices are no exception, increasing by more than 200 percent over the last 11 years;

03 Numerous barriers to cheap and effective competition in the insulin market exist, including a heavy and expensive regulatory burden in bringing generic insulins to market; abuses in the patent system; and high concentrations of market power among the dominant drug manufacturers and the PBMs that often dictate which insulin products will be covered by private and public health insurance plans, and at what cost;

04 Through a first-of-its-kind survey of Colorado residents struggling with diabetes, we report on the challenges of finding affordable insulin and diabetes-related supplies. The responses paint a sobering picture of health care gone awry, with too many people unable to afford a life-saving medication invented more than a century ago and decades after more efficient insulin analog's first hit the market; and

[11] *See* COLO. REV. STAT. § 24-31-110(4) (2019).

05 There are numerous state and national policies that must be pursued to ensure the availability of insulin, and of insulin supplies, to all Americans, regardless of their income or ability to pay.

Most importantly, the Department has learned that prescription insulin pricing is complex. This report is an important part of a larger discussion, and the Department welcomes feedback, comments and additional information. Addressing high prescription drug prices, and high insulin prices in particular, will remain a top priority—and will continue to be a core part of our consumer protection mission.

Study Methodology

Based on the mandate in House Bill 19-1119 ("HB 19-1119") and codified at Section 24-31-110, C.R.S., the Department investigated insulin pricing in Colorado over the course of 2019 and 2020. The investigation sought to understand the market and regulatory forces impacting insulin drug pricing and determine policy recommendations as required by Section 24-31-110(4)(b), C.R.S. to prevent overpricing of insulin products made available to Colorado consumers. To fulfill the requirements of the HB 19-1119 study and investigation, the Department assembled a cross-sectional study team of staff with experience in the areas of consumer protection, antitrust, health services, Medicaid and Medicare, and community outreach.

The Department issued civil investigative demands ("CIDs") to industry participants at all levels of the drug distribution chain, requesting documents and information relating to insulin pricing. The three dominant manufacturers of insulin drugs—Eli Lilly, Sanofi-Aventis, and Novo Nordisk—provided written responses and documents concerning their insulin products and relationships with PBMs. Department staff also sought information from the three largest PBMs—OptumRX, Express Scripts, and CVS Caremark. Finally, insurance carriers with significant Colorado presences, including Denver Health Medical Plan, Anthem, Colorado Access Group, Aetna, Humana, Friday Health Plans, and United HealthCare, provided information, including documents regarding formularies, advertising, information provided to patients, prescription savings programs, copays, policies and procedures, pharmacy benefits, responses to questions, litigation materials, and position statements. The Colorado Department of Health Care Policy and Financing ("HCPF") also produced data for use in an expert analysis.

Notably, CID respondents declined to disclose information they claimed as confidential trade secrets,[12] such as the actual rebates or other incentives in manufacturers' contracts with PBMs. The information we received informed our thinking and analysis, but our

[12] HB 19-1216 authorized the Attorney General to serve investigative subpoenas but prohibited the Attorney General from compelling the discovery of trade secrets. *See* COLO. REV. STAT. § 24-31-110(3) (2019).

task was hampered by the lack of visibility into drug pricing dynamics in the Colorado prescription insulin marketplace.

In addition to the issuance of formal process to large industry players, the Department study team sought to better understand the experience of diabetes patients in Colorado. To that end, the Department's Office of Community Engagement ("OCE") developed and distributed a survey seeking to learn more about Coloradans' experiences and how they are impacted by the cost of insulin and supplies.[13]. OCE administered the survey online in both English and Spanish languages to Colorado residents from May 20, 2020 to August 3, 2020. To encourage participation, OCE promoted the survey through social media, Colorado diabetes and community organizations, patient advocates, endocrinologists, elected officials' newsletters, and other avenues. The survey questions addressed the monthly cost and frequency of rationing insulin and supplies, frequency of expired insulin use, general affordability of insulin and supplies, effects of insulin costs on respondents' lives, and respondents' experiences using pharmacies and discount cards for insulin and supplies. The Department received 391 responses from 44 of the 64 Colorado counties. The Department study team also interviewed a range of players in the healthcare system, including patients, physicians, nurses, pharmacists, and advocates. These conversations helped refine our understanding of the economic and logistical challenges faced by insulin-dependent individuals. A summary of the survey results is attached as Appendix A.

In addition to the information obtained from Colorado industry players and patients, the Department study team researched and reviewed relevant academic literature analyzing various aspects of the insulin market, including law review articles, medical journals, reports from the Colorado Department of Public Health and Environment ("CDPHE"), and state and federal agency reports. The literature review examined not only general issues involving pharmaceutical pricing but also the role of patents and availability of biosimilars, analyzing how the intellectual property landscape has impacted pricing and availability. These materials offered further context for narrowing down the key factors impacting insulin pricing in the United States and in Colorado specifically.

In an effort to understand the application to the Colorado market, the Department consulted with Robin Feldman, a nationally renowned expert in the areas of intellectual property law, innovation in drug pricing, and health care law. Professor Feldman used Medicaid Part D data, data on patents from the FDA's Orange Book, and Medicaid data produced by HCPF to analyze insulin accessibility in Colorado. Specifically, Professor Feldman's team sought to address four central questions:

- What impact do patents, exclusivities, and patent term extensions have on the price of insulin?

[13] *See* Colorado Department of Law Insulin Pricing Report Survey, attached as Appendix A.

- How much do Colorado patients pay, directly and out-of-pocket, for insulin and how much does the federal government pay in subsidies for Colorado patients?
- Does irrational tiering contribute to high insulin prices in Colorado?
- What is the relationship between the rebate structure and insulin pricing?

In answering each of these questions, Professor Feldman's team compared Colorado with a national average of all other states. Her report is attached as Appendix B.

The Department study team's review of the information gathered from industry participants, relevant literature, patient survey responses, and Professor Feldman's work greatly informs this report.

Overview of Diabetes and Impact of Insulin Pricing in Colorado

The cost of insulin, and critical diabetes supplies, overwhelmingly affects the lives of Coloradans who rely on insulin to survive. This section provides an overview and background on diabetes, the history of insulin, and the burdens facing Coloradans due to the rising costs of insulin and diabetes-related supplies.

Diabetes and the Discovery of Insulin

Diabetes falls into three categories: type 1,[14] type 2, and gestational.[15] Type 1 diabetes is an autoimmune disease caused when the body's immune system attacks the pancreas, killing insulin-producing beta cells.[16] Without insulin, blood glucose, also referred to as blood sugar, reaches abnormally high levels. If a patient can no longer produce insulin, glucose stays in the patient's blood stream and does not reach cells to be converted into energy.[17] Having too much glucose in the blood stream can cause numerous severe health complications, including death. Type 1 diabetes is neither preventable nor curable, and patients living with type 1 diabetes must inject insulin several times a day to survive.[18] Without insulin, patients with type 1 diabetes will die.[19]

Type 2 diabetes results from the body's ineffective use of insulin, also known as "insulin-resistance."[20] Type 2 diabetes patients may use insulin and/or antidiabetic drugs to

[14] Patients who have undergone a total pancreatectomy become insulin-dependent diabetics for life.
[15] Gestational diabetes is diabetes diagnosed for the first time during pregnancy and often resolves itself after delivery. *See* Mayo Clinic Staff, *Gestational Diabetes*, Aug. 26, 2020, https://www.mayoclinic.org/diseases-conditions/gestational-diabetes/symptoms-causes/syc-20355339. While some patients may take medication, including insulin, to treat gestational diabetes, it is not the focus of this study.
[16] Beyond Type 1, https://beyondtype1.org/type-1-diabetes/.
[17] Congressional Diabetes Caucus Co-Chairs Representatives Diana DeGette and Tom Reed, *Insulin: A Lifesaving Drug Too Often Out of Reach* (Apr. 2, 2019), at 6 ("Congressional Report").
[18] Beyond Type 1, *supra* note 16.
[19] Elizabeth Snouffer, *Insulin insecurity and death by DKA*, Diabetes Voice (June 14, 2019).
[20] Beyond Type 1, *supra* note 16.

control blood glucose levels.[21] From 2006 to 2013, insulin use among type 2 diabetics increased from 17.1 to 23.0 percent.[22]

Prior to the discovery of insulin, a diagnosis of type 1 diabetes was fatal. In 1921, Canadian scientists Frederick Banting, J.J.R. Macleod, Charles Best, and James Collip produced the first form of insulin intended for use as a treatment for humans.[23] The scientists successfully treated their first patient with type 1 diabetes in 1922, and, in 1923, the team received the Nobel Prize for their discovery.[24] Many countries, including the U.S., granted the scientists patents for their insulin solution, but they sold the patents to the University of Toronto for one dollar to ensure that affordable insulin would be available to anyone who needed it.[25]

In the decades that followed, pharmaceutical manufacturers have continued to develop and improve insulin to better manage diabetes.[26] "In the 1970s, scientists found that they could use recombinant DNA to manufacture real human insulin,"[27] and, by the 1990s, analog insulins were first patented, acting "more like the insulin naturally produced and regulated by the body."[28] Patients typically take rapid- and short-acting insulins just before mealtime, which can begin to reduce blood glucose levels within 20-30 minutes.[29] In 1996, lispro became the first short-acting insulin analog to receive FDA approval; aspart followed in 2000, and glulisine in 2004.

Scientists developed intermediate and longer-acting insulins for slower, more consistent treatment for 24 or even 36 hours using the same technologies.[30] Glargine became the first long-acting analog insulin in 2000, followed by detemir in 2005. The first patents on these products expired in 2015.[31]

Although the market has largely shifted to analog insulin, human insulins remain available without a prescription for as little as $25 per vial. Human insulin thus, in theory, remains a viable option to higher costs alternatives, particularly for patients with type 2 diabetes who cannot afford analog insulin. There are two categories of human insulin: R and N or NPH.[32] R is a short-acting insulin which peaks after about 90

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[21] International Diabetes Federation, *About Diabetes*, Mar. 3, 2020, https://www.idf.org/aboutdiabetes/type-2-diabetes.html.
[22] Kasia J. Lipska et al., *Trends in Drug Utilization, Glycemic Control, and Rates of Severe Hypoglycemia, 2006-2013,* 40 Diabetes Care 468, 470 (Apr. 2017).
[23] Congressional Report, *supra* note 17 at 5.
[24] Lydia Ramsey Pflanzer, *The Incredible History of Insulin, a Lifesaving Diabetes Drug that was Discovered Almost a Century ago and is now at the Center of Drug Pricing Outrage*, BUSINESS INSIDER, Apr. 11, 2019, https://www.businessinsider.com/diabetes-insulin-banting-history-2016-11.
[25] Congressional Report, *supra* note 17 at 5.
[26] *Id.*
[27] Pflanzer, *supra* note 24.
[28] *Id.*; *see also* George Grunberger, *Insulin Analogs—Are They Worth It? Yes!*, 37 Diabetes Care 1767, 1767-68 (June 2014).
[29] American Diabetes Association, *Insulin Basics*, https://www.diabetes.org/diabetes/medication-management/insulin-other-injectables/insulin-basics.
[30] *Id.*
[31] Initiative for Medicines, Access and Knowledge, *Overpatented, Overpriced Special Edition: Lantus, Initiative for Medicines, Access, and Knowledge*, 2018, at 3.
[32] Dana Howe, *The Patient's Bottom Line: Human Insulin is Not the Answer*, Beyond Type 1, June 18, 2020, https://beyondtype1.org/the-patients-bottom-line-human-insulin-is-not-the-answer.

minutes and stops working after 4 to 6 hours.[33] R insulin is used at mealtimes and for corrections on a human insulin regimen.[34] N or NPH is longer acting than R insulin.[35] NPH insulin begins working after 1 to 3 hours, peaks between 6 and 8 hours, and continues working for up to 24 hours.[36] NPH is used to provide baseline insulin.[37]

While several studies have found that human insulin can work well for patients with Type 2 diabetes,[38] that is not necessarily true for Type 1 diabetics who can experience difficulty in accurately calculating correct dosages. Each person has a different blood-glucose profile.[39] And many factors can affect blood-glucose levels, including what a diabetic eats, time and amount of exercise, where insulin is injected, when insulin injections are taken, illness, and stress.[40] Moreover, differences in human insulin and insulin analogs make switching between the two difficult. Because human insulin takes longer to work, diabetics must carefully plan insulin injections up to an hour before a meal.[41] To maintain a steady baseline insulin rate with NPH human insulin, a diabetic must adhere to specifically timed meals every day.[42] Moreover, "[h]uman insulin types are not short acting enough to efficiently cover meals and correct highs, and not long-acting enough to provide a stable basal rate."[43] The inconvenience and uncertainty around maintaining adequate glucose levels is heightened by the fact that most insulin pumps are only approved for use with insulin analogs.[44] In contrast, analog insulin starts acting about 20 minutes after injection and lasts four hours.[45] Insulin analogs do not have a peak, and they can be taken right before a meal.[46]

Consistent with these observations, one review of studies assessing the effects of short-acting insulin analogs versus human insulin in Type 1 diabetics found that short-acting insulin analogs are superior to regular human insulin in total hypoglycemic episodes, nocturnal hypoglycemia, severe hypoglycemia, glucose levels after meals, and HbA1c.[47]

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[33] *Id.*
[34] *Id.*
[35] *Id.*
[36] *Id.*
[37] *Id.*
[38] *See generally* Jing Luo et al., *Implementation of a Health Plan Program for Switching from Analogue to Human Insulin and Glycemic Control Among Medicare Beneficiaries with Type 2 Diabetes*, 321 JAMA 374 (Jan. 29, 2019); Kasia J. Lipska et al., *Association of Initiation of Basal Insulin Analogs vs Neutral Protamine Hagedorn Insulin with Hypoglycemia-Related Emergency Department Visits or Hospital Admissions and With Glycemic Control in Patients with Type 2 Diabetes*, 320 JAMA 53 (June 23, 2018).
[39] Kelly McLaughlin, *Insulin is getting so expensive that people with diabetes are switching to older versions of the drug. It's having deadly consequences.*, INSIDER, Aug. 16, 2019, https://www.insider.com/safety-tips-for-switching-insulins-type-1-diabetes-patients-2019-8.
[40] American Diabetes Association, *Insulin Routines*, https://www.diabetes.org/diabetes/medication-management/insulin-other-injectables/insulin-routines.
[41] Kate Ruder, *What to Know Before You Use OTC Insulin*, EVERYDAY HEALTH,, Apr. 23, 2019, https://www.everydayhealth.com/diabetes/otc-insulin-what-know-before-you-buy/.
[42] Howe, *supra* note 32.
[43] *Id.*
[44] *Id.*
[45] McLaughlin, *supra* note 39.
[46] Ruder, *supra* note 41.
[47] Karla Melo et al., *Short-acting insulin analogues versus regular human insulin on postprandial glucose and hypoglycemia in type 1 diabetes mellitus: a systematic review and meta-analysis*, DIABETOLOGY & METABOLIC SYNDROME, vol. 11:2 (2019). "The term

Short-acting insulin analogs resulted in a reduction of 7 percent in total hypoglycemic episodes, 32 percent in severe hypoglycemia, and 45 percent in nocturnal hypoglycemia levels.[48] Another recent study found that insulin analogs have much improved safety and efficacy profiles over human insulin.[49]

Nevertheless, endocrinologists advise that taking human insulin is still preferable to rationing analog insulin, but any switch between the two should be done in consultation with a doctor.

Patient Experiences and Survey Results of the Economic Impact of Diabetes on Coloradans

Approximately 300,000 Coloradans live with type 1 or type 2 diabetes, with as many as 110,000 additional undiagnosed diabetes patients.[50] Nationally, out of more than 30 million people with diabetes, approximately 24.6 percent use some form of insulin.[51] That would mean that nearly 73,800 Coloradans rely on insulin to manage their diabetes. Thus, the cost of both insulin and necessary supplies have a significant impact on diabetic Coloradans. The Department analyzed the results of the survey it conducted to better understand how the cost of insulin and supplies impacts Coloradans.

Coloradans' Experience with High Insulin Prices

Survey Respondent 1 has been a type 1 diabetic since 1972 and is a diabetes patient advocate. When Survey Respondent 1 was first diagnosed, insulin cost 99 cents a vial, and until 1996, insulin was available without a prescription. Now, Survey Respondent 1's insurance limits access to certain pharmacies and prices. Survey Respondent 1 states that: "[I]nsulin is not part of the free market economy." Despite living with diabetes for decades, Survey Respondent 1 suffers from no complications from diabetes, stating:

> *but that's only because I have been able to take care of myself in the best way that I can. Type 1s are living longer, which means we need insulin LONGER, for more years. It's not like we take insulin on Sunday and don't need it again until Friday. Insulin is more vital than water to stay alive.*

HbA1c refers to glycated haemoglobin. It develops when haemoglobin, a protein within red blood cells that carries oxygen throughout your body, joins with glucose in the blood, becoming 'glycated'. By measuring glycated haemoglobin (HbA1c), clinicians are able to get an overall picture of what our average blood sugar levels have been over a period of weeks/months. For people with diabetes this is important as the higher the HbA1c, the greater the risk of developing diabetes-related complications." *Guide to HbA1c*, DIABETES.CO.UK, Jan 15, 2019, https://www.diabetes.co.uk/what-is-hba1c.html.

[48] Melo et al., *supra* note 47.

[49] Andrej Janež et al., *Insulin Therapy in Adults with Type 1 Diabetes Mellitus: a Narrative Review*, 11 DIABETES THERAPY 387, 393 (Feb. 2020) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6995794/.

[50] Colorado Department of Public Health & Environment, *Diabetes' Impact in Colorado, Facts for Actions: Chronic Diseases and Related Risk Factors in Colorado*, DC Factsheet Facts for Action Diabetes in Colorado (Nov. 2015).

[51] William Cefalu et al, *Insulin Access and Affordability Working Group: Conclusions and Recommendations*, vol 41(6), DIABETES CARE 1299, 1299-1311 (June 2018).

> *You can go for three days without water. But you can't go for more than 12 hours, MAYBE without insulin.*

Survey Respondent 2 is a type 1 diabetic who lost her insurance after her husband lost his employment due to COVID-19. She recently stayed in hospital for three-weeks because her blood sugar spiked, resulting in complications. Although she took short-acting insulin, she did not have access to the long-acting insulin she usually takes or the necessary supplies to check her blood sugar. Survey Respondent 2 said, "had I had the supplies that I needed at a reasonable price, that hospital stay could have been avoided."

Before Colorado capped co-pays at no more than $100 per month for insured patients in January 2020,[52] survey respondents reported insulin co-pays of $2,500 for a 3-month supply of insulin. Many respondents reported difficulty in budgeting for insulin costs because their insurance would not notify them of changes in coverage of certain brands. As one certified diabetes resident nurse explained:

> *Many patients are unable to obtain coverage for their prescribed or preferred brand of insulin. This forces patients to not only pay for their insurance but to also pay out-of-pocket for their insulin. Further marginalizing individuals that are already struggling with their health and many who already face economic adversity, especially families.*

What was previously affordable can become unaffordable overnight, and a patient will only learn about the change when picking up an insulin refill from their pharmacy. Many patients reported that when faced with paying thousands of dollars out of pocket, their insurance coverage pushed them into a new prescription for the insurance preferred brand of insulin. But getting a new prescription can take time. If patients do not have enough insulin on hand to bridge that gap, they have no alternative but to pay themselves, if they can.

To combat the escalating costs of insulin, survey respondents reported going into debt, selling homes, and buying prescription insulin in Canada and Mexico. A certified diabetes resident nurse noted, "Patients shop around for jobs with insurance that cover the insulin they need to stay alive," and "people quit jobs that they are passionate about too so that they can afford their insulin."

Many respondents stated that they receive insulin from family members or friends. More than one survey respondent reported sending insulin to loved ones who need it but cannot afford it. And it is not uncommon to hear that patients must choose between food, rent, bills, and insulin every month. Some patients even reported they cannot get their insulin prescription renewed because they cannot afford a doctor's appointment.

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[52] *See* COLO. REV. STAT. § 10-16-151 (2019).

Survey respondents were asked to list their average monthly costs for insulin:

Item	*Responses*	*Percentage (%)*
$0-99	166	47.29
$100-499	111	31.62
$500-999	16	4.56
$1,000-1499	5	1.42
$1,500+	17	4.84
"It Varies"	9	2.56
"I don't Know"	4	1.14
Did not answer	23	6.55

Measure: Monthly Cost of Insulin

The survey also asked respondents to describe the effect of insulin prices on their daily lives:

Item	*Responses*	*Percentage (%)*
Very Much	152	43.18
Somewhat	118	33.52
Very Little	71	20.17
"I don't Use Insulin"	2	0.57
Did Not Answer	9	2.56

Measure: Effect of Cost of Insulin on Life

Many survey respondents reported rationing because of cost. Survey respondents reported that patients who cannot afford their insulin often resort to using less insulin than prescribed, skipping doses, and using expired insulin. Sonya Walker, a type 1 diabetic, nurse, and certified diabetes educator at the Barbara Davis Center, indicated that she often sees patients who are rationing insulin and diabetes supplies. Survey Respondent 2 reported underdosing, so she can "stretch [her] short-acting Humalog." In one study of 354 eligible patients at the Yale Diabetes Center in Connecticut, 25.5 percent of patients reported cost-related insulin underuse.[53]

[53] Darby Herkert et al., *Cost-Related Insulin Underuse Among Patients with Diabetes*, 179 JAMA INTERNAL MED. 112 (2019).

The findings from the Department's investigation and study paint a grimmer picture. Over 40 percent of survey respondents replied that they ration insulin due to cost at least once per year, with over 6 percent of respondents rationing insulin every day:

Item	Responses	Percentage (%)
Never	197	55.97
About Once per Year	44	12.5
About Once per Month	59	16.76
About Once per Week	22	6.25
Every Day	22	6.25
Did Not Answer	8	2.27

Measure: Frequency of Rationing Insulin due to Cost

Others reported skipping doses due to cost:

Item	Responses	Percentage (%)
Never	245	69.6
About Once per Year	36	10.23
About Once per Month	36	10.23
About Once per Week	16	4.55
Every Day	13	3.69
Did Not Answer	6	1.7

Measure: Frequency of Skipping Insulin Doses due to Cost

Or, even used expired insulin to stretch their supplies:

Item	Responses	Percentage (%)
Never	210	59.66
About Once per Year	73	20.74
About Once per Month	42	11.93
About Once per Week	9	2.56
Every Day	7	1.99
Did Not Answer	11	3.13

Measure: Frequency of Use of Expired Insulin

The underuse and rationing of insulin results in poor glycemic control potentially leading to diabetic ketoacidosis ("DKA") in the short term and microvascular and macrovascular complications in the long term, including retinopathy, kidney disease, neuropathy, and heart disease.[54] Overall, the Centers for Disease Control reported that between 2000 to 2009, the age-adjusted rate of hospitalizations from DKA among persons with diabetes fluctuated but declined at an average annual rate of 1.1 percent, but that those hospitalizations increased 54.9 percent from 2009 to 2014 (or from 19.5

[54] H. Peter Chase & David M. Maahs, Barbara Davis Center for Childhood Diabetes, Understanding Diabetes 157, 229-35 (12th ed. 2011).

to 30.2 per 1,000 persons).[55] In severe cases, insulin underuse can result in death. From 2017 to 2019, at least 13 people in the United States died from rationing insulin.[56]

The high cost of insulin not only results in physical manifestations for those patients struggling to afford their insulin, but also impacts their mental health. Coloradan diabetes patients report persistent high anxiety, depression, and insomnia along with pervasive worry, stress, and fear about their ability to afford insulin. Walker noted, "This is a chronic disease—there is so much burden on the part of the patient to care for themselves—this results in high rates of depression and anxiety."

The mental and physical toll for diabetes patients has only increased as the COVID-19 pandemic has continued. Early research observed that severe and fatal cases of COVID-19 are often associated with underlying chronic conditions, including diabetes.[57] Further, survey respondents reported job loss, furloughs, and salary reductions due to the pandemic, which have made survival even more difficult. As one respondent said, "I was laid off…I am high risk for a number of reasons. Haven't been able to find work still. Insurance ended the last day of June. Really scared." Another respondent shared, "I am unemployed at the moment. Still waiting to get a call to come back to work. The unemployment [benefits] are running out and one income ain't gonna cut it. It's gonna come down to paying bill or getting meds very quickly. And I can't go back to trying to balance those decisions. I will die from it. Then who takes care of my kid?"

Another common issue involves health plan limitations on which brands or forms of insulin the plans will cover, which presents a separate set of challenges. Both survey respondents and medical professionals report that insurance companies will often cover only a preferred brand of insulin. If a patient needs a different brand, they must obtain prior authorization from the insurance company. As one nurse explained,

> *The entire prior authorization process is time consuming and costly. There is one person in the office devoted almost entirely to doing prior authorizations, so that is yet another burden on our entire healthcare system. It is also ridiculous that prior authorizations have to be renewed annually. If a patient has an allergy or intolerance to a certain insulin, they will still have that allergy or intolerance in a year. But we still have to complete the prior authorization the following year, even if their insurance is the same…The insurance companies dictate which type of insulin patients will use. It is often a type of insulin that is not optimal for the patient. Having an allergy to a certain type of insulin is*

[55] Stephen Benoit et al., *Trends in Diabetic Ketoacidosis Hospitalizations and In-Hospital Mortality* — United States, 2000–2014, Morbidity and Mortality Weekly Report (Mar. 30, 2018), at 362-65.
[56] Right Care Alliance, *Insulin*, 2020, https://rightcarealliance.org/actions/insulin/.
[57] Akhtar Hussain et al., *COVID-19 and diabetes: Knowledge in progress*, Diabetes Research and Clinical Practice vol. 162, at 4 (2020), https://www.sciencedirect.com/science/article/pii/S0168822720303922.

> *the ONLY reason an insurance company will accept for NOT using that certain type of insulin. The insurance company will NOT accept other medically valid reasons such as 'this person's body does not react optimally with this type of insulin.' To help rectify this situation, doctors and nurses often lie when doing pre authorizations and falsely claims [sic] that the patient has an 'allergy' to the type of insulin that the insurance company wants the patient to use. A person should be on the right insulin for their body. Insulins have many differences and are unique from each other and to have to switch insulin can be detrimental to a body.*

Another problem arises when patients are forced to switch to a different insulin brand or formulation—over their physician's objections—because their insurance company no longer covers their existing insulin, and the new formulation either does not work as well or does not last as long.[58] As one physician interviewed shared:

> *A lot of patients are on a long acting insulin injection called Tresiba. There is not any other equivalent – there is just one insulin like this. As of July 1 for patients on UnitedHealth Care they DROPPED Tresiba from their formulary! We can't even do a planned exemption – they say it's a plan exclusion. We have to switch them to a different long acting insulin – but for many patients nothing else works the same or as well. This has been VERY upsetting for a lot of people. Tresiba is more consistently absorbed and therefore the patient is less prone to hyperglycemia – the number one killer for an overdose of insulin. Tresiba has been proven to have less incidents of hyperglycemia – but for the insurance company not to cover is really tragic.*

And even if the insurance company approves a non-preferred brand, survey respondents report out-of-pocket costs of thousands of dollars per prescription. Survey respondents also report that some insurance companies have started limiting how much insulin the plan will cover for a patient per month, though it is unclear if the limits apply to all insulin or only those types not on the formulary. These limits are too low for some patients, causing them to ration their insulin.

[58] Where a new brand of insulin runs out too early, a patient may struggle with his insurance company to get an early refill. *See* Stephanie Talmadge, *Sticker Shock in the Pharmacy*, THE NEW YORK TIMES, Sept. 23, 2020, https://www.nytimes.com/2020/09/23/well/live/sticker-shock-in-the-pharmacy.html?smid=em-share.

Cost Impact of Diabetes-Related Supplies on Coloradans

The cost of insulin is not the only financial burden facing Coloradans. A national survey of privately insured patients with type 1 diabetes revealed that diabetes-related supplies accounted for more out-of-pocket spending than insulin.[59] Many survey respondents similarly reported that the cost of diabetic supplies needed to administer insulin and monitor blood glucose levels was even more onerous than the cost of insulin.

Item	Responses	Percentage (%)
$0-99	136	38.64
$100-499	153	43.47
$500-999	20	5.68
$1,000-1499	4	1.14
$1,500+	5	1.42
"It Varies"	0	0
"I don't Know"	4	1.14
Did not answer	34	9.66

Measure: Monthly Cost of Supplies

Managing diabetes requires continuous monitoring and treatment. Type 1 diabetics and many type 2 diabetics must either inject insulin multiple times a day—which requires the purchase of needles or syringes—or use an insulin pump that can deliver insulin as needed. Survey respondents reported reusing needles to defray costs. Diabetics must also check their blood glucose levels multiple times a day using a blood glucose meter, test strips, and continuous glucose monitors ("CGMs"). Patients rely on CGMs to monitor and improve glycemic control and lower A1C levels, [60] which reflect a patient's average blood glucose level over the past three months.

Insulin pump therapy along with the use of CGMs are crucial but costly supplies. For those who use pumps, respondents stated insurance companies will often cover only one brand of pump, whether the pump adequately meets a patient's needs or not. The retail cost for newer generation pumps can be as high as $8,000,[61] and ongoing insulin pump supplies frequently cost an additional $3,000-$6,000 annually.[62] Although insurance covers some portion of the costs for qualifying patients, that coverage varies widely. To control costs, survey respondents reported reusing sensors and pump supplies against physician and manufacturer recommendations. Respondents also expressed frustration

[59] Kao-Ping Chua et al., *Out-of-Pocket Spending for Insulin, Diabetes-Related Supplies, and Other Health Care Services Among Privately Insured US Patients with Type 1 Diabetes*, 180 JAMA Internal Medicine 1013, E1 (July 2020).
[60] David M. Maahs et al., *Epidemiology of type 1 diabetes*, 39 ENDOCRINOLOGY AND METABOLISM CLINICS OF NORTH AM. 481, 489 (2010).
[61] Jimmy McDermott et al., *FDA Approves Medtronic MiniMed 670G Hybrid Closed Loop for 7–13 Year Olds*, DIATRIBE LEARN, July 13, 2018, https://diatribe.org/fda-approves-medtronic-minimed-670g-hybrid-closed-loop-7-13-year-olds.
[62] Healthline, *Insulin Pumps*, https://www.healthline.com/health/type-2-diabetes/insulin-prices-pumps-pens-syringes#insulin-pumps.

that insurance does not often cover sensors and pump supplies, even though these products keep blood sugar well controlled and keep patients out of physicians' offices and emergency rooms.

Because of the costs associated with pumps, sociodemographic characteristics play a significant role in whether patients use insulin pump therapy.[63] For example, the SEARCH for Diabetes in Youth study[64] found that 26.3 percent of white children reported using insulin pump therapy compared with only 12.3 percent of Hispanic children and 5.3 percent of Black children.[65]

Diabetics also adopt measures to minimize their glucose testing costs. Survey respondents reported limiting how often they test blood glucose levels. As one certified diabetes resident nurse explained, "Due to the cost of testing supplies, many people with low incomes will skip testing and hope for the best. This leads to drastic difference in the effect that diabetes plays in the outcome of people's lives." And like prescription insulin and insulin pumps, insurance often covers only the preferred brand. A CGM with the necessary sensors and transmitters can cost up to $6,000 per year, depending on insurance coverage.[66] Walker noted that "[m]ost patients on Medicaid could never afford a [CGM]—this is a life-saving device." Diabetics also require prescriptions for Glucagon or Baqsimi for the emergency treatment of severe hypoglycemia[67]—when a patient's blood glucose falls to a severely low level—but a prescription for Glucagon or Baqsimi can cost almost $300 for a single dose.[68]

Using an insulin pump in conjunction with a CGM is optimal for managing diabetes, but, for many, these treatment and management tools are unaffordable. Survey Respondent 2 reported that if she had all the necessary diabetes-related supplies, she would be paying $1,200 per month without insurance, but even with insurance, the necessary supplies cost her over $600. As a result, she sometimes goes without the supplies. And even for those who can afford the supplies, the costs are staggering. Survey respondents report paying as much as $30,000 annually for prescription insulin supplies, even with insurance. Many respondents stated that the cost of all diabetic supplies, not just prescription insulin, must be addressed.

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[63] Carolyn Paris et al. *Predictors of Insulin Regimens and Impact on Outcomes in Youth with Type 1 Diabetes: The SEARCH for Diabetes in Youth Study*. 155 THE J. OF PEDIATRICS 183, 187 (Apr. 27, 2009).

[64] A total of 2743 subjects participated in the SEARCH for Diabetes in Youth study, an observational population-based study of youth diagnosed with type 1 diabetes, conducted at six centers.

[65] Steven Willi et al., *Racial-Ethnic Disparities in Management and Outcomes Among Children With Type 1 Diabetes*, 135 PEDIATRICS 424, 425 (Mar. 2015).

[66] David Spero, *Is Continuous Glucose Monitoring Worth It? Diabetes Self-Management*, DIABETES SELF-MANAGEMENT, Mar. 18, 2015, https://www.diabetesselfmanagement.com/blog/is-continuous-glucose-monitoring-worth-it.

[67] JDRF, *What is glucagon?*, https://www.jdrf.org/t1d-resources/daily-management/what-is-glucagon/ (Severe hypoglycemia occurs when a patient's blood glucose falls to a dangerously low level where he or she becomes confused or unconscious or suffers from other symptoms that require assistance from another person to treat. "Glucagon is a hormone that helps the liver release glucose in order to raise blood-sugar levels. It can be administered through injection, auto-injection pen, or nasal spray.").

[68] Jordan Dakin, *Nasal Glucagon Baqsimi Approved by the FDA*, Beyond Type 1, https://beyondtype1.org/nasal-glucagon-baqsimi-approved-by-the-fda/.

Pharmaceutical Industry

Understanding the pharmaceutical supply chain—including both the physical distribution of drugs and the payment system[69]—is important for understanding insulin pricing.

The physical distribution of a drug begins at the point of manufacture. The manufacturer decides what products to manufacture and then typically sells its products to wholesale distributors, which in turn sell the drug products to pharmacies. The pharmacies then dispense the drug to patients.[70]

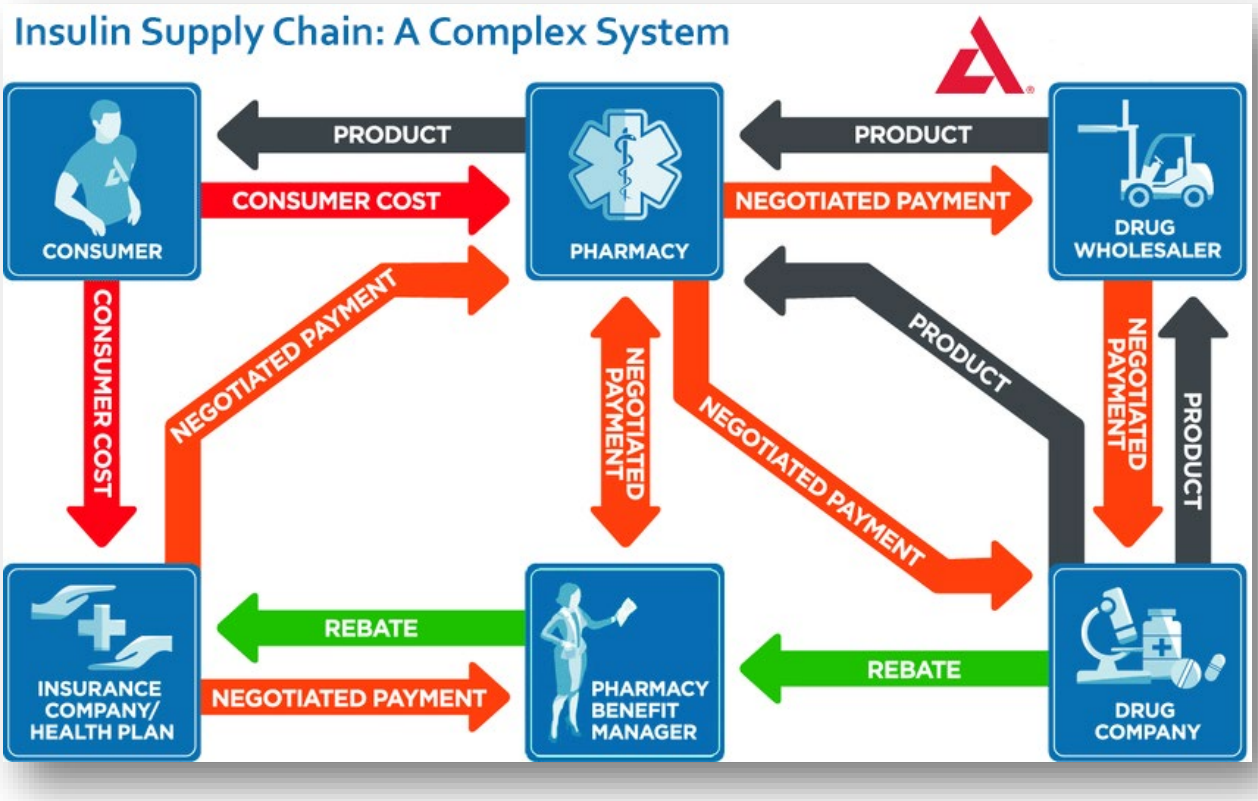
The purchase/payment system also begins with the manufacturer, which sets the product's list price. The *net* price manufacturers receive for a drug is the list price less any fees paid to wholesalers, discounts paid to pharmacies, and rebates paid to PBMs or health plans for including the drug in the formulary.[71] When the pharmacy sells a drug to the patient, the patient pays his or her out-of-pocket cost as determined by insurance coverage—assuming the patient has coverage—and the dispensing pharmacy then sends a bill to the PBM, which passes the bill to the patient's health insurer. After the PBM receives the insurer's payment, it sends a portion of the payment back to the dispensing pharmacy.[72]

The interplay among drug manufacturers, PBMs, insurers, and pharmacies has a significant impact on the out-of-pocket cost of drugs to a patient. This section discusses in more detail the various roles of the players in the pharmaceutical supply chain.

[69] Congressional Report, *supra* note 17 at 7.
[70] The Health Strategies Consultancy, LLC., *Follow the Pill: Understanding the US Commercial Pharmaceutical Supply Chain*, Kaiser Family Foundation, at 3, 5.
[71] Cefalu, *supra* note 51 at 1301.
[72] Congressional Report, *supra* note 17 at 7.

How the Pharmaceutical Supply Chain Operates

The American Diabetes Association depicted the pharmaceutical supply chain, and its key players—with a focus on insulin—as follows:[73]



Manufacturers

Drug manufacturing is the process of producing pharmaceutical drugs on an industrial scale, which includes small molecule drugs and biopharmaceuticals such as insulin. A manufacturer must decide what drugs to manufacture and supply to the marketplace. Drug manufacturers also manage the sale and supply of insulin products from their manufacturing facilities to drug wholesalers, although manufacturers sometimes deliver directly to pharmacies, hospitals, and certain health plans. Because drug manufacturers control the distribution and initial pricing, they play a significant role in the cost of insulin to patients.[74]

Currently, there are only 10 independent insulin manufacturers globally,[75] with the three largest companies supplying 90 percent of the world's insulin and nearly 100

[73] Cefalu, *supra* note 51 at 1303.
[74] *Follow the Pill, supra* note 70 at 6.
[75] David Beran et al., *Access to Insulin: Current Challenges and Constraints*, ACCIS/Health Action International at 5 (Mar. 2017 Update), http://haiweb.org/wp-content/uploads/2017/03/Issues_Paper_2017.pdf.

percent of the insulin in the United States.[76] This highly concentrated market with minimal competition, few consumer options, and tightly controlled product availability directly influences the difficulty of reducing the price of insulin,[77] as discussed in more detail in later Sections.

Manufacturers set the initial sales price of their drugs—often referred to as the manufacturer's "list price."[78] A manufacturer's list price frequently serves as the starting point for a drug's pricing as it moves along the supply chain. When a manufacturer raises the list price, the price wholesaler distributors charge to pharmacies increases. In turn, the pharmacy passes those price increases onto the patient. An increase in the list price also impacts the amount that health plans will cover or reimburse members when a plan member is prescribed the drug.

Although the list price is defined as the price manufacturers set for their pharmaceutical, the list price is not what patients pay at the pharmacy, unless—as described below—they are underinsured, uninsured, or have high-deductible health plans. Nor is the list price the amount that manufacturers receive for their drugs. The *net* price manufacturers receive for the drug is the list price less: (1) any fees paid to wholesalers; (2) discounts paid to pharmacies; and (3) rebates paid to PBMs or health plans for including the drug in the formulary.[79] This complex pricing formula, and how it impacts what patients pay for insulin, is described in more detail below.

Pharmacy Benefit Managers

A pharmacy benefit manager, or PBM, acts as a middleman in the drug supply chain. PBMs have relationships with three important entities in the sales chain that influence drug pricing: manufacturers; health plans; and retail pharmacies.[80]

Third-party payers (private insurers, self-funded employers, and public health programs) hire PBMs to manage all or part of the drug benefit provided to plan members on the plan's behalf.[81] The PBM typically outlines and develops the policies specifying which drugs are covered, the amounts that pharmacies will receive for a drug, and what the consumers must pay out-of-pocket when the prescription is filled.[82]

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[76] JUDITH A. JOHNSON, CONGRESSIONAL RESEARCH SERVICE, 7-5700, INSULIN PRODUCTS AND THE COST OF DIABETES TREATMENT 2 (Nov. 19, 2018), https://fas.org/sgp/crs/misc/IF11026.pdf.

[77] Margaret Ewen et al., *Insulin Prices Profile*, ACCISS/Health Action International, Apr. 2016, at 82, https://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf.

[78] Office of MN AG Keith Ellison, *Report of the MN Attorney General's Advisory Task Force on Lowering Pharmaceutical Drug Prices* at 21, Feb. 2020 ("MN AG Report") https://www.ag.state.mn.us/Office/Communications/2020/docs/DPTF_Feb2020Report.pdf.

[79] Cefalu, *supra* note 51 at 1303.

[80] MN AG Report, *supra* note 78 at 21.

[81] *Id.*

[82] *Follow the Pill, supra* note 70 at 14-15.

PBMs manage the drug benefit for third-party payers by creating and managing what is known as a "formulary." Formularies list the drugs for which the health plan will reimburse when prescribed. Formularies typically group drugs into tiers, and the "tier" determines the price a patient pays. For example, a "Tier 1" drug usually encompasses preferred generic drugs, "Tier 2" includes preferred brand-name drugs, "Tier 3" includes non-preferred drugs (generic and brand-name), and "Tier 4" are specialty drugs.[83] If a drug is not included on the formulary at all, a patient—even if insured—must generally pay the full list price of the drug out of pocket.[84] PBMs develop and manage formularies by processing the drug through quality and utilization management screens. "Utilization management" or "utilization review" is the evaluation of the appropriateness and medical necessity of health care services, procedures, and facilities according to evidence-based criteria or guidelines and under the provisions of an applicable health insurance plan. PBMs, citing trade secrets, do not disclose what role rebates and other negotiated fees play in exclusive or preferred placement in drug formularies.[85]

"Just as three players dominate insulin manufacturing, three PBMs together manage more than 85% of the pharmaceutical and biopharmaceutical markets in the United States."

Within Medicare Part D plans, most formularies cover insulin on Tier 3.[86] In 2019, insulin typically had a $47 copayment in the initial coverage phase, but incurred a 25 percent coinsurance rate during the so-called "donut hole" [87] coverage gap, which could cost $100 or more in out-of-pocket costs for insulin.[88]

PBMs represent insurers by negotiating prices with the manufacturers of brand-name drugs, which results in the manufacturers providing rebates, discounts, and paying fees

[83] *See* Kaiser Permanente, *Colorado Commercial Formulary* at 4, Oct. 2020, http://providers.kaiserpermanente.org/info_assets/cpp_cod/co_marketplace_formulary_sec.pdf.
[84] MN AG Report, *supra* note 78 at 21.
[85] This information was not even available to Congress as it tried to investigate high insulin prices. *See* Congressional Report, *supra* note 17 at 10-11.
[86] Juliette Cubanski et al., *Insulin Costs and Coverage in Medicare Part D*, Kaiser Family Foundation, June 4, 2020, https://www.kff.org/medicare/issue-brief/insulin-costs-and-coverage-in-medicare-part-d/.
[87] The Medicare "donut hole" is the "temporary limit on what most Medicare Part D Prescription Drug Plans or Medicare Advantage Prescription Drug plans pay for prescription drug costs." The "donut hole" occurs after a Medicare insured has met their deductible and reached their out-of-pocket threshold in the initial coverage phase. While in the "donut hole," Medicare insureds typically pay up to 25% of the plan's cost for both branded and generic drugs. https://medicare.com/medicare-part-d/coverage-gap-donut-hole-made-simple/.
[88] *Id.*

to PBMs in exchange for getting their drugs on health plan formularies.[89] Insurers pay PBMs based on some percentage of the discount from the list price negotiated with the drug manufacturer—whether through rebates, administrative fees, or otherwise. It is reported that several PBMs recently created their own group purchasing organizations to assist in the negotiation of rebates, fees and other discounts.[90] Commentators speculate that, among other things, use of the organizations allow for even less transparency into rebates, fees, and other discounts.[91]

Just as three players dominate insulin manufacturing, three PBMs—OptumRx (owned by United Health), CVS Caremark (owns Aetna), and Express Scripts (owned by Cigna)—together manage more than 85 percent of the pharmaceutical and biopharmaceutical markets in the United States. This resulted from tremendous consolidation in the PBM market, where, since 2000, the market has contracted into these three dominant players through various mergers and acquisitions. For the Medicaid managed-care population, these three PBMs alone appear to handle 50 percent of the prescription drug benefits outside of the commercial insurance market as of 2015.[92]

Carriers/Payers

Insurance carriers play a significant role in a patient's access to insulin and insulin-related products. The formularies that PBMs create for carriers largely determine patient access: if a drug does not appear on a formulary, the patient either cannot access the drug or must pay the list price, which may be prohibitive, because the drug is not available through their specific plan. Patients' options are further limited because they have no influence over what drugs appear on the formulary or in what tier. The patient interacts with their insurer and rarely with the PBM.

Wholesalers/Distributors

Wholesale drug distributors, or wholesalers, purchase drugs directly from manufacturers and then sell those drugs to pharmacies.[93] The wholesaler acquires the drugs at a wholesale acquisition cost (WAC), less negotiated rebates or discounts, and is reimbursed by the pharmacy at a price above the wholesaler's acquisition cost. In Colorado, a wholesaler must be registered with the Colorado Board of Pharmacy to distribute drugs into the State of Colorado.[94] The top three wholesale distributors (McKesson, Cardinal Health, and AmerisourceBergen) account for almost 90 percent of

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[89] Ge Bai et al., *Pharmacy Benefit Managers, Brand-Name Drug Prices, and Patient Cost Sharing*, 168 ANNALS OF INTERNAL MEDICINE 436, 436 (Feb. 13, 2018).
[90] Rebecca Pifer, *CVS reportedly creating group purchasing organization for PBM business*, HealthCareDive, July 1, 2020, https://www.healthcaredive.com/news/cvs-reportedly-creating-group-purchasing-organization-for-pbm-business/580889/.
[91] Adam J. Fein, *Express Scripts + Prime Therapeutics: Our Four Takeaways From This Market Changing Deal*, Drug Channels, Jan. 7, 2020, https://www.drugchannels.net/2020/01/express-scripts-prime-therapeutics-our.html.
[92] Feldman Report, *supra* note 5 at 23.
[93] *Follow the Pill, supra* note 70 at 8.
[94] *See* COLO. REV. STAT. § 12-280-303 (2019).

the wholesale drug distribution market and therefore play an important role and exercise significant control over insulin prices.[95]

> ***"The top three wholesale distributors account for almost 90% of the wholesale drug distribution market and therefore play an important role and exercise significant control over insulin prices."***

Pharmacies

Pharmacies serve as the final stop before a drug reaches the patient. Pharmacies break down into 5 basic categories: chain drug stores, pharmacies located in retail establishments (e.g., grocery store pharmacies), independent pharmacies, hospital pharmacies, and mail-order pharmacies. Pharmacies typically purchase their drugs from wholesalers (sometimes directly from manufacturers) and then stock the drugs for dispensing to the patient.[96]

Pharmacies act as an important link among PBMs, drug manufacturers, and wholesalers. Because pharmacies serve as the final point of sale for medications and as the interface between the supply chain and the patient, pharmacies generate the prescription drug claims information that PBMs, as well as health plans, employers, governments, and other payers, rely upon to measure consumer activity. As the last point of contact in the supply chain, it is incumbent on the pharmacy to contact the prescribing physician if the drug prescribed is not on the patient's health plan formulary or if a lower-cost therapeutic alternative is available.[97]

How this Supply Chain Structure Affects Drug Prices

This complicated distribution scheme significantly impacts the pricing of pharmaceutical drugs in the United States. A March 2020 study from the University of Pittsburgh found that, when adjusted for inflation, list prices set by drug manufacturers increased over the last decade by 159 percent, while the prices paid to manufacturers (net price) increased by 60 percent—more than three times the rate of inflation.[98] List prices for insulin increased by 262 percent during the period studied, while the net price increased by 51 percent. Among other things, these heavy discounts may be "applied to

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[95] *Follow the Pill, supra* note 70 at 9 (citing to Standard & Poor's, *GICS Sub-Industry Revenue Share* at 3, Sept. 4, 2004)).
[96] *Id. at 10.*
[97] *Id.*
[98] Hernandez, *supra* note 1 at 860.

stave off competition from biosimilars."[99] For patients, this widening gap between list and net prices may expose the uninsured or those with high-deductible plans to the ever-growing list prices.[100]

Another recent study focused on 49 top-selling drugs between 2012 and 2017 and found "substantial cost increases" among all of them.[101] Of the 36 drugs in the study that have been available since 2012, 28 (78 percent) had seen an increase in insurer and out-of-pocket costs by more than 50 percent.[102] In total, 16 drugs (44 percent) more than doubled in costs, including several insulin products.[103] Significantly, insulin products in the study "demonstrated highly correlated price increases, coinciding with some of the largest growth in drug costs."[104]

Researchers from the National Academy of Sciences published a Consensus Study Report finding that annual expenditures on biopharmaceuticals[105] in the United States[106] far exceeded that of other developed countries. The Consensus Study Report noted:

> *Most other developed countries have explicit price controls or bargaining mechanisms in place for prescription drugs, some of which use cost-effectiveness metrics. In the United States, currently there are no centralized price controls, and payers do not explicitly deny access to treatments on the basis of costs, thus enabling biopharmaceutical companies to set higher prices than in other countries.*[107]

Americans pay more for their prescription drugs than consumers in any other country. Per capita pharmaceutical drug spending is 54 percent to 209 percent higher in the United States than other high-income countries.[108] Net spending on prescription drugs in the United States reached $324 billion in 2017 and is expected to increase 2 to 5 percent annually over the next 5 years.[109] And the amount Americans spend on

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[99] *Id.* at 861.
[100] *Id.*
[101] Nathan E. Wineinger et al., *Trends in Prices of Popular Brand-Name Prescription Drugs in the United States*, JAMA NETWORK OPEN, vol. 2(5), at 1 (May 31, 2019).
[102] *Id.* at 4.
[103] *Id.*
[104] *Id.* at 1.
[105] A biopharmaceutical (or biologic medical product, or biologic) is any pharmaceutical drug product manufactured in, extracted from, or synthesized from biological sources.
[106] A Consensus Study Report of the National Academies of Sciences, Engineering, and Medicine, *Making Medicines Affordable – A National Imperative* at 25, 2018 ("NAS Consensus Study").
[107] *Id.* at 26. The federal government is prohibited from negotiating lower drug prices on behalf of Medicare Part D beneficiaries, although that prohibition does not extend to Medicaid or VA programs, resulting in much higher brand name drug prices for Medicare Part D patients. *See* House Oversight Committee, *The Medicare Drug Price Negotiation Act of 2017 (Discussion Draft Summary)*, https://oversight.house.gov/sites/democrats.oversight.house.gov/files/documents/Negotiation%20Bill%20Two-Pager%20for%20Release%20-%20Final_0.pdf.
[108] *See* Irene Papanicolas et al., *Health care spending in the United States and other high-income countries*, 319 JAMA 1024, 1024 (2018).
[109] Wineinger, *supra* note 101 at 2.

prescription drugs only continues to increase. By 2018, annual spending on biopharmaceuticals exceeded half a trillion dollars.[110]

What makes this marketplace different from other consumer goods is (i) the existence of payers (both public and private) who pay the majority of drug costs and (ii) the involvement of intermediaries, including PBMs, to negotiate deep discounts—in the form of rebates and other fees—and control formulary placement. For several reasons, traditional and expected market dynamics are not at play, changing the incentives and barriers typically present in other industries.

First, in contrast to other industries, the party paying for the product, and thus holding the market power, is not the ultimate consumer. In the prescription drug market, the principal party that directly pays the bill, in part or in its entirety, is usually not the consumer but rather an insurer, the government, or some other third-party payer, such as an employer or union. Because patients are not the direct payer, patients do not hold the purchasing power for prescription drugs and insulin specifically. The insurer's ability to pass through price increases as overall increases in premiums temper incentives to hold down costs.

Second, in contrast to other markets, patients not only have little purchasing power, but they also do not generally make the decisions about which products they will consume. Before purchasing a prescription drug, the purchaser (patient) generally must obtain permission in the form of a prescription from a licensed practitioner. The decision as to what prescription drug a pharmacy will dispense is typically made by the prescribing physician, and the drug dispensed also depends on what the insurance plan will authorize. As a result, decision-making authority does not lie with the patient but rather falls under the controls of other players in the pharmaceutical supply chain.

Third, heavy regulation creates significant barriers to entry for new manufacturers to enter and compete. The pharmaceutical industry is highly regulated ostensibly due to health and safety considerations. As a result of these regulatory requirements, entry may be stifled, which lessens competition and often results in oligopoly pricing. This phenomenon, however, is not new or unique to insulin and applies to a range of pharmaceutical products. The regulatory regime on its own does not explain high insulin prices.[111]

Fourth, as part of this regulatory landscape, even where generic or biosimilar products have been approved in a foreign country, U.S. law prohibits importation of that drug into this country without FDA approval.[112] This is a somewhat unique benefit to the prescription drug biopharmaceutical industry as compared to other industries that experience foreign competition. The regulatory scheme thus also provides these

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[110] NAS Consensus Study, *supra* note 106.

[111] *See* Regulatory Process of Biosimilars on page 39.

[112] 21 U.S.C. § 331; *see also* Division of Import Operations and Policy, Food and Drug Administration, Information on Importation of Drugs, https://www.fda.gov/industry/import-program-food-and-drug-administration-fda/importations-drugs.

manufacturers and other actors in the drug supply chain with additional protection and control over the U.S. prescription drug market.

Fifth, patents play a significant role in impacting drug prices and changing normal market dynamics and incentives. It is important to note that a new drug manufacturer files its patent application before it undertakes what can be years or testing and clinical trials, which occurs before the manufacturer even has FDA approval. Compliance with these requirements "eats into" a substantial portion of the patent protection period.[113] A manufacturer stands to make the most profit when it is a sole source of a particular prescription drug, which is the time period when the manufacturer is protected by its patent(s) and before generic or biosimilar entry.

"Americans pay more for their prescription drugs than consumers in any other country. Per capita pharmaceutical drug spending is* 54% higher in the United States *than other high-income countries."

Rising Insulin Prices—The High Cost of Diabetes

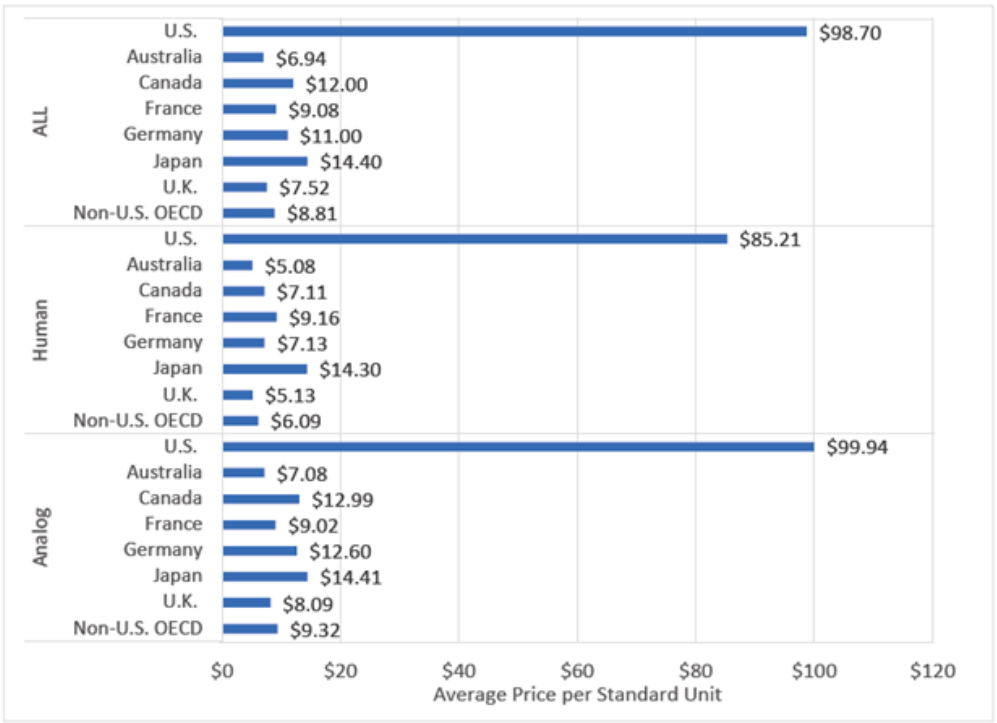
Even aside from the market dynamics at play in the pharmaceutical industry that differentiate it from other industries, the market for insulin presents unique challenges that have led to dramatic increases in costs for patients. This section examines the factors and policies that have contributed to the rising cost of insulin.

[113] NAS Consensus Study, *supra* note 106 at 15-18; *see also* Feldman Report, *supra* note 5 at 3.

Insulin Prices in the United States are Higher than Other Developed Countries

As with prescription drugs generally, insulin prices in the United States far exceed those in other developed countries. Although the United States in 2018 accounted for 31.6 percent of insulin volume measured in standard units among the OECD[114] countries included in a just-released study, it accounted for 83.8 percent of sales in U.S. dollars.[115] The following tables from this Rand Health Group Report demonstrate just how much of an outlier the US in terms of insulin prices:[116]

Figure 2.8. Average Price per Standard Unit, by Insulin Type, Selected Comparisons, 2018



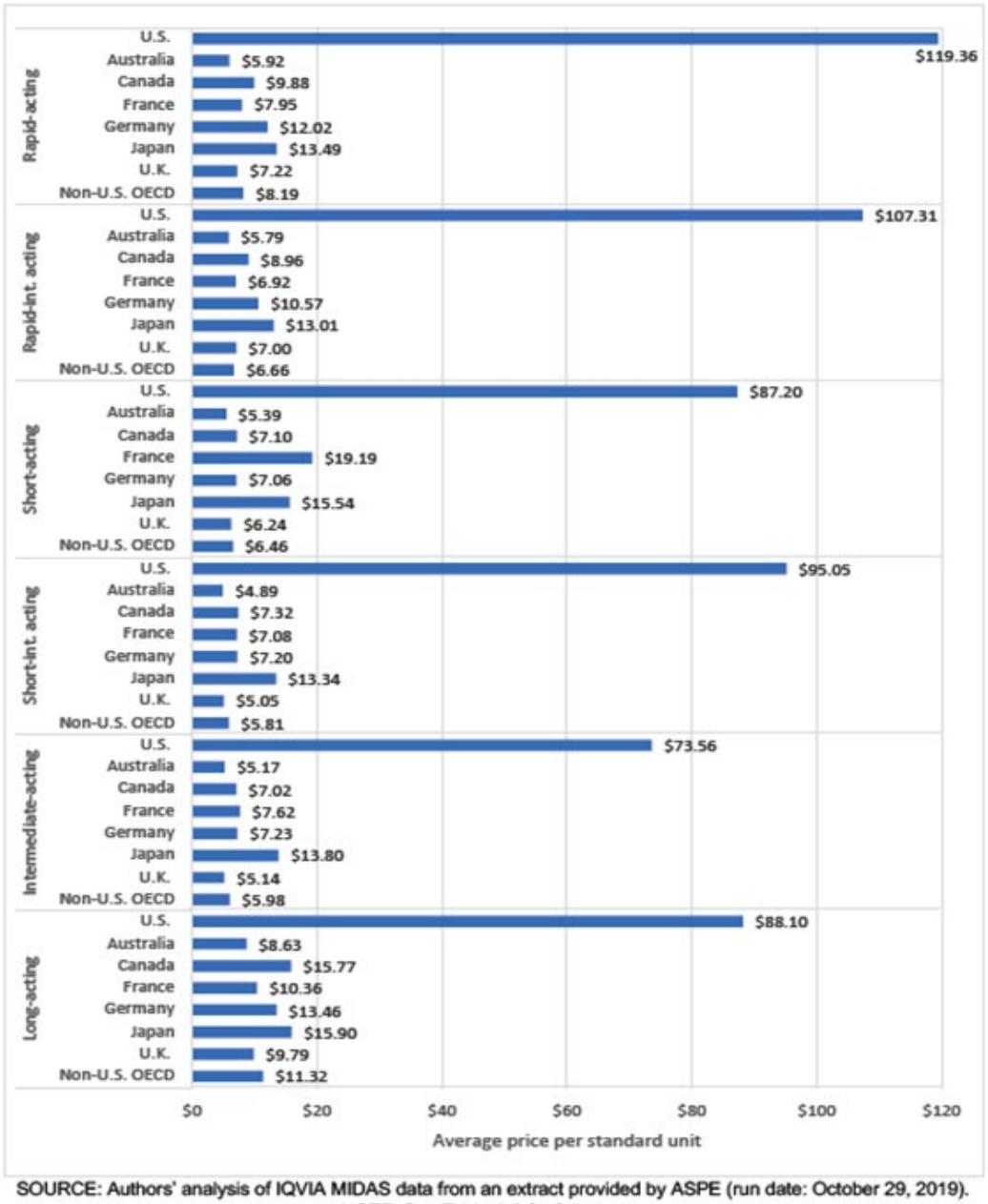
SOURCE: Authors' analysis of IQVIA MIDAS data from an extract provided by ASPE (run date: October 29, 2019).
NOTE: See Table A.3 for full results.

[114] OECD refers to the Organization for Economic Co-operation and Development, an intergovernmental economic organization with 37 member countries.

[115] Andrew W. Mulcahy et al., *Comparing Insulin Prices in the United States to Other Countries – Results from a Price Index Analysis*, RAND HEALTH CARE, Oct. 6, 2020, https://www.rand.org/pubs/research_reports/RRA788-1.html at 5.

[116] *Id.* at 10-11.

Figure 2.9. Average Price per Standard Unit, by Insulin Timing Category, Selected Comparisons, 2018



SOURCE: Authors' analysis of IQVIA MIDAS data from an extract provided by ASPE (run date: October 29, 2019).
NOTE: See Table A.3 for full results.

Insulin Prices Have Increased in the U.S. in Recent Decades

The American Diabetes Association ("ADA") regularly analyzes the cost of diabetes in America and published data in both 2012 and 2017. In 2012, the ADA estimated the total cost of diabetes in the U.S. at $245 billion,[117] which included some $176 billion in direct medical costs and $69 billion in lost productivity due to diabetes-related absences from work. Hospital care was the largest cost driver, at 43 percent of total costs, with prescription medications accounting for 28 percent, and antidiabetic drugs and supplies accounting for 4 percent of the total costs.[118]

> ***"For patients with diabetes, the ADA estimates patients paid $9,600 annually to manage the disease, reflecting an increase of 26% from 2012 to 2017"***

By 2017—with an estimated 24.7 million people in the U.S. living with a diabetes diagnosis and approximately 7.4 million of those using some form of insulin[119]— the total cost of diabetes in the U.S. had increased to $327 billion, including $237 billion in direct medical costs and $90 billion in reduced productivity.[120] This increase is attributed to the increased prevalence of diabetes and the increased cost per person with diabetes.[121] For patients with diabetes, the ADA estimates patients paid $9,601 annually to manage the disease, reflecting an increase of 26 percent from 2012 to 2017.[122] The growth in diabetes prevalence and medical costs is primarily among the population aged 65 years and older, contributing to a growing economic cost to the Medicare program."[123]

For those diabetics whose survival depends on access to affordable insulin, the last twenty years have seen a dramatic increase in the cost of all formulations of insulin.[124] This steady increase occurred even though scientists first learned how to use DNA code to develop artificial insulins that worked as well or better than the body's own natural insulin in the 1980's, and short- and long-acting insulin analogs have been available since 2000.[125] Very little new science has developed since that time.

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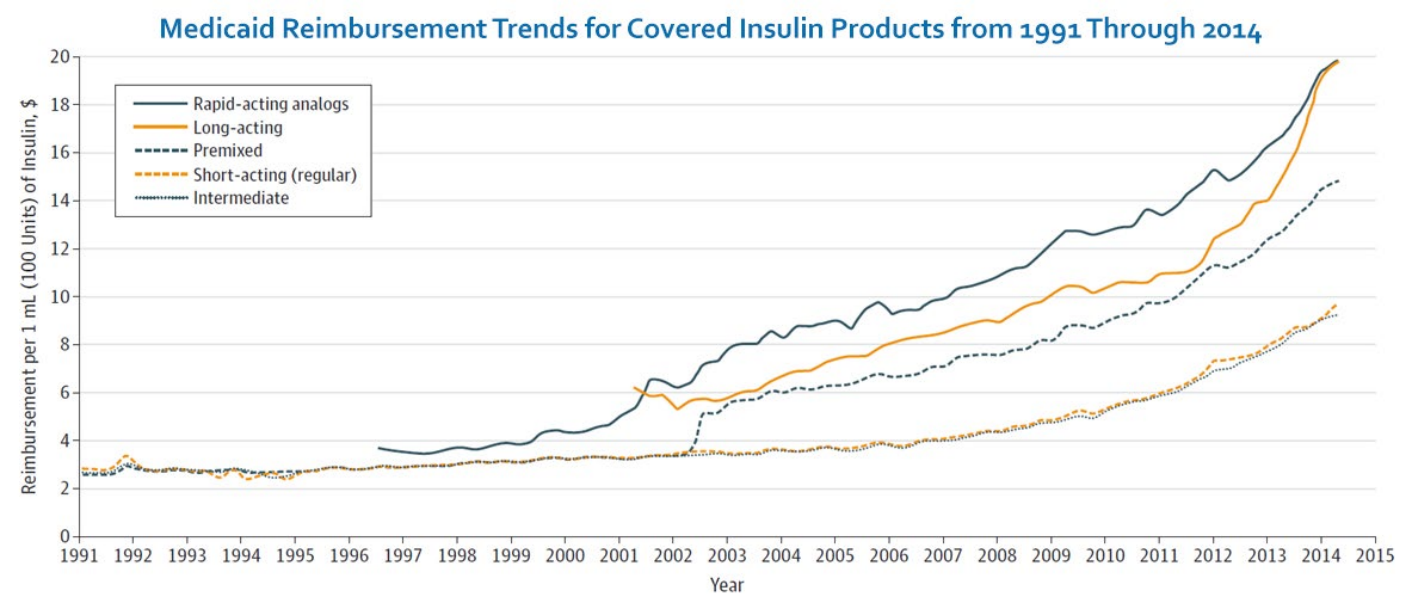
[117] Wenya Yang et al., *Economic Costs of Diabetes in the U.S. in 2012*, 36 DIABETES CARE 1033, 1038 (Apr. 2013).
[118] *Id.* at 1039.
[119] Wenya Yang, *Economic Costs of Diabetes in the U.S. in 2017*, 41 DIABETES CARE 917, 924 (May 2018); Cefalu, *supra* note 51 at 1300.
[120] *Id.*
[121] *Id.*
[122] *Id.* at 926
[123] *Id.* at 917.
[124] Jing Luo et al., *Trends in Medicaid Reimbursements for Insulin From 1991 Through 2014*, 175 JAMA INTERNAL MED. 1681, 1683 (2015).
[125] Jeremy A. Greene & Kevin R. Riggs, *Why Is There No Generic Insulin? Historical Origins of a Modern Problem*, 372 THE NEW ENGLAND J. OF MED. 1171, 1172 (Mar. 19, 2015).

Medicaid reimbursements for rapid-acting insulin evidence this steep escalation in cost, increasing from $3.69 per unit when this class of insulins first appeared on the US market in 1996[126] to $19.81 per unit in 2014.[127] By 2020, the unit cost to Colorado's Medicaid program for some formulations of insulin had increased to as much as $33 per unit, an increase of 66.5 percent in just six years. This increase in unit cost has had a significant impact on this vulnerable population. In 2017, 24 percent of adults with diabetes living below the poverty line use insulin, either alone or with other medications.[128] The graph below depicts these trends for the period 1991 through 2014 examining Medicaid reimbursement:[129]

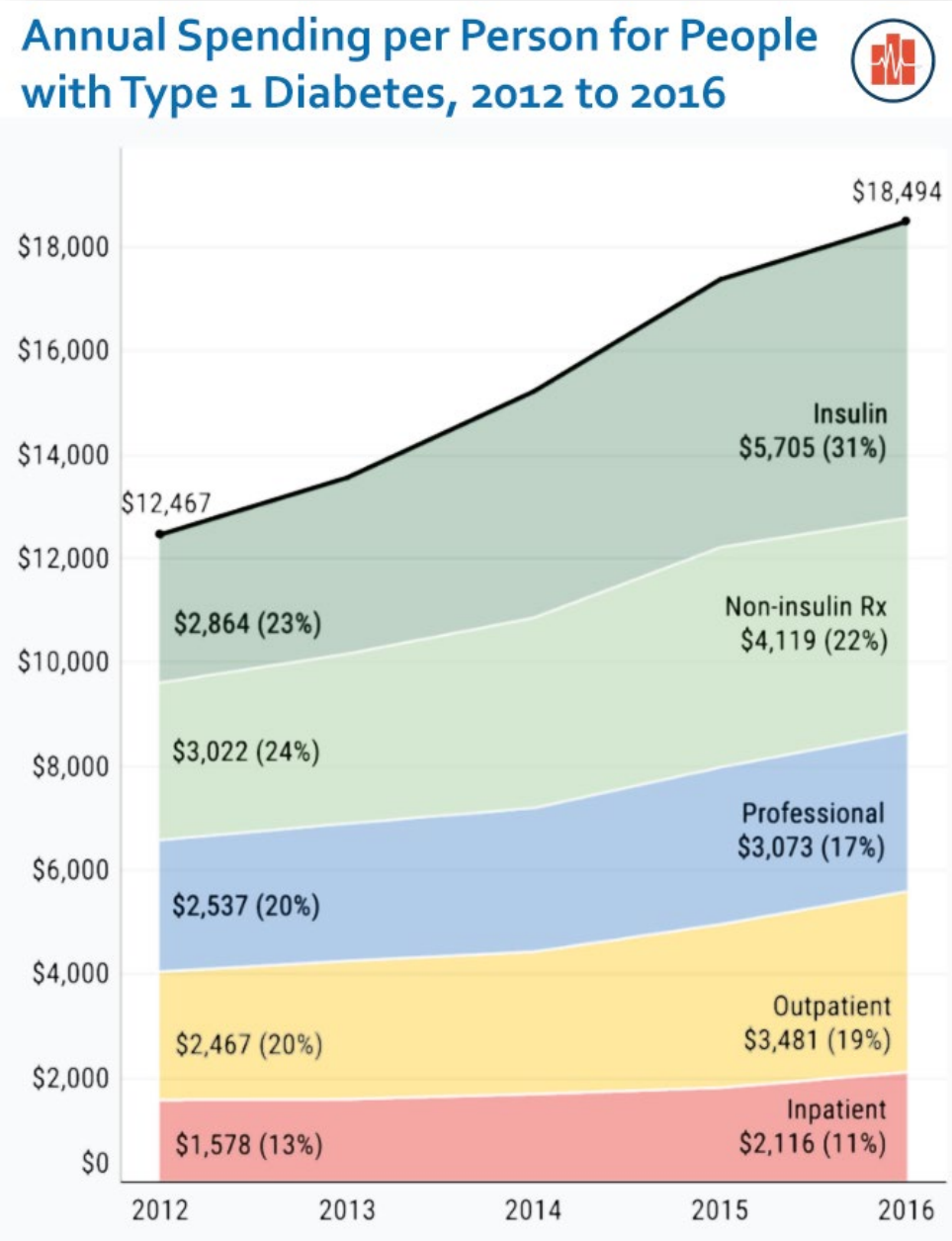


**Reimbursements were adjusted by the Bureau of Labor Statistics' annual Consumer Price Index for All Urban Consumers.*

"Medicaid reimbursements for rapid-acting insulin evidence this steep escalation in cost, increasing from $3.69 per unit when this class of insulins first appeared on the US market in 1996 to $19.81 per unit in 2004"

[126] *Id.*
[127] Luo, *supra* note 124 at 1684.
[128] Cefalu, *supra* note 51 at 1300.
[129] Luo, *supra* note 124 at 1683.

Another study found that, in 2016, individuals with type 1 diabetes spent $5,705 per-person on insulin, approximately 31 percent of the $18,494 in total per-person spending on diabetes-related care.[130] That was an increase of $2,841 in annual expenditures for insulin from 2012 to 2016, the largest increase among various diabetes-related healthcare expenditures: [131]



[130] Jean Biniek & William Johnson, *Spending on Individuals with Type 1 Diabetes and the Role of Rapidly Increasing Insulin Prices* at 2, Health Care Cost Institute, Jan. 2019.
[131] *Id.*

This increase appeared across all insulin products, with average point-of-sale prices nearly doubling. For a patient using an average amount of insulin (60 units per day), the prices increased from $7.80 a day in 2012 to $15 a day in 2016.[132] This represents a 92 percent increase, far in excess of inflation during those same years.[133] The following chart shows the relevant price increases during this period by insulin type:[134]

				Average Price Per Product ($)					
	Product	Delivery	Description	2012	2013	2014	2015	2016	5-yr chg. (5)
Basal	Humulin N	Vial	10mL, 100 units/mL	68	79	95	116	131	93%
		Pen	5 pens, 3mL each, 100 units/mL	219	257	290			
		KiwiPen	5 pens, 3mL each, 100 units/mL			314	370	415	
	Novolin N	Vial	10mL, 100 units/mL	67	75	89	108		
	Lantus	Vial	10mL, 100 units/mL	123	152	211	244	243	98%
		SoloStar Pen	5 pens, 3mL each, 100 units/mL	217	258	325	368	367	69%
	Levemir	Vial	10mL, 100 units/mL	124	152	216	252	264	113%
		FlexPen	5 pens, 3mL each, 100 units/mL	217	253	315			
		FlexTouch	5 pens, 3mL each, 100 units/mL			353	380	398	
	Toujeo	SoloStar Pen	3 pens, 1.5mL each, 300 units/mL				333	328	
	Tresiba	U-100 Pen	5 pens, 3mL each, 100 units/mL					440	
		U-200 Pen	3 pens, 3mL each, 200 units/mL					524	
Mealtime	Humulin R	Vial	10mL, 100 units/mL	68	80	96	116	132	94%
		U-500 Vial	20mL, 500 units/mL	563	804	961	1152	1319	134%
		U-500 KwikPen	2 pens, 3mL each, 500 units/mL					513	
	Novolin R	Vial	10mL, 100 units/mL	68	79	93			
	Apidra	Vial	10mL, 100 units/mL	97	124	169	209	240	147%
		SoloStar Pen	5 pens, 3mL each, 100 units/mL	196	244	332	408	466	138%
	Humalog	Vial	10mL, 100 units/mL	127	147	178	213	241	90%
		Cartridge	5 cart, 3mL each, 100 units/mL	235	271	334	398	449	91%
		Pen	5 pens, 3mL each, 100 units/mL	247	285	346	415	469	90%
		KwikPen	2 pens, 3mL each, 200 units/mL					381	
	Novolog	Vial	10mL, 100 units/mL	127	146	176	209	237	87%
		Cartridge	5 cart, 3mL each, 100 units/mL	242	275	333	397	443	83%
		FlexPen	5 pens, 3mL each, 100 units/mL	247	286	344	409	461	87%

What likely further contributes to these price increases is that the three major manufacturers of insulin tend to mirror each other's list price increases—when one raises its list price, the others are quick to follow.[135] A series of lawsuits have been filed accusing the three insulin manufacturers (Sanofi, Novo Nordisk and Eli Lilly) of consumer fraud and racketeering in connection with the dramatic increases in the costs of insulin.[136]

[132] *Id.* at 7.
[133] Inflation ranged from 1.7 percent per annum in 2012 to 2.1 percent in 2016.
[134] *Id.* at 10.
[135] Feldman Report, *supra* note 5 at 6.
[136] *See, e.g.*, *In re Insulin Pricing Litigation*, Civil Action No. 3:17-cv-00699 (D.N.J.); *State of Minnesota v. Sanofi-Aventis U.S. LLC. et al.*, Civil Action No. 3:18-cv-14999 (D.N.J.); *MSP Recovery Claims, Series LLC v. Sanofi-Aventis US LLC, et al.*, Civil Action No. 3:18-cv-02211 (D. N.J.).

The victims of these alleged schemes are uninsured consumers, consumers in high-deductible health plans, consumers who reach the Medicare Part D "donut hole," and consumers with high coinsurance rates. One of the complaints graphically depicts each manufacturer increasing its prices in lockstep with its competitors:

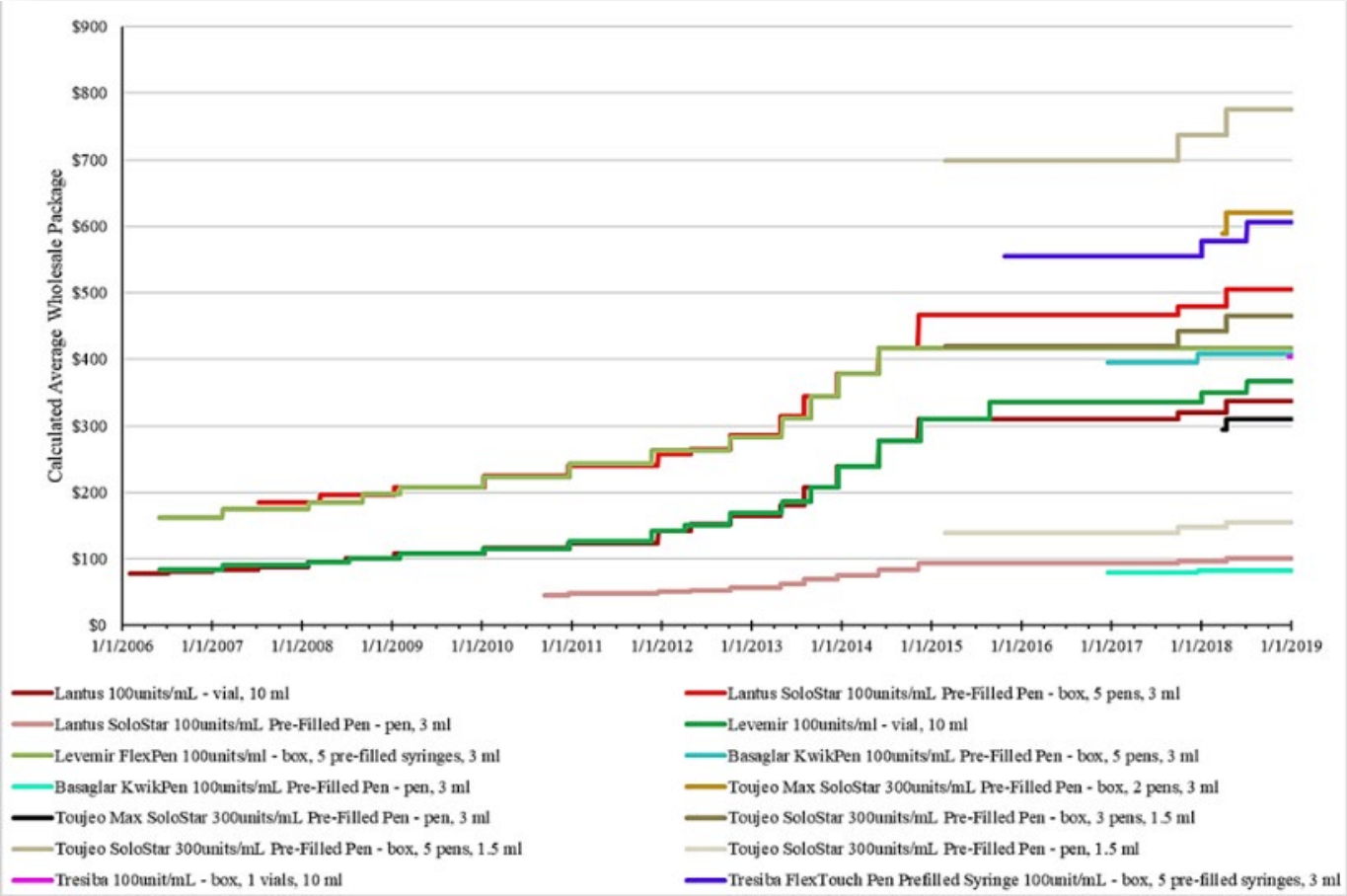


Figure 1: Defendant Drug Manufacturers increase long-acting insulin benchmark prices in lockstep.[137]

[137] *In re Insulin Pricing Litigation*, *supra* note 136 at 5 ¶ 9.

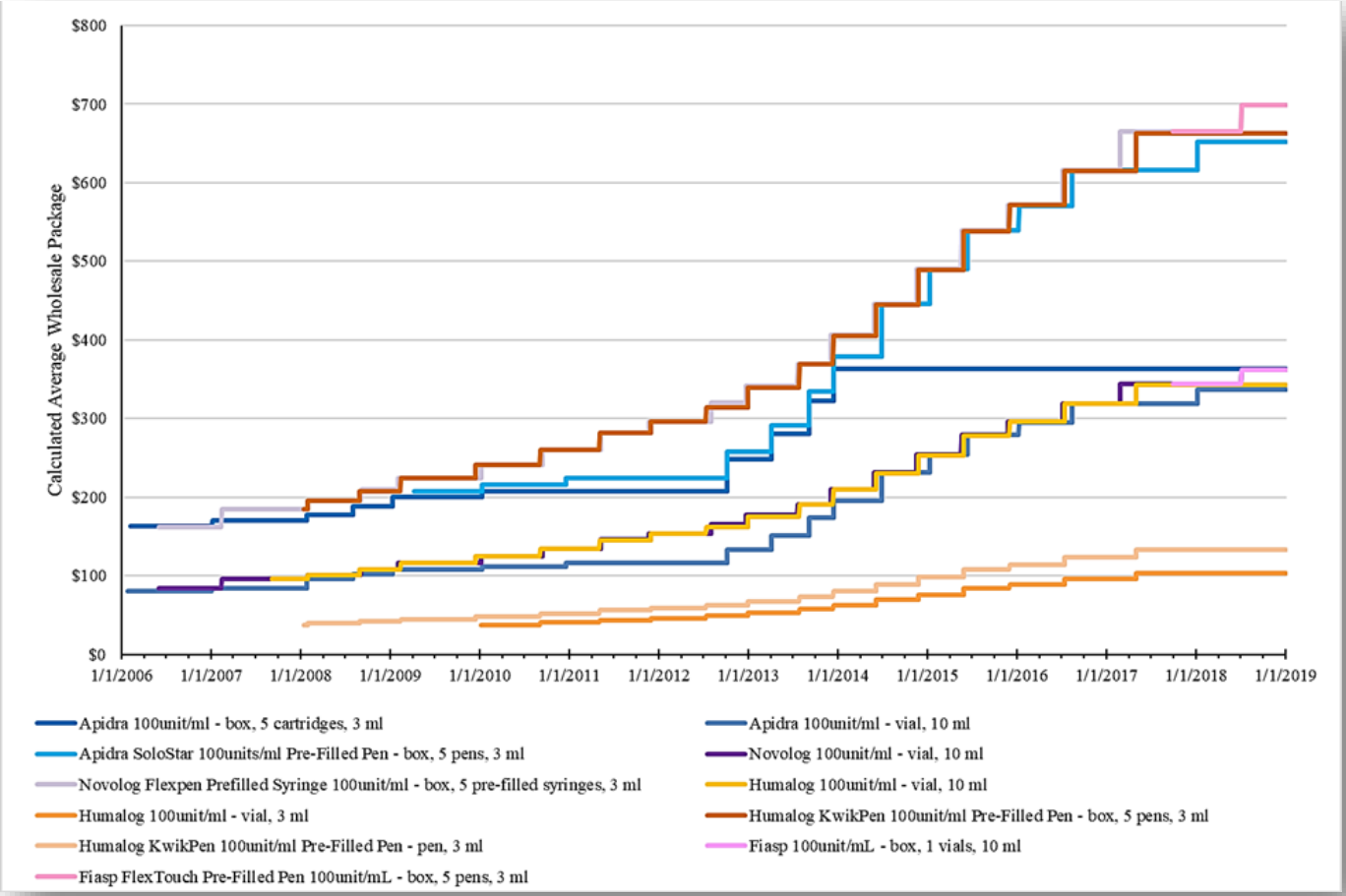


Figure 2: Defendant Drug Manufacturers increase rapid-acting insulin benchmark prices in lockstep.[138]

As the time of this report, these cases remain open and pending, though some of the claims alleged have been trimmed.

The Increased Cost of Diabetes in Colorado

At the Attorney General's request, Professor Feldman conducted an analysis of insulin pricing in Colorado. The "Feldman Report" is attached as Appendix B. Professor Feldman has written expansively and published widely on the various players and complexities of the pharmaceutical market, drug pricing, and the intersection of patent law and drug price increases. After examining some key findings in The Feldman Report, this study will examine the numerous factors that might impact those prices and which may constrain open competition in the inulin market.

[138] *Id.* at 6 ¶ 9.

The Feldman Report

Based on years of study of prescription drug pricing and the structure of those markets and her analysis of both Medicare and Medicaid spending on insulin, Professor Feldman's report contains the following findings:

- **Colorado Insulin Cost Increased 280 percent**: In Colorado, the average dosage unit cost (pre-rebate) of all insulin types increased roughly 280 percent between 2010 and 2018.[139] Analog insulin is more expensive than other human insulins.[140]
- **Colorado Insulin Out-of-Pocket Costs More than Doubled in 7 years**: For Colorado Medicare patients, the insulin out-of-pocket burden more than doubled between 2011 and 2018. The average annual out-of-pocket payment rose from $360 to $816, with some Colorado Medicare patients paying as much as $15,120 annually.
- **Colorado Insulin Patients Pay More in the Gap Phase (the "donut hole") than Other States:** According to Professor Feldman:

> *The Medicare Part D program has four coverage phases: deductible, initial, gap, and catastrophic. In the deductible stage, the patient is responsible for 100% of expenses until the deductible threshold is met. During the initial coverage phase, patients pay a copay or coinsurance, and the health plan covers the remainder. After the patient and plan collectively reach the Part D initial coverage threshold—$4020 in 2020—the patient enters the gap phase, also known as the donut hole. The health plan is then limited in how much it can spend, and the patient must cover about 25% of all prescription drug costs. Finally, the patient enters the catastrophic phase once the patient has reached a certain level of out-of-pocket costs—$6,350 in 2020. In the catastrophic phase, the patient pays for 5% of the drug cost, with the remainder covered by the federal government reinsurance program and the plan.*[141]

Colorado patients on average paid more for their monthly supply of insulin than patients in other states. This is largely because Colorado patients pay more during the gap phase compared to patients in other states. In 2018, for example, this difference amounted to $26 more each month that a patient was in the gap phase.

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[139] Feldman Report, *supra* note 5 at 2; *see also* Cefalu, *supra* note 51 at 1301 (noting that "human insulins are available at the pharmacy for $25 to $100 per vial compared with human insulin analogs at $174 to $300 per vial").
[140] Feldman Report, *supra* note 5 at 2; *see also* Biniek, *supra* note 129 at 1. ("increases in insulin spending were primarily driven by increases in insulin prices, and to a lesser extent, a shift towards use of more expensive products").
[141] Feldman Report, *supra* note 5 at 10.

- **Insulin Tiering:** The majority of insulin drugs were prescribed from Tier 3 of five-tier formularies commonly used in Medicare Part D. Since there is no truly interchangeable tiering system, we cannot say the insulin market exemplifies irrational tiering, a practice in which brand drugs are misplaced compared to their generics. Nevertheless, all diabetics are forced to buy brand-price insulin, and it is possible that preferred-drug lists limit patient choice to a single brand or form of insulin.
- **Evergreening of Patents Has Extended Monopoly Protections:** Many insulin products have received additional patents, exclusivities, and extensions, adding decades of protection and monopoly prices. Evergreening is a familiar tactic for best-selling insulin products: Eli Lilly's Humalog added 17 years of protection; Novo Nordisk's Novolog added 27 years of protection; Sanofi's Lantus added 28 years of protection. In addition, we note that many cheaper, trailing-edge insulin products have been discontinued, effectively removing them from the market and blocking generic competition.

Factors Impacting Price

Numerous factors contribute to the high cost of insulin in the United States and Colorado, including the unique regulatory environment surrounding biologic medicines like insulin,[142] rebates, drug formularies, patent laws and exclusivity, including the manipulation of those laws, and various other barriers to entry of biosimilar competition.[143]

Regulatory Process for Biosimilars

The United States Congress passed the Biologics Price Competition and Innovation Act of 2009 ("BPCIA") as part of the Affordable Care Act signed into law by President Obama on March 23, 2010.[144] After BPCIA, the FDA spent ten years developing the procedures for considering new biologic medicines and biosimilars and moved all biologics and biosimilars into a new regulatory regime in March 2020. Biosimilars are traditionally more expensive to develop compared to traditional, small molecule drugs because of their complexity and manufacturing process.[145]

The BPCIA provides biologic drugs with two patent exclusivity periods that—although meant to foster innovation—impact and delay generic entry.[146] During the first period,

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[142] Most prescription drugs are referred to as "small molecule" drugs which are created directly from natural ingredients, or synthetic versions of those substances. "Biologics," on the other hand, are large molecule drugs derived from the manipulation of living cells.

[143] Biosimilar competition is analogous to the concept of a "generic" for small molecule drugs in that it provides an alternative to more costly "branded" prescription drugs.

[144] Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, 124 Stat. 804.

[145] John White & Jennifer Goldman, *Biosimilar and Follow-on Insulin: The Ins, Outs, and Interchangeability*, 35 J. OF PHARMACY TECHNOLOGY, 25, 26 (2019).

[146] 42 U.S.C. § 262(k)(6).

the FDA will not accept an application from a biosimilar (generic) manufacturer for four years after the innovator biologic (known as the reference drug) product's approval.[147] In the next period, beginning after the four years has passed, the FDA has authority to accept biosimilar applications but is not able to grant approval for eight years. This exclusivity for the branded reference drug grants these branded drugs strong protection in the marketplace but results in higher prices to the consumer until a biosimilar (generic) is approved and available.

To gain approval as a biosimilar under the BPCIA, an applicant must demonstrate that: (1) the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and (2) there are no clinically meaningful differences between the biological product and the reference product in term of safety, purity, and potency of the product.[148] By contrast, obtaining FDA approval of a small molecule generic drug is relatively easier because it is chemically identical to the brand name product (referred to as "bioequivalence"). With a small molecule drug, the generic manufacturer has access to the brand name manufacturer's chemical formulations and its numerous testing and clinical trials and is not required to replicate that work. The precise DNA sequencing and modification in developing a biologic are considered "proprietary information" [149] and are not available to a biosimilar developer.[150]

Although the FDA intended the new regulatory scheme to create an "abbreviated licensure pathway" for biosimilar biological products (similar to the Hatch-Waxman Act for small molecule "generic" drugs),[151] it has taken almost a decade for the new biologics regime to be established. Under the previous regulatory structure, the FDA approved several "follow-on" insulin products,[152] but the FDA only recently approved a biosimilar version of Sanofi's Lantus (insulin glargine) produced by a new entrant into the U.S. insulin market (though not a new player in generic pharmaceuticals generally)—Mylan Pharmaceuticals. [153] The FDA continues to review other biosimilar insulin applications.

In addition to biosimilar products generally, the BPCIA also introduced the concept of "interchangeability," which are biosimilar products that show that the biosimilar version: (1) is highly similar to and has no clinically meaningful differences from the reference product; and (2) can be expected to produce the same clinical result as the

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[147] 42 U.S.C. § 262(k)(6)(B).
[148] 42 U.S.C. § 262(i)(2).
[149] White, *supra* note 145 at 26.
[150] Michael A. Carrier, *Don't Die! How Biosimilar Disparagement Violates Antitrust Law*, 115 Nw. U. L. Rev. Online 119, 132 (2020).
[151] Leah Christl, *FDA's Overview of the Regulatory Guidance for the Development and Approval of Biosimilar Products in the US* at 4.
[152] "Basaglar" produced by Eli Lilly as a follow-on to Sanofi's Lantus (insulin glargine), and "Admelog" produced by Sanofi as a follow-on to Lilly's Humalog (insulin lispro). Because they were approved under section 505(b)(2) of the FDA governing "generic" drugs, these are classified as "follow-on" drugs, not biosimilars. *See* White, *supra.* note 154 at 28-29.
[153] "Follow-on" biologics generally refer to drugs approved under section 505(b)(2) of the Food, Drug, and Cosmetics Act while a "biosimilar" refers to those biologics approved as "highly similar" to the reference drug under the BPCIA. *See* White, *supra* note 145 at 25.

reference product in any given patient, [154] a concept known as "immunogenicity." For products administered more than once to an individual, the follow-on biosimilar manufacturer must show that the risk of switching between products is not greater than the risk of *not* switching.[155] If the manufacturing applicant seeking interchangeability can meet this standard, it will receive exclusivity, which expires (if certain other litigation thresholds are not earlier reached) one year after commercial marketing.[156]

Unlike generic small molecule drugs applications, the first-to-file a biosimilar applicant does not benefit from a market exclusivity period against other generic manufacturers.[157] For example, with Abbreviated New Drug Applications for small molecules, the first-to-file generic receives six months of exclusivity as to other generics (but not branded drug or an "authorized generic" of the branded drug). Rather, with biosimilars, exclusivity is granted only to the first biosimilar that clears the higher threshold of interchangeability.[158]

Biosimilar Interchangeability and State Substitution Laws

The interchangeability of a biosimilar has particular importance under state drug substitution laws, which govern when a pharmacist can, or in some cases must, fill a prescription with a less expensive generic version of the prescribed drug. In Colorado, Section 12-42.5-122, C.R.S. (2019), allows a pharmacist to:

> *substitute an equivalent drug product if the substituted drug product is the same generic drug type and, in the pharmacist's professional judgment, the substituted drug product is therapeutically equivalent, is interchangeable with the prescribed drug, and is permitted to be moved in interstate commerce.*

After passage of the BPCIA, most states, including Colorado, amended their drug substitution law to reference biosimilars.[159] But unlike generic small molecule drugs, under most of these state laws—again, including Colorado's—a biosimilar drug may be substituted only if "the FDA has determined that the biological product to be substituted *is interchangeable* with the prescribed biological product."[160] Without that FDA determination of interchangeability, a Colorado pharmacist cannot substitute a biosimilar product, which means that the consumer has no biosimilar alternative to the branded insulin drug and consequently pays a higher price.

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[154] 42 U.S.C. § 262(k)(2)(A)(i).
[155] 42 U.S.C. § 262(k)(4)(B).
[156] 42 U.S.C. § 262(k)(6).
[157] 42 U.S.C. § 262(k)(6).
[158] 42 U.S.C. § 262(k)(2)(A)(i).
[159] SB 15-071 (2015); *see also* Nat'l Conference of State Legislatures, *Generic Drug Substitution Laws* at 3, May 3, 2019, https://www.ncsl.org/portals/1/documents/health/Generic_Drug_Substitution_Laws_32193.pdf.
[160] *Id.* Colorado's law is found at COLO. REV. STAT. §12-12-280-125(1)(a)(A) (2019).

This interchangeability restriction is significant because follow-on biosimilars—although potentially cheaper alternatives to the referenced insulin products—are treated as alternative brand name drugs, and not interchangeable. They require a specific prescription written by a health care practitioner. An early prediction of the importance of an interchangeable insulin concluded:

> *A designation of interchangeability may make physicians view a biosimilar more positively and allow the market for biosimilar insulin to expand beyond new users. It may also ease the concerns of [health care practitioners] who are hesitant about switching patients currently taking branded insulins to biosimilars that are not interchangeable because of immunogenicity concerns . . . . interchangeability will also drive how it is reimbursed and managed at the insurance level.*[161]

Unfortunately, the FDA has not yet approved an interchangeable biosimilar insulin.[162] However, some relief may be on the horizon. In November 2019, the FDA published draft guidelines that could dramatically streamline the certification of a biosimilar as interchangeable with its reference product.[163] Specifically noting that, among biosimilar products, insulin is a "relatively small, structurally uncomplicated and well-characterized" biologic, the FDA proposes to drop the additional requirement for clinical immunogenicity tests required for a determination of interchangeability if the biosimilar is otherwise proved to be "highly similar" to the reference product.[164] The FDA has not yet issued a final guidance on this topic.

Formularies and Rebates

Formularies

As discussed in the Pharmacy Benefit Managers section, drug formularies serve as a means for third-party payers to control drug spending.[165] Placement on a preferred tier in a formulary typically means a patient will have a lower cost-sharing obligation. According to Professor Feldman: "tiering should be part of a virtuous cycle, creating proper market and systemic incentives. The reality, however, falls short of the ideal."[166] In fact, both high rebates and the spread created between net price and list price—a

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[161] Lisa Rotenstein et al., *Opportunities and Challenges for Biosimilars: What's on the Horizon in the Global Insulin Market*, 30 CLINICAL DIABETES 138, 141 (2012).
[162] White, *supra* note 145 at 30.
[163] 84 Fed. Reg. 65822 (November 29, 2019); U.S. Dep't of Health and Human Services et al., *Clinical Immunogenicity Considerations for Biosimilar and Interchangeable Insulin Products*, *Guidance for Industry* (Draft Guidance), Nov. 2019, https://www.fda.gov/media/133014/download.
[164] Mariana Socal & Jeremy Greene, *Interchangeable insulins – New pathways for safe, effective, affordable diabetes therapy*, 382 THE NEW ENGLAND J. OF MED. 981, 982 (Mar. 12, 2020).
[165] Feldman Report, *supra* note 5 at 19.
[166] *Id.*

significant profit margin for a PBM—may have more to do with a formulary placement.[167]

Rebates Paid to PBMs in Exchange for Formulary Placement

Insulin pricing, like most prescription drugs, involves a complex web of list prices, net prices, rebates, and other fees. As discussed in the Manufacturers Section, most consumers with public or private insurance do not pay the list price at the pharmacy, and manufacturers do not receive the list price for their products.[168] Instead, PBMs negotiate discounts—through rebates and other fees—with the manufacturers and may pass some or all of those discounts on to their insurance company clients. The PBM's profit margin has been described as the "spread" between what it receives from the insurance company and what it pays to the pharmacy for dispensing that drug.[169] The secrecy behind this process—where even the insurance companies are in the dark about the actual discounts off of the list price negotiated by the PBM—and the structure of this industry is "problematic."[170] To calculate the net price manufacturers actually receive, the amount of any fees paid to wholesalers, discounts paid to pharmacies, and any rebates paid to PBMs or health plans must be subtracted from the list price.[171] Rebates, in particular, play a significant role in drug pricing, and there is little, if any, public information about rebates for insulin products.

Professor Feldman explains how the rebate system works:

> *Insurers pay their PBMs based on the extent of the discount that a PBM can negotiate with individual drug companies. In other words, the greater the distance between the list price and the final price, the more money a PBM makes. In theory, this might encourage PBMs to drive prices down, given that their pay is directly tied to the level of discounts and rebates. In reality, the incentives are operating to drive prices higher. Quite simply, the drug company raises prices so that the PBM can demonstrate a greater spread between the original price and the post-rebate price. The technique is reminiscent of raising the price on a suit before a sale so that the final price looks like a great bargain. Indeed, one private firm found that PBMs have likely profited billions of dollars per year by taking advantage of insulin price increases and the hyper-concentrated insulin market.*[172]

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[167] *Id.*
[168] Cefalu, *supra* note 51 at 1300.
[169] Robert Langreth et al., *The Secret Drug Pricing System Middlemen Use to Rake in Millions,* BLOOMBERG, Sept. 11, 2018, https://www.bloomberg.com/graphics/2018-drug-spread-pricing/.
[170] Feldman Report, *supra* note 5 at 22.
[171] *Id.*
[172] Feldman Report, *supra* note 5 at 22-23.

Pharmaceutical manufacturers often are willing to pay high rebates and other fees in exchange for exclusive placement on a PBM's formulary. [173] Formulary placement, in exchange for rebates and fees, often results in channeling patients into higher priced brand name drugs and away from generics.

> *"Rebates, in particular, play a significant role in drug pricing, and there is little, if any, public information about rebates for insulin products.*

Unfortunately, there is little or no public information about negotiations between PBMs and insulin manufacturers, including the rebate structure, and the Department's staff has been unable to obtain that information as part of the study. PBMs claim the details of rebates and net prices are proprietary confidential trade secrets and refuse to disclose or make rebates publicly available. As the NAS Consensus Study Report notes, "no meaningful information exists to determine the size of those rebates, what portion of the rebates eventually results in lower prices for patients, or the portion that the PBMs retain as profit."[174] Not even the U.S. Congress had access to this information for its report on insulin pricing.[175]

It is also not known how much of any negotiated rebates get passed on to insurance carriers and ultimately to consumers.[176] At best, and to the extent that a PBM passes on any rebate to a health insurance plan, that plan may apply aggregate rebates received across all drug classes to lower premiums or co-pays to all its insureds.[177] One report found that insulin rebates average between 30 and 50 percent, and often reach as high as 70 percent for the most commonly used insulin products.[178] These rebates are significantly higher than the average rebate for other types of drugs.[179] Several federal initiatives were introduced—but ultimately without success—to prohibit this PBM rebate structure, including the withdrawal of federal Medicare anti-kickback safe harbors that some

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[173] *Id.* at 22.
[174] NAS Consensus Study, *supra* note 106 at 2-3.
[175] Congressional Report, *supra* note 17 at 10-11.
[176] Some PBMs point to a couple of government reports indicating that they pass on as much as 99 percent of rebates to Medicare Part D plan sponsors, and that growth in rebates reduced the growth in spending from 2011 to 2105. *See* U.S. Gov't Accountability Office, *MEDICARE PART D - Use of Pharmacy Benefit Managers and Efforts to Manage Drug Expenditures and Utilization*, GAO-19-498 (July 2019); U.S. Department of Health & Human Services, Office of Inspector General, *Rebates for Brand-Name Drugs in Part D Substantially Reduced the Growth in Spending from 2011 to 2015*, OEI-03-19-00010 (Sept. 2019). It should be noted, however, that regulations governing Medicare Part D plans may "create a disincentive to engage in spread pricing that is not present in the commercial sector." GAO-19-498, *supra* at 49 (citing 42 C.F.R. § 423.308 (2020) which provides that rebates or price concessions are "administrative costs" that must be included in determination of bid amounts.)
[177] *Id.*
[178] O'Neill Hayes et al., *Insulin Cost and Pricing Trends*, AMERICAN ACTION FORUM, Apr. 2, 2020, https://www.americanactionforum.org/research/insulin-cost-and-pricing-trends/.
[179] *Id.*

believed insulated this industry, and these practices, from scrutiny. [180]Professor Feldman concluded that list prices are rising faster than rebates. The Department's research similarly shows a dramatic increase in net prices. While studying Medicare claims of roughly one million patients from 2005-2017, Professor Feldman found that the average dosage unit cost of branded drugs after rebates increased from $38 to $157, representing an increase of almost 313 percent.[181] The rate of increase in rebates continues to accelerate, and rebates now approach approximately half of the list price of insulin.[182] These discounts or rebates are in addition to the fees paid to PBMs by the payers to provide services such as establishing networks of pharmacies, negotiating rebates and other price concessions from manufacturers, and drug utilization management.

A working group convened by the ADA in 2018, which met with all stakeholders in this complex marketplace to better understand the cause of escalating drug prices, reached similar conclusions about rebates and PBMs as Professor Feldman.[183] The ADA working group found that negotiations between insulin manufacturers and PBMs coalesced around the manufacturer's desire for favorable formulary placement—which alone can determine whether a manufacturer's insulin will be either the lowest priced drug or even the exclusive product on a formulary—and the PBM's desire to obtain the deepest discounts for its health insurance clients and the greatest profits for itself.

The ADA working group concluded that "the insulin manufacturers still control the list price of insulin, but a meaningful share of the negotiating power has shifted from manufacturers to the PBMs." [184] According to the ADA working group, the market power of the PBMs is "directly related" to their design of and control over drug formularies, especially their ability to negotiate for greater rebates in exchange for favorable placement within a formulary, or perhaps even exclusive placement.[185]

Representatives of health insurance plans confirmed that PBMs have a financial incentive to select prescription drugs, including insulin, for preferred placement on a plan's formulary that pay the highest rebates and other fees.[186] This, in turn, causes drug manufacturers to raise their list prices[187] in response to the demands for ever-higher

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[180] Press Release, U.S. Dep't of Health and Human Services, Trump Administration Proposes to Lower Drug Costs by Targeting Backdoor Rebates and Encouraging Direct Discounts to Patients (Jan. 31, 2019), https://www.hhs.gov/about/news/2019/01/31/trump-administration-proposes-to-lower-drug-costs-by-targeting-backdoor-rebates-and-encouraging-direct-discounts-to-patients.html; *see also* Elizabeth Seeley & Aaron Kesselheim, *Pharmacy Benefit Managers: Practices, Controversies, and What Lies Ahead*, THE COMMONWEALTH FUND, Mar. 26, 2019, https://www.commonwealthfund.org/publications/issue-briefs/2019/mar/pharmacy-benefit-managers-practices-controversies-what-lies-ahead.

[181] Feldman Report, *supra* note 5 at 23-24.

[182] *Id.*

[183] Cefalu, *supra* note 51 at 1299.

[184] *Id.* at 1304.

[185] *Id.*

[186] *Id.* at 1305.

[187] Increasing list prices may not be relevant to those with comprehensive prescription drug coverage in their insurance plan, where they have a set co-pay requirement. However, as Professor Feldman notes, patients without insurance (estimated as 10% of Americans in 2017), or with plans that carry high deductibles (patients pay 100% of their prescription drug costs until

rebates.[188] Again, "no meaningful information exists to determine the size of those rebates, what portion of the rebates eventually results in lower prices for patients, or the portion that the PBMs retain as profit."[189]

"Formulary placement, in exchange for rebates and fees, often results in channeling patients into higher priced brand name drugs and away from generics."

Recently, while testifying before the U.S. Congress, representatives from the three insulin analog manufacturers and the three dominant PBMs also confirmed that these misaligned incentives significantly impact and increase the cost of insulin.[190] For example, a Novo Nordisk representative testified that the PBMs "are able to exert considerable leverage in negotiations. If the PBMs do not extract the rebate concessions they demand (recognizing that PBMs are under pressure from employers and health plans to deliver certain dollar amounts in savings), they can and do exclude products from formularies, essentially making them unavailable to patients who rely on them every day."[191] Sanofi and Eli Lilly representatives echoed this sentiment.[192]

Patent Laws and Exclusivity

Drug manufacturers use a variety of tactics to extend the patent exclusivity of their products, referred to as "evergreening," which impacts drug pricing.[193] Such tactics may include "product hopping," (withdrawing older versions of a drug coming off patent from the market in favor of a new version with slight modifications to the drug or the

some high level of expenditures are reached), will either pay list price or some price calculated on the list price. Feldman Report, *supra* note 5 at 22.

[188] Cefalu, *supra* note 51 at 1301.

[189] NAS Consensus Study, *supra* note 106 at 2-3.

[190] *Hearing on Priced Out of a Lifesaving Drug: Getting Answers on the Rising Cost of Insulin Before the Oversight and Investigations Subcommittee of the House Committee on Energy & Commerce*, 116th Cong. (Apr. 10, 2019).

[191] *Hearing on Priced Out of a Lifesaving Drug: Getting Answers on the Rising Cost of Insulin Before the Oversight and Investigations Subcommittee of the House Committee on Energy & Commerce*, 116th Cong. (Apr. 10, 2019) (statement of Douglas J. Langa, President, Novo Nordisk Inc.).

[192] *Hearing on Priced Out of a Lifesaving Drug: Getting Answers on the Rising Cost of Insulin Before the Oversight and Investigations Subcommittee of the House Committee on Energy & Commerce*, 116th Cong. (Apr. 10, 2019) (statement of Kathleen W. Tregoning, Executive Vice President, External Affairs Sanofi) ("discounts apparently not being passed on to patients, but patients are in fact being asked to pay more when PBMs and health plans are paying less for the medicine"); *Hearing on Priced Out of a Lifesaving Drug: Getting Answers on the Rising Cost of Insulin Before the Oversight and Investigations Subcommittee of the House Committee on Energy & Commerce*, 116th Cong. (Apr. 10, 2019) (statement of Michael B. Mason, Senior Vice President, Connected Care and Insulins at Eli Lilly and Company) ("the market began moving to restrictive formularies, which limit the number of medications covered on someone's health plan. In some classes like meal-time insulin, insurers started covering only a *single* brand of medication.").

[193] Feldman, *May Your Drug Price be Evergreen*, 5 J.L. & Biosci. 590, 596 (2018).

delivery device),[194] pay-for-delay settlements,[195] creating a patent thicket by patenting every aspect of the drug, including formulation, manufacturing, method of treatment for different conditions, and auxiliary devices and supplies needed to use the drug; and other methods.

Manufacturers have financial incentives to manufacture and supply products that return the highest net profit, and profit-margins have a direct link to patent protections.[196] In the pharmaceutical industry, manufacturers frequently net the most profit by being the sole supplier of a drug, which most often occurs when the manufacturer holds a patent (or patents) covering the drug. It is not unusual for a patent holder to attempt to extend its exclusive right to sell a drug, using time-consuming patent infringement litigation and other tactics,[197] in an effort to protect its exclusivity. These tactics include, among others, efforts to switch the market to a newer, patent-protected version by ceasing to manufacture the now readily available product (typically in a generic format) or negotiating with PBMs to exclude the less-profitable product from their formularies to keep demand for the generic product so low that it forces the generic producers out of the market.[198]

Manufacturers of biopharmaceutical insulin have successfully controlled the market and have thus far prevented many generics or biosimilars from entering the marketplace through the use of patents and tactics to extend their exclusivity period.[199] Until June 2020, when the FDA approved the biosimilar Semglee, there were no true generic options available on the market. The success of these tactics in conjunction with the fact that analog insulin is generally preferred over regular human insulin[200] has resulted in a significant increase in the production and consumption of analog insulin.

In addition, manufacturers have influenced the market such that physicians are more likely to prescribe analog insulin products over human insulin.[201] Analog insulin continues to be protected by the patent protection schemes discussed above. Manufacturers have ensured that analog insulin is the preferred treatment option for patients, which has solidified their control over the market. Not surprisingly, analog insulin products are more expensive than human insulin, which means that health

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[194] Feldman Report, *supra* note 5 at 9.
[195] Robin C. Feldman & Prianka Misra, *The Fatal Attraction of Pay-for-Delay*, 18 CHI.-KENT J. INTELL. PROP. 249, 249 (2019). ("Pay-for-delay settlements [are] a strategic tactic in which brand-name drug manufacturers induce generic companies to agree to stay off the market by sharing portions of their monopoly profits."); *see also* https://www.ftc.gov/news-events/media-resources/mergers-competition/pay-delay online, available (8/28/2020).
[196] NAS Consensus Study, *supra* note 106 at 7.
[197] *See also* Feldman Report at 5-8.
[198] Feldman, *May Your Drug Prices be Evergreen*, *supra* note 193; Feldman, *The Fatal Attraction of Pay-for-Delay, supra* note 195.
[199] Feldman Report, *supra* note 5 at 5.
[200] Grunberger, *supra* note 28 at 1769.
[201] Laura Newman, *Global Drug Companies Go for Gold with Aggressive Insulin Analogue Marketing*, Guest Blog, SCIENTIFIC AMERICAN, Aug. 10, 2012, https://blogs.scientificamerican.com/guest-blog/ninety-years-after-insulins-discovery-the-worlds-poor-are-still-dying/.

expenditures have increased overall, resulting in higher tax burdens, insurance premiums, and individual household expenditures.[202]

According to Professor Feldman, many insulin products have received additional patents, exclusivities, and extensions, adding decades of protection and monopoly prices. While manufacturers sought to expand their patent protections, cheaper, trailing-edge insulin products have been discontinued, effectively removing them from the market and blocking generic competition.[203] The major three manufacturers have employed extensive evergreening techniques to maintain their hold on the insulin market. These evergreening techniques have added 17 years of protection to Eli Lilly's Humalog, 27 years of protection to Novo Nordisk's Novolog, and 28 years of protection to Sanofi's Lantus. The Feldman Report details the numerous patents and extensions these manufacturers have acquired over the years.[204]

Professor Feldman concluded:

> *In short, insulin manufacturers regularly game patents, exclusivities, and extensions in an effort to maintain monopoly pricing, block generic competitors, and force patients, in Colorado and elsewhere, to consume the latest, most expensive insulin products. Aided by extreme consolidation within the industry, the major three insulin companies face little competition and tend to raise their prices in lockstep.*[205]

One case study is Lantus, an insulin glargine product first patented by Sanofi in 1994 and approved by the FDA in April 2000.[206] Since that time, Sanofi has filed 74 additional patent applications on Lantus in an attempt to extend its patent exclusivity a total of 37 years.[207] Extensive litigation to support some of these patents resulted in one preliminarily-approved competitor deciding to withdraw its FDA application.[208] Another competitor, Mylan Pharmaceuticals, engaged in three years of litigation before the US Patent & Trademark Office to finally defeat Sanofi's infringement claims. The FDA approved this biosimilar insulin in June 2020.[209]

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[202] Veronika Wirtz et al., *Insulin Market Profile,* HEALTH ACTION INTERNATIONAL at 47, Apr. 2016.
[203] Feldman Report, *supra* note 5 at 8-9.
[204] *Id.*
[205] *Id.* at 9 (citing to *Chaires et al v. Sanofi, U.S. et al,* No. 1:2017cv10158 (D. Mass. 2017), https://static01.nyt.com/science/01-30-17_Insulin_Class_Action_Complaint_Hagens_Berman.PDF.
[206] *Overpatented, Overpriced*, *supra* note 31 at 3.
[207] *Id.*
[208] *Id.* at 4.
[209] U.S. Food and Drug Administration, *FDA In Brief: FDA Approves Insulin Product Providing Patients with an Additional Safe and Effective Treatment Option,* June 11, 2020, https://www.fda.gov/news-events/fda-brief/fda-brief-fda-approves-insulin-product-providing-patients-additional-safe-and-effective-treatment.

Barriers to Entry

Multiple entry barriers limiting the number of U.S. biosimilars have exacerbated the rigorous regulatory regime created for biologics and biosimilars.

First, developing a biosimilar comes with a hefty price tag. Unlike generic drugs, the regulations do not require biologic manufactures to disclose exactly how a biologic is developed.[210] Recent reports estimate that it costs at least $100 million to bring a biosimilar to market (as opposed to $5 million for a generic).[211]

Second, manufacturers' manipulation of the patent regime serves as an additional barrier. Manufacturers hoping to bring a biosimilar to market may face years of patent litigation before they receive FDA approval.

"According to Professor Feldman, many insulin products have received additional patents, exclusivities, and extensions, adding decades of protection and monopoly prices. While manufacturers sought to expand their patent protections, cheaper, trailing-edge insulin products have been discontinued, effectively removing them from the market and blocking generic competition."

Third, reference biologic products receive exclusive or preferential treatment over biosimilars on many drug formularies or preferred drug lists. Unable to compete with brand name manufacturers in the scope of rebates and other negotiated fees the brand manufacturers may pay, a biosimilar may face exclusion from a formulary or be relegated to a non-preferred status.[212] For example, a non-preferred formulation of a rapid-acting follow-on insulin can be prescribed and dispensed under Colorado's Medicaid program only "following trial and failure of treatment with two preferred products (failure is defined as allergy [hives, maculopapular rash, erythema multiforme, pustular rash, severe hypotension, bronchospasm, and angioedema] or intolerable side effects)."[213]

Finally, established patients may be unwilling or unable to switch medications, even in the face of a price increase.[214] Patients' unwillingness to switch may be exacerbated if

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[210] Carrier, *supra* note 150 at 132 ("As a result, unlike generics, which cost an average of $5 million to bring to market, biosimilar development involves more intensive and uncertain research and development, which could result in costs of at least $100 million.").

[211] *Id*.

[212] *Id*. at 132-33.

[213] Preferred Drug List at 52, effective July 1, 2020, https://www.colorado.gov/pacific/sites/default/files/7-1-20%20PDL%20v4.pdf.

[214] Carrier, *supra* note 150 at 133.

the incumbent manufacturer suggests in its advertising and marketing that biosimilars are not the exact same product and switching to a biosimilar may cause adverse consequences.[215] These advertising and marketing representations may also influence the prescribing physicians.

Research and Development Costs

Drug manufacturers frequently cite the costs of research and development as one of the primary reasons for rising drug prices. This is especially true for biosimilars, whose complexity and specialized equipment needs make them much more expensive than generic small molecule drugs.[216] In the range of biopharmaceuticals, however, insulin is a " relatively small, structurally uncomplicated proteins that are well-understood and well-characterized."[217] Insulin products received approval many years ago, and, while modest improvements have been made in some formulations, price increases exceeding rates of inflation cannot be accounted for on the basis of new research and development alone. [218]

Unavailability of Authorized Generics

The term "authorized generic" describes an approved brand name drug that is marketed, often by the brand manufacturer, without the brand name on its label.[219] Other than the name on the label, the product is identical to the branded product.[220] Manufacturers typically sell the authorized generic at a lower cost than the brand name drug.[221] Although authorized generics are common among small molecule drugs, authorized generics are not as common with biosimilars and insulin in particular.

In March 2019, Eli Lilly announced that it would begin selling an authorized generic version of its rapid acting insulin Humalog.[222] The company claimed that its authorized generic would be sold at a list price 50 percent lower than Humalog. In December 2019, U.S. Senators Elizabeth Warren (MA) and Richard Blumenthal (CT) released the results of their investigation into the availability of Eli Lilly's authorized generic insulin.[223] They found that Eli Lilly's authorized generic insulin is not widely available in pharmacies across the country, with 83 percent of surveyed pharmacies reporting that it was not in stock and available to customers.[224] Colorado patients echo these findings, reporting

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[215] *Id.*
[216] White, *supra* note 145 at 26.
[217] Draft Guidance, *supra* note 163 at 5.
[218] Julia Belluz, *The Absurdly High Cost of Insulin, Explained*, Vox, Nov. 7, 2019, https://www.vox.com/2019/4/3/18293950/why-is-insulin-so-expensive.
[219] *FDA List of Authorized Generic Drugs*, FDA (July 1, 2019), https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/fda-list-authorized-generic-drugs.
[220] *Id.*
[221] *Id.*
[222] Elizabeth Warren & Richard Blumenthal, *Inaccessible Insulin: The Broken Promise of Eli Lilly's Authorized Generic* at 1, Dec. 2019, https://www.warren.senate.gov/imo/media/doc/Inaccessible%20Insulin%20report.pdf.
[223] *Id.*
[224] *Id.*

that they are unable to find Eli Lilly's authorized generic in stock in their local pharmacies.

Moreover, even the recent introduction of the biosimilar glargine Semglee is unlikely to "alter current market dynamics."[225] According to Professor Feldman, this is due to the absence of an "interchangeability" designation for Semglee; the presence of so-called "approved generics" by Sanofi and Eli Lilly further concentrating the market for long-acting insulins; and questions about whether this biosimilar can "navigate through contracts between existing insulin manufacturers and health plans.[226] One recent study suggests that further insulin biosimilar development will be minimal "due to technical complexities of manufacturing insulin and the extremely deep market discounts that predominate and thus limit potential financial returns."[227] Insulin lispro, for example, has the highest market concentration of biologic drugs where the originator launched an authorized generic "effectively blunting biosimilar uptake."[228]

"They found that Eli Lilly's authorized generic insulin is not widely available in pharmacies across the country, with 83% of surveyed pharmacies reporting that it was not in stock and available to consumers. Colorado patients echo these findings, reporting that they are unable to find Eli Lilly's authorized generic in stock in their local pharmacies."

How Health Insurance Impacts Privately Insured Diabetes Patients

The cost of insurance coverage has a significant impact on diabetes patients who do not qualify for Medicaid or Medicare. Most Coloradans obtain health insurance through their employer. The Affordable Care Act ("ACA") requires large employers, generally defined as employers with 50 or more full-time employees, to either provide health

[225] Feldman Report, *supra* note 5 at 6.
[226] *Id.*
[227] Murray Aitken et al., IQVIA Institute for Human Data Science, *Biosimilars in the United States 2020-2024* at 5, Sept. 29, 2020, https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/iqvia-institute-biosimilars-in-the-united-states.pdf?_=1602283178492.
[228] *Id.* at 8.

benefits to their employees or pay a penalty.[229] The ACA requires the coverage to be affordable, meaning that employees do not pay more than a fixed percentage of their household income, adjusted annually for inflation.[230] The affordability percentage for those between 330 percent and 400 percent of the federal poverty level for 2020 is 9.78 percent.[231] For 2021, the affordability percentage for that income level will be 9.83 percent.[232]

According to the most recent report from the Colorado Division of Insurance, 98 percent of large employers (those with more than 1000 employees) in Colorado offered insurance coverage to employees in 2017.[233] That same year, approximately 28 percent of Colorado companies with fewer than fifty employees offered insurance coverage.[234] Colorado employees paid 21 percent of the total premium for individual coverage and 27 percent for family coverage when splitting costs with their employers.[235]

The pricing of health insurance coverage is complicated and involves many variables specific to different types of plans. The ACA mandates 5 plan categories: Catastrophic, Bronze, Silver, Gold, and Platinum.[236] Plans with lower premiums generally require higher out-of-pocket expenditures when a patient needs care. Consumers may also choose a high deductible health plan ("HDHP"), which offers a lower monthly premium but has a higher deductible that patients must meet before insurance starts paying for care.[237] HDHPs are available in most areas and may be available as qualified health plans at the Bronze, Silver, or Gold levels.[238] HDHPs may also be available for enrollment directly through health insurance companies or offered by employers.[239] Most survey respondents either pay for a more expensive plan to get better prescription insulin coverage or have an HDHP that requires them to pay out-of-pocket for insulin until they reach their deductible. Many also stated that they suffer financial difficulty each year until their deductible is met.

Under the ACA, insurance companies can account for only five factors when setting premiums: age, location, tobacco use, individual or family enrollment, and plan

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[229] Kaiser Family Foundation, *Employer Responsibility Under the Affordable Care Act*, July 2, 2019, https://www.kff.org/infographic/employer-responsibility-under-the-affordable-care-act/.
[230] Internal Revenue Service, Examination of returns and claims for refund, credit, or abatement; determination of correct tax liability, 26 C.F.R. 601.105, https://www.irs.gov/pub/irs-drop/rp-19-29.pdf.
[231] *Id.* at 3. For those at 133 percent of the federal poverty level, the percentage is 2.06 percent.
[232] *Id.*
[233] Colorado Department of Regulatory Agencies, Division of Insurance, *Health Insurance Cost Report* at 15 (Dec. 10, 2018), https://drive.google.com/file/d/1Cff9sUyj8vhSTAPswEC8YaUJ-XlJ1XCn/view.
[234] *Id.*
[235] *Id.* at 6.
[236] U.S. Centers for Medicare & Medicaid Services, *How insurance companies set health premiums*, https://www.healthcare.gov/how-plans-set-your-premiums/.
[237] U.S. Centers for Medicare & Medicaid Services, *What are HDHPs & HSAs?*, https://www.healthcare.gov/high-deductible-health-plan/hdhp-hsa-information/.
[238] U.S. Centers for Medicare & Medicaid Services, *How HSAs work with HDHPs*, https://www.healthcare.gov/high-deductible-health-plan/hdhp-hsa-work-together/.
[239] *Id.*

category.[240] Premiums can be up to 3 times higher for older individuals.[241] Differences in competition, state and local rules, and cost of living have a large impact on premiums.[242] Survey respondents expressed anxiety about the future of the ACA and what will happen to their healthcare if the Supreme Court ever strikes down the law, ending the Medicaid expansion and removing protections against discrimination for those with pre-existing conditions, among other impacts.

The Colorado Division of Insurance ("Division") reviews plans and premiums health insurance carriers submit for the individual market, small group market, and large group market.[243] The Division also reviews plans in the individual and small group markets for compliance with the ACA.[244] The Division's review requires carriers to provide justifications for premiums. According to the Division, a wide range of factors drive the increases in health premiums, such as medical service costs, general inflation, medical inflation in excess of general inflation, increased utilization of health care services, higher priced technologies and new drugs, increases in wages and cost of materials, consumer demand, demographics, benefit mandates and regulations, aging, and cost shifting.[245]

Many survey respondents reported they feel hostage to jobs they would like to leave but need to keep for the insurance because they could not afford insulin and supplies without it. One survey respondent expressed the fear of expanding his small business because of high insulin costs and overall expensive insurance costs. Others expressed fear of starting their own business because of high insurance costs. At least one recent study has found that while patients with a private health insurance plan have been relatively shielded from insulin price increases, commercial health insurers have accommodated higher insulin prices by increasing premiums or deductibles for all members.[246] The COVID-19 pandemic has given diabetes patients another reason to worry—many survey respondents fear what will happen to them if they lose their jobs, and consequently their health insurance.

The Colorado General Assembly has taken steps to address the cost of health insurance premiums. In 2019, the legislature enacted House Bill 19-1168 creating the Colorado Reinsurance Program intended to reduce premiums in high cost regions and increase stability in Colorado's individual market.[247] The Program pays a portion of higher-cost claims in the individual insurance market, such as those incurred after major accidents

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[240] *How Insurance Companies set Health Premiums, supra* note 236.
[241] *Id.*
[242] *Id.*
[243] Colorado Department of Regulatory Agencies, *Step-by Step Guide on Accessing Health Insurance Filings* at 2, https://drive.google.com/file/d/0BwguXutc4vbpWVNVd21Td3Q2Vkk/view.
[244] *Id.*
[245] *Health Insurance Cost Report*, *supra* note 233 at 14.
[246] Amir Meiri, et al, *Trends in Insulin Out-of-Pocket Costs and Reimbursement Price Among US Patients with Private Health Insurance, 2006-2017*, 180 JAMA Internal Med. at E2 (June 2020).
[247] Colorado Department of Regulatory Agencies, *Colorado Reinsurance Program Public Forum*, June 30, 2020, https://drive.google.com/file/d/1anVGiBCjoPBhRJkDYhOjYVhlSYuCFWCp/view; 2019 Colo. Sess. Laws 2176.

or due to serious health conditions.[248] In return, health insurers agree to offer lower premiums to consumers in the individual insurance market. As a result of the Program, nearly 150,000 Coloradans had lower premiums in 2020, with an average premium reduction of 20 percent statewide. [249] The original legislation provided for a two-year reinsurance program starting in 2020.[250] Once the law was passed, the U.S. Department of Health and Human Services approved Colorado's application to run a reinsurance program and the Program was recently extended through 2026 in Senate Bill 20-215.[251]

Public Policy Recommendations

Many factors impact insulin prices. Because the pharmaceutical industry is complex and opaque, a combination of federal and state legislation and policy solutions are likely necessary to provide any noticeable relief for diabetes patients. In this section, we discuss proposed federal legislation and our recommendations for future legislation and policy solutions in Colorado.

Federal Policy Proposals

1. Use Patent Workarounds

To address manufacturers' use of evergreening tactics, commentators have suggested workarounds in patent law and modifying patent standards.[252] One group proposed modifying the "inventiveness" standard for patents so that non-inventive and commonly practiced techniques in the pharmaceutical field cannot be patented; allowing public participation in patent litigation and disputes; and removing secondary and tertiary patents from the FDA's Orange Book.[253] State attorneys general continue to challenge manufacturers' efforts to expand patent exclusivity through pay-for-delay deals and other strategies.[254]

There are several existing—although rarely used—options in federal patent law. One permits the federal government to rescind a drug's patent and allow other companies to develop competing products—a process known as "march-in rights." That option might be available where the government helped fund the drug's development and rescission is necessary, for example, to counter a threat to public safety.[255] It is unclear whether high

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[248] *Id.*

[249] CO Governor Jared Polis, *2020 ACA Premiums Going Down by an Average of 20.2%* (Oct. 10, 2019), https://www.colorado.gov/governor/news/gov-polis-2020-aca-premiums-going-down-average-202.-

[250] Colorado Reinsurance Program Public Forum, *supra* note 247.

[251] *Id.*

[252] Shefali Luthra, *In The Battle To Control Drug Costs, Old Patent Laws Get New Life*, KAISER HEALTH NEWSm Oct. 5, 2018, https://khn.org/news/in-the-battle-to-control-drug-costs-old-patent-laws-get-new-life/.

[253] *Overpatented, supra* note 31 at 10-11.

[254] *See* Brief for States of Washington, et al. as Amici Curiae Supporting Plainitffs-Appellants, *UCFW Local 1500 Welfare Fund, et al. v. AbbVie Inc., et al.*, No. 20-2402 (7th Cir. 2020) (filed October 13, 2020).

[255] 1980 Bayh-Dole Act (Pub. L. 96-517, December 12, 1980).

drug prices, alone would trigger this provision.[256] This provision has never been invoked, despite a small handful of applications.[257]

Another suggestion relies on Section 1498, which allows the federal government to bypass patent protection if the government fairly compensates the patent holder.[258] The federal government routinely used its authority under Section 1498 to obtain generic versions of patented pharmaceuticals from the late 1950s through the 1970s.[259] In the case of pharmaceuticals, the U.S. Department of Health and Human Services could authorize a drug manufacturer to produce a low-cost biosimilar version, which it could then buy in bulk.[260] Alternatively, the federal government could purchase biosimilars from existing foreign manufacturers.[261] The drawback to this proposal is that Section 1498 authority has traditionally involved the purchase and use of pharmaceuticals by federal agencies. It is unclear how patients with commercial insurance would benefit from Section 1498.

2. Reduce Market Exclusivity Period for Biologics

The BPCIA grants biologics 12 years of market protection from generic competition—an increase over the 7 years of potential exclusivity granted under the Hatch-Waxman Act.[262] The FDA has stated that insulin products that were previously approved under the Hatch-Waxman Act were deemed to be approved under the BPCIA on March 23, 2020. But these insulin products are not entitled to any portion of the 12-year exclusivity afforded under the BPCIA and, in fact, lose any remaining exclusivity they had under the Hatch-Waxman Act.[263] Existing manufacturers, however, have focused on building a patent portfolio around injectors and other delivery methods. Observers expect that these new patents will be used to extend exclusivity for insulin products.[264]

These exclusivities do not require proof of a useful therapeutic advance. [265] Commenters also note that additional exclusivities are unnecessary because biosimilar products are not automatically substitutable for the original biologic, assuring a profitable market for

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[256] Joseph Allen, *The Washington Post Misses the Mark on March-In Rights,* IP Watchdog (April 22, 2019) (noting that march-in right authority has never been invoked), https://www.ipwatchdog.com/2019/04/22/washington-post-misses-mark-march-rights/id=108499/.

[257] John R. Thomas, *March-In Rights Under the Bayh-Dole Act,* CONG. R. SERV. (August 22, 2016)at 1, https://fas.org/sgp/crs/misc/R44597.pdf.

[258] The Editorial Board, *How the Government Can Lower Drug Prices*, THE NEW YORK TIMES, June 20, 2018, https://www.nytimes.com/2018/06/20/opinion/prescription-drug-costs-naloxone-opioids.html.

[259] Hannah Brennan et al., *A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health*, 18 YALE J.L. & TECH. 275, 303-307 (2016).

[260] NEW YORK TIMES, *supra* note 261.

[261] Brennan, *supra* note 262 at 303-07.

[262] Tony Hagen, *New Battleground Shaping Up Over Insulin Deliverables*, THE CENTER FOR BIOSIMILARS, July 20, 2020, https://www.centerforbiosimilars.com/view/new-battleground-shaping-up-over-insulin-deliverables.

[263] *Id.*

[264] *Id.*

[265] Alfred B. Engelberg, *Memo To The President: The Pharmaceutical Monopoly Adjustment Act Of 2017*, HEALTH AFFAIRS, Sept. 13, 2016, https://www.healthaffairs.org/do/10.1377/hblog20160913.056548/full/.

the biologic even after exclusivities expire.[266] Reducing the term of, or even eliminating, these exclusivities could allow earlier entry of biosimilars.

3. Prevent Manufacturer from Delaying the Introduction of Biosimilars

To remove barriers to entry for more affordable biosimilar insulin, the U.S. Senate Finance Committee Chairman Charles Grassley (IA) and Senate Judiciary Subcommittee on Antitrust, Competition Policy and Consumer Rights Ranking Member Amy Klobuchar (MN) introduced S.64, the "Preserve Access to Affordable Generics Act."[267] This proposal seeks to limit anticompetitive pay-for-delay deals that prevent or delay the introduction of affordable generic and biosimilar pharmaceuticals.[268]

Another bill,[269]introduced by Congressional Diabetes Caucus co-chairs, Rep. Diane DeGette (CO) and Rep. Tom Reed (NY),[270] would make permanent an FDA policy to help speed up the time it takes for biosimilars to be approved and made available to consumers.[271] The guidelines issued by the FDA in 2018 created a new fast-track approval process for biosimilars, such as insulin.[272]

4. Reduce the Price of Insulin through Importation or Price Pegging

Right now, federal law does not allow the importation of biologics—like insulin—for personal use in the U.S. Several bills have been introduced to fix that. In Canada, patients needing insulin pay up to one-tenth the price for insulin than patients in the U.S.[273] U.S. Senators Chuck Grassley (IA) and Amy Klobuchar (MN) introduced S.61—the Safe and Affordable Drugs from Canada Act of 2019. The Act would permit American consumers to buy prescription drugs from Canadian pharmacies for personal use.[274] Specifically, this Act would allow individuals to import drugs from a list of Canadian pharmacies published by HHS.[275] HHS would require that approved pharmacies be at least five years old and exist for a purpose other than participating in

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[266] *Id.*

[267] S. 64, the "Preserve Access to Affordable Generics and Biosimilars Act," was introduced on January 9, 2019. No further action has been taken.

[268] Dan Fleshler, *The Government's Big Ideas to Bring Down Insulin Prices*, HEALTH LINE, Apr. 3, 2019, https://www.healthline.com/diabetesmine/government-big-ideas-insulin-prices#1.

[269] H.R. 2011, the "Protecting Access to Biosimilars Act of 2019," was introduced on April 1, 2019. No further action has been taken.

[270] *Id.*

[271] *Id.*

[272] U.S. Food and Drug Administration, *Questions and Answers on Biosimilar Development and the BPCI Act Guidance for Industry*, 83 FR 63900 (Dec. 12, 2008).

[273] Fleshler, *supra* note 271.

[274] *Id.*

[275] *Grassley, Klobuchar Introduce Bill to Allow Importation of Canadian Drugs*, FDANews (Jan. 17, 2019), https://www.fdanews.com/articles/189911-grassley-klobuchar-introduce-bill-to-allow-importation-of-canadian-drugs.

the program.[276] The bill has been referred to the Committee on Health, Education, Labor, and Pensions.

Other federal legislation introduced similarly promotes Canadian or other foreign imports. [277] The Affordable and Safe Prescription Drug Importation Act, S.97, co-authored by U.S. Senators Cory Booker (NJ) and Bob Casey (PA) and introduced by U.S. Senator Bernie Sanders (VT) allows U.S. wholesalers, pharmacies, and individuals to import medications from Canada.[278] After two years, the bill also permits imports from other countries.[279] Legally imported drugs under this bill must be purchased from an FDA-certified foreign seller and have the same ingredient(s), route of administration, and strength as drugs approved in the U.S.[280] Some types of drugs, such as certain biologics, could only be imported by wholesalers or pharmacies.[281]

5. Support the Insulin Price Reduction Act

On October 29, 2019, Rep. DeGette introduced HR 4906—the Insulin Price Reduction Act. The bill was referred to the Committee on Energy and Commerce/Committee on Ways and Means, which has not held any hearings. The bill includes several important components, including:

- A reduction in the list price of most insulin products by more than 75 percent. The bill creates an incentive for drug manufacturers to set the list price of their insulin products at, or below, the list price they had in 2006. This would lower the list prices for some of the most popular insulin products by more than 75 percent.
- A requirement that Medicare and all private insurers cover insulin with no deductible. The bill requires Medicare and all private insurers to waive the deductible requirements for any insulin product that's been reduced to its 2006 price.
- Protections for drug manufacturers who reduce their prices from the pressure of having to offer any additional rebates. The bill would prohibit any drug maker that sets the price of their insulin products at, or below, its 2006 list price from offering any additional rebates to further lower the cost of that product for insurers. Lowering the list price of insulin benefits consumers. It also allows drug makers who reduce their insulin products to their 2006 prices to sell their

[276] *Id.*
[277] This report does not analyze whether importation is likely to lead to substantial savings for Medicaid programs, which already receive discounts through the Medicaid Rebate Program. Department of Health and Human Services, "Medicaid Drug Rebate Program," https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/index.html.
[278] Fleshler, *supra.* note 271.
[279] *Id.*
[280] The Affordable and Safe Prescription Drug Importation Act, S. 97, 116th Cong. § 804(a)(5)(A)(iii) (2019), https://www.sanders.senate.gov/download/final_-affordable-and-safe-prescription-drug-importation-act-of-2019---bill-summary?id=3F55AA41-4A20-426D-8CEB-987A30F3A838&download=1&inline=file.
[281] *Id.*

products without having to offer additional rebates and gives them an incentive to do so.

- Prohibitions on insurers from refusing to cover any insulin product that's been priced at, or below, its 2006 list price. Under the current system, insurers may refuse to cover a drug that doesn't come with a significant rebate to reduce the cost for them. This power to deny coverage of a manufacturer's product has led many drug manufacturers to increase the list price of their products in order to offer a larger rebate to insurers. The Insulin Price Reduction Act would prohibit insurers from refusing to cover any insulin product that's priced at, or below, its 2006 list price—thus removing the leverage many insurers currently have to pressure drug makers into raising both their prices and the rebates they offer.

State Policy Recommendation

1. Require Price Transparency from Each Link in the Pharmaceutical Supply Chain

During the 2019 legislative session, the Colorado legislature passed, and Governor Polis signed into law, "HB19-1131, Prescription Drug Cost Education."[282] HB19-1131 requires manufacturers or their representatives to disclose the wholesale acquisition cost of a drug when engaging in marketing activities with health care providers and other prescribers.[283] This disclosure must be in writing and accompanied by at least three generic drug alternatives. If less than three generic alternatives are available, then all possible alternatives must be provided.[284] A more comprehensive price transparency bill was introduced in the 2020 legislative session, but it did not pass.[285]

The Department recommends more comprehensive, transactional price transparency reporting to the Division of Insurance from each link in the pharmaceutical supply chain, including manufacturers, PBMs, insurance carriers and wholesalers. A recent study analyzed 166 price transparency laws to assess which accomplished the goal of better understanding the economic forces behind drug pricing. It found that six states passed moderately successful transparency laws, but that all 166 fell short by "failing to require release of real transaction prices at each stage of the pharmaceutical distribution process."[286]

Any future drug price legislation should require each participant in the distribution chain to report all transaction price information to the Division of Insurance, including

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[282] HB19-1131, *Prescription Drug Cost Education*, https://leg.colorado.gov/bills/hb19-1131.
[283] *Id.*
[284] *Id.*
[285] HB 20-1160, *Drug Price Transparency Insurance Premium Reductions*, http://leg.colorado.gov/bills/hb20-1160.
[286] Martha Ryan & Neeraj Sood, *State Drug Pricing Transparency Laws Numerous Efforts Most Fall Short*, University of Southern California (Sept. 25, 2019), https://healthpolicy.usc.edu/research/state-drug-pricing-transparency-laws-numerous-efforts-most-fall-short/.

the discounts and rebates received.[287] Such pricing information should not be made publicly available to avoid price coordination among market participants. It should also make the failure to provide the required information a violation of the Colorado Consumer Protection Act.

2. Expand Mandatory Coverage for Diabetes Supplies

Additional study should be pursued regarding the cost and availability of diabetes supplies that are processed through insurance, including blood glucose meters, blood glucose test strips, blood ketone meters, blood ketone test strips, needles, lancets, insulin pumps (as well as accompanying infusion sets and reservoirs), and continuous glucose monitors (and accompanying sensors). Consideration should be given to mandating coverage for all such supplies and capping copayments or coinsurance for such supplies.

3. Join a Bulk Purchasing Plan to Increase Purchasing Power

Colorado may opt to explore joining a bulk purchasing plan to lower its prescription drug costs.[288] Because bulk purchasing gives the purchasers greater purchasing and bargaining power than they would have on their own individually, bulk purchasing may be one way for Colorado to reduce insulin costs. Bulk purchasing also presents the opportunity to replace the traditional role of the PBM with the state.[289] There are two dominant models of bulk purchasing: "(1) middlemen that leverage large membership bases to obtain upfront discounts from drug manufacturers, and (2) group purchasing organizations ("GPOs") that purchase drugs in sufficient quantities to lower the acquisition cost."[290]

Since 1999, many states adopted or promoted bulk purchasing plans.[291] States can begin their own bulk purchasing plans, or they can join one of five multi-state bulk buying pools. The more states and public entities that enter a pool, the greater the pool's power to negotiate more favorable prices.[292]

The largest bulk purchasing pool, the Minnesota Multistate Contracting Alliance for Pharmacy ("MMCAP INFUSE"), follows the large membership base model to obtain lower drug prices.[293] The Minnesota Department of Administration runs MMCAP

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[287] *Id.*

[288] Katherine Young & Rachel Garfield, *Snapshots of Recent State Initiatives in Medicaid Prescription Drug Cost Control*, THE KAISER FAMILY FOUNDATION, Feb. 2018, http://www.advancingstates.org/sites/nasuad/files/Issue-Brief-Snapshots-of-Recent-State-Initiatives-in-Medicaid-Prescription-Drug-Cost-Control.pdf.

[289] John Agwunobi & Paul London, *Removing Costs From The Health Care Supply Chain: Lessons From Mass Retail*, HEALTH AFFAIRS, Sept./Oct. 2009, https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.28.5.1336.

[290] MN AG Report, *supra* note 78 at 50.

[291] Nat'l Conference of State Legislatures, *Pharmaceutical Bulk Purchasing*, Mar. 2, 2020, https://www.ncsl.org/research/health/bulk-purchasing-of-prescription-drugs.aspx.

[292] *Id.*

[293] MMCAP Infuse, http://www.mmd.admin.state.mn.us/MMCAP/background/Default.aspx.

INFUSE, and the pool includes over 5,000 non-profit pharmacies, public entities, and agencies in 49 states, including agencies in Colorado. Through negotiation and bulk purchasing, MMCAP is able to purchase drugs at 23.7 percent below average wholesale prices for brand name drugs and 63 percent below average wholesale prices for generic drugs. These savings are 4 percent greater than what any other bulk purchaser currently provides.[294] The Minnesota Report recommended leveraging and increasing the power of MMCAP as a bulk purchaser.[295] Colorado should consider joining a Medicaid interstate pooling agreement and working with Minnesota to increase MMCAP's focus on achieving better insulin prices.

One limitation of MMCAP and Medicaid purchasing pools is that they do not allow private purchasers to benefit from the savings they achieve. The Northwest Prescription Drug Consortium ("NDCP"), however, opens the benefits of bulk purchasing to private residents. Oregon and Washington formed NDCP, a government-run organization that provides its benefits to participating states[296] through an interstate agreement. It offers individual consumers the ability to purchase prescriptions directly at the discounted rates available to the NDCP's organizational members.[297] Colorado may also want to consider joining the NDCP or advocate for implementation of the private purchaser approach in other pooled purchasing programs.

4. Challenge the Pharmaceutical Industry to Pass Rebates Through to Consumers

Passing rebates through to consumers at the point of sale is one way to reduce consumers' insulin costs.[298] In recent years, dramatically increasing list prices and a growing spread between list and net prices suggests that rebates and other discounts on insulin negotiated by PBMs have also increased.[299] Many of these rebates and other discounts are not regularly passed onto patients.[300] Care will have to be taken, however, to ensure that this pass through does not result in higher overall premiums, especially in Medicare Part D.[301]

CVS Caremark has voluntarily adopted a business model that passes 100 percent of rebates to plan sponsors.[302] CVS Caremark's model provides a mechanism for plan

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[294] *Pharmaceutical Bulk Purchasing*, *supra* note 290.
[295] MN AG Report, *supra* note 78 at 10.
[296] Northwest Prescription Drug Consortium, *Integrating Solutions for Best Value*, https://etf.wi.gov/boards/wpcsc/2020/02/27/item3/direct#:~:text=The%20Northwest%20Prescription%20Drug%20Consortium%20(NW%20Consortium)%20is%20an%20inter,in%20participating%20NW%20Consortium%20states.
[297] *Id.*
[298] MN AG Report, *supra* note 78 at 22.
[299] The net price is the list price minus any fees that the manufacturer pays, such as rebates. Cefalu, *supra* note 51 at 1032.
[300] Hernandez, *supra* note 1 at 861.
[301] Steven Lieberman et al., *Sharing Drug Rebates With Medicare Part D Patients: Why And How*, HEALTH AFFAIRS, Sept. 14, 2020, https://www.healthaffairs.org/do/10.1377/hblog20200911.841771/full/.
[302] Evan Sweeney, *CVS Caremark Shifts PBM Model to 100% Pass-Through Pricing and Focus on Net Cost*, FIERCE HEALTH CARE, Dec. 5, 2018, https://www.fiercehealthcare.com/payer/cvs-caremark-launches-guaranteed-pbm-model-100-pass-through-pricing.

sponsors to audit annual rebates.[303] Plan sponsors also receive standard annual financial audits allowing them to verify net costs instead of calculating individual drug AWP discounts.[304] What is uncertain, however, is whether a rebate structure will be replaced with another model—perhaps utilizing PBM-controlled group purchasing organizations "to shift discounts to less transparent fee structures that are more difficult for its PBM customers to audit."[305]

Assuming full transparency of all rebates, discounts, and fees collected from drug manufacturers, other PBMs should follow CVS Caremark's lead and provide 100 percent of rebates to plan sponsors. If the industry fails to act, Colorado should consider more directly regulating the business practices of PBMs, including requiring increased transparency around rebates and other pricing drivers, as discussed above.[306] In addition, legislation requiring rebates to be passed through to consumers at the point of sale—thus allowing consumers to pay their coinsurance based on the net price of their insulin rather than the list price—would ensure consumer prices are not artificially inflated and that the incentives better align.[307] Rebates for many insulin products average between 30 and 50 percent, so the savings to consumers would be substantial.[308]

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The high prices of insulin continue to force diabetics in Colorado to confront unthinkable choices—purchase access to this life-saving drug or skimp on other necessities. In this report, we have outlined the market dynamics that explain how this concentrated industry continues to raise prices well above the inflation rate. With the first entry of an authorized biosimilar into this marketplace, there is a glimmer of hope that consumers may begin to benefit from competition. But policymakers should not adopt this hope as a strategy. Rather, the proposals outlined above all merit consideration as strategies for addressing this critical public health challenge.

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[303] CVSHealth, *Frequently Asked Questions; Guaranteed Net Cost*, https://payorsolutions.cvshealth.com/sites/default/files/cvs-health-payor-solutions-guaranteed-net-cost-executive-summary-december-2018.pdf.
[304] CVSHealth, *Frequently Asked Questions; Guaranteed Net Cost*, https://payorsolutions.cvshealth.com/sites/default/files/cvs-health-payor-solutions-guaranteed-net-cost-executive-summary-december-2018.pdf.
[305] Pifer, *CVS Reportedly Creating Group Purchasing Organization for PBM Business*, Health Care Dive (July 1, 2020), https://www.healthcaredive.com/news/cvs-reportedly-creating-group-purchasing-organization-for-pbm-business/580889/.
[306] CVSHealth, *Frequently Asked Questions, supra* note 306 at 53.
[307] Patient Assistance Plans offered by manufacturers appear to provide an avenue to ease the high cost of insulin. The American Diabetes Association provides a link to programs offered by all 3 manufacturers. https://www.insulinhelp.org/ The survey reports from consumers suggest that these programs were not particularly helpful. Survey responses included: "Most insulin coupon discounts only pay up to $100 if you have insurance so the cost for insulin is too high to afford;" "I cannot use discount cards because of medicare [sic];" "When I check discount cards usually price is higher than what I am paying;" "Since I have health insurance with prescription coverage, cannot use discount cards." But one consumer noted "I [now] make less, but Eli Lilly started a covid [sic] discount program that applies to people without insurance that I will try." In addition, with health plans having different deductibles, co-insurance and co-pays, patient assistance programs, like rebates at point of sale, can be difficult to administer. Moreover, while appearing to help those struggling to pay for needed medicines, from a policy point of view rebates and patient supplements misalign incentives to consumers that can drive up costs overall.
[308] Tara O'Neill Hayes et al., *Federal and State Actions to Address Insulin Costs*, FIERCE HEALTHCARE, Apr. 29, 2020, https://www.fiercehealthcare.com/payer/cvs-caremark-launches-guaranteed-pbm-model-100-pass-through-pricing.

APPENDIX A:
INSULIN PRICING REPORT SURVEY NARRATIVE

Insulin Pricing Report Survey Narrative

The Department of Law's Report on Insulin Pricing in Colorado sought to learn more about Coloradans' experiences with, and how they are impacted by, the cost of insulin and supplies. How, and to what extent, do high insulin prices, coupled with high prices for diabetes supplies, affect Coloradans with diabetes? What is the financial burden on these consumers, whether insured, underinsured with high-deductible plans, or uninsured? Do they take extraordinary steps just to survive: rationing their insulin, skipping doses or using expired products, looking elsewhere for their medicine and supplies? How does all of this affect their daily lives? To begin to answer some of these questions, the Department's Office of Community Engagement developed the Insulin Pricing Report Survey to hear from patients and caregivers about the realities of obtaining insulin and diabetes supplies and the ways in which their lives have been affected by the high costs of these life-saving products. Although other surveys of individuals struggling to afford insulin and diabetes supplies have been conducted,* this Survey is unique in that it focuses solely on the experience of Coloradans. This provides a real first-hand look at the physical, financial, and emotional struggles of this vulnerable population.

*See e.g., Maria Muccioli, Thrivable Study Sounds the Alarm on Insulin Access in the US, Diabetes Daily (July 29, 2020), accessed at https://www.diabetesdaily.com/learn-about-diabetes/living-with-diabetes/thrivable-study-sounds-the-alarm-on-insulin-access-in-the-us/; Darby Herkert, et al., Cost-Related Underuse Among Patients With Diabetes, JAMA Internal Medicine January 2019 Volume 179, Number 1.

With the onset of the COVID-19 pandemic, the Department viewed conducting the survey online as the safest means for engaging with the public. The insulin survey allowed us to hear from diverse voices as well as provide an anonymous and safe format where diabetics could share their stories, be included in our process, and provide critical data and insights to inform our analysis.

The Department developed the Survey by consulting with leading Colorado health agencies and diabetes organizations, including: Colorado Department of Public Health and Environment, Colorado Department of Health Care Policy and Financing, Rocky Mountain Area of the American Diabetes Association, Barbara Davis Center for Diabetes, The CU School of Medicine, Rocky Mountain Chapter of the Juvenile Diabetes Research Foundation, CU Diabetes and Endocrinology Clinical Trial Program, T1International, Rocky Mountain Diabetes Educators, and individual patient advocates. These institutions and individuals provided input about patient experiences and hardships, diabetes education and awareness, types of insulin, and different implications and options for obtaining needed supplies. This information formed the basis of possible survey questions that would help illuminate important aspects of the experiences and challenges faced by patients accessing insulin. In addition to supporting the development of the survey, these organizations also assisted in the editing and distribution of the first version of the survey to a small sample size to test its effectiveness and inform the final version. We translated the final version of the survey into Spanish.

To promote interest in the Survey and facilitate easy access to the survey form, the Department created a website to house the English and Spanish surveys.** The website has information on the survey itself, the legislation (HB19-1216) that spurred the insulin pricing report, and pertinent information about the partner organizations that guided our process. To help explain the purpose of the report and the goals of the survey, we included a letter in English and Spanish, as well as a video from Attorney General Phil Weiser. Eventually, this website will host the final Insulin Pricing Report for the public to read.

**That page is accessible at coag.gov/insulin

Developing and distributing this survey during the past few months highlighted the importance of patient outreach and equitable healthcare. The Department's team worked diligently to build awareness of the survey and distribute the link to diverse groups across the state. The organizations that helped develop the survey provided critical assistance in achieving a wide distribution of the survey. Additionally, the Department rolled out a social media campaign to aid in outreach in collaboration with several organizations, including the Colorado Black Health Collaborative, Servicios De La Raza, and tribal representatives.

To elicit responses from individuals in a range of ages, the Department distributed the survey to organizations that work with older adults, including nursing homes, grandparent support groups, and groups that serve young adults and children, like social media groups for parents of children with diabetes and on college campuses. To promote geographic diversity, the Department sent the survey to endocrinologists, county health departments, and elected officials from all 64 Colorado counties. Additionally, the Department promoted the survey in churches, homeless shelters, food pantries, and organizations serving homeless communities, including Samaritan House Homeless Shelter, Catholic Charities, Colorado House & Resource Center, Boulder Shelter, Springs Rescue Mission, Greeley Transitional House, Denver Rescue Mission, and Colorado Coalition for the Homeless.

Survey Results

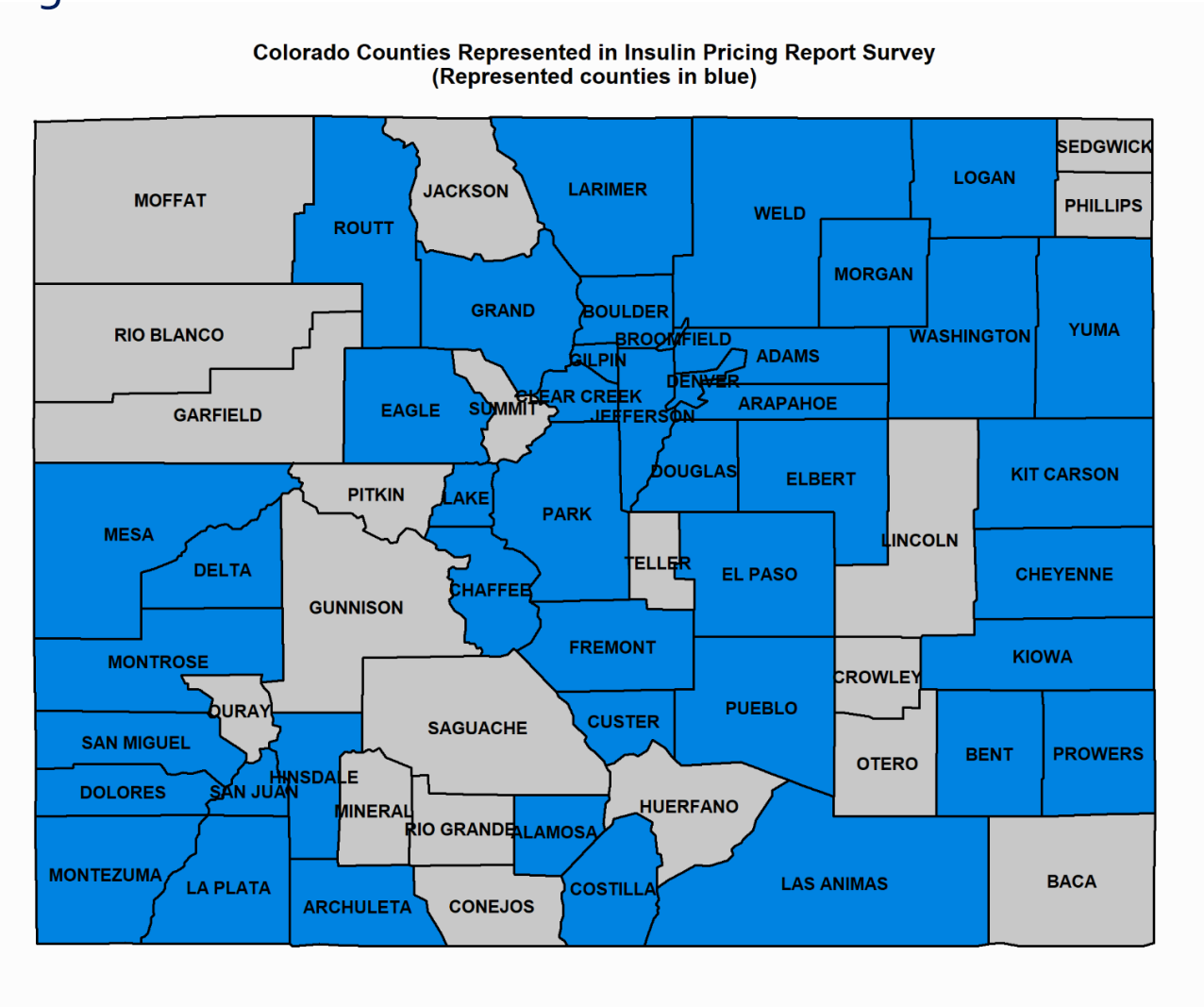
The Department distributed the survey questionnaire as a Google Form that aggregated accumulated survey responses into a Google Sheet. The Department then aggregated and analyzed the responses as illustrated in Tables 1 and 2, below.

Demographics

The Department administered the Insulin Pricing Report Survey online in English and Spanish to Colorado residents from May 20 through August 3, 2020. The Department received a total of 391 responses from 44 of Colorado's 64 counties (see Figure 1). Of the 391 respondents, 39 reported that no one in their household has diabetes and thus were excluded from the analysis. See Table 1 for respondent demographics.

According According to the United States Census Bureau (2019), Colorado's population breaks down as follows; 86.9% White, 4.6%Black or African American, 1.6% American Indian and Alaska Native, 3.5% Asian, 0.2% Hawaiian and Other Pacific Islander, 3.1% two or more races; as well as 21.8% Hispanic or Latino, and 67.7% White (not Hispanic or Latino)***. Table 1 offers more specific demographic information provided by Survey respondents.

Figure 1:



***United States Census Bureau, Quick Facts - Colorado at census.gov/quickfacts/co.

Table 1: Demographic Data (Survey Questions 1-12

Measure	Answer	Count	Percentage (%)
Language	English	353	90.00
	Spanish	38	10.00
Diabetic in Household	Yes	352	90.03
	No	39	9.97
Diabetes Type	Type 1	243	66.76
	Type 2	113	31.04
	Other	7	1.92
	Did Not Answer	1	0.27
Sex of Person with Diabetes	Male	149	40.38
	Female	214	57.99
	Other (multiple in home)	1	0.27
	Did Not Answer	5	1.36
Age of Person with Diabetes	0 to 18	82	22.28
	19 to 35	71	19.29
	36 to 50	94	25.54
	51 to 65	71	19.29
	66 to 80	45	12.23
	Over 80	3	0.82
	Did Not Answer	2	0.54
Race and Ethnicity of Person with Diabetes	White	271	75.7
	Hispanic or Latino	64	17.88
	African American	10	2.79
	Native American	1	0.28
	Asian/Pacific Islander	0	0.00
	Other (multiple)	7	1.96
	Did Not Answer	5	1.40
Annual Household Income	0 to $15,000	17	4.35
	$16,000 to $30,000	48	12.28
	$31,000 to $45,000	57	14.58
	$46,000 to $60,000	53	13.55
	$61,000 to $75,000	43	11.00
	$76,000 to $90,000	24	6.14
	$91,000 to $100,000	32	8.18
	$101,000 to $150,000	59	15.09
	Over $150,000	39	9.97
	Did Not Answer	19	4.86

Measure	Answer	Count	Percentage (%)
Number of People in Household	1	35	8.95
	2	100	25.58
	3	69	17.65
	4	73	18.67
	5	53	13.55
	6	29	7.42
	7	6	1.53
	8	4	1.02
	9	4	1.02
	Did Not Answer	18	4.60
Insulin(s) Used	Humalog	179	32.31
	Novolog	104	18.77
	Fiasp	14	2.53
	Lantus	88	15.88
	Levemir	29	5.23
	Tresiba	30	5.42
	Toujeo	11	1.99
	Basaglar	26	4.69
	NPH	8	1.44
	Humulin R	28	5.05
	Novolin R	13	2.35
	Other	16	2.89
	Did Not Answer	8	1.44
Health Insurance	Yes	341	87.21
	No	39	9.97
	Did Not Answer	11	2.81
Prescription Drug Coverage	Yes	309	79.03
	No	49	12.53
	Did Not Answer	33	8.44

Insulin & Pharmacy Survey Questions

The insulin and pharmacy survey questions addressed, among other things, the monthly cost of insulin and supplies, the manner in which consumers manage costs of insulin and supplies, the effects of the costs of insulin on respondents' lives, and experiences using pharmacies and discount cards for insulin and supplies. For the questions addressing "supplies," supplies include items necessary for diabetes management in addition to insulin such as glucose meters, needles, syringes, test strips, and lancets. See Table 2 for summary statistics.

Table 2: Insulin and Pharmacy Data (Survey Questions 13-28)

Measure	Answer	Count	Percentage (%)
Monthly Cost of Insulin	$0-99	166	47.29
	$100-$499	111	31.62
	$500-$999	16	4.56
	$1,000-$1,499	5	1.42
	$1,500 or more	17	4.84
	It Varies	9	2.56
	I Don't Know	4	1.14
	Did Not Answer	23	6.55
Monthly Cost of Supplies	$0-99	136	38.64
	$100-$499	153	43.47
	$500-$999	20	5.68
	$1,000-$1,499	4	1.14
	$1,500 or more	5	1.42
	It Varies	0	0.00
	I Don't Know	0	0.00
	Did Not Answer	34	9.66
Frequency of Rationing of Insulin due to Cost	Never	197	55.97
	About once/year	44	12.50
	About once/month	59	16.76
	About once/week	22	6.25
	Every day	22	6.25
	Did Not Answer	8	2.27
Frequency of Rationing of Supplies due to Cost	Never	150	42.61
	About once/year	51	14.49
	About once/month	60	17.05
	About once/week	40	11.36
	Every day	44	12.50
	Did Not Answer	7	1.99
Frequency of Skipping Insulin Doses due to Cost	Never	245	69.60
	About once/year	36	10.23
	About once/month	36	10.23
	About once/week	16	4.55
	Every day	13	3.69
	Did Not Answer	6	1.70
Frequency of Use of Expired Insulin	Never	210	59.66
	About once/year	73	20.74
	About once/month	42	11.93
	About once/week	9	2.56
	Every day	7	1.99
	Did Not Answer	11	3.13

Measure	Answer	Count	Percentage (%)
Affordability of Insulin	Yes (Affordable)	156	44.32
	No (Not affordable)	153	43.47
	It Depends	25	7.10
	I Don't Use Insulin	2	0.57
	I Don't Know	1	0.28
	Did Not Answer	15	4.26
Increase in Cost of Insulin over the Past Year	Yes (increased)	174	49.43
	No (not increased)	116	32.95
	I Don't Know	56	15.91
	Did Not Answer	6	1.70
Effect of Cost of Insulin on Life	Very Much	152	43.18
	Somewhat	118	33.52
	Very Little	71	20.17
	I Don't Use Insulin	2	0.57
	Did Not Answer	9	2.56
Frequency of Paying for Necessities instead of Insulin	Never	227	64.49
	About once/year	55	15.63
	About once/month	39	11.08
	About once/week	16	4.55
	Every day	8	2.27
	Did Not Answer	7	1.99
Alternative Insulin(s) Offered by Pharmacy due to Cost	Yes	85	24.15
	No	253	71.88
	Did Not Answer	14	3.98
Awareness of Less Expensive Alternatives to Prescribed Insulin	Yes (Aware)	132	37.50
	No (Not aware)	211	59.94
	Did Not Answer	9	2.56
Use of Discount Cards	Yes (Use cards)	104	29.55
	No (Don't use cards)	233	66.19
	Did Not Answer	15	4.26
Ease of Use of Discount Cards	Yes (Easy to use)	49	13.92
	Somewhat	72	20.45
	No (Not easy to use)	130	36.93
	Did Not Answer	101	28.69

Measure	Answer	Count	Percentage (%)
Cost Savings of Using Discount Card	$0-$15	141	40.06
	$16-$50	25	7.10
	$51-$100	17	4.83
	$101-$150	7	1.99
	$151-$300	8	2.27
	Over $300	10	2.84
	Did Not Answer	144	40.91
Obtaining of Insulin by means other than a U.S. Pharmacy	Never	232	58.44
	Family	33	8.31
	Friends	45	11.34
	Internet	17	4.28
	International Pharmacy	36	9.07
	Other	10	2.52
	Did Not Answer	24	6.05

Survey Respondent Narratives

The final two survey questions asked respondents to share 1) their stories about how high costs of managing diabetes have affected them, and 2) how the novel Coronavirus has affected their ability to pay for insulin. These questions had 237 responses and 260 responses, respectively. In many instances, the details in the narratives are specific and personal; as such, they have been excluded from this report to avoid the potential for identifying individual respondents.

Several themes emerged from the survey respondent narratives and may warrant further analysis:

- High costs associated with diabetes:
  - High cost of insulin and supplies
  - High cost of medical insurance (premiums, copays, deductibles, out of pocket maximums)
  - Gaps in medical insurance coverage
  - Reliance on Medicaid for insulin
  - Necessity of emergency room visits for diabetes management and to obtain insulin
  - Significant effects on quality of life (i.e., strict budgeting, staying in a job simply for the health insurance, sacrificing vacations and other luxuries)
  - Effects of COVID-19 pandemic on ability to pay (i.e., job loss or cuts to hours, furloughs, loss of insurance)
- Methods of coping with high costs:
  - Rationing and use of expired insulin
  - Diet changes and skipping meals to preserve insulin supply
  - Obtaining insulin by means other than a U.S. pharmacy

APPENDIX B:
THE FELDMAN REPORT

CENTER FOR INNOVATION (C4i)

INSULIN COSTS IN THE STATE OF COLORADO[1]

Report Presented to the Colorado Attorney General's Office
By Professor Robin Feldman
Arthur J. Goldberg Distinguished Professor of Law
Albert Abramson '54 Distinguished Professor of Law Chair
Director of the Center for Innovation
UC Hastings Law

I. Introduction

Skyrocketing insulin prices, borne out of poor market incentives and extreme pharmaceutical consolidation, have created a human tragedy. Diabetics unable to afford their insulin report under-dosing or injecting expired insulin; others starve themselves to restrain blood sugar levels; in more extreme cases, patients purposefully lapse into Diabetic Ketoacidosis to obtain free insulin from emergency rooms. Bankruptcy and economic ruin are routine experiences for diabetics, many of whom spend over 50% of their monthly income on insulin. One patient's words speak for many: "I often cry, and I think, have I done something wrong that I can't afford to take care of myself?"[2]

The most recent empirical evidence corroborates the pain of these price increases. One 2020 report from the RAND Corporation, for instance, found that insulin patients in the United States oftentimes pay 5-10 times as much in list price for insulin, depending on the type of insulin, compared to 32 other OECD countries. Even after applying a standard 50% rebate discount, insulin-dependent patients in the US pay several times as much as comparable patients in other advanced economies.[3]

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[1] I wish to thank Chief Data Scientist Ramy Alsaffar and Research Fellow David Toppelberg, who led the research team. I am also grateful to Research Fellows Nathan Brown, Christopher Kim, Nick Massoni, and Sophia Tao for their work on this report.

[2] *Chaires et al v. Sanofi, U.S. et al,* 1:2017cv10158 (D. Mass. 2017), https://static01.nyt.com/science/01-30-17_Insulin_Class_Action_Complaint_Hagens_Berman.PDF

[3] Andrew Mulcahy, Daniel Schwam, and Nathaniel Edenfield, *Comparing Insulin Prices in the United States to Other Countries: Results from a Price Index Analysis,* RAND INST. 16 (6 Oct. 2020); For standard rebate discounts for insulin, *see* Jean Fuglesten Biniek and William Johnson, *Spending on Individual with Type 1 Diabetes and the Role of Rapidly Increasing Insulin Prices,* HEALTH CARE COST INST. (Sept.

This report analyzes insulin accessibility in Colorado. Specifically, we seek to answer four central questions. 1) What is the impact of patents, exclusivities, and extensions on the price of insulin? 2) How much do Colorado patients pay for insulin, directly and out-of-pocket, and how much does the federal government pay in subsidies for Colorado patients? 3) Does irrational tiering contribute to high insulin prices in Colorado? 4) What is the relationship between the rebate structure and insulin pricing? In each of these questions, we compare Colorado with nationwide averages.

We utilized a variety of methodological approaches and datasets to paint a clear picture of Colorado's insulin market. For quantitative analyses of insulin pricing, tiering, and formularies, we relied upon Medicare Part D data during the years 2006-2018 from the Centers for Medicaid and Medicare Services (CMS). We sourced analyses of insulin patents and related intellectual property from the FDA's Orange Book data, 2005-2018.

Medicare provides a reasonable research venue to answer the questions above. It accounts for roughly 29 percent of prescription drug spending in the United States. In addition, problems within Medicare are likely to echo or amplify across private markets. From a practical perspective, direct claims information is easily available.[4] We considered our quantitative Medicare findings in the broader contexts of the insulin market, pharmaceutical industry, regulations, and intellectual property law.

Key empirical results from this report include:

- **Colorado Insulin Cost Increased 280%:** The average dosage unit cost (pre-rebate) of all insulin types increased roughly 280% between 2010 and 2018. Analog insulin is more expensive than other human insulins.[5]
- **Colorado Insulin Out-of-Pocket Costs More than Doubled in 7 years:** For Colorado Medicare patients, the insulin out-of-pocket burden more than doubled between 2011 and 2018.[6] The average annual out-of-pocket payment rose from $360 to $816, with some Colorado Medicare patients paying as much as $2,500 in 2018.
- **Colorado Insulin Patients Pay More in the Gap Phase than Other States:** Colorado patients on average paid more for their monthly supply of insulin than patients in other states. This is largely because Colorado patients pay more during the gap phase compared to patients in other states. In 2018, for example, this difference amounted to $26 more each month that a patient was in the gap phase.[7]
- **Insulin Tiering:** The majority of insulin drugs were prescribed from Tier 3 of five-tier formularies commonly used in Medicare Part D. Since there is no truly interchangeable

2020), https://healthcostinstitute.org/diabetes-and-insulin/spending-on-individuals-with-type-1-diabetes-and-the-role-of-rapidly-increasing-insulin-prices

[4] CENTERS FOR MEDICARE AND MEDICAID SERVICES, NATIONAL HEALTH EXPENDITURES 2018 HIGHLIGHTS (DEC. 5, 2019); US DEPARTMENT OF HEALTH & HUMAN SERVICES, HHS FY 2018 BUDGET IN BRIEF – CMS – MEDICARE (2018)

[5] Note: analog insulin is a genetically altered and laboratory-grown subcategory of human insulin. It is considered the most cutting-edge insulin type on the market.

[6] This statistic covers the period 2011-2018 while the previous statistic covers the period 2010-2018 because the 2010 data for out-of-pocket costs was a strong outlier in the overall dataset.

[7] *See infra* text accompanying notes 40-44 (explaining the concept of phased coverage under Medicare, including the gap phase).

generic or biosimilar insulin available,[8] we cannot say the insulin market exemplifies irrational tiering, a practice in which brand drugs are misplaced compared to their generics. Nevertheless, all diabetics are forced to buy brand-price insulin, and it is possible that preferred-drug lists limit patient choice to a single brand or form of insulin.

- **Evergreening of Patents Has Extended Monopoly Protections:** Many insulin products have received additional patents, exclusivities, and extensions, adding decades of protection and monopoly prices. Evergreening is a familiar tactic for best-selling insulin products: Eli Lilly's Humalog added 17 years of protection; Novo Nordisk's Novolog added 27 years of protection; Sanofi's Lantus added 28 years of protection.[9] In addition, we note that many cheaper, trailing-edge insulin products have been discontinued, effectively removing them from the market and blocking generic competition.

II. Patents, Exclusivities, and Extensions in the Insulin Market

The modern system for drug approval in the United States is a long and arduous process.[10] Companies wishing to bring an entirely new drug to market must develop the drug, prove its safety and efficacy to the FDA through rigorous clinical trials, and mass-scale its production. Survivors of this marathon – at least those whose innovation is significant enough to earn a patent – are rewarded with the right to exclude others from making, using, or selling the drug.[11] As a result, patented drugs command monopoly-level prices on the market until their patents, exclusivities, and extensions expire.

The cost of obtaining the patent itself is minuscule compared to the hundreds of millions of dollars necessary to take a drug through clinical safety and efficacy trials.[12] Because of this, companies try to plant their patent stake in the ground as soon as possible, to mark off their

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[8] Lily and Novo Nordisk have released half-price versions of their own drugs. These can be described as authorized generics, but they do not inject the competition that a true generic or biosimilar would bring. Eli Lilly, likewise, has released a branded generic version of Sanofi's long-acting insulins. More recently, the FDA approved a long-acting generic insulin from Mylan/Biocon for market release in the summer of 2020. However, there are several reasons why Eli Lilly's branded generic and Mylan/Biocon's likewise fail to inject price competition. For a full treatment of the market and legal dynamics at play, *see infra* text accompanying notes 23-32

[9] For access to the searchable evergreening database, *see* Robin Feldman, *Evergreening Drug Patent Search*, CENTER FOR INNOVATION, UC HASTINGS (last accessed Sept. 22nd, 2020) https://sites.uchastings.edu/evergreensearch/about/

[10] For more in-depth descriptions of the drug approval process, *see* US FOOD AND DRUG ADMIN., DEVELOPMENT & APPROVAL PROCESS (DRUGS) (Oct. 5, 2017), www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm; *see also* US FOOD AND DRUG ADMIN., HOW DRUGS ARE DEVELOPED AND APPROVED (Aug. 18, 2015), www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/default.htm; *see generally* BERNICE SCHACTER, THE NEW MEDICINES: HOW DRUGS ARE CREATED, APPROVED, MARKETED, AND SOLD (2005); *see generally* Kimiya Sarayloo, *A Poor Man's Tale of Patented Medicine: The 1962 Amendments, Hatch-Waxman, and the Lost Admonition to Promote Progress*, 18 QUINNIPIAC HEALTH L.J. 1 (2015); *see generally* Martin S. Lipsky & Lisa K. Sharp, *From Idea to Market: The Drug Approval Process*, 14 J. AM. BOARD FAM. PRACTIC. 362 (2001).

[11] 35 U.S.C. § 154(a)(2) (providing for 20 years of protection from the date of the patent application).

[12] Aylin Sertkaya et al., *Key Cost Drivers of Pharmaceutical Clinical Trials in the United States*, 13 CLIN. TRIALS 117 (2016), www.ncbi.nlm.nih.gov/pubmed/26908540 (noting that costs for clinical trials can range from $1.4 million to $52.9 million, depending on the therapeutic area of the drug and the phase of the trial); *see* Rebecca S. Eisenberg & W. Nicholson Price, *Promoting Healthcare Innovation on the Demand Side*, 4 J.L. & BIOSCI. 3, 8–9 (2017) (outlining the various incentives surrounding the high cost of clinical trials).

territory and keep others out. Consequently, drug companies own many patents that sit idly on the shelf, never translating into viable products.

Since patenting occurs early in the drug development cycle, some of the 20-year patent term will have expired before the drug gets to market. Some estimates suggest that the average remaining patent period for a new drug is 12 years.[13] Although considerably less than the 20 years that begins with a patent application, 12 years of exclusivity is a substantial reward, particularly for a blockbuster drug that will garner billions of dollars a year in revenue.

Given that a generic will have nothing new to patent, the generic's company has no potential for monopoly returns, unlike a branded drug company. Thus, the financial incentive for engaging in any clinical trials is seriously limited for generic drugs, and repeating those trials in their entirety does not necessarily represent a good use of societal resources.[14] With this in mind, the federal Hatch-Waxman system for rapid entry of generic small-molecule drugs allows generic companies to reference certain safety and efficacy data from the brand-name company's original drug application, known as a new drug application (NDA).[15] In the biologics space, the Biologics Price Competition & Innovation Act (Biosimilars Act) governs the similar system for biosimilars and interchangeable drugs; here, the original application is known as a biologics licensing application (BLA). Insulin spans both systems. For historic reasons, insulin was treated as a small molecule drug until the FDA shifted it to the biologics system in March 2020.[16]

The introduction of generics or biosimilars is a shock to the system for a drug company. Prices can drop by as much as 20 percent when the first generic enters the market; with multiple generics, the prices may eventually drop by 80–85 percent.[17] Although biosimilars have not initiated as sharp a price drop in the United States, biosimilar entry still erodes the original biologic's monopoly pricing. As a result, drug companies have a powerful incentive to delay competitive entry for as long as possible. Given that sales of blockbuster drugs reach billions of

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[13] *See e.g.* Jan Berger, Jeffrey Dunn, Margaret Johnson, et. al., *How Drug Life-Cycle Management Patent Strategies May Impact Formulary Management*, 22 AM. J. MANAG. CARE S487 (JAN. 2017); Aaron Kesselheim, *Determinants of Market Exclusivity for Prescription Drugs in the United States*, COMMONWEALTH FUND (Sept. 13, 2017) https://www.commonwealthfund.org/publications/journal-article/2017/sep/determinants-market-exclusivity-prescription-drugs-united

[14] *See generally* Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417 (informally referred to as the Hatch Waxman Act). The generic equivalent of a biologic drug is known as a "biosimilar," or an "interchangeable." Such drugs are governed by the Biologics Price Competition and Innovation Act of 2009 (the Biosimilars Act), rather than the Hatch-Waxman Act. Greater safety and efficacy testing is required for biosimilars than for generics. Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111–148, Title VII, Subtitle A, 124 Stat. 119 (2010).

[15] ROBIN FELDMAN & EVAN FRONDORF, DRUG WARS: HOW BIG PHARMA RAISES PRICES AND KEEPS GENERICS OFF THE MARKET, 22 (2017) (citing 21 U.S.C. § 355(j)(2)(A) (i)–(v) (2012)).

[16] Press Release, FDA, Insulin Gains New Pathway to Increased Competition (March 23rd, 2020) https://www.fda.gov/news-events/press-announcements/insulin-gains-new-pathway-increased-competition

[17] ROBIN FELDMAN & EVAN FRONDORF, DRUG WARS: HOW BIG PHARMA RAISES PRICES AND KEEPS GENERICS OFF THE MARKET, 20 (2017), citing Ernst R. Berndt & Murray Aitken, *Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century after the 1984 Waxman-Hatch Legislation*, Working Paper No. 16431, NAT'L BUREAU OF ECON. RES. 10 (2010), www.nber.org/papers/w16431.pdf; US Food & Drug Admin., Generic Drugs Facts, www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm67991.htm (last visited Oct. 30, 2018).

dollars a year, delaying a generic's entry by just a few months can be worth hundreds of millions to drug companies.[18]

Although the Hatch-Waxman and Biosimilars Acts encourage the rapid entry of generics and biosimilars once patents expire, drug companies have proven extraordinarily adept at maintaining their protections. Drug companies can deploy a sequence of tactics to prevent or delay entry from potential market competitors. One of the most common of these tactics is *evergreening*—when companies artificially extend patents and exclusivities to block generic or biosimilar approval.[19]

Evergreening techniques can come in many shapes and forms. Simple evergreening techniques involve obtaining new protections on existing drugs; for example, a company can file additional patents based on new methods of manufacturing or packaging a drug. More complex evergreening strategies involve developing new formulations, dosage schedules, or drug combinations. These can be combined with attempts to push the market toward the slightly altered product through advertising, pressuring doctors to write prescriptions including terms such as "Dispense as Written" or "Brand Medically Necessary," or even by withdrawing the old product from the market entirely. Using these techniques, brand-name companies try to prevent pharmacists from being able to fill a prescription with a cheaper version, or deter patients from moving to the generic or biosimilar.[20] At the very least, the brand-name company may be able to bifurcate the market through its efforts, with some patients moving to their new version, for which no generic or biosimilar is available.

Our research has found that evergreening tactics were the norm rather than the exception. Analyzing more than a decade of data published by the US Food and Drug Administration (FDA), including all small-molecule drugs on the market, we found that pharmaceutical companies were recycling and repurposing old medicines, rather than creating new ones. In fact, 78 percent of the drugs associated with new patents were not new drugs, but existing ones.[21]

Adding new patents and exclusivities to extend the protection cliff is particularly pronounced among blockbuster drugs. Of the roughly 100 bestselling drugs, more than 70 percent had their protection extended at least once, with more than 50 percent having the protection cliff extended more than once. Patents or exclusivities were added to almost 40 percent of all drugs available on the market. Of the companies that added protections, 80 percent added more than one.

The problem is also growing across time. The number of drugs shielded by an additional patent almost doubled during the period of study. The addition of certain other protections, such as the Orphan Drug exclusivity, increased at an even greater rate – even tripling in frequency for some protection types.

Small changes to drugs may be of some value to segments of the population. Nevertheless, the research and development cost for making adjustments to existing drugs may

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[18] *See id.*, at 67–69 (noting that branded drugs making large yearly sales, such as the $1.3 billion annual sales of the drug Flonase, have the potential to gain hundreds of millions of dollars in only months of delay).

[19] *See e.g.* ROBIN FELDMAN, RETHINKING PATENT LAW 170–78 (2012) (describing evergreening and providing case history examples); *see also infra* notes 33–39 and accompanying text (explaining evergreening and identifying quantity within our data set of those who apply repeatedly for patent and exclusivity extensions).

[20] For a detailed description of these and other evergreening techniques, *see* ROBIN FELDMAN & EVAN FRONDORF, DRUG WARS: HOW BIG PHARMA RAISES PRICES AND KEEPS GENERICS OFF THE MARKET (2017), at 69–79.

[21] Robin Feldman, *May Your Drug Price Be Evergreen*, OXFORD J.L. AND THE BIOSCIENCES (Dec. 2018), available at SSRN: https://ssrn.com/abstract=3061567 or http://dx.doi.org/10.2139/ssrn.3061567

be far less than the cost of research and development for entirely new drugs. Thus, society may be lavishing expensive rewards on suboptimal innovation, when a market reward would be sufficient.

The world of insulin production is no exception to these trends. The vast majority of insulin products are manufactured by three companies: Eli Lilly, Novo Nordisk, and Sanofi-Aventis. Together, these three insulin manufacturers produce 90% of the global insulin supply and nearly 100% of the US insulin supply.[22] There are no truly interchangeable generic or biosimilar competitors for these companies' drugs. Observers have noted that the three major insulin manufacturers tend to mirror each other's price increases; when one raises prices, the others are quick to follow.[23]

In the summer of 2020, the FDA approved a long-acting biosimilar insulin, Semglee.[24] However, Semglee—which is manufactured by a partnership between the generic manufacturers Biocon and Mylan—is unlikely to substantially alter current market dynamics. First, Semglee is not approved for interchangeability, meaning that automatic substitution will not apply.[25] This inhibits Semglee from attaining market share or competing on price in the same manner as a generic. Without automatic substitution, it is up to patients and doctors to specifically request and prescribe biosimilar insulin.[26]

Beyond interchangeability, Semglee does not actually compete with the entire insulin market; rather, it competes only with other long-acting insulins. There are only three other long-acting insulins, two of which are produced by Sanofi and the third of which is Eli Lilly's branded generic, priced almost equivalently to a regular branded insulin.[27] The long-acting insulin market remains incredibly consolidated, inhibiting the extent to which competition reduces price.

Moreover, it is too soon to tell whether Semglee will be able to navigate through the contracts between existing insulin players and health plans, along with the tactics used by companies with large market positions to prevent new entrants from challenging those positions.[28] Finally, some recent forecasts have predicted limited potential savings from biosimilar entrants, as well as a limited ability to capture market share over the medium-term.[29] For instance, a 2020 IQVIA analysis found that the 22 biosimilars launched in the US have only secured about 20% of the accessible market by volume and a roughly 30% price discount.[30]

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[22] Judith Johnson, *Insulin Products and the Cost of Diabetes Treatment*, CONGRESSIONAL RESEARCH SERVICE (19 Nov. 2018), https://fas.org/sgp/crs/misc/IF11026.pdf

[23] Lydia Ramsey, *There's Something Odd About the Way Insulin Prices Change*, BUSINESS INSIDER (17 Sept. 2016), https://www.businessinsider.com/rising-insulin-prices-track-competitors-closely-2016-9

[24] Tony Hagen, *Biocon, Mylan Launch Semglee and Seek Biosimilar, Interchangeable Status*, CENTER FOR BIOSIMILARS (Aug. 31, 2020) https://www.centerforbiosimilars.com/view/biocon-launches-semglee-and-seeks-biosimilar-interchangeable-status

[25] Richard Cauchi, *State Laws and Legislation Related to Biologic Medications and Substitution of Biosimilars*, NATIONAL CONFERENCE OF STATE LEGISLATURES (May 3, 2019) https://www.ncsl.org/research/health/state-laws-and-legislation-related-to-biologic-medications-and-substitution-of-biosimilars.aspx

[26] Ibid. Cauchi

[27] Christopher Curley, *Will This New, Cheaper Insulin Product Help the Diabetes Community?* HEALTHLINE (June 18, 2020) https://www.healthline.com/health-news/new-cheaper-insulin-may-help-diabetes-community#Competition-may-not-lower-prices

[28] For an explanation of the dynamics of volume-based rebate games, PBM contracting, and formulary placement, *see infra* text accompanying notes 67-69

[29] *See generally* Murray Aitken, Michael Kleinrock, and Elyse Muñoz, *Biosimilars in the United States 2020-2024*, IQVIA INSTITUTE FOR HUMAN DATA SCIENCE (Oct. 2020), 14. Note: patient costs are estimated using average invoice amounts, which are the prices patients pay at the pharmacy.

[30] *Id.* at 2, 3

These results are far less impressive than what occurs with generic entry, in which the brand drug generally loses 80-90% of its market share within a year after the first generic enters, and the price of the drug can eventually drop 80-85% when multiple generics have entered.[31] In short, although any competition is encouraging, it is simply too early to tell what impact Semglee will have on market-wide insulin prices. As former FDA Commissioner Scott Gottlieb cautiously described the state of biosimilar competition, "We'll know that we've been successful when there's a biosimilar market that can sustain multiple competing biosimilar and biologic options."[32]

Beyond any potential shortcomings of the nascent biosimilar insulin market, the three major insulin manufacturers have also employed extensive evergreening techniques to extend their protections in the insulin market.[33] In recent decades, incremental innovation has introduced versions of insulin, such as insulin analogs, that cost significantly more than human synthetic and animal insulin products.[34] Some studies of these new insulin analogs found that they are not clearly superior to prior insulins, though they cost up to ten times more.[35] Furthermore, these newer, more expensive insulins seem to quickly replace older insulins on preferred formulary tiers, such that more than 90% of privately insured patients with type 2 diabetes are prescribed the latest versions of insulin.[36]

The Center for Innovation's Evergreen Database shows that insulin producers have frequently used evergreening techniques to extend their protection cliff and maintain exclusivity.[37] The tables below detail all insulin-related drugs in the FDA's Orange Book from 2005 to 2018, listed according to manufacturer. The "Additional Time" column details the

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[31] *See e.g.,* ROBIN FELDMAN & EVAN FRONDORF, DRUG WARS: HOW BIG PHARMA RAISES PRICES AND KEEPS GENERICS OFF THE MARKET 7 (2017); Henry G. Grabowski et al., *Evolving Brand- Name and Generic Drug Competition May Warrant a Revision of the Hatch- Waxman Act,* 30 HEALTH AFF. 2157, 2163 (2011).

[32] Scott Gottlieb, Commissioner, Food and Drug Administration, Remarks on Capturing the Benefits of Competition for Patients (March 7, 2018) (transcript available at https://www.fda.gov/news-events/speeches-fda-officials/capturing-benefits-competition-patients-03072018)

[33] Why Is There No Generic Insulin? Historical Origins of a Modern Problem (Jeremy Greene, NEJM), https://search-proquest-com.uchastings.idm.oclc.org/docview/1664805626?rfr_id=info%3Axri%2Fsid%3Aprimo

[34] Note: Both human and analog insulin are grown in labs, but insulin analogs are molecularly altered forms of insulin that have been developed in recent years. Animal insulin, which was the original form of insulin, is rarely used in the United States anymore. Analog insulin's cost-effectiveness is much debated and controversial. Insulin analogs have been found to be faster acting with slightly shorter onset periods, but they do not appear to be more or less efficacious overall compared to human insulin. *See* Diabetes.co.uk, *Analogue Insulin,* 15 Jan. 2019, https://www.diabetes.co.uk/insulin/analogue-insulin.html; Diabetes.co.uk, *Animal Insulin,* 15 Jan. 2019, https://www.diabetes.co.uk/insulin/animal-insulin.html; Kasia Lipska, Joseph Ross, Holly Houten, *Use and Out-of-Pocket Costs of Insulin for Type 2 Diabetes Mellitus from 2000 Through 2010,* JAMA, https://jamanetwork.com/journals/jama/fullarticle/1878705. https://www.diabetes.co.uk/insulin/analogue-insulin.html

[35] Jing Luo, Nazleen Khan, Thomas Manetti, *Implementation of a Health Plan Program for Switching from Analogue to Human Insulin and Glycemic Control Among Meidcare Beneficiaries with Type 2 Diabetes,* 321 JAMA 374 (29 Jan. 2019), https://jamanetwork.com/journals/jama/article-abstract/2722772; Elizabeth Bashoff, *Human Insulin may be a lower-cost option for some people with diabetes,* HARVARD HEALTH BLOG (6 JUNE 2019), https://www.health.harvard.edu/blog/human-insulin-may-be-a-lower-cost-option-for-some-people-with-diabetes-2019060316747

[36] Julia Belluz, *The absurdly high cost of insulin, explained,* VOX (7 Nov. 2019), https://www.vox.com/2019/4/3/18293950/why-is-insulin-so-expensive

[37] Robin Feldman, *Evergreening Drug Patent Search,* CENTER FOR INNOVATION, UC HASTINGS (last accessed Sept. 22nd, 2020) https://sites.uchastings.edu/evergreensearch/about/

amount of time between the date at which the protection beginning with the patent period should have expired and the latest expiration date from all additional protections.

As the tables demonstrate, evergreening has secured insulin manufacturers decades of additional protections and monopoly pricing. At the end of the day, patients, government budgets, and insurance plans must bear the brunt of artificially extended monopoly pricing.

ELI LILLY

Drug Name	# of Additions	# of Additions that Extend Time	Additional Time	Latest Protection Date	# of Unique Patents
Humalog	11	2	17 years	Aug 2024	3
Humalog Kwikpen	5	-	6 years	Aug 2024	3
Humalog Mix 75/25	13	1	11 years	Aug 2024	5
Humalog Mix 50/50	13	1	11 years	Aug 2024	5
Humulin R	2	-	10 years	Aug 2024	1
Humulin 70/30	1	-	-	Aug 2024	1
Humalin N	1	-	-	Aug 2024	1
Basaglar	1	-	-	Dec 2018	-

NOVO NORDISK

Drug Name	# of Additions	# of Additions that Extend Time	Additional Time	Latest Protection Date	# of Unique Patents
Novolog	64	5	27 years	Sept 2032	23
Novolog Mix 70/30	43	3	27 years	Sept 2032	12
Novolog Mix 50/50	14	-	4 years	December 2017	5
Levemir	46	7	23 years	Sept 2032	23
Ryzodeg 70/30	20	1	15 years	May 2033	17
Tresiba	20	-	12 years	Feb 2032	15

Xultophy 100/3.6	23	-	14 years	Feb 2032	20
Fiasp Flextouch	16	1	11 years	Feb 2032	14
Admelog; Solostar	20	2	12 years	April 2033	18

SANOFI AVENTIS

Drug Name	**# of Additions**	**# of Additions that Extend Time**	**Additional Time**	**Latest Protection Date**	**# of Unique Patents**
Lantus	37	4	28 years	April 2033	23
Apidra Solostar	33	2	24 years	April 2033	23
Toujeo Solostar	41	2	13 years	May 2031	19

In addition to adding protections, our analysis shows that insulin manufacturers have frequently removed older versions of insulin from the market. Discontinuing trailing-edge insulin products prevents patients from accessing cheaper insulins; it also blocks potential generic competitors from obtaining necessary samples of the now-unprotected drug in order to file for generic approval.

Specifically, using New Drug Application numbers and the FDA's Orange Book data, we found that six insulins were discontinued between 1982 and 2020, which left 13 insulin products in the Orange Book. Going by unique branded drug name, 52 drugs were discontinued in the same period, with 31 remaining on the market in 2020.[38] The sheer amount of discontinued insulin products could suggest underlying evergreening strategies, such as product hopping, in which a drug company moves the market to a new version of a drug—a version protected by new protection periods.

In short, insulin manufacturers regularly game patents, exclusivities, and extensions in order to maintain monopoly pricing and block generic competitors. Their efforts force patients, in Colorado and elsewhere, to consume the latest, most expensive insulin products, even when such products are not necessarily the most efficacious. Further aided by extreme consolidation within the industry, the three major insulin companies face little competition and tend to raise their prices in lockstep.[39] As the next section details, these high prices are borne directly by Colorado patients.

[38] Note: data for insulin discontinuations and related analyses come from the FDA's Orange Book prior to March 2020, which was when insulin was reclassified in the Purple Book. *See* FDA, *Orange Book,* *https://www.fda.gov/drugs/information-healthcare-professionals-drugs/electronic-orange-book*

[39] *Chaires et al v. Sanofi, U.S. et al,* 1:2017cv10158 (D. Mass. 2017), https://static01.nyt.com/science/01-30-17_Insulin_Class_Action_Complaint_Hagens_Berman.PDF

III. Colorado Patient Burdens for Insulin in Colorado

Using data from the Centers for Medicare and Medicaid Services related to Medicare retail drug claims (Part D of Medicare), we were able to assess both what Colorado Medicare patients pay for insulin and how those costs compare to nationwide averages.

Medicare patients do not typically pay a standard price for their prescription drugs. Rather, the coverage phase of a patient's Medicare plan dictates prescription drug costs at any given time. The Medicare Part D program has four coverage phases: deductible, initial, gap, and catastrophic.[40] These phases are separated by spending thresholds that reset annually.

In the deductible stage, the patient is responsible for 100% of expenses until the deductible threshold is met. (With $0 deductible plans, patients skip to the next phase, known as initial coverage.) During the initial coverage phase, patients pay a copay or coinsurance, and the health plan covers the remainder. After the patient and plan collectively meet the Part D initial coverage threshold—$4020 in 2020—the patient enters the gap phase, also called the donut hole.[41] Here, the health plan is limited in how much it can spend, requiring the patient to cover up to 25% of all prescription drug costs, as of 2019.[42] After paying a certain amount of out-of-pocket costs—$6,350 in 2020—the patient enters the catastrophic phase.[43] In the catastrophic phase, the patient foots 5% of a drug bill, with the remainder covered by the health plan and federal government reinsurance program.[44] With high-cost drugs, however, 5% can still present a significant burden.

Given the piecemeal coverage structures that shape prescription drug costs under Medicare Part D, our analysis found average patient costs for each of the four phases. Moreover, given the role of formulary design in determining insulin costs, as described below, our analysis controlled for insulin tier placement.

i. Average Out-of-Pocket Costs

Tier 3 of the various health plans covered the vast majority of insulin products for Medicare patients during the study period. For example, in 2018, Tier 3 sourced 87% of the insulin utilized in Colorado. Thus, we focused on Tier 3 claims to analyze the actual out-of-pocket costs for Colorado Medicare patients.[45]

Our results demonstrate the substantial burdens that Colorado patients bear for their insulin. Even with Medicare coverage in place, these burdens continue to worsen. Between 2011 and 2018, the average insulin out-of-pocket cost more than doubled for Colorado Medicare

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[40] Blue MedicareRx (PDP), *The Four Stages of Medicare's Part D Program,* https://www.rxmedicareplans.com/Learn/Stages;

[41] Medicare.gov, *Costs in the Coverage Gap*, https://www.medicare.gov/drug-coverage-part-d/costs-for-medicare-drug-coverage/costs-in-the-coverage-gap

[42] *Id.*, Medicare.gov

[43] Medicare.gov, *Catastrophic coverage, https://www.medicare.gov/drug-coverage-part-d/costs-for-medicare-drug-coverage/catastrophic-coverage*

[44] *Id.*, Blue MedicareRx; Medicare Rights Center, *Medicare Interactive: Phase of Part D coverage, https://www.medicareinteractive.org/get-answers/medicare-prescription-drug-coverage-part-d/medicare-part-d-costs/phases-of-part-d-coverage*

[45] The results were derived by combining all coverage phases on Tier 3 of five-tier formularies.

patients, rising from $360 to $816 annually. Some Colorado Medicare patients paid as much as $2,500 for one year of insulin.

When compared to generic drug costs, these findings highlight the limited availability of interchangeable true generics or competition in the insulin market.[46] For perspective, consider the cost of generic drugs. In 2017, the average dosage unit cost for generic drugs in the Medicare system was $4 a month, or $48 annually. Even during the deductible phase, in which patients must pay the full cost, generic drugs proved far cheaper.[47]

We also found that some Colorado patients pay more for insulin than patients in other states. During the deductible, initial and catastrophic phases, we do not find that Colorado patients paid significantly more than patients from other states for their insulin.[48] The disparity in out-of-pocket costs is caused largely by plans charging Colorado patients more during the gap phase compared to patients in other states.[49] For example, in 2018, Colorado patients in the gap phase paid roughly $26 more for a monthly supply of insulin compared to patients nationwide. Though changes to Part D have reduced patient cost-sharing burdens in the gap phase—from 50% in 2011 to no more than 25% in 2019—Colorado patients on average pay more during this coverage phase than patients in other states.[50]

Moreover, in several of the years we studied, Colorado patients paid more for a monthly supply of insulin in the gap phase than in any other coverage phase. For example in 2015, when an average monthly supply of insulin cost $20.70 in the deductible phase, $35.50 in the initial phase, and $23.90 in the catastrophic phase, Colorado patients in the gap phase paid $111.60 on average for a month's supply.[51] Many patients may spend more time in the initial phase, for instance, than the gap phase, with the result that their total out-of-pocket costs during the initial phase may exceed what they pay across the gap phase. Nevertheless, we highlight the gap phase because these costs are not insubstantial and because Colorado patients end up paying more than patients in other states. As a result, this period of coverage may be disproportionately challenging for many Colorado patients.[52]

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[46] For an in-depth explanation of recent biosimilar attempts at insulin and the associated shortcomings, *see supra* text accompanying notes 23-33

[47] Now that the FDA has shifted insulin from the Hatch-Waxman system to the biosimilars system, the costs of approval may be greater, substitution may be more limited, and the competitive reduction in price may be less.

[48] In certain years, for certain phases (e.g. 2014 initial phase) Colorado patients paid more than patients in other states. However, our analysis did not find that what Colorado patients paid out-of-pocket during these three phases across the study period differed significantly from patients from other states (*see* note 45).

[49] Our results were confirmed using a variety of statistical tests with significance at the .01 level. We confirmed that Colorado patients pay more for insulin out-of-pocket during the gap phase than patients in other states, while paying similar amounts during the other three phases (deductible, initial, and catastrophic). Since the vast majority of insulin drugs are placed on the third tier, we only tested third-tier statistical significance and ignored the other tiers. The charts below illustrate insulin costs for Colorado patients in each phase.

[50] Q1 Medicare, *What kind of discount can we expect in the coverage gap?*, *https://q1medicare.com/q1group/MedicareAdvantagePartDQA/FAQ.php?faq_id=470*

[51] For average patient paid amounts for insulin in Colorado by year and coverage phase, *see infra* Tables 1, 3, 5, and 7.

[52] Regarding the question of why Colorado patients paid more in the gap phase compared to patients from other states, it is possible that fewer Colorado patients were enrolled in enhanced alternative Medicare plans, some of which include a reduction in cost-sharing during the gap phase. *See* Q1 Medicare, *What is meant by the Medicare Part D abbreviations*, *https://q1medicare.com/q1group/MedicareAdvantagePartDQA/FAQ.php?faq=What-is-meant-by-the-Medicare-Part-D-abbreviations--EA-BA-DS-AE-in-the-plan-benefit-type-&faq_id=407&category_id=*; We also considered the low-income subsidy as a possible driver of lower gap phase out-of-pocket costs for patients in other states, but we found that Colorado patients received a similar average low-

To provide a complete picture of the insulin burden on Colorado patients, the charts and tables below detail patient cost figures by coverage phase. Our analysis disaggregated all Part D coverage phases and averaged out-of-pocket costs for a one-month supply of insulin across tiers. Note that patient costs are based on an average one-month insulin supply, rather than per year.

income subsidy during the gap phase compared to patients in other states. This rules out the low-income subsidy as an explanation for Colorado's gap phase out-of-pocket cost discrepancy. In 2018, however, changes in Medicare coverage gap rules reduced patient burden to no more than 25% but also disincentivized this type of gap assistance coverage. *See Seema Verma, The Part D Senior Savings Model*, HEALTH AFFAIRS (11 Mar. 2020*),* *https://www.healthaffairs.org/do/10.1377/hblog20200311.582575/full/* (noting that under current Medicare rules, if a patient pays less than 25% of a drug's cost, then the 70% manufacturer discount only applies to the patient's post-discount price, not the full amount*)*. Thus, even if enhanced alternative plans provide a possible explanation for the gap phase disparity during our 2006-2018 study period, that factor would likely be irrelevant going forward.

Figure 1: Average Patient Paid Amount by Tier on Deductible Coverage Phase

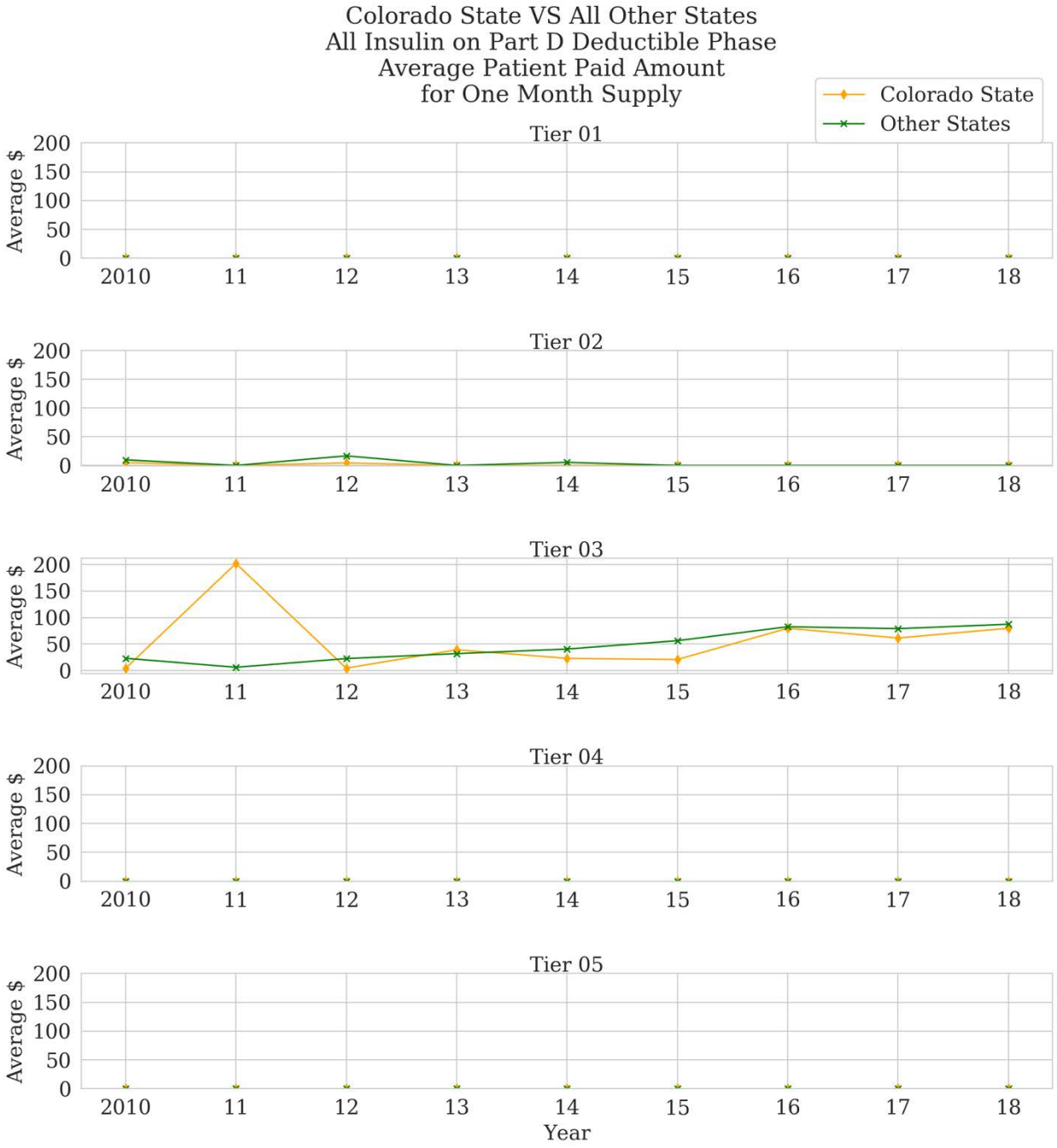

Table 1. Colorado State – All Insulin – Deductible Phase – Patient Paid Amount for One-Month Supply

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	5	4.1	0	0
2011	0	0	202	0	0
2012	0	4.5	4.5	0	0
2013	0	0	39.2	0	0
2014	0	0	23	0	0
2015	0	0	20.7	0	0
2016	0	0	79.7	0	0
2017	0	0	61.3	0	0
2018	0	0	79.8	0	0

Note: Zero values indicate no data were found for patient amount paid on that tier.

Table 2. All Other States– All Insulin – Deductible Phase – Patient Paid Amount for One-Month Supply

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	9.8	23.1	0	0
2011	0	0	6.1	0	0
2012	0	16.7	22.5	0	0
2013	0	0	31.9	0	0
2014	0	5.3	40.5	0	0
2015	0	0	56.3	0	0
2016	0	0	82.6	0	0
2017	0	0	79	0	0
2018	0	0	87.3	0	0

Note: Zero values indicate no data were found for patient amount paid on that tier.

Figure 2. Average Patient Paid Amount by Tier on Initial Coverage Phase

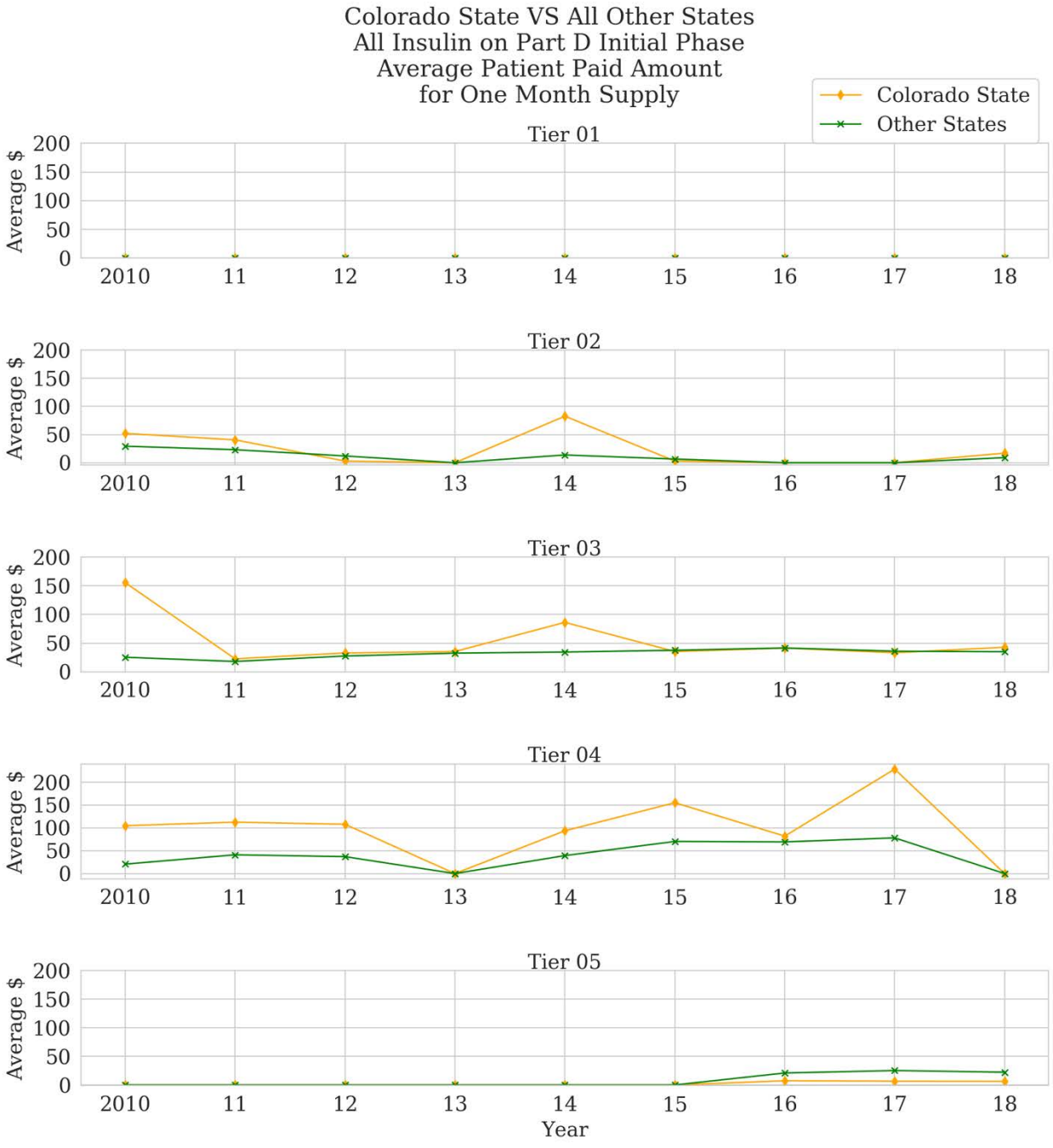

Table 3. Colorado State – All Insulin – Initial Phase – Patient Paid Amount for One-Month Supply

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	52.2	155.6	104.8	0
2011	0	40.6	22.8	112.6	0
2012	0	3	33	107.9	0
2013	0	0	35.5	0	0
2014	0	82.7	86.2	93.6	0
2015	0	3	35.5	155.1	0
2016	0	0	41.5	82	7.3
2017	0	0	33.3	228.7	6.5
2018	0	17	43	0	6.3

Note: Zero values indicate no data were found for patient amount paid on that tier.

Table 4. All Other States – All Insulin – Initial Phase – Patient Amount Paid Amount for One-Month Supply

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	29.4	25.6	20.7	0
2011	0	23.2	18.2	41	0
2012	0	12	27.7	37.1	0
2013	0	0	32.7	0	0
2014	0	13.9	34.6	39.4	0
2015	0	6.5	37.7	70.3	0
2016	0	0	41.7	69.3	21
2017	0	0	36.1	78.1	25.2
2018	0	9.1	35.2	0	22.3

Note: Zero values indicate no data were found for patient amount paid on that tier.

Figure 3. Average Patient Paid Amount by Tier on Gap Coverage Phase

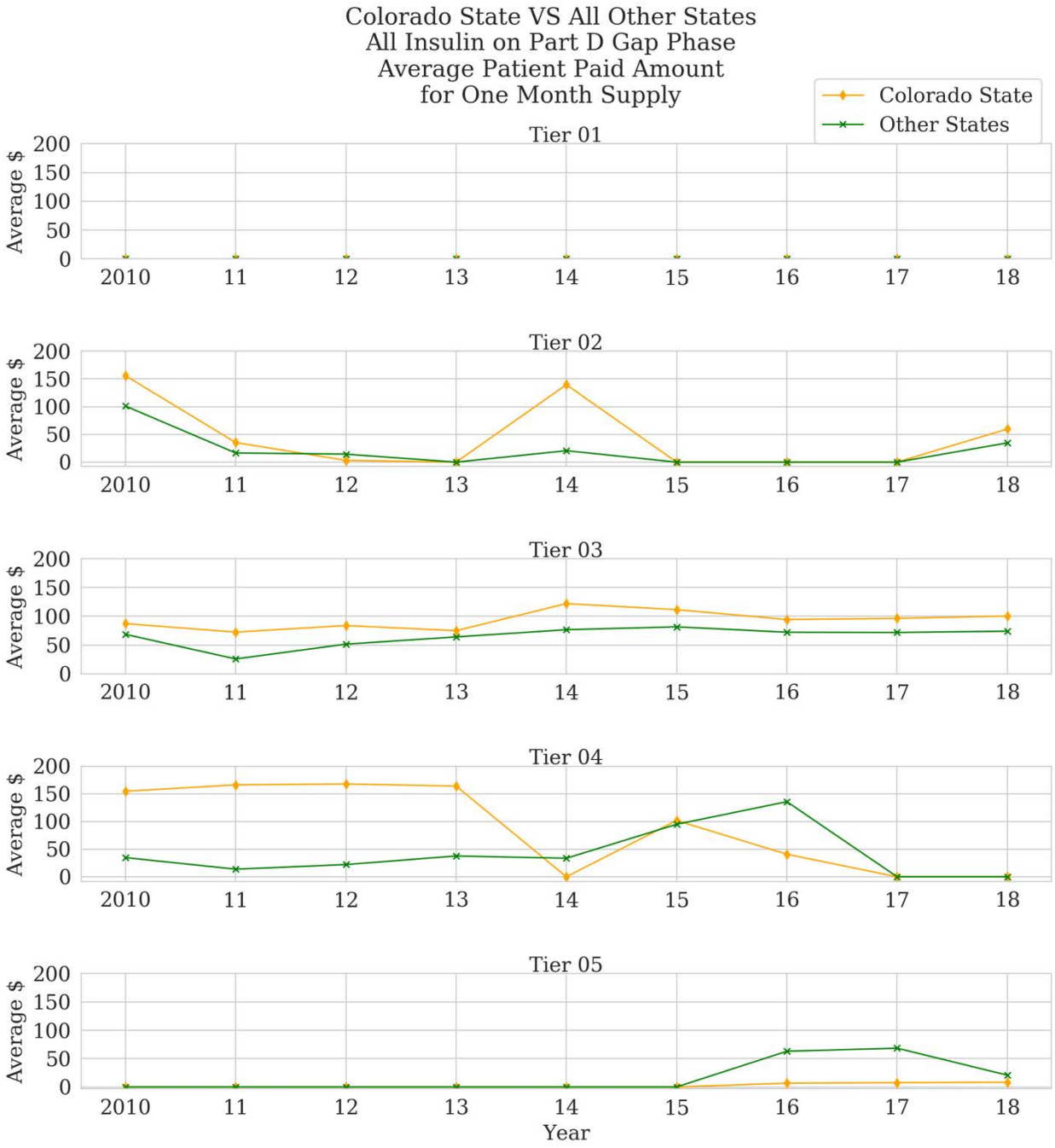

Table 5. Colorado State – All Insulin – Gap Phase – Patient Paid Amount for One-Month Supply

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	155.9	87.3	154.6	0
2011	0	35.3	72.5	166.2	0
2012	0	3.2	84	167.8	0
2013	0	0	75.1	164	0
2014	0	139.6	122	0	0
2015	0	0	111.6	101.7	0
2016	0	0	94.4	40.8	6.7
2017	0	0	96.4	0	7.5
2018	0	59.7	100.3	0	8.4

Note: Zero values indicate no data were found for patient amount paid on that tier.

Table 6. All Other States– All Insulin – Gap Phase – Patient Paid Amount for One-Month Supply

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	101.1	68.7	34.6	0
2011	0	16.5	26	13.7	0
2012	0	14.4	51.7	22	0
2013	0	0	64.2	37.6	0
2014	0	20.6	76.7	33.5	0
2015	0	0	81.7	94.9	0
2016	0	0	72.3	135.7	63
2017	0	0	72	0	68.4
2018	0	34.7	74.2	0	20.8

Note: Zero values indicate no data were found for patient amount paid on that tier.

Figure 4. Average Patient Paid Amount by Tier on Catastrophic Coverage Phase

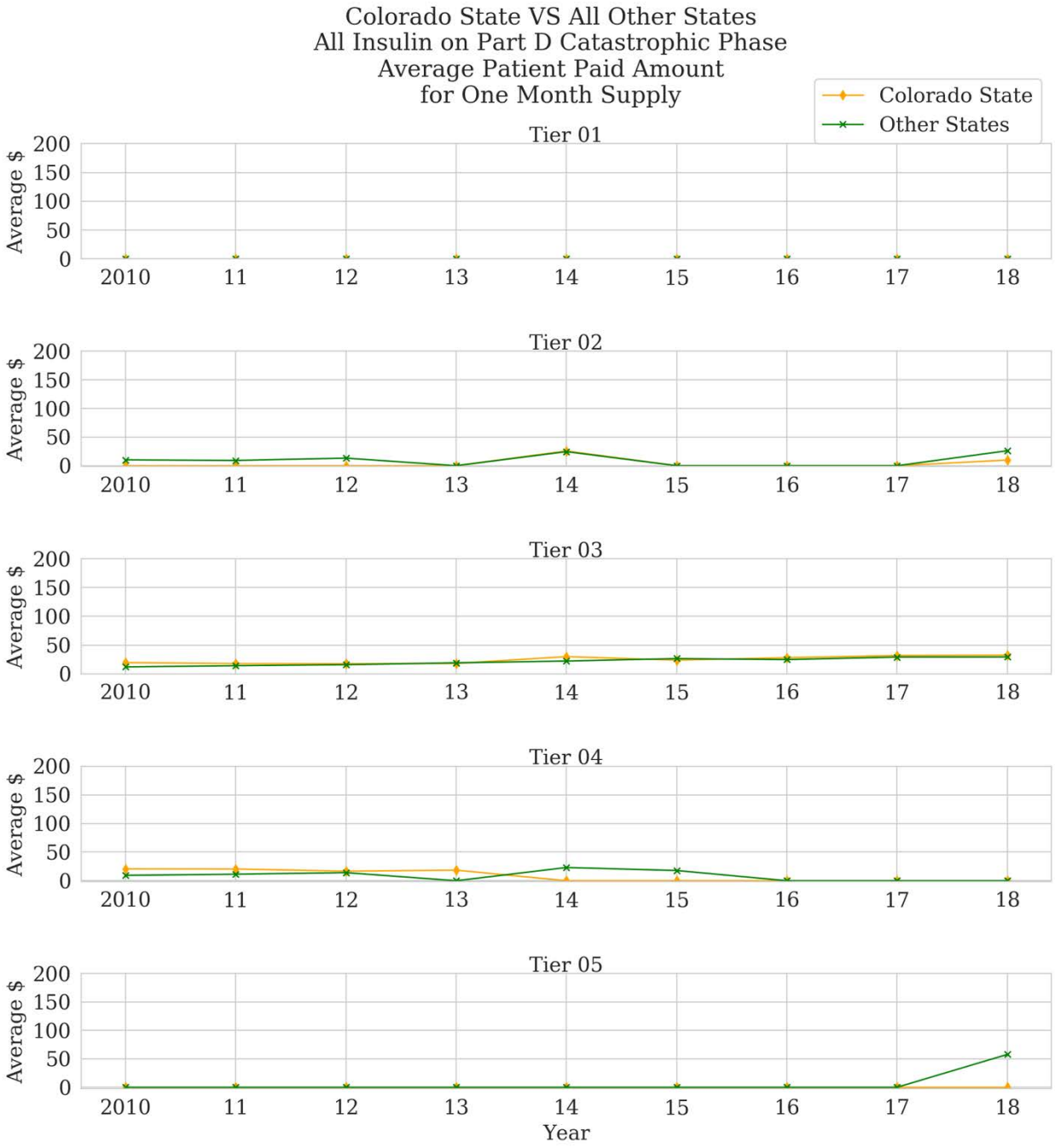

Table 7. Colorado State – All Insulin – Catastrophic Phase – Patient Paid Amount for One-Month Supply

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	0	19.7	20.7	0
2011	0	0	18	20.5	0
2012	0	0	17.8	16.7	0
2013	0	0	18.2	18.5	0
2014	0	25.7	30	0	0
2015	0	0	23.9	0	0
2016	0	0	28.3	0	0
2017	0	0	32	0	0
2018	0	9.9	32.6	0	0

Note: Zero values indicate no data were found for patient amount paid on that tier.

Table 8. All Other States – All Insulin – Catastrophic Phase – Patient Paid Amount for One-Month Supply

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	10.2	12.2	9.4	0
2011	0	9.2	14.3	11.4	0
2012	0	13.2	16	14.1	0
2013	0	0	19.3	0	0
2014	0	24.6	22.4	23.1	0
2015	0	0	26.6	17.9	0
2016	0	0	24.9	0	0
2017	0	0	29.3	0	0
2018	0	26.2	29.5	0	57.8

Note: Zero values indicate no data were found for patient amount paid on that tier.

IV. Formulary Design and Insulin Prices

The formulary system is a critical mechanism for restraining drug spending. Formulary tiers determine which drugs will be covered under a health plan and how much patients will pay to access those drugs through their plans. Patients may pay in the form of a flat co-pay, a percentage of the drug's list price (known as co-insurance), or a combination of both. No matter the form, out-of-pocket payments are tied to a drug's formulary placement.

When health insurers place drugs on lower, preferred tiers, patients enjoy lower cost-sharing burdens; when health insurers place drugs on higher, less-preferred tiers, the patient pays more. Specialty drugs and other rare medications occupy the highest tier in most formularies because they are the most expensive or challenging for insurers to cover. In five-tier Medicare formularies, these high-cost drugs would occupy the fifth tier. On the other end, we would expect the first tier to feature mainly low-cost, generic drugs. In prioritizing certain drugs over others, the tiering system should drive patients towards the most cost-effective drugs. As such, tiering should be part of a virtuous cycle, creating sensible, cost-saving market incentives. The reality, however, falls short of the ideal.[53]

The tier placement of drugs is shaped by deals between insurers and drug manufacturers. Insurers who guarantee a certain amount of revenue (i.e., sales volume) for drug companies receive large rebates off pharmaceutical list prices. Pharmacy benefit managers (PBMs) act as intermediaries, negotiating rebates on behalf of their health plan clients. PBMs help design a health plan's formulary by deciding which drugs to include, and tiering drugs based on factors like clinical effectiveness, cost and availability. [54] As a product of price-based negotiations, we would expect that the tiering system arranges its drugs according to price. A more expensive therapeutic equivalent—the FDA's classification for drugs that can be substituted with identical clinical efficacy and safety—of a drug should occupy a higher tier than its cheaper alternative, disincentivizing the costlier option as a result.[55]

In the world of pharmaceuticals, however, price is rarely a simple matter. Prescription drug costs can be contextualized by two distinct metrics: list price and net price. A list price is calculated as the average wholesale price a company charges to retailers for a certain drug.[56] List prices might be inconsequential if no patient ever had to pay the list price. Many people *do* pay full list price, however, or pay a co-insurance based on it. Although the passage of the 2010 Affordable Care Act substantially expanded health insurance coverage,[57] 10 percent of Americans under the age of 65 still had no insurance in 2017. Moreover, not all who had health insurance enjoyed prescription drug coverage.[58] Even with prescription drug coverage, insurance

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[53] ROBIN FELDMAN, DRUGS, MONEY, AND SECRET HANDSHAKES: THE UNSTOPPABLE GROWTH OF PRESCRIPTION DRUG PRICES, (2018) 18-43 (describing perverse incentives in the health insurance rebate system).

[54] CENTER FOR MEDICARE AND MEDICAID SERVICES, MEDICARE MODERNIZATION ACT FINAL GUIDELINES – FORMULARIES CMS STRATEGY FOR AFFORDABLE ACCESS TO COMPREHENSIVE DRUG COVERAGE, (JAN. 24, 2005)

[55] *FDA Glossary of Terms*, FDA (Nov. 14, 2017), https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms#TE

[56] *See* Julie Appleby, *Tracking Who Makes Money on a Brand-Name Drug*, KAISER HEALTH NEWS (Oct. 6, 2016), https://khn.org/news/tracking-who-makes-money-on-a-brand-namedrug/; *see also* WELLPOINT, INC. & EXPRESS SCRIPTS, INC., PHARMACY BENEFIT MGMT. SERVICES AGREEMENT (EX-10.30) (Dec. 1, 2009) (specifying that the AWP refers to the average wholesale price of a prescription drug "as established and reported by the Pricing Source" and that a drug's applied AWP will be the AWP for the actual 11-digit National Drug Code).

[57] Patient Protection and Affordable Care Act., Pub. L. No. 111–148, 124 Stat. 119 (2010).

[58] NAS REPORT at 98.

plans often require patients to contribute a percentage of a drug's list price, especially for more expensive drugs.[59] Studies have observed dramatic reductions in coverage and increased cost-sharing burdens for higher-priced drugs over time.[60]

List prices, however, are only the beginning of the story. Drug companies and PBMs agree to contracts, ensuring rebates to discount the list price. Rebates are a closely guarded secret, so it is difficult to tease out the actual net price that different parties pay along the drug supply chain.[61] Nevertheless, the net price paid to the drug company is substantially less than the initial list price.[62] PBMs are uniquely situated, with the bargaining power, drug information, and data to negotiate the most aggressive price concessions from drug companies. Unfortunately, PBM behavior has been distorted by reimbursement schemes that reward them most significantly when drug prices and drug spending increases. The problem starts with a payment structure that, though seemingly procompetitive, minimizes the pressure to reduce prices.[63] Here is how it works: health plans pay their PBMs based on the size of the discount that a PBM can negotiate with each drug company.[64] In other words, the greater the distance between the list price and the net price, the more money a PBM earns.[65]

In theory, since PBM earnings are directly tied to rebate amounts, this structure might encourage PBMs to drive prices down.[66] In reality, these incentives operate to drive prices

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[59] MEDICARE PAYMENT ADVISORY COMM'N, REPORT TO THE CONGRESS: MEDICARE PAYMENT POLICY 408–09 (2017) [hereinafter MEDPAC 2017 REPORT]

[60] NAS Report at 98.; Jalpa Doshi et al., Specialty Tier-Level Cost Sharing & Bio. Agent Use in the Medicare Part D Initial Coverage Period among Beneficiaries with Rheumatoid Arthritis, 68 ARTHRITIS CARE & RES. 1623 (2016); Jeah K. Jung et al., Coverage for Hepatitis C Drugs in Medicare Part D, 22 AM. J. OF MANAGED CARE 220 (2016); Jennifer M. Polinski, Penny E. Mohr & Lorraine Johnson, Impact of Medicare Part D on Access to and Cost Sharing for Specialty Biologic Medications for Beneficiaries with Rheumatoid Arthritis, 61 ARTHRITIS CARE & RES. 745 (2009); Jinoos Yazdany et al., Coverage for High-Cost Specialty Drugs for Rheumatoid Arthritis in Medicare Part D, 67 ARTHRITIS & RHEUMATOLOGY 1474 (2015).

[61] Dylan Scott, *Inside the Impossibly Byzantine World of Prescription Drug Prices*, STAT (Dec. 21, 2015), www.statnews.com/2015/12/21/prescription-drug-prices-confusion/ (describing secretive discount and rebate systems, and explaining that the list price is the company's opening bid; quoting acting administrator of the federal Centers for Medicare and Medicaid Services as saying that "we have list prices, wholesale prices, average wholesale prices, rebates, supplemental rebates, mark-ups . . . Most of that information is not available of well understood by the public," and University of Pittsburgh Professor Walid Gellad as referring to pricing as a black hole and noting that "[i]t's impossible to understand what people are paying").

[62] Industry reports indicate that the gap between prices and rebate prices has increased in recent years. *See* Adam J. Fein, *Payor Power: Why Eli Lilly, Janssen, and Merck Deeply Discount Their Drug Prices*, DRUG CHANNELS (Apr. 5, 2018), www.drugchannels.net/2018/04/payer-power-why-eli-lillyjanssen-and.html (publicly reported earnings note that, comparing 2016 to 2017, Janssen's average discount rose from 32 percent off list to 42 percent off list, Merck's rose from 41 percent to 45 percent off list, and Lilly's grew only marginally, from 50 percent to 51 percent off list).

[63] *See* Express Scripts Holding Co., Form 10-K, *Annual Report* 4-5, 18-19 (Dec. 31, 2017)

[64] Some forms are modeled as price protections; others, as anticipated rebate amounts.

[65] *See* Mark Meador, *Squeezing the Middleman: Ending Underhanded Dealing in the Pharmaceutical Benefit Management Industry through Regulation*, 20 ANNALS OF HEALTH LAW 77, 82 (2011) (noting that PBMs take advantage of the price range in various price lists for generic drugs, negotiating with manufacturers for a lower price and setting reimbursement rates with plan sponsors using a higher list price, to maximize the spread); *cf*. Fiona Scott Morton & Lysle T. Boller, *Enabling Competition in the Pharmaceutical Markets*, WORKING PAPER 30, HUTCHINS CTR. ON FISCAL & MONETARY POL'Y AT BROOKINGS 3 (May 2017), www.brookings.edu/wp-content/uploads/2017/05/wp30_scottmorton_competitioninpharma1.pdf (noting that PBMs may use rebates to grow profits by keeping a share of the high prices paid by insurers for costly medication).

[66] *See id.* Morton & Boller at 21–22 (noting that contracts between plan sponsors and the PBM are often based on list price without rebates, in part because this incentivizes the PBM to bargain for larger rebates). Accounting

higher. Quite simply, the drug company raises prices so that the PBM can demonstrate a greater "spread" between the original price and the post-rebate price. The technique is like a store raising the price on a suit before a sale so that the final price looks like a great bargain. The insulin market is no exception to this practice. According to one private firm, PBMs have likely profited billions of dollars annually by exploiting insulin price increases and the heavy concentration of the insulin market.[67]

In addition, rebate amounts can be crafted as volume discounts, creating more power for companies that already hold a large market position and making it difficult for new entrants to gain much of a foothold in the market.[68] It would be like a major beer company offering all bar owners in Denver the following deal: "I will pay you 50 cents for every bottle of my beer that you sell next year. Better yet, I will make it $1 a bottle if you don't put any of that craft beer on the menu." If the craft beer company starts out by selling a limited number of bottles, it could never offer enough off the price of its few beers to compensate for the millions of dollars in rebates that the bar owner would have to forgo by turning down the major company's offer.[69]

In the same vein, a pharmaceutical company whose protections have just expired could easily command most or all of the volume in the market, depending on whether substitutes exist. The volume power of protected drugs blocks new, lower-cost entrants from adequate placement on health plan formularies, thus limiting who may participate in the market.

Such perverse pricing incentives are exacerbated by the PBM industry's remarkable consolidation. Three PBMs – Express Scripts, CVS Health, and OptumRX – dominate 85 percent of the commercial insurance market.[70] Beyond the private market, the three major PBMs also reportedly handled 50 percent of the prescription drug benefits for the Medicaid managed-care population in 2015.[71]

This market structure, with all its perverse incentives, has real-world pricing implications. Our prior research has demonstrated that list prices are growing faster than rebates. Studying Medicare claims of roughly one million patients from 2005-2017, we found that the average

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methods for PBMs are also problematic: PBMs report their revenue based on the total value of drugs flowing through their contracts and their income as a percentage of that total revenue. Thus their earnings per share (EPS) stock valuations increase as the total revenue increases – a figure that is, in part, a function of prices.

[67] Duane Schulthess, *Insulin Prices and Pharmacy Benefit manager rebates: pin the tail on the patient*, STAT+ (19 March 2020), https://www.statnews.com/2020/03/19/insulin-prices-pbm-rebates/

[68] In economic terms, this could be characterized as a form of "raising rivals' costs." *See* Thomas G. Krattenmaker & Steven C. Salop, *Anticompetitive Exclusion: Raising Rivals' Costs To Achieve Power over Price*, 96 YALE L.J. 209 (1986); *See also* Robin Feldman, *Defensive Leveraging in Antitrust*, 87 GEO. L.J. 2079 (1999) (for an explanation of raising rivals' costs in the pharmaceutical context).

[69] For additional discussion of the beer example and the implications of volume rebating in the pharmaceutical industry, see ROBIN FELDMAN, DRUGS, MONEY, AND SECRET HANDSHAKES: THE UNSTOPPABLE GROWTH OF PRESCRIPTION DRUG PRICES (2019) at 22.

[70] *See* Neeraj Sood, *Understanding Competition in Prescription Drug Markets: Entry and Supply Chain Dynamics*, FED. TRADE COMM'N WORKSHOP SLIDES 101 (2017), www.ftc.gov/news-events/events-calendar/2017/11/understanding-competition-prescription-drug-markets-entry-supply; *see also* Murray Aitken, *Medicines Use and Spending in the U.S.: A Review of 2016 and Outlook to 2021*, Quintiles IMS Inst. 2 (2017), www.iqvia.com/institute/reports/medicines-use-and-spending-inthe-us-a-review-of-2016.

[71] Jon Roberts, CVS/Caremark Executive Vice President & President, Gaining Lives with Our Unique PBM Capabilities 27 (2014), http://investors.cvscaremark.com/~/media/Files/C/CVS-IR-v3/documents/16-12-2014/jonroberts-
presentation.pdf.

dosage unit cost of branded drugs *after* rebates increased from $38 to $157.[72] This represents an increase of almost 313%.

Furthermore, we have found strong evidence of widespread abuses in the tiering system. We followed over 1 million Medicare patients between 2010 and 2015, utilizing claims and tiering data from the Centers for Medicare and Medicaid Services.[73] The results show that while generics are the most cost-effective drugs in many healthcare systems, they are increasingly disadvantaged in formularies. Between 2010 and 2015, the percentage of generics on the most preferred tier nationwide fell from 73% to 31%. The percentage of generics on all other tiers increased. Thus, an increasing share of generics has been shifted to more expensive—and therefore less accessible—tiers. This is true despite the fact that generic drugs are vastly cheaper than brand drugs, even accounting for rebates. Finally, we found substantial evidence of irrational tiering, in which brand drugs (which are more expensive) were placed on the same or even a better tier than a generic with the same active ingredient.[74]

In the short run, improper tiering can force patients to use costlier drugs, increasing out-of-pocket payments and overcharging government programs that subsidize health care. In the long run, this behavior can reduce competition in the pharmaceutical market by raising a cheaper competitor's costs, driving the competitor out of business, or deterring the competitor from entrance in the first place. In both cases, irrational tiering burdens society.

In the context of irrational tiering, the insulin market is unusual in that it is composed of a few manufacturers operating without limited competition from generics or biosimilars. Since irrational tiering describes the tier placement of brand drugs relative to their generic or biosimilar equivalent, the concept does not apply to insulin drugs. Nevertheless, irrational tiering may come to light as more generic and biosimilar insulin products, such as Semglee, emerge on the market.

Our quantitative findings, tabled below, reaffirm the absence of irrational tiering: formularies in Colorado place the vast majority of their insulins together on Tier 3. As a result, we found that the vast majority of Colorado patients obtained their insulin from the third tier of five-part Part D formularies. This tier placement is largely consistent with formularies in all other states nationwide, as the charts below illustrate.

[72] Robin Feldman, *The Devil Is in the Tiers*, UC HASTINGS RESEARCH PAPER NO. 380, Fig. 1, text accompanying notes 110-111 (NOV. 2019). Available at SSRN: https://ssrn.com/abstract=3490065

[73] Robin Feldman, *The Devil Is in the Tiers*, UC HASTINGS RESEARCH PAPER NO. 380 (NOV. 2019). Available at SSRN: https://ssrn.com/abstract=3490065

[74] *Id.* at 28-44

Figure 5. Insulin Placement Percentage by Tier on Part D Five-Tier Formularies

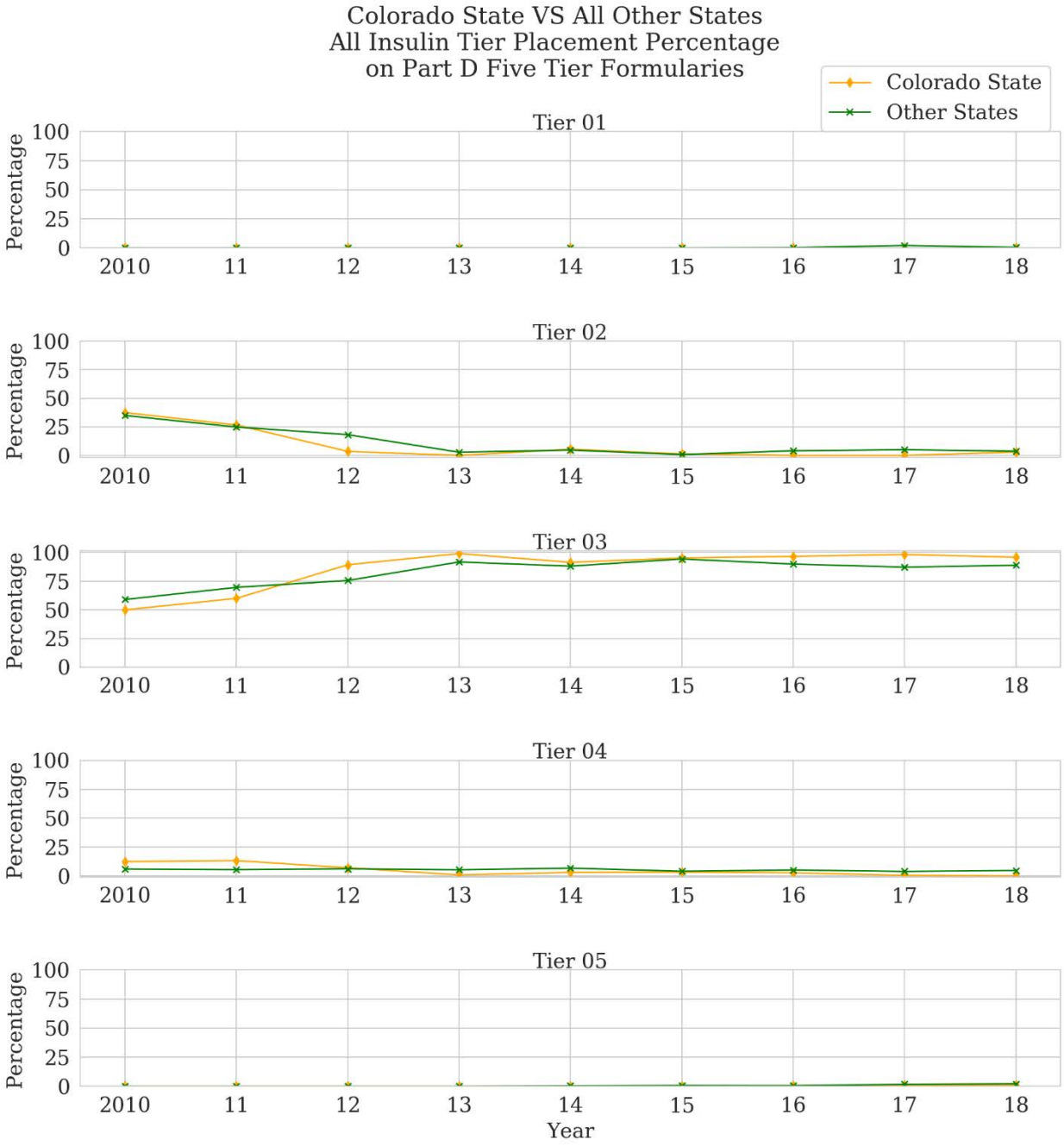

Table 9. Colorado State – All Insulin – Formulary Tier Placement Percentages

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	37.5	50	12.5	0
2011	0	26.67	60	13.33	0
2012	0	3.57	89.29	7.14	0
2013	0	0	99.06	0.94	0
2014	0	5.47	91.41	3.13	0
2015	0	1.35	95.27	3.38	0
2016	0	0	96.63	2.81	0.56
2017	0	0	98.27	0.58	1.16
2018	0	2.96	95.86	0	1.18

Note: Zero values indicate no data were found for insulin options on that tier.

Table 10. All Other States – All Insulin – Formulary Tier Placement Percentages

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	35	59	6	0
2011	0	24.88	69.59	5.53	0
2012	0	18.2	75.58	6.22	0
2013	0	2.85	91.74	5.41	0
2014	0	4.73	88.12	6.79	0.36
2015	0	0.79	94.35	4.18	0.68
2016	0.24	4.11	89.89	5.21	0.55
2017	2.04	5	87.24	4.01	1.71
2018	0.48	3.77	88.86	4.79	2.1

Note: Zero values indicate no data were found for insulin options on that tier.

Figure 6. Insulin Utilization Percentage by Tier on Part D Five-Tier Formularies

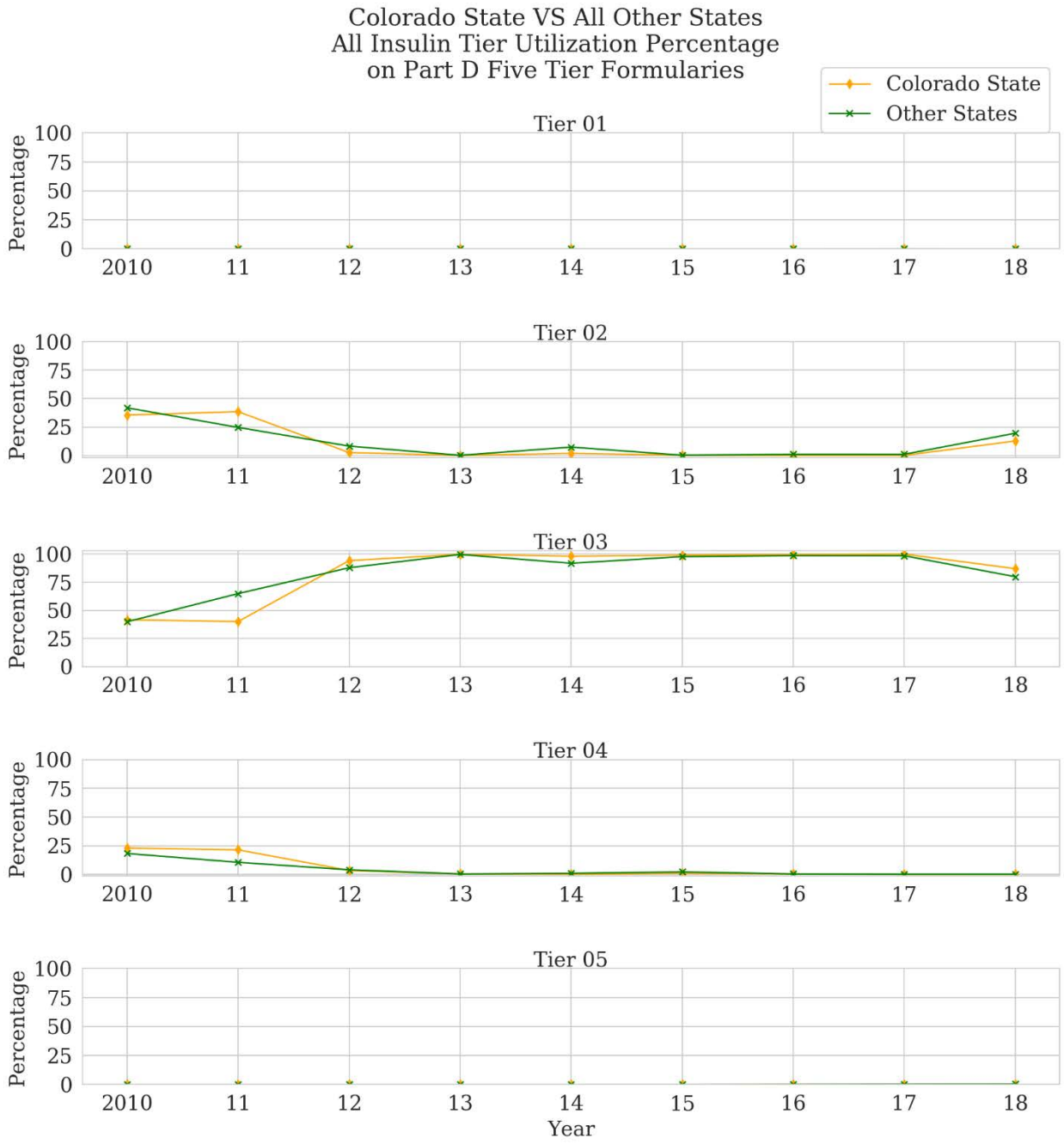

Table 11. Colorado State – All Insulin – Formulary Tier Utilization Percentages

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	35.51	41.59	22.9	0
2011	0	38.5	40.11	21.39	0
2012	0	2.54	94.07	3.39	0
2013	0	0	99.66	0.34	0
2014	0	1.82	98.03	0.15	0
2015	0	0.21	98.88	0.91	0
2016	0	0	99.49	0.41	0.11
2017	0	0	99.89	0.02	0.09
2018	0	12.74	86.94	0	0.32

Note: Zero values indicate no data were found for insulin options on that tier.

Table 12. All Other States – All Insulin – Formulary Tier Utilization Percentages

Year	Tier 01	Tier 02	Tier 03	Tier 04	Tier 05
2010	0	41.9	39.88	18.21	0
2011	0	24.67	64.84	10.5	0
2012	0	8.23	87.8	3.97	0
2013	0	0.11	99.54	0.35	0
2014	0	7.36	91.74	0.89	0.01
2015	0	0.19	97.61	2.17	0.03
2016	0	1.01	98.48	0.34	0.18
2017	0.04	1	98.41	0.21	0.35
2018	0.01	19.54	79.81	0.2	0.45

Although most Colorado health plans place insulins on Tier 3 of their formularies, competition in the insulin market remains limited. For a start, diabetics are limited to brand insulins, which tend to raise prices in lockstep. Even if a patient might prefer a slightly less expensive, less state-of-the-art insulin formulation or delivery system, few such products are available. Moreover, these generic or biosimilar insulin products may be unlikely to gain traction in a market dominated by practices of evergreening and product hopping.

Even with most insulins covered on the third tier, patient choice may still be stymied. Plans may choose to cover a select few insulin brands on Tier 3 and exclude all other options. In this case, despite the appearance of equivalent tiering, patient choice would still be limited.

We found evidence of product exclusion in Colorado Medicare claims. While there are three main insulin manufacturers, and Tier 3 contained a vast majority of all insulin drugs, our data showed an average of fewer than three insulin products on Tier 3 of Colorado plans. In other words, someone was left out, although that party may have varied by health plan.[75] We noticed that the majority of Novo Nordisk insulin drugs appeared on Tier 3 of plans, while the majority of Eli Lilly's appeared on Tiers 3 and 5. The majority of Sanofi Aventis insulin drugs appeared on Tier 3, with a relatively small percentage on Tier 4. One could hypothesize that these irregularities may be the product of formulary tiering negotiations, whose rebates serve to drive prices higher.

V. Conclusion

The pain wrought by rising insulin prices stems from misaligned, anticompetitive market incentives. Drug companies and PBMs alike benefit from rising drug prices. Concentration in both markets, combined with tactics like evergreening, product hopping, and volume rebates ensure that no meaningful, cost-reducing competition can get a seat at the table. In the words of one patient quoted in a class action complaint, "[f]inancially, it's killing me…"[76] For other patients, the consequences have been even more tragic. [77]

[75] We noticed that the inhaled insulin drug, Afrezza—which failed to gain popular acceptance—had different tier placement percentages in Colorado that the other states combined. Afrezza appeared only on Tier 4 in Colorado while appearing on Tiers 3, 4, and 5 in other states.

[76] *Chaires et al v. Sanofi, U.S. et al*, 1:2017cv10158 (D. Mass. 2017), https://static01.nyt.com/science/01-30-17_Insulin_Class_Action_Complaint_Hagens_Berman.PDF

[77] Shefali Luthra, *Is Insulin's High Cost Keeping Diabetes Patients From Taking their Medicine?*, KAISER HEALTH NEWS (2019), HTTPS://KHN.ORG/NEWS/IS-INSULINS-HIGH-COST-KEEPING-DIABETES-PATIENTS-FROM-TAKING-THEIR-MEDICINE/


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