2021

DRUG TRENDS & STRATEGIC INSIGHTS

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Introduction

2021 DRUG TRENDS & STRATEGIC INSIGHTS

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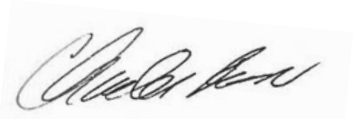
Foreword

Welcome to the second annual HBM+ Drug Trends and Strategic Insights report. Much has happened in the last year since we published our inaugural report – the successive waves of the COVID-19 pandemic have continued to cause challenges for Canadians and our health care system. As we prepared this report, the successful rollout of vaccines stirred optimism that the pandemic may be nearing its end, yet the emergence of new variants calls into question that timeline.

In this year's report*, we provide updates on trends we are seeing with drug claims, particularly relating to specialty drugs, biologics, and biosimilars, as well as the impact of new, costlier chronic disease therapies. We also take a closer look at how the pandemic has fundamentally changed health care delivery. In particular, the use of virtual health care services has exploded in the last year. This trend is impacting how Canadians access their medications with the rise of digital pharmacies as an exciting and convenient new alternative.

Mindful of the rapid pace of innovation and the resulting cost challenges this is presenting to Canadian payors and plan sponsors, we have taken a close look at the pipeline of new drug therapies likely to have a significant impact on benefit plans in 2021 and onwards. In particular, we zero in on gene therapies, as well as a new treatment for Alzheimer's disease that has reinvigorated questions around assessing the value of a drug treatment from the vantage points of both patients and payors. Finally, recognizing the tremendously negative impact the pandemic has had on Canadians' mental health, we examine this important area through the lens of our drug data, but also beyond that into extended health data and how they intertwine.

Through all the changes and challenges, at HBM+ we continue to remain steadfastly focused on serving our partners and their plan members in achieving sustainable health care solutions now and into the future.



Charles Rosen, Senior Vice President and Managing Director, HBM+

Steve Laberge, Vice President-Quebec and Strategic Solutions, HBM+

*Data for this analysis was conducted by IQVIA based on claims reported by HBM+.

Terminology

Term	Definition
Biologic drug	A drug product that is produced from living organisms.
Biosimilar	A biologic drug that is highly similar to another biologic drug known as the "originator biologic." Biosimilars are produced after patent expiry of the originator biologic.
Cardiovascular health coaching	Service provided by pharmacists that focuses on cardiovascular health and offers blood pressure and cholesterol management to eligible plan members. Its main objective is to empower patients diagnosed with hypertension and elevated cholesterol to take ownership and responsibility for their overall cardiovascular health.
Claimant	Any covered individual who has submitted at least one claim.
Gene therapy	A treatment method that involves modifying a patient's genes to treat a disease.
Generic penetration rate	Proportion of claims that were filled for generic drugs.
Maintenance drugs	Medications used to treat chronic and ongoing conditions on a regular basis. For example, drugs used to treat hypertension, asthma, or diabetes.
Non-specialty drug	Refers to drug products that cost less than $10,000 per claimant. The cost is solely determined by its annual average claimant cost without dispensing fees.

Term	Definition
Originator biologic	Biologic drug that is first to market. Sometimes referred to as "reference biologic" or "innovator biologic."
Preferred pharmacy networks	Group of pharmacies that provide plan members with reduced drug claim costs when they fill their prescriptions at a participating pharmacy.
Product listing agreement (PLA)	Negotiated agreement between a drug plan and a pharmaceutical manufacturer to list a drug on a formulary at a confidentially discounted price.
Proportion of days covered (PDC)	Method used to calculate medication adherence by analyzing drug claims data. A patient is defined as being highly adherent if their adherence based on PDC is greater than 80 per cent.
Specialty drug	Refers to drug products that cost $10,000 or more per claimant. The cost is solely determined by its annual average claimant cost without dispensing fees.
Total drug cost	Amount paid by the plan and patient. Includes drug costs, markups, and dispensing fees.
Value-based Pharmacy	Pharmacy provider initiative with the goal of increasing quality of care through measuring pharmacy performance, providing feedback to facilitate improvement, and aligning reimbursement with the delivery of high-quality care to plan members.

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Drug Utilization Trends

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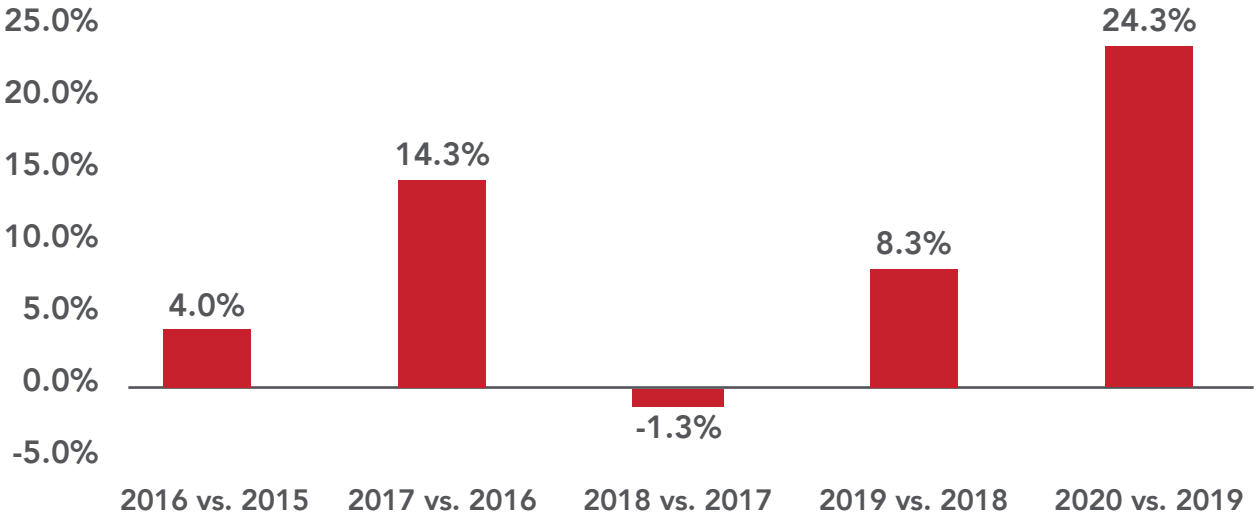
Overall Trends

Since 2016, the total drug costs adjudicated by HBM+ have risen from about $1.3 billion to over $1.9 billion in 2020. At the same time, the number of claimants has increased from 1.7 million to over 2.1 million. As outlined in Figure 2.1, there was a 24.3 per cent growth in total adjudicated drug cost between 2019 and 2020. A large proportion of this increase is attributable to the addition of a new Quebec-based partner as of January 1, 2020.

FIGURE 2.1 | Year-over-year growth in total adjudicated drug cost, 2016 to 2020



The number of overall drug claims adjudicated by HBM+ approached 30 million in 2020. While there was a steady increase in drug cost per claim from 2016 to 2019, the average cost per claim actually declined by 2.6 per cent in 2020. This is due to the overall increase in claims with a shorter days' supply, which was affected by two factors – the increase in the share of claims from the province of Quebec (due to the addition of a new partner) and the temporary COVID-19-related relaxation of minimum days' supply policies.* While some provincial drug plans require a minimum days' supply

* "Provincial changes in provision of services and dispensing practices related to COVID-19," Canadian Foundation for Pharmacy, https://cfpnet.ca/bank/document_en/149-cfp-covid-19-chart-july-27-2020.pdf.

quantity for specific medications, chronic medications in Quebec are routinely filled for 30 days to align with the public plan's monthly patient contributions, which is a shorter days' supply on average compared to the rest of Canada. Looking at non-Quebec-based claims, there was a 0.6 per cent increase in drug cost per claim in the rest of the country.

TABLE 2.1 | Total drug cost, claims, claimants, and total drug cost per claim, 2016 to 2020

Metric	2016	2017	2018	2019	2020
Total Drug Cost	$1,267M	$1,448M	$1,429M	$1,548M	$1,923M
Claims	20.4M	22.7M	22.3M	23.5M	29.9M
Claimants	1.7M	1.9M	1.8M	2.0M	2.1M
Total Drug Cost per Claim	$62.0	$63.7	$64.2	$66.0	$64.3

Cost Concentration

As evident in previous years, a relatively small portion of claimants is responsible for a disproportionately large share of overall expenditures. In 2020, just under 54 per cent of the total adjudicated HBM+ drug cost was associated with the top five per cent of claimants and about 32 per cent was associated with the top one per cent of claimants. And that cost concentration appears to be intensifying – the share of cost for the top five per cent of HBM+ claimants made up an increasing share of total drug cost over the years, from 50.6 per cent in 2016 to 53.8 per cent in 2020.

In 2020, the top five per cent most expensive claimants cost 21 times more on average, compared to the remaining 95 per cent of the claimant population ($10,020 versus $454). These high-cost claimants had six times more claims (78 claims versus 11) at an average cost per claim that was more than double that of the rest of the claimant population ($128 versus $41).

TABLE 2.2 | Total drug cost distribution by claimant group, 2020

Claimant Group	2016 Share of Total Drug Cost	2020 Share of Total Drug Cost	2020 Average Claims per Claimant	2020 Average Cost per Claim	2020 Average Annual Cost per Claimant
Top 1%	29.3%	32.1%	78	$385	$29,913
Top 5% (Includes Top 1%)	50.6%	53.8%	78	$128	$10,020
All Other 95%	49.4%	46.2%	11	$41	$454

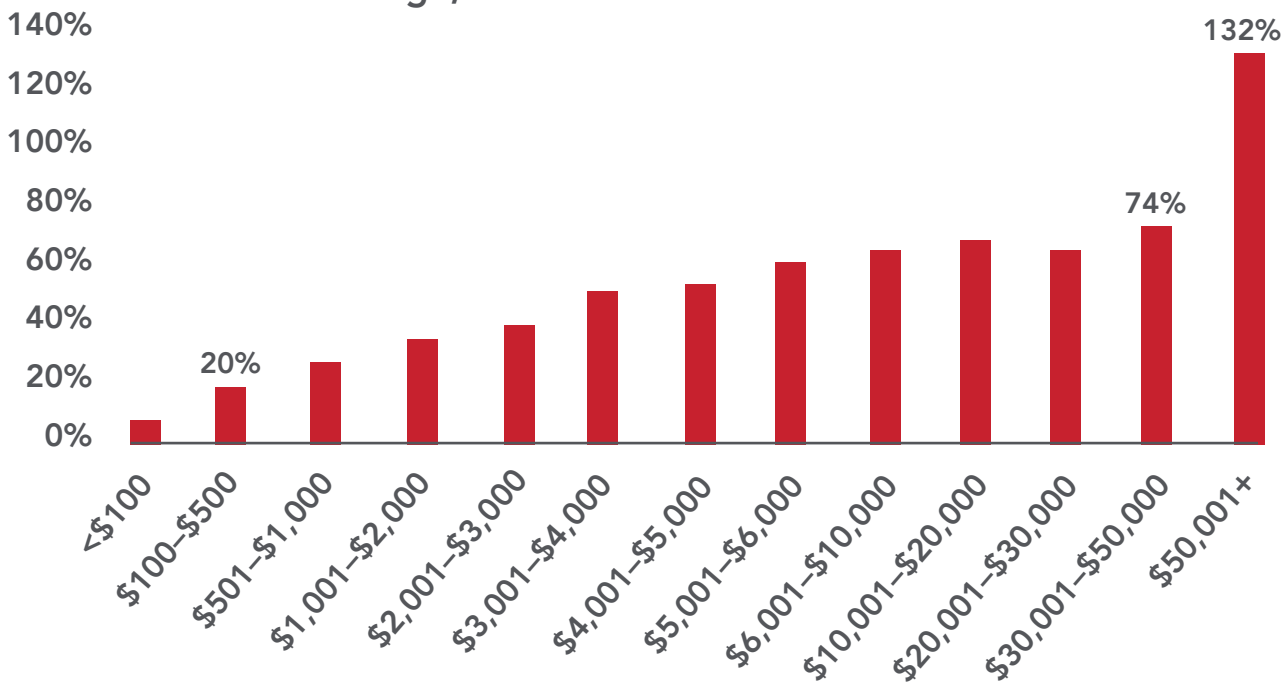
The high-cost claimants not only made up most of the total drug cost, but a large percentage of them also stayed a high-cost claimant for three or more consecutive years. About 48 per cent of the top five per cent of claimants from 2018 were also ranked in the top five per cent in both 2019 and 2020. This relatively high persistence of high-cost claimants warrants not only the consideration of strategies to ensure both appropriateness of continued usage of high-cost drugs, but also patient support through strategies such as more comprehensive case management.

TABLE 2.3 | Proportion of high-cost claimants that remain in the same group for three consecutive years

Claimant Group	2016-2018	2017-2019	2018-2020
Top 1%	46.3%	48.2%	49.0%
Top 5% (Includes Top 1%)	44.5%	46.4%	47.9%

The importance of effective high-cost claimant management is underscored by the fact that the most expensive sub-group ($50,000+ per year) is growing the fastest (132 per cent between 2016 and 2020). Indeed, as indicated in Figure 2.2, there is a near-linear relationship between the rate of growth of a particular sub-group of claimants and their annual treatment cost with more expensive claimants growing faster.

FIGURE 2.2 | Change in the number of claimants by annual treatment cost range, 2016 vs. 2020



Delving a bit deeper into the characteristics of the high-cost claimants, patients suffering from rheumatoid arthritis (RA), Crohn's disease, colitis, and psoriasis represented the largest share of total drug cost in both the top one per cent and top five per cent high-cost claimant groups (Table 2.4). While the claimants in the top one per cent typically required specialty medications to manage their conditions, the top five per cent high-cost claimants, in contrast, suffered from more common chronic diseases, such as diabetes, asthma, anxiety and depression, and high cholesterol.

The top five per cent high-cost claimants suffered from more common chronic diseases, such as diabetes, asthma, anxiety and depression, and high cholesterol.

Diabetes in particular had a different dynamic in the two categories; it represented the second-largest share of drug costs in the top five per cent claimant group, compared to the 10th largest share in the top one per cent group. This was owing to the high prevalence of the disease, paired with an escalating cost of treatment per patient driven by utilization of newer antidiabetic agents. In the top one per cent category, 2020 was the first year that saw the emergence of a skin condition in the top one per cent claimant category, primarily driven by the rapidly growing utilization of Dupixent – a biologic drug for the treatment of eczema, as well as other conditions.

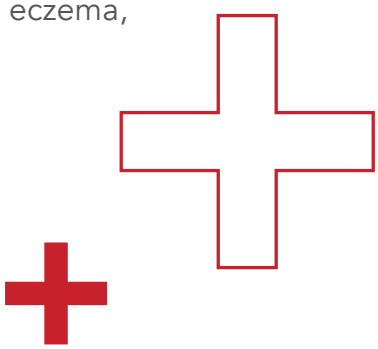


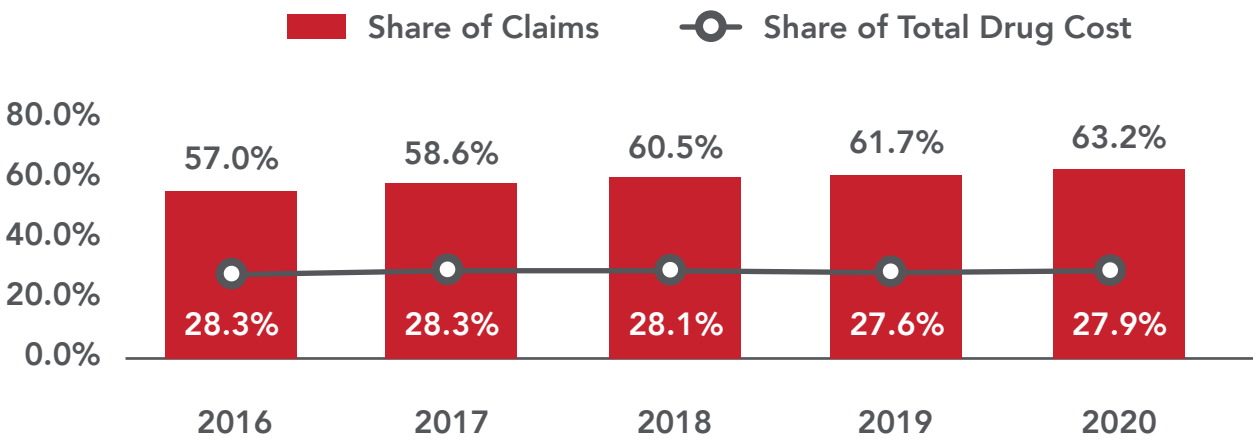
TABLE 2.4 | Top 10 disease states by share of total drug cost for top one per cent and top five per cent of high-cost claimants

Top 1%			Top 5%		
Rank	Disease State	Share of Total Drug Cost	Rank	Disease State	Share of Total Drug Cost
1	RA/Crohn's/ Colitis/Psoriasis	44.4%	1	RA/Crohn's/Colitis/ Psoriasis	29.0%
2	Cancer	13.0%	2	Diabetes	9.0%
3	Multiple Sclerosis	7.7%	3	Cancer	8.9%
4	Asthma and COPD	4.4%	4	Multiple Sclerosis	5.1%
5	HIV	3.1%	5	Asthma and COPD	4.6%
6	Cystic Fibrosis	2.8%	6	Anxiety/Depression	2.5%
7	Skin Irritations/ Conditions	2.0%	7	HIV	2.3%
8	Paroxysmal nocturnal haemoglobinuria (PNH)	1.9%	8	Pain	2.0%
9	Macular Degeneration	1.7%	9	ADHD	2.0%
10	Diabetes	1.4%	10	Elevated Cholesterol	1.9%

Generic Utilization

Increasing the utilization of generic drugs continues to be an important element of cost management in private drug plans, and mandatory generic policies are an essential vehicle to achieving those savings. Generic products continued to make up a greater share of claims within HBM+, accounting for 63 per cent of all claims in 2020 up from 61.7 per cent in 2019 (Figure 2.3). While this growth in generic penetration is encouraging, there is room for upwards growth. For reference, public plans in Canada have achieved generic penetration rates of 71 per cent, and in the United States, generic penetration has reached over 80 per cent.*

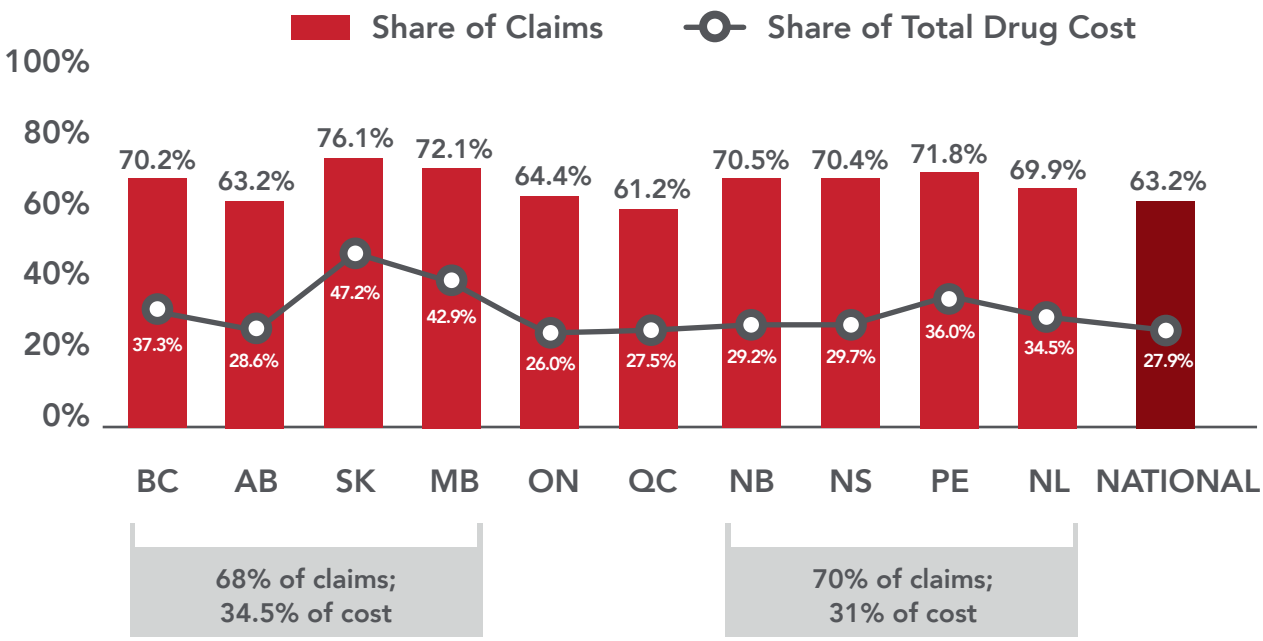
FIGURE 2.3 | Generic share of claims and total drug cost, 2016 to 2020



At the provincial level, the Atlantic provinces had the highest generic penetration rate at close to 70 per cent, followed by the western provinces at 68 per cent on average, with Alberta as a bit of an outlier. The two most populous provinces, Ontario and Quebec, had some of the lowest generic-fill rates at 64.4 per cent and 61.2 per cent, respectively.

* "CompassRx", 6th Edition 2018-2019, and "Generics360" report, 2018 edition; NPDUIS (National Prescription Drug Utilization Information System) Analytical Studies; Patented Medicine Prices Review Board; Government of Canada website; http://www.pmprb-cepmb.gc.ca/en/npduis/analytical-studies.

FIGURE 2.4 | Generic share of claims and costs by province, 2020



Top 10 Therapeutic Classes*

Despite only 5.5 per cent of claimants submitting claims for rheumatoid arthritis (RA)/Crohn's/colitis/psoriasis in 2020, these inflammatory conditions made up the largest share of total drug cost, accounting for over 16 per cent (Table 2.5). Diabetes continues to grow not only in prevalence at 6.4 per cent but also in overall share of costs (7.4 per cent in 2020 compared to 5.9 per cent in 2016). The most prevalent condition continues to be infection, but there was a sizeable drop in the proportion of patients claiming for this condition in 2020 (37.8 per cent) compared to 2016 (48.3 per cent). This is in large part due to measures introduced to manage COVID-19, including masking and disinfection as well as stay-at-home orders.

* Note that the disease states are determined using the primary indication of an individual drug. The prevalence rates are calculated as a share of the total number of HBM+ claimants who claimed drugs associated with a specific disease state.

The sizeable drop in the rate of infections is also supported by data showing the near non-existence of influenza infections during the 2020 flu season.* Anxiety and depression show a pronounced increase in prevalence rising to almost 21 per cent of all claimants, which is an increase of 2.7 per cent from 2016. The dynamics and impacts of COVID-19 are also evident in this disease category and will be explored in greater detail in section 5 of this report.

TABLE 2.5 | Top therapeutic classes by share of prevalence and total drug cost

Disease State	2020		2016	
	Prevalence Rate	Share of Total Drug Cost	Prevalence Rate	Share of Total Drug Cost
RA/Crohn's/Colitis/Psoriasis	5.5%	16.4%	5.3%	13.4%
Diabetes	6.4%	7.4%	5.1%	5.9%
Anxiety/Depression	20.8%	5.9%	18.1%	6.7%
Asthma and COPD	14.2%	5.8%	15.1%	5.6%
Cancer	1.6%	5.1%	1.2%	3.5%
ADHD	5.2%	4.6%	3.9%	4.3%
Hypertension	18.5%	4.4%	14.9%	5.4%
Acid Related Gastrointestinal Conditions	16.4%	3.2%	14.2%	3.9%
Infection	37.8%	2.9%	48.3%	4.7%
Elevated Cholesterol	13.3%	2.8%	10.5%	3.3%

* "FluWatch annual report: 2019-2020," Government of Canada website, https://www.canada.ca/en/public-health/services/publications/diseases-conditions/fluwatch/2019-2020/annual-report.html; and "Flu cases hit record lows during pandemic: researcher," Global News, https://globalnews.ca/news/7696427/influenza-low-case-numbers-pandemic/.

3 Specialty Drugs

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Overall Trends

In 2020, there were over 23,000 claimants that used a specialty drug to treat their medical conditions. These specialty drug products were associated with $554 million in total drug costs (Table 3.1). Specialty drug costs grew by 37 per cent from 2019 to 2020. It is important to note that this relatively large growth in total adjudicated specialty-drug costs is a reflection of both an increase in utilization as well as the addition of a large Quebec-based partner as of January 1, 2020.

TABLE 3.1 | Specialty drugs total cost, number of claims, and number of claimants, 2016 to 2020

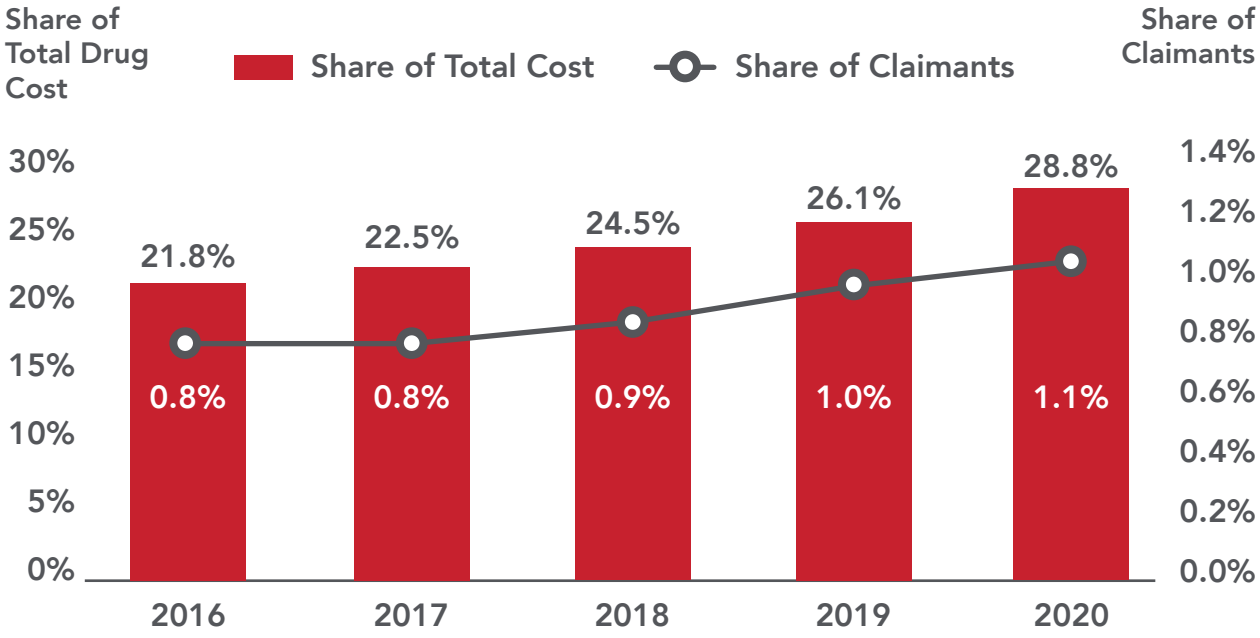
Period	Total Drug Cost		Claims		Claimants	
	Amount	YOY Growth	Number	YOY Growth	Number	YOY Growth
2016	$276.1M	7.5%	99.1K	9.7%	13.0K	3.0%
2017	$326.3M	18.2%	115.9K	17.0%	15.5K	19.4%
2018	$349.8M	7.2%	123.6K	6.6%	16.9K	8.8%
2019	$404.3M	15.6%	138.6K	12.1%	19.2K	14.0%
2020	$553.8M	37.0%	183.8K	32.6%	23.2K	20.6%

Cost and Utilization

The proportion of overall drug spending owing to specialty drugs rose from just over 26 per cent in 2019 to 28.8 per cent in 2020. As in previous years, a very small proportion (1.1 per cent) of claimants was responsible for a large share of overall costs. As evident in Figure 3.1, the contribution of specialty drugs to overall spending has steadily climbed since 2016, and it is not expected to slow down in the near future. The pharmaceutical industry pipeline continues to be dominated by specialty drugs, including biologics and gene therapies.

In a 2020 report by the Patented Medicines Price Review Board (PMPRB), 16 late-stage new medicines, including five gene therapies, were identified based on their potential to significantly impact the Canadian health care system. Additionally, four new medicines currently under review by Health Canada were forecasted to reach global revenues over US$1 billion annually by 2026.* In the United States, specialty drugs are expected to exceed 50 per cent of total prescription drug spending in 2021.** While Canada has not reached this level yet, the current growth rates do put us on a pathway towards it within the next five years. Given these trends, continued vigilance and effective cost and health management strategies are essential in ensuring the sustainability of drug plans – public and private.

FIGURE 3.1 | Specialty drugs share of total drug cost and share of claimants, 2016 to 2020



* "Meds Pipeline Monitor, 2020"; NPDUIS (National Prescription Drug Utilization Information System) Analytical Studies; Patented Medicine Prices Review Board; Government of Canada website; http://www.pmprb-cepmb.gc.ca/en/npduis/analytical-studies.

** Eric M Tichy, et al., "National trends in prescription drug expenditures and projections for 2021;" Am J Health Syst Pharm. 2021; 78(14): 1294-1308. doi: 10.1093/ajhp/zxab160; https://pubmed.ncbi.nlm.nih.gov/33880494/.

Understanding these dynamics, HBM+ has developed an essential toolkit of high-cost drug management strategies necessary to manage this category (Table 3.2). Each of these strategies has been demonstrated to reliably and consistently manage spending while ensuring patients have access to effective drug therapies.

TABLE 3.2 | HBM+ High-cost drug management toolkit

Strategy		Key Components
Product Listing Agreements (PLAs)		Negotiated agreement between a drug plan and a pharmaceutical manufacturer to list a drug on a formulary at a confidentially discounted price.
Specialty Drug Preferred Pharmacy Network (PPN)*		Group of pharmacies that provides plan members with reduced drug claim costs (pharmacy markup or upcharge) when they fill their prescriptions at a participating pharmacy. PPNs are structured to not only reduce the standard pharmacy markup for these claims but also bundle additional value-added services, such as adherence support. When combined, these programs can control claim costs and ensure patients are appropriately using these high-cost therapies.
Disease Case Management		A value-added service that coordinates patient-specific medical needs over the lifespan of their illness. These services may vary depending on the individual and specific illness but are designed to complement the patient's current health care team and journey.
Biosimilar Strategies	**Biosimilar New Start Program**	This program lists biosimilars as preferred products for all patients newly starting biologic therapy. Originator products are only permitted in exceptional circumstances.
	Biosimilar Transition Program	This program supports plan members being treated with an impacted originator biologic drug as they transition to the corresponding biosimilar product.

* Does not apply in Quebec

As noted below, in 2020 over 23,000 claimants utilized a specialty drug product for the treatment of their condition. The vast majority (95 per cent) of these claimants used products costing between $10,000 and $49,999 per year. Products costing between $50,000 and $99,999 and between $100,000 and $499,999 saw significant claimant growth in 2020, with Imbruvica, Revlimid, Tagrisso, and Lynparza, used for oncology treatments, responsible for 85 per cent of the cost growth in the $50,000–$99,999 category. In comparison, the combination of cystic fibrosis, paroxysmal nocturnal hemoglobinuria (PNH), and X-linked hypophosphatemia (XLH) were the conditions responsible for three-quarters of the cost growth from the products costing $100,000–$499,999. There were five claimants that used specialty products costing more than $500,000. These high-cost claimants represented a 66.7 per cent growth year-over-year. Four of these claimants used Vimizim to treat a genetic disorder, and one claimant used Strensiq for enzyme replacement therapy.

TABLE 3.3 | Number of claimants by cost of specialty products

Range of Specialty Product Cost	Number of Claimants			
	2018	2019	2020	YOY Growth Rate in 2020
$10,000 – $49,999	16,030	17,747	22,601	20.5%
$50,000 – $99,999	292	379	471	22.7%
$100,000 – $499,999	96	136	216	32.5%
$500,000 +	2	3	5	66.7%
Grand Total	16,372	18,200	23,222	20.6%

The summation of Number of Claimants across different cost ranges could be higher than the Grand Total because some claimants might use more than one specialty product with a different cost range.

The Specialty Product Cost interval is assigned to each specialty product according to its largest annual average drug cost per claimant between 2011 and 2020.

From a disease-state perspective, rheumatoid arthritis (RA)/Crohn's/colitis/psoriasis medications made up about 53 per cent of the specialty products in 2020, reaching nearly $300 million in total spending. Cystic fibrosis expenditures, while not in the top five, continued to rise at a fast pace, reaching over $15 million in annual expenditures in 2020. In contrast, the hepatitis C expenditure maintained its negative growth in 2020, as in prior years, partly due to declining utilization. A new entrant in the top 10 disease-states category is X-linked hypophosphatemia (XLH), a condition treated by a recently approved drug called Crysvita.

TABLE 3.4 | Top 10 disease states treated by specialty drugs in 2020 and associated year-over-year cost growth

Top 10 Disease States	2016 vs. 2015	2017 vs. 2016	2018 vs. 2017	2019 vs. 2018	2020 vs. 2019*
RA/Crohn's/Colitis/Psoriasis	17.2%	17.1%	2.9%	14.5%	38.3%
Cancer	-2.7%	31.4%	18.5%	5.2%	44.6%
Multiple Sclerosis	5.4%	10.6%	1.1%	8.9%	10.6%
Asthma and COPD	27.3%	21.0%	9.4%	13.3%	40.2%
HIV	30.3%	27.3%	3.8%	12.4%	13.4%
Cystic Fibrosis	267.2%	123.6%	37.8%	44.1%	68.3%
Skin Irritations/Conditions	N/A	N/A	N/A	141.0%	75.3%
Paroxysmal nocturnal haemoglobinuria (PNH)	-49.3%	126.8%	39.3%	21.1%	61.7%
Hepatitis C	-51.1%	-30.3%	-14.0%	-15.5%	-12.2%
X-linked Hypophosphatemia (XLH)		N/A	N/A	N/A	214.3%

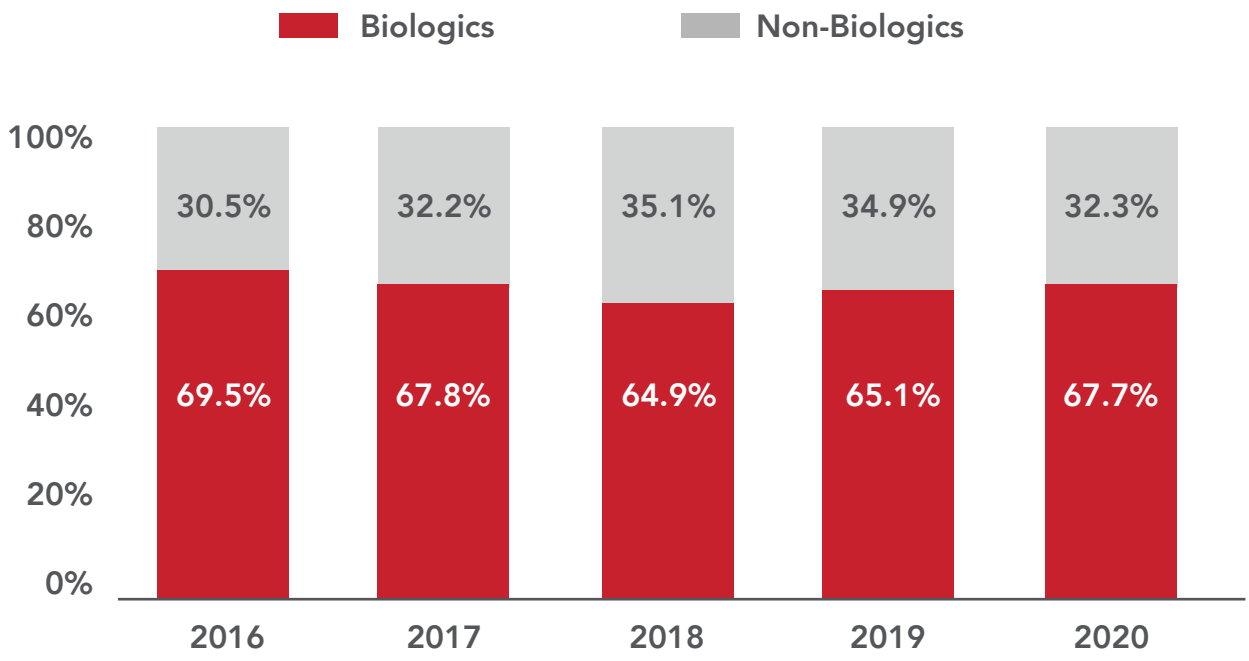
N/A - Not Available

* Key drugs driving the change include: Remicade, Humira, Stelara (RA/Crohn's/colitis/psoriasis); Imbruvica, Ibrance (cancer); Xolair, Fasenra, Nucala (asthma and COPD); Symdeko, Orkambi (cystic fibrosis); Dupixent (skin irritations/conditions); Soliris (PNH); Crysvita (XLH).

Focus on Biologics and Biosimilars

Biologic drugs are the main contributors within specialty product expenditures – they made up 67.7 per cent of the specialty total drug cost in 2020, which includes 1.7 per cent from biosimilars.

FIGURE 3.2 | Biologic and non-biologic share of specialty drug cost by year



Since 2014, more than 27 biosimilar products impacting private drug plans have been approved and marketed in Canada, 15 of which were approved after 2019 (Table 3.5). Biosimilars present comparable safety and efficacy to their originator products, but at a significantly lower cost; in fact, the discount attributable to a biosimilar relative to a reference product is up to 50 per cent for some products.

TABLE 3.5 | Approved biosimilars in Canada*

Biosimilar	Originator Reference Product	Approval Date	Condition(s)	Discount (Relative to Originator)
Inflectra	Remicade	2014	RA/Crohn's/Colitis/ Psoriasis	47%
Basaglar	Lantus	2015	Diabetes	25%
Grastofil	Neupogen	2015	Neutropenia	17%
Brenzys	Enbrel	2016	RA/Psoriasis	40%
Admelog	Humalog	2017	Diabetes	25%
Erelzi	Enbrel	2017	RA/Psoriasis	40%
Renflexis	Remicade	2017	RA/Crohn's/Colitis/ Psoriasis	50%
Glatect**	Copaxone**	2017	Multiple Sclerosis	32%
Hadlima	Humira	2018	RA/Crohn's/Colitis/ Psoriasis	40%
Fulphila	Neulasta	2018	Neutropenia	44%
Lapelga	Neulasta	2018	Neutropenia	44%
Truxima	Rituxan	2019	RA/Granulomatosis with Polyangiitis (GPA)/ Microscopic Polyangiitis (MPA)	38%
Avsola	Remicade	2020	RA/Crohn's/Colitis/ Psoriasis	50%
Riximyo	Rituxan	2020	RA	38%

(continued onto next page)

* This table reflects biosimilars that are relevant to private plans and were approved as of July 1, 2021.

** Glatect and Copaxone are considered non-biologic complex drugs.

TABLE 3.5 | Approved biosimilars in Canada* (continued)

Biosimilar	Originator Reference Product	Approval Date	Condition(s)	Discount (Relative to Originator)
Ruxience	Rituxan	2020	RA/GPA/MPA	38%
Nivestym	Neupogen	2020	Neutropenia	17%
Ziextenzo	Neulasta	2020	Neutropenia	44%
Nyvepria	Neulasta	2020	Neutropenia	44%
Trurapi	NovoRapid	2020	Diabetes	17%
Amgevita	Humira	2020	RA/Crohn's/Colitis/ Psoriasis	40%
Hulio	Humira	2020	RA/Crohn's/Colitis/ Psoriasis	40%
Hyrimoz	Humira	2020	RA/Crohn's/Colitis/ Psoriasis	40%
Idacio	Humira	2020	RA/Crohn's/Colitis/ Psoriasis	40%
Noromby	Lovenox	2020	Thromboembolic disorders	25%
Inclunox	Lovenox	2020	Thromboembolic disorders	25%
Redesca	Lovenox	2020	Thromboembolic disorders	25%
Riabni	Rituxan	2021	RA/GPA/MPA	38%

* This table reflects biosimilars that are relevant to private plans and were approved as of July 1, 2021.

Biosimilars continued gaining strong momentum through HBM+ business in 2020. Their total drug cost reached $20.7 million, which represents an increase of 54.8 per cent from the previous year (Figure 3.3). This significant growth was led by the biosimilars of Remicade (Inflectra and Renflexis). Their combined total drug cost rose 66 per cent year-over-year to $6.2 million in 2020 (Figure 3.4). They were responsible for 33 per cent of the biosimilar total drug cost growth followed by the biosimilars of Neulasta and Neupogen which contributed 23 per cent and 14 per cent, respectively.

FIGURE 3.3 | Biosimilar expenditures at HBM+, 2016 to 2020

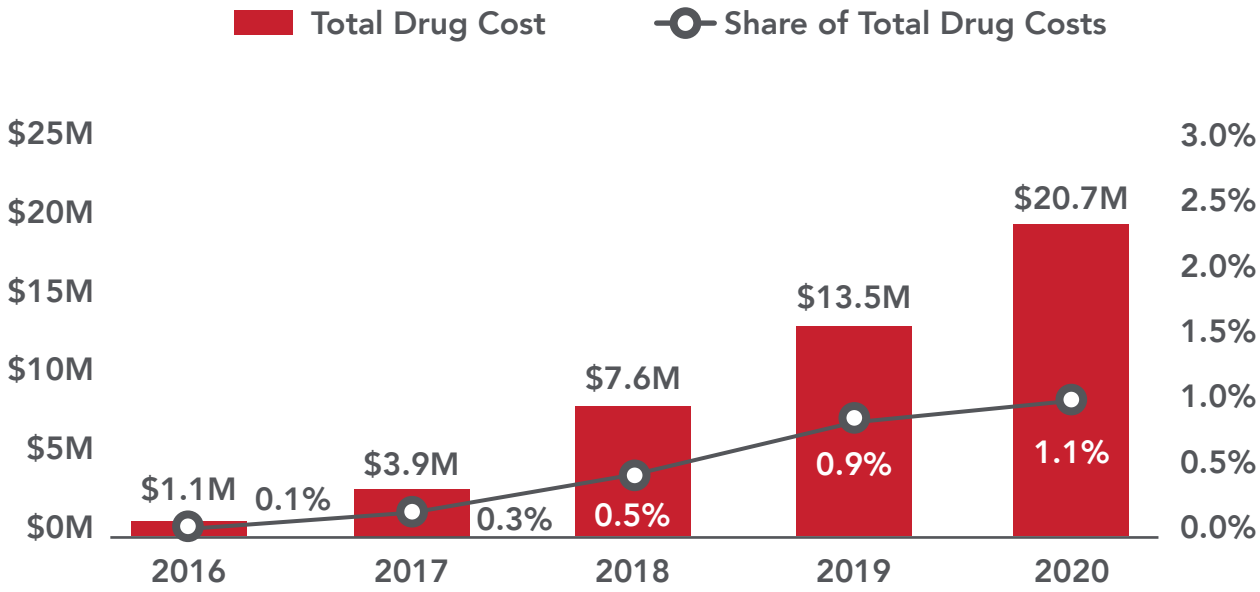
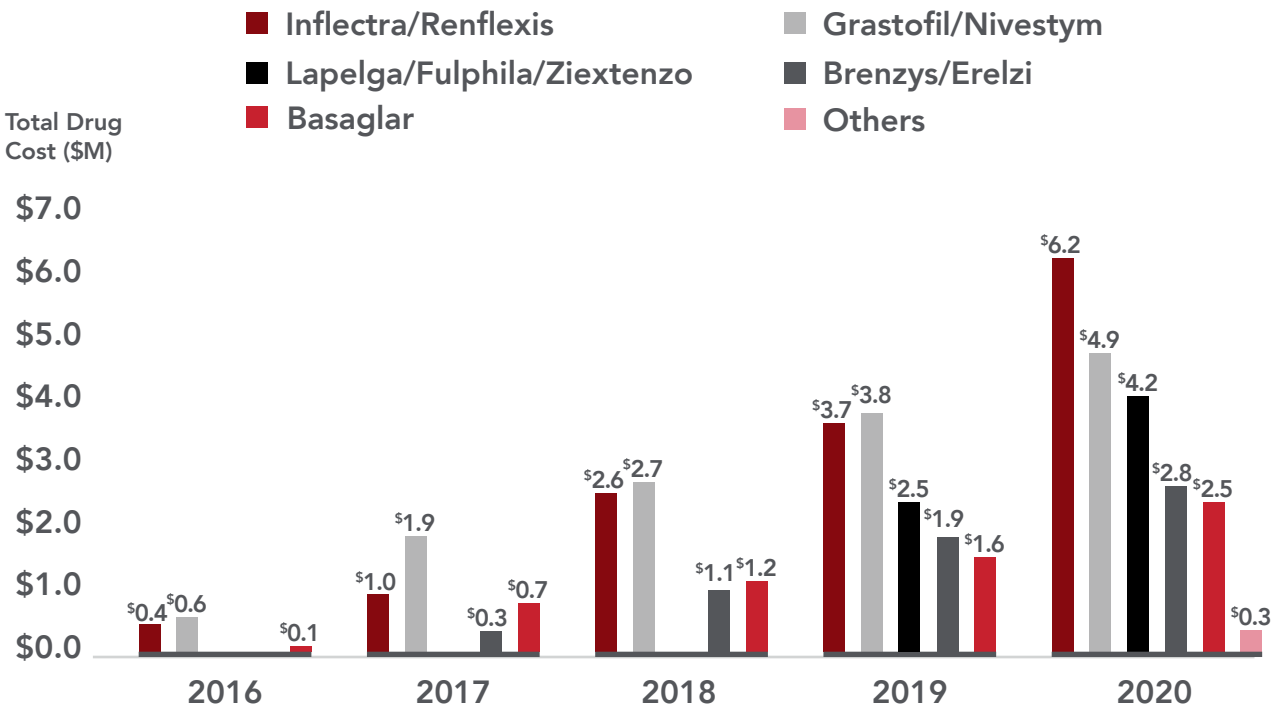


FIGURE 3.4 | Biosimilar total drug costs by drug, 2016 to 2020



Since 2015, HBM+ has been an avid supporter of a strong biosimilar market in Canada to ensure the necessary conditions are in place to drive the continued arrival of new biosimilars into the system. The HBM+ biosimilar strategy has two key elements:

- New Start Program that ensures that bio-naive patients (newly prescribed biologic drugs) are required to start on the biosimilar version of the medication.
- Biosimilar Transitioning Program that responsibly transitions patients from originator to biosimilar products using our nurse-led support service for assistance and navigation.

Together, these two programs have driven biosimilar penetration at HBM+ to levels beyond the rest of the private payor industry for each of the major molecules, including infliximab, etanercept, insulin glargine, filgrastim, and pegfilgrastim. Focusing in on infliximab specifically, while biosimilar penetration continues to grow, the originator market share continues to remain high at over 88 per cent, six years post market-entry of biosimilar products. It is expected that the rapidly growing uptake of the HBM+ Biosimilar Transitioning Program will continue to drive biosimilar penetration higher in 2021 and onwards.

HBM+ Biosimilar Transitioning Program will continue to drive biosimilar penetration higher in 2021 and onwards.

Provincial government policies that implement biosimilar transitioning under their health care plans have now been launched in British Columbia, Alberta, New Brunswick, and Quebec. These policies have had a positive effect on the private payor market, providing reassurance to plan sponsors that such policies can be implemented safely and generate substantial savings.

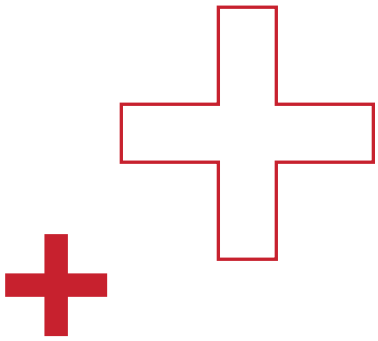


TABLE 3.6 | Biosimilars share of claims by molecule, 2020

Molecule	HBM+	Other Private Drug Programs*	Ontario Public Drug Program*	RAMQ
	Biosimilar Share of Claims	Biosimilar Share of Claims		
Infliximab (Remicade)	11.8%	9.2%	17.9%	13.7%
Etanercept (Enbrel)	27.2%	22.1%	30.8%	20.0%
Insulin Glargine (Lantus)	43.6%	20.2%	2.0%	29.4%
Filgrastim (Neupogen)	88.1%	87.7%	92.6%	97.4%
Pegfilgrastim (Neulasta)	97.6%	83.0%	100%	100%

* Source: IQVIA, PharmaStat

One additional development generating continued interest in biosimilar transitioning is the arrival of the Humira biosimilars in the Canadian market. Currently, five distinct Humira biosimilars, with discounts of 40 per cent relative to originators, have now been approved in Canada and are listed on HBM+ formularies (Table 3.7).

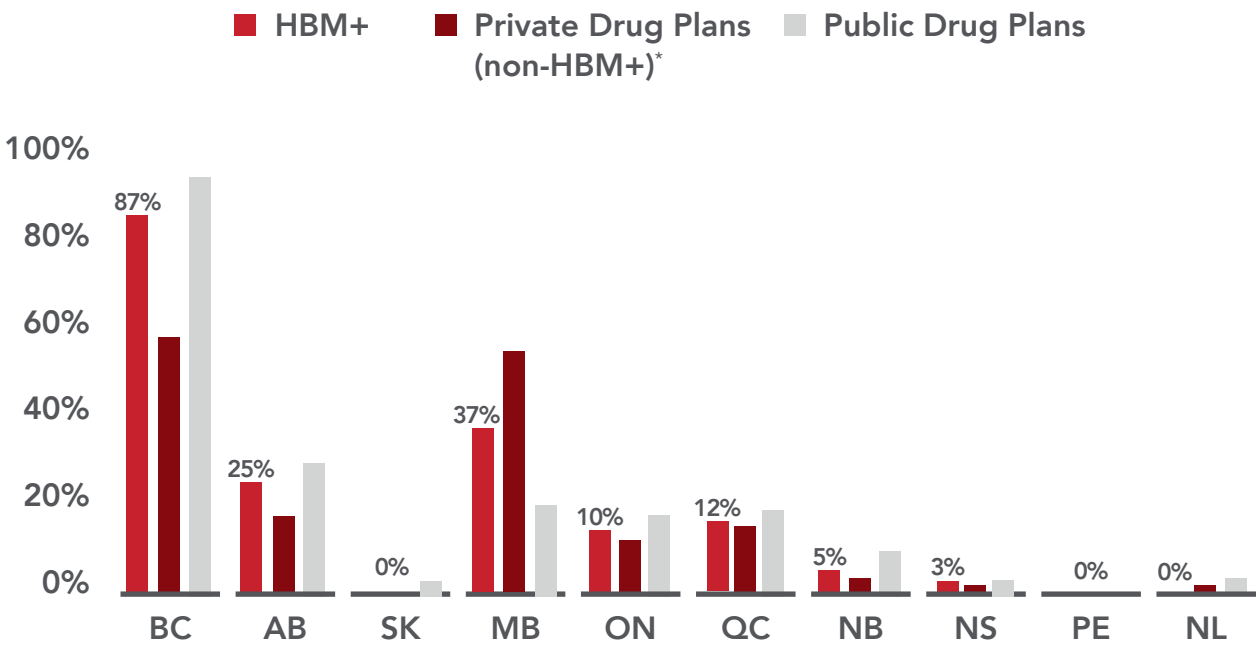
TABLE 3.7 | Approved adalimumab biosimilars in Canada

Biosimilar Name	Manufacturer	Discount (Relative to Originator)
Amgevita	Amgen Canada Inc.	40%
Hadlima	Samsung Bioepis	40%
Hulio	BGP Pharma ULC	40%
Hyrimoz	Sandoz Canada Inc.	40%
Idacio	Fresenius Kabi Canada Ltd.	40%

At a provincial level, biosimilar penetration shows a dramatic difference across the country, with a strong west to east gradient. For example, biosimilars of Remicade had the highest market share in British Columbia at nearly 90 per cent in 2020, which was mainly influenced by the biosimilar transition policy from the public drug program. Biosimilar penetration rates for this product decline gradually from the west to the east, with 12 per cent and 10 per cent penetration in Quebec and Ontario, respectively, as these two provinces made up 65 per cent and 30 per cent of the infliximab claims within HBM+ in 2020.

At a provincial level, biosimilar penetration shows a dramatic difference across the country.

FIGURE 3.5 | Biosimilar penetration of infliximab by province, 2020



* Source: IQVIA, PharmaStat

4 Non- Specialty Drugs

2021 DRUG TRENDS & STRATEGIC INSIGHTS

hbm+®

Overall Trends

While specialty drugs continue to dominate industry conversations and planning efforts within private plans, there are important trends pertaining to non-specialty drugs that are starting to emerge and which also require close attention. The dynamics of non-specialty drugs are best illustrated by dividing claimants into cost intervals (Table 4.1). Each of these cost intervals is dominated by specific therapeutic categories such as hyperlipidemia, migraines, and diabetes. The overarching theme is the growing utilization of biologic drugs to treat these relatively common conditions. This utilization is driving unprecedented growth in spending and will require closer management not only of the appropriateness of drug therapy but also overall disease management. The two fastest growing claimant-cost-interval categories in 2020 were the $1,000–$1,999 and the $5,000–$9,999 intervals; the dynamics of each are outlined below.

TABLE 4.1 | Utilization by claimant cost intervals, 2020

Claimant Cost Interval	Total Drug Cost Growth 2020 vs. 2019	Claimant Growth 2020 vs. 2019
<$500	17.5%	4.8%
$500–$999	22.8%	14.7%
$1,000–$1,999	**23.5%**	**10.3%**
$2,000–$2,999	24.2%	8.2%
$3,000–$3,999	16.8%	12.9%
$4,000–$4,999	26.0%	15.3%
$5,000–$9,999	**36.3%**	**26.4%**
Non-Specialty	**19.8%**	**4.9%**
Specialty	**37.0%**	**20.6%**

Claimant Cost Interval $5,000–$9,999

Total costs for claimants in the **$5,000–$9,999** cost interval grew by 36.3 per cent in 2020 rising to a total of $46.4 million. This exceptional growth was mainly caused by greater utilization of biologic treatments for the top five disease states within this group of medications, including macular degeneration, cancer, high cholesterol, migraines, and HIV. Given the rapidly growing utilization of products in this category, ensuring the appropriate utilization of biologics in this cost interval is going to become increasingly important for effective overall drug-plan cost management. Traditional tools such as prior authorization continue to be an essential element of drug plan management for this category, but equally important are disease-based case management approaches. In a case management framework, claimants with specific chronic diseases, such as high cholesterol and diabetes, work with a case manager one-to-one to manage all aspects of their disease, including medication adherence, diet, and exercise among others. Case management, delivered through the combination of technology and human guidance, can be a powerful tool for enabling effective disease control as well as long-term cost management.

TABLE 4.2 | Top five disease states for claimants in the $5,000–$9,999 cost interval, 2020

Rank	Disease State	Share of Total Drug Cost	Total Drug Cost Growth 2020 vs. 2019	Claimant Growth 2020 vs. 2019
1	Macular Degeneration	31.7%	32.4%	17.7%
2	Cancer	14.2%	34.0%	48.5%
3	Elevated Cholesterol	12.9%	38.8%	22.4%
4	Migraines	12.0%	155.4%	93.2%
5	HIV	7.3%	-10.6%	-14.9%

Macular degeneration

Total drug cost for eye diseases such as macular degeneration reached $14.7 million in 2020, with Eylea and Lucentis as the only medications in this class. Eylea made up 70 per cent of the total drug cost, but it was responsible for 90 per cent of the cost growth in 2020.

Cancer

Lapelga (Neulasta biosimilar) claimants almost doubled in 2020 and were responsible for most of the 34 per cent total cancer drug-cost growth in 2020.

Elevated cholesterol

Praluent and Repatha total drug cost grew by 37.5 per cent and 39.3 per cent year-over-year, respectively. These biologic treatments for high cholesterol have been available in the market for some time (with the first initially approved in 2015), and their number of claimants reached 1,100 in 2020, up by 22 per cent from the previous year.

Migraines

Total migraine drug cost jumped by 155 per cent year-over-year thanks to the 93.2 per cent increase in claimants taking the new biologic treatments Aimovig, Ajovy, and Emgality. Moreover, this substantial utilization growth also means migraine contributed 27.4 per cent of the total drug-cost growth within the category of $5,000–$9,999 products relative to its 12 per cent share of total drug cost.

HIV

This therapeutic category was the only one in the top five that saw an annual decline in cost growth. It made up just 7.3 per cent of total drug cost in 2020 – down from 35.2 per cent in 2016 owing to the lower utilization of Truvada, Viread, Isentress, and Prezista which faced strong generic competitors.

Claimant Cost Interval $1,000–$1,999

Total costs for claimants in the **$1,000–$1,999** cost interval grew by 21.8 per cent over the past five years due to consistent double-digit claimant growth. Diabetes is the significant cost driver within this interval, accounting for 67 per cent of the total drug-cost growth in 2020. This increase is mainly attributed to the GLP-1 inhibitors and insulins, where Ozempic and Trulicity made up 63.5 per cent and 19.3 per cent of the total drug cost in 2020 respectively, followed by 10.6 per cent for Toujeo and 4.4 per cent for Levemir. Attention deficit hyperactivity disorder (ADHD) was another stand-out condition within this claimant cost interval since it contributed 20 per cent of the total drug-cost growth in 2020, with the increase mainly driven by the greater utilization of Intuniv XR.

TABLE 4.3 | Top five disease states for claimants in the $1,000–$1,999 cost interval, 2020

Rank	Disease State	Share of Total Drug Cost	Contribution to Total Drug Cost Growth	Total Drug Cost Growth 2020 vs. 2016 (Annually)	Claimant Growth 2020 vs. 2016 (Annually)
1	Diabetes	26.4%	67.0%	51.3%	34.4%
2	ADHD	9.7%	19.9%	23.5%	19.3%
3	Weight Control	8.3%	9.0%	62.5%	50.0%
4	Cervical Dystonia	7.1%	0.6%	14.5%	13.7%
5	Rheumatoid Arthritis/Crohn's/ Colitis/Psoriasis	6.1%	10.3%	11.7%	9.2%

5 Emerging & Future Trends

2021 DRUG TRENDS & STRATEGIC INSIGHTS

hbm+®

Digital Pharmacy

The global COVID-19 pandemic has dramatically shifted Canadians' utilization of various health care services. Lockdowns and distancing requirements have resulted in more Canadians turning to virtual options to obtain their care.

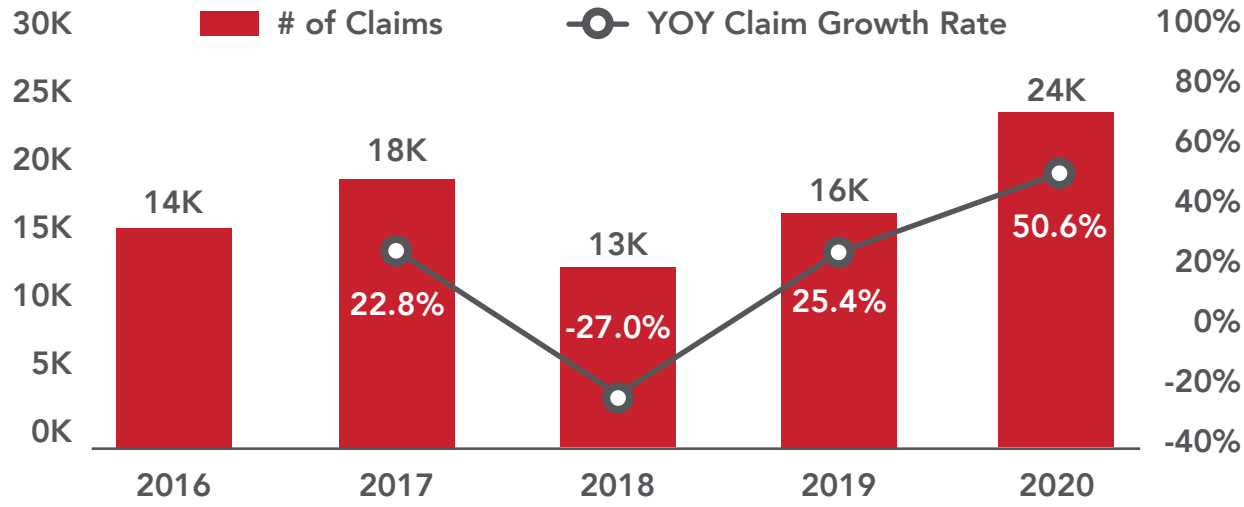
Pharmacy has absolutely been affected by this movement. Even in advance of COVID-19, a number of new digital pharmacy startups entered the Canadian marketplace, including PocketPills, Pillway, Mednow, Health Depot, and others. Digital pharmacies rely on the same model of drug distribution as "mail-order" pharmacies, but they elevate the patient experience to a much higher level. The distinguishing line between the two pharmacy types is not always clear, and many of the traditional mail-order pharmacies are adding a digital experience layer to their services.

In general though, digital pharmacy has provided patients with new ways of interacting with their pharmacy providers, including through mobile applications combined with home delivery of medications.

Throughout the pandemic, Canadians have relied more and more on online shopping and home delivery for obtaining a wide array of products. It is expected that these online behaviours will inevitably translate into growing adoption of digital pharmacy as a means of obtaining medications.

HBM+ data trends support this assertion – the number of claims for non-specialty medications obtained through digital pharmacies has grown over 50 per cent in 2020 compared to 2019 (Figure 5.1). Specifically, there were 24,000 non-specialty prescriptions delivered by digital pharmacies in 2020, with an associated $1.76 million total drug cost. This represents 0.08 per cent of HBM+ claims in 2020, up from 0.01 per cent in 2019.

FIGURE 5.1 | Number of claims and annual growth rate for digital pharmacies



Delving a bit deeper into the dynamics of the traditional versus digital pharmacy models reveals some interesting trends.

- First, digital pharmacies charge lower dispensing fees than their traditional counterparts – on average under $8 per prescription compared to $9–$11 for traditional pharmacies (Table 5.1).
- In addition, digital pharmacies tend to dispense larger quantities (days' supply) of medications compared to traditional pharmacies – on average 54 days per claim compared to 33–47 days for traditional pharmacies (Table 5.2).

For both of these reasons – lower dispensing fees and higher quantity supplied – digital pharmacies have garnered growing interest from Canadian plan sponsors, offering the opportunity to provide their plan members with a convenient pharmacy option while saving plan dollars.

TABLE 5.1 | Average dispensing fees by pharmacy type and province

Average Dispensing Fee per Claim				
Province	Chain Banners	Food Stores	Independent	Digital Pharmacy
BC	$10.42	$8.57	$10.14	$7.83
AB	$11.99	$10.63	$11.89	$8.04
SK	$11.43	$10.65	$11.37	$8.19
MB	$11.80	$9.82	$12.32	$7.50
ON	$11.53	$8.84	$10.88	$7.57
NB	$11.55	$8.65	$11.90	$7.86
NS	$12.06	$9.45	$11.88	$9.31
PE	$12.22	$11.49	$12.32	Not Available
NL	$11.48	$7.80	$11.71	$7.16
National*	$11.39	$9.12	$10.86	$7.63

*Excluding Quebec

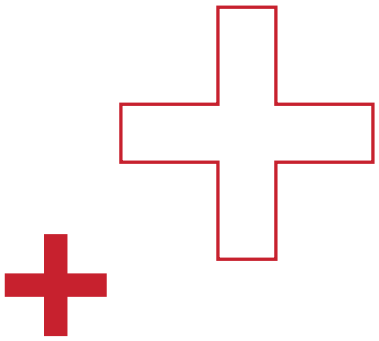


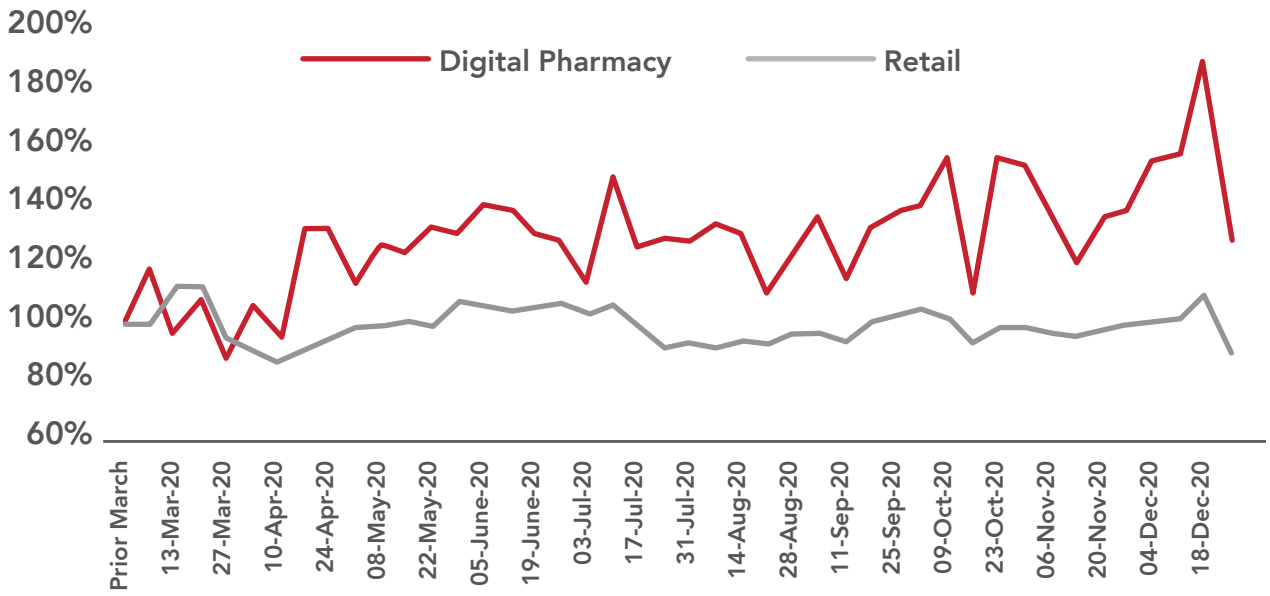
TABLE 5.2 | Average quantities dispensed by pharmacy type and province

Average Day Supply per Claim				
Province	Chain Banners	Food Stores	Independent	Digital Pharmacy
BC	45.0	53.5	40.4	64.3
AB	36.6	42.1	31.7	59.5
SK	34.8	37.4	24.9	63.6
MB	40.3	46.8	37.6	55.4
ON	36.3	45.1	32.5	51.5
NB	42.5	49.7	52.4	64.6
NS	45.5	48.3	39.2	52.8
PE	44.6	44.0	42.8	Not Available
NL	42.4	48.3	39.5	53.3
National*	38.1	47.2	33.5	54.3

*Excluding Quebec

Digital pharmacy demonstrated more resilient growth than its retail counterpart during the COVID-19 pandemic. As outlined in Figure 5.2, the number of claims through digital pharmacies grew throughout 2020, and the gap between retail and digital pharmacy channels widened, indicating faster growth through the digital channel.

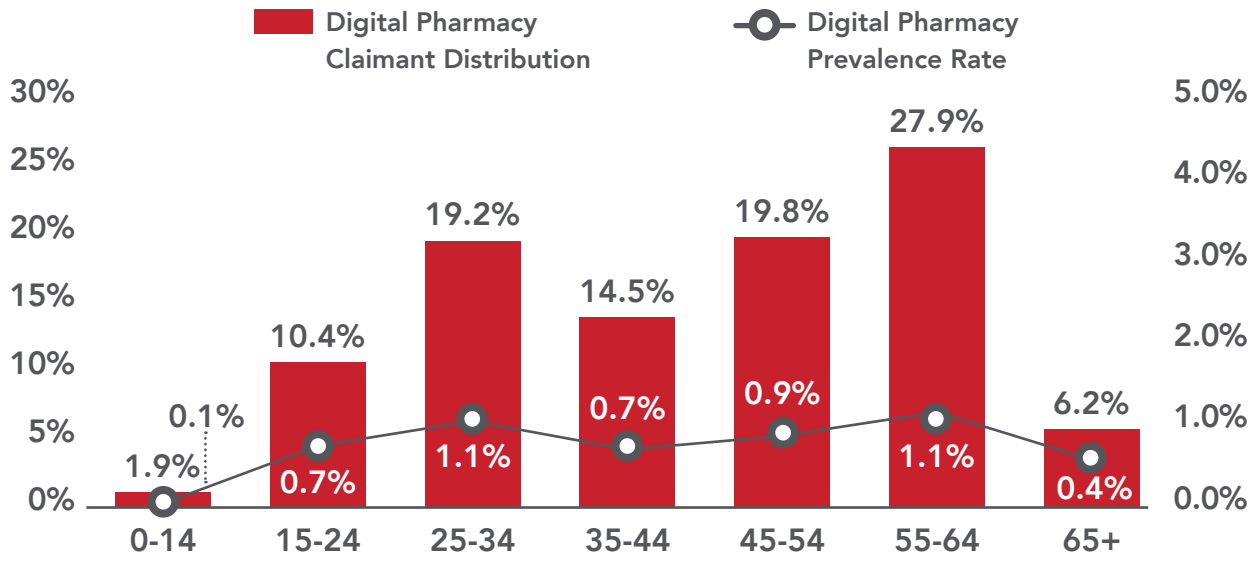
FIGURE 5.2 | Weekly claim count comparison 2019 to 2020 by delivery channel



Looking at the demographics of patients utilizing the digital pharmacy channel, it is evident that a relatively older population – more prone to chronic diseases – makes up most of the claimants taking advantage of digital pharmacy services (Figure 5.3). Claimants aged 55 to 64 are the main consumers in the digital pharmacy channel, and they accounted for 27.9 per cent of the total digital pharmacy population in 2020, followed by claimants 45–54 and 25–34 who accounted for 19.8 per cent and 19.2 per cent of the claimants, respectively.

Chronic medications are in many ways an ideal category for distribution through digital pharmacies given the predictable nature of dispensing, compared to acute medications which are often required on short notice.

FIGURE 5.3 | Digital pharmacy claimant age distribution



The prevalence of chronic disease in the digital pharmacy claimant population is also evident in the distribution of the top disease states (Table 5.3). All of the top 10 disease states are typically chronic in nature with hypertension plus anxiety and depression leading the way.

TABLE 5.3 | Top 10 diseases among patients utilizing digital pharmacy channels

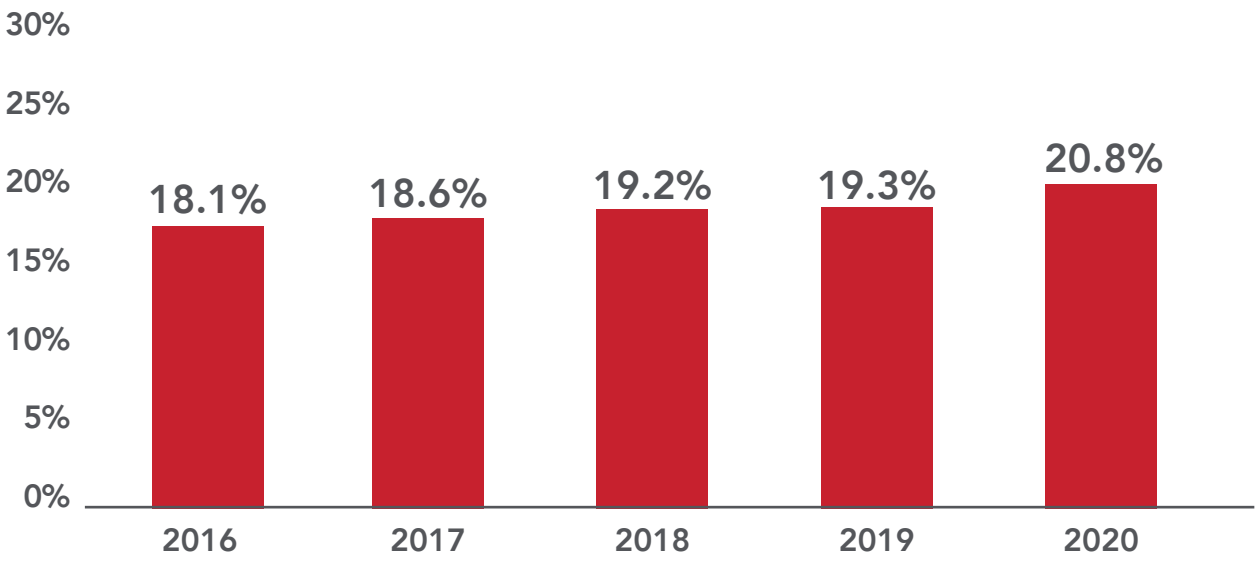
Disease State	Share of Claims	Share of Total Drug Costs
Hypertension	13.9%	4.8%
Anxiety/Depression	11.9%	6.7%
Birth Control	10.9%	7.0%
Diabetes	8.8%	18.3%
Elevated Cholesterol	7.8%	2.9%
Acid Related Gastrointestinal Conditions	5.1%	5.0%
Asthma and COPD	5.0%	6.8%
Thyroid Condition	3.4%	0.8%
Skin Irritations/Conditions	3.3%	4.0%
Allergies	3.1%	2.3%
Top 10 Subtotal	**73.2%**	**58.5%**

Mental Health

A growing body of evidence has shown that the COVID-19 pandemic has negatively affected the mental health of many individuals both in Canada and globally. A number of underlying pandemic-caused changes have been at fault, including persistent lockdowns, social isolation, economic issues, and worries about infection.

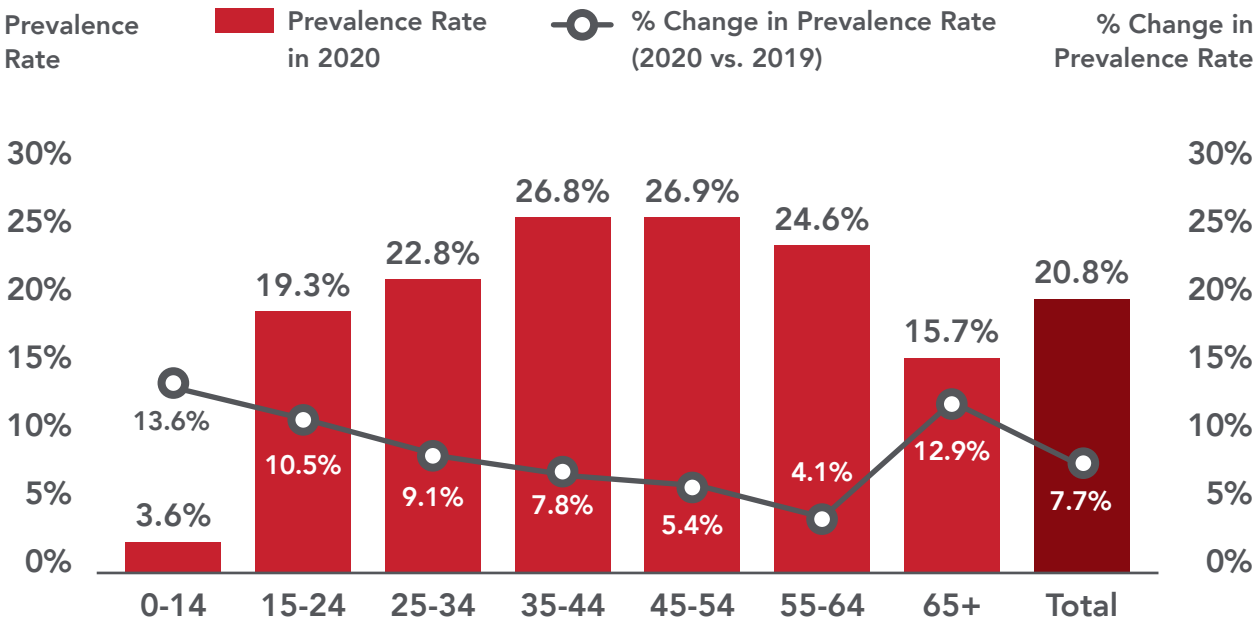
The HBM+ claims data supports the assertion of a growing mental health crisis. In 2020, approximately 429,000 claimants utilized medications that are typically used to manage depression and anxiety representing a prevalence rate of 20.8 per cent of all claimants. This is an increase from 19.3 per cent in 2019 and 18.1 per cent in 2016. Not all of the growth is due necessarily to the pandemic, as there has been a focus in recent years on destigmatizing mental health which resulted in more individuals seeking appropriate care.

FIGURE 5.4 | Prevalence of mental health conditions among HBM+ claimants, 2016–2020



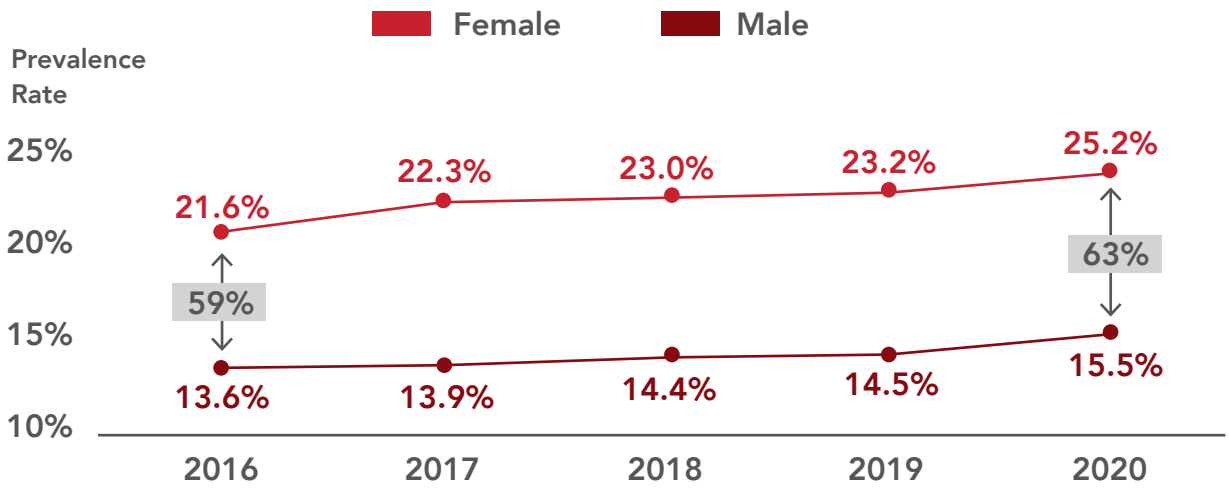
The highest prevalence rate was for claimants in the 45–54 age group, though rates were generally high across a number of age groups. Substantial increases in prevalence from 2019 to 2020 were among younger cohorts, namely the 0-14 (13.6 per cent increase) and 15–24 (10.5 per cent increase) age groups, and the older (age 65+) claimant population.

FIGURE 5.5 | Prevalence rates of mental health conditions by age group, 2020



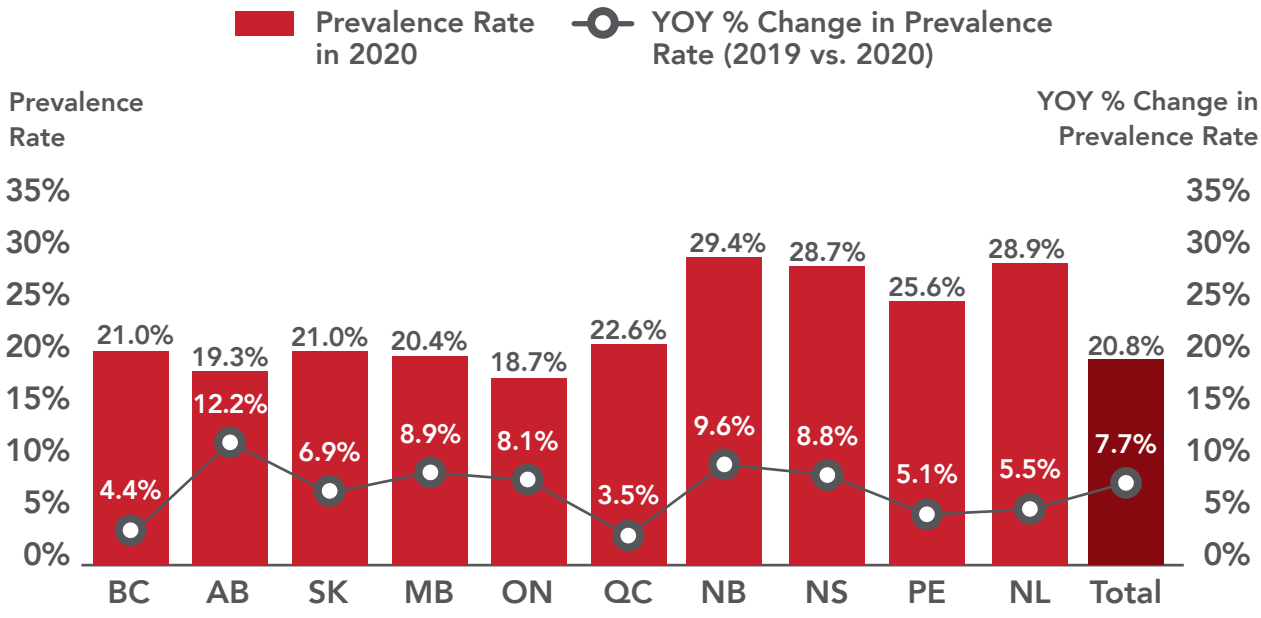
Females were 63 per cent more likely to claim medications to treat mental health conditions than males, and the gap between genders for the prevalence of mental health conditions has widened since 2016 (Figure 5.6).

FIGURE 5.6 | Prevalence of mental health conditions by gender, 2016–2020



The prevalence of mental health conditions varied by province with eastern provinces having generally higher rates than the rest of Canada (Figure 5.7). Alberta was the province with the highest annual increase (12.2 per cent) in prevalence of mental health conditions.

FIGURE 5.7 | Prevalence of mental health conditions by province, 2020



Over 80 per cent of the total drug costs (or 71.1 per cent of the claims) for treating mental health conditions were concentrated among the top 10 products (Table 5.4).

TABLE 5.4 | Top 10 products used to treat mental health conditions, 2020

Ranking by Total Drug Cost	Products	Share of Claims	Share of Total Drug Costs
1	Escitalopram	12.3%	19.2%
2	Venlafaxine	15.0%	10.0%
3	Duloxetine	5.7%	8.7%
4	Vortioxetine	2.1%	8.6%
5	Sertraline	9.7%	8.2%
6	Desvenlafaxine	2.3%	7.7%
7	Citalopram	10.1%	6.4%
8	Bupropion	7.8%	5.6%
9	Fluoxetine	3.4%	4.2%
10	Paroxetine	2.8%	3.3%
Top 10		**71.1%**	**82.0%**

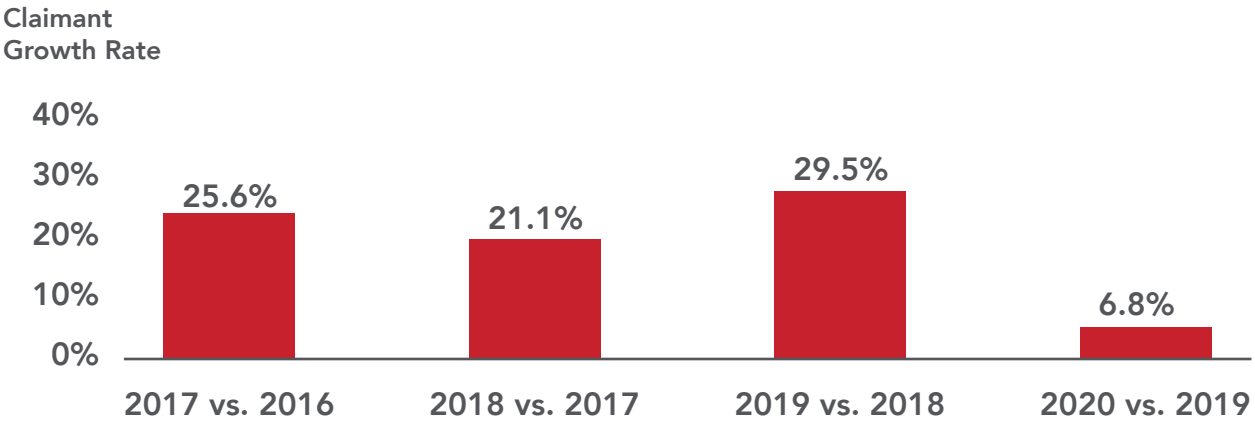
Mental health – beyond medication therapy

The treatment of mental health conditions can involve a variety of different tools and approaches. For many patients, medications are the mainstay of treatment, particularly for severe depression and anxiety. However, increasingly, patients are choosing to either supplement or complement their medication-based treatment with talk therapy of various kinds – including cognitive behavioural therapy, psychoanalysis, humanistic therapy, and others. These types of therapy, typically covered under extended health benefits (EHB) plans, are delivered by health professionals such as social workers, psychologists, and counsellors. The modalities of delivery are also wide-ranging – some involve one-on-one counselling with a qualified practitioner while others involve carefully curated and self-guided approaches combined with therapist support, such as therapy provided by MindBeacon. As well, a number of innovative startups, such as Inkblot, are using technology to not only increase access to care, but also to enhance the matching process between provider and patient using artificial intelligence technology.

Patients are choosing to complement their medication-based treatment with talk therapy of various kinds.

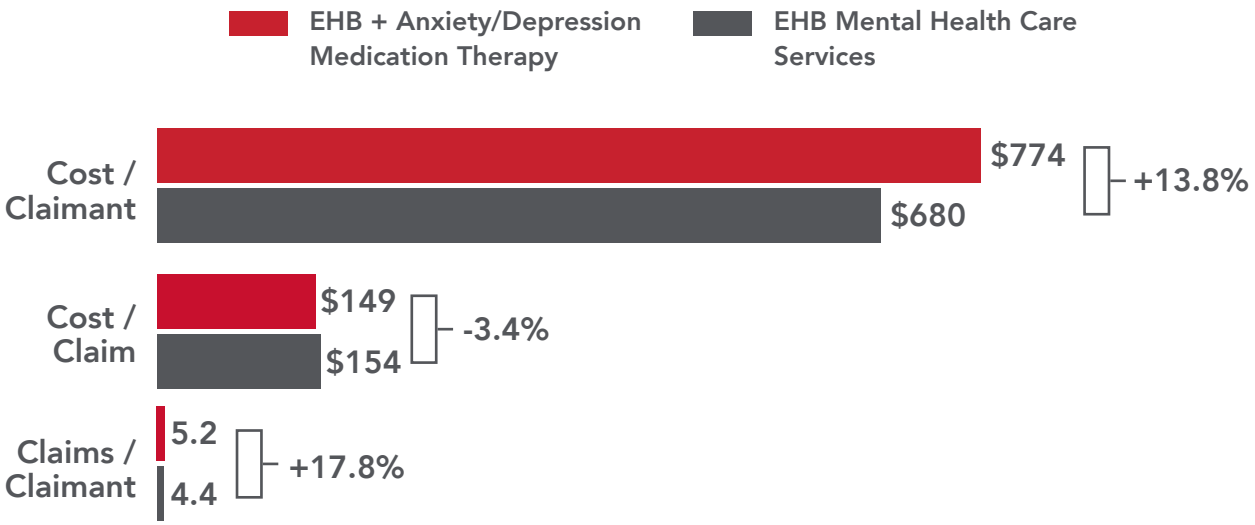
The number of claimants that utilized EHB mental health care services doubled between 2016 and 2020 (34,000 and 71,500 respectively). Overall, 2.2 per cent of HBM+ eligible claimants used EHB mental health services in 2020 up from 1.8 per cent in 2016. Claimant utilization for EHB mental health care services slowed down noticeably in 2020 (Figure 5.8), which could be partially attributable to the lockdown and social distancing measures during the pandemic which may have discouraged patients from seeking counselling in person.

FIGURE 5.8 | Year-over-year claimant growth for EHB mental health care services



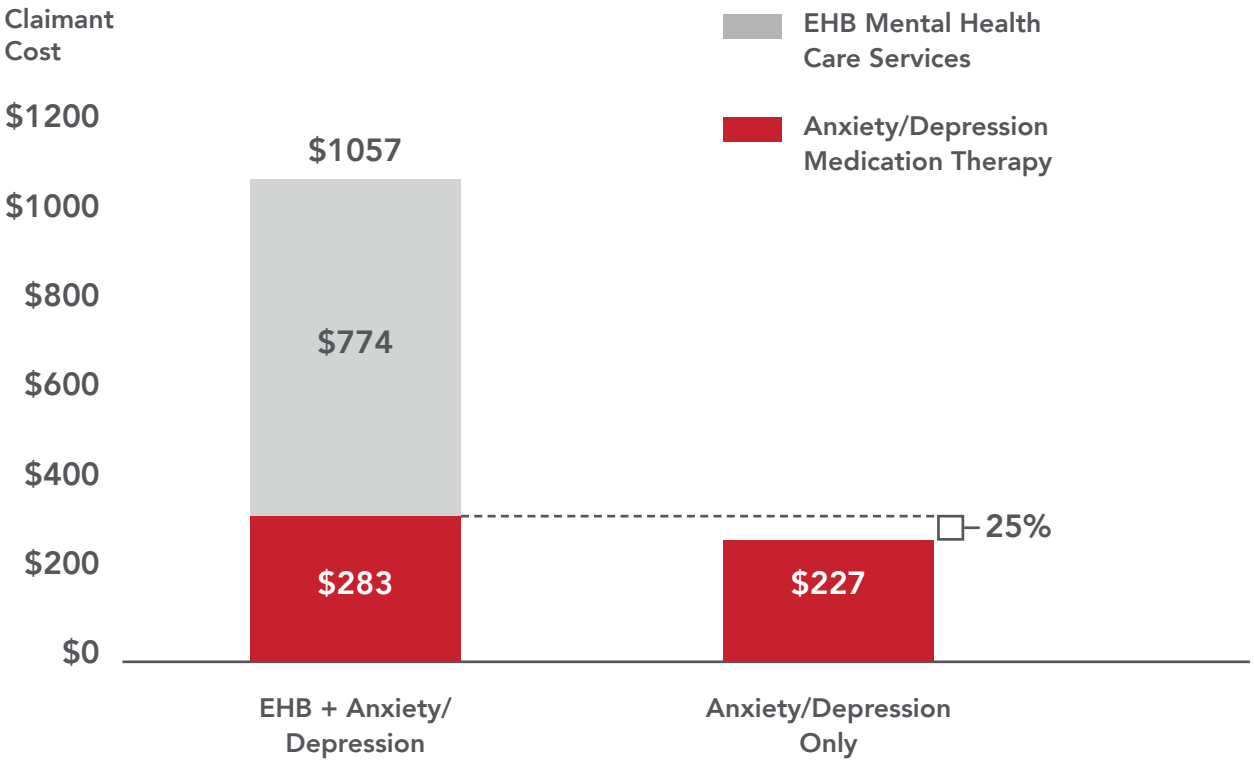
Nearly 29 per cent of the claimants utilizing EHB mental health care services also used anxiety/depression medications to manage their condition. Those claimants had 13.8 per cent higher expenditures on EHB mental health services, perhaps reflecting a greater complexity of their disease state that required multiple modalities and higher intensity treatment.

FIGURE 5.9 | Comparison of patients utilizing EHB services with and without medication therapy



Across HBM+ in 2020, about 282,000 claimants were utilizing medication therapy to treat their mental health condition. About 7.2 per cent (20,000) of these patients also utilized EHB mental health care services. On average, these patients had a total mental health care treatment cost of $1,057; about 73 per cent of that total cost was attributable to the EHB benefit, and the remainder (27 per cent) was due to medication therapy costs (Figure 5.10). Interestingly, the patients utilizing combined modalities had 25 per cent higher medication costs, again potentially indicating greater disease severity.

FIGURE 5.10 | Average claimant cost by benefit type and claimant type, 2020



Value-Based Pharmacy

In 2017, HBM+ became the first pharmacy benefits manager in Canada to introduce a system for measuring the performance of community pharmacies on a number of important quality-of-care metrics (Table 5.5). This system, called Value-based Pharmacy, sets a foundation for the first pharmacy-based pay-for-performance system in Canada (note that this program does not apply in Quebec). Value-based Pharmacy was created out of a desire to utilize pharmacists to their maximum scope of practice and improve overall patient care and health outcomes.

TABLE 5.5 | Value-based Pharmacy quality improvement measures

Measure	Description
Hypertension	Proportion of patients age 18 and older taking at least one renin-angiotensin-system-antagonist (RASA) drug who were adherent to their therapy.
High Cholesterol	Proportion of patients age 18 and older taking a statin drug who were adherent to their therapy.
Diabetes	Proportion of patients age 18 and older taking at least one non-insulin diabetes drug who were adherent to their therapy.
Statin Use in Diabetes	Proportion of patients age 40–75 who were dispensed a medication for diabetes and also received a statin medication.
Asthma – Suboptimal Control	Proportion of patients who were dispensed asthma medications during the measurement period and received more than three canisters of a short-acting beta agonist (rescue medication) within a 90-day period.
Asthma – Absence of Controller Therapy	Proportion of patients who did not receive controller asthma therapy during the same 90-day period in which they received more than three canisters of a short-acting beta agonist.
Cardiovascular (CV) Health Coaching	Proportion of patients who met the eligibility criteria for cardiovascular health coaching services and received the service.
High-risk Medications	Proportion of patients age 65 and older who were dispensed two or more fills for a high-risk medication.

Phase I of Value-based Pharmacy was implemented in 2017 when pharmacies across Canada began receiving site-specific performance reports, called Patient Impact Scorecards. In 2018, Phase II was implemented, which made pharmacy performance information available to plan members in the form of a searchable online portal. This information provided patients with the ability to search for providers based on quality-of-care delivery, not merely location and convenience. Finally, Phase III of this program, which introduces the pay-for-performance component, was slated to be implemented on July 1, 2021. Recognizing the challenges that COVID-19 has posed for pharmacies and the important role that pharmacists have played in the vaccination campaign over the last six months, HBM+ made the decision to defer the implementation of Phase III of this program to July 1, 2022. There is growing evidence that routine care, including for chronic disease management, has suffered over the course of the pandemic. Recent data also shows that screening and diagnoses rates are lower than typically expected and that there is a growing backlog of new patients who will need future treatment for these chronic conditions. With pharmacies engaged on the COVID-19 front-line, HBM+ recognized that the intense focus on the pandemic has left limited time for quality improvement and disease management efforts aimed at chronic conditions, which make up the bulk of the Value-based Pharmacy metrics.

In comparing the 2020 pharmacy performance to 2019, several themes emerge that are primarily driven by the impact of the pandemic. First, adherence to medication therapy (for diabetes, hypertension, and high cholesterol) has increased with over 80 per cent of patients highly adherent to all three measures. At the regional level, Alberta pharmacies show lagging scores relative to other provinces, with adherence four to five percentage points lower on average.

Second, there appeared to be reduced performance across a number of chronic disease measures. This is an expected outcome as pharmacists shifted their focus from proactively managing diseases to supporting pandemic efforts and ensuring patients had continuous access to their

prescribed medications and reduced risk of interruptions to therapy. The most noticeable change in performance was in the asthma measures, specifically with increased rates of suboptimal control. Some of this is due to asthmatic patients utilizing more inhalers than usual last year, either because their disease truly worsened and/or because some patients stockpiled inhalers due to pandemic fears. One surprising trend was with respect to the high-risk medication use in the elderly: there was a noticeable decline in the proportion of patients in this age group utilizing potentially high-risk medications. This is a very encouraging finding as the over-use of medications in the elderly is a well-documented issue that can lead to significant health complications for these patients.

TABLE 5.6 | Pharmacy performance on quality of care measures by province, 2020

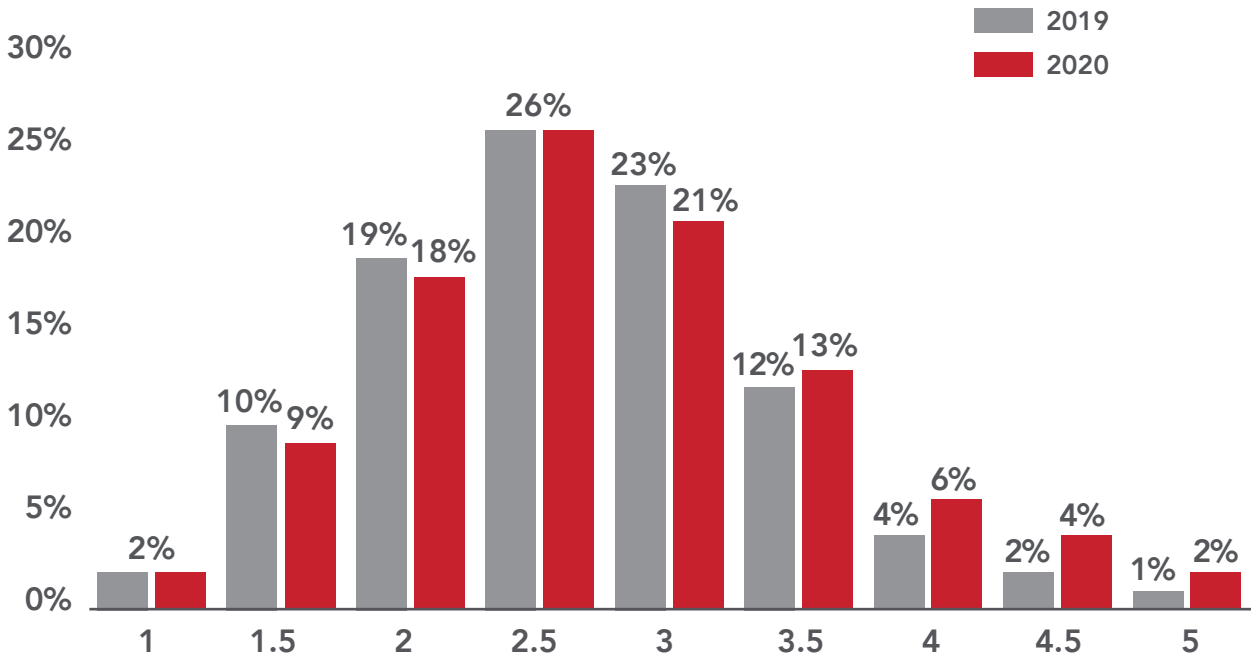
Measure Name	Canada**		Ontario + Others*		British Columbia		Alberta	
	2019	2020	2019	2020	2019	2020	2019	2020
RASA Proportion of Days Covered (PDC)	80.5%	82.7%	80.7%	82.1%	80.9%	85.7%	77.5%	79.7%
Cholesterol PDC	79.8%	81.1%	79.9%	80.3%	81.1%	85.0%	75.1%	76.2%
Diabetes PDC	82.1%	82.1%	82.1%	81.9%	83.3%	84.4%	73.3%	73.1%
Statin Use in Diabetes	75.3%	74.4%	77.2%	75.9%	70.5%	71.4%	68.2%	66.6%
Asthma – Suboptimal Asthma Control (SAC)	12.9%	17.7%	14.1%	18.7%	21.5%	--	9.5%	13.7%
Asthma – Absence of Controller Therapy (ACT)	--	--	--	--	--	--	--	--
CV Health Coaching	0.3%	0.1%	0.4%	0.2%	0.1%	0.0%	0.1%	0.0%
High Risk Medications	15.1%	13.0%	14.4%	12.0%	15.7%	13.6%	--	--

Table reflects the performance of pharmacies with a minimum of 10 patients qualifying for the measures.
* Includes all provinces and territories, except Alberta, British Columbia, and Quebec.
** Quebec data is not included in performance calculations.

In order to derive a summary of pharmacy performance, we combined the eight quality-of-care measures (Figure 5.11) into one overall composite score or star rating, called the Pharmacy Quality Rating. This is generated through valuing the individual measures, with adherence-based measures bearing single weight and chronic disease management and safety measures bearing double weight towards the overall star rating.

There was an overarching improvement in the overall distribution of the Pharmacy Quality Rating in 2020 compared to 2019 (Figure 5.11). Fifty-seven per cent of pharmacies in 2019 had a score of 2.5 stars or lower compared to 55 per cent of pharmacies in 2020. Conversely, about 43 per cent of pharmacies had a three-star or higher rating in 2019 compared to 45 per cent of pharmacies in 2020.

FIGURE 5.11 | Pharmacy Quality Rating distribution 2020 vs. 2019



Percentage is based on total number of eligible pharmacies for the program. Total percentages may not add up to 100 per cent due to rounding.

Drug Pipeline

In recent years, private drug plans have shown a growing interest in forecasting the impending arrival of new drugs to the Canadian market. This has been driven by both a desire to understand potential cost implications of those drugs as well as to ensure effective formulary management. Forecasting the success of clinical trials and subsequent commercial efforts of pharmaceutical manufacturers is a challenging practice; however, certain trends are starting to appear that will dominate 2021 and onwards. Here we discuss a few of these with a focus on Alzheimer's disease, mental health, gene therapies, and biosimilars.

Alzheimer's disease

Alzheimer's disease is a very common condition particularly among the elderly in Canada – over 747,000 Canadians are living with this disease or another form of dementia, with 70,000 individuals newly diagnosed each year. The cause of Alzheimer's disease is not known though it does have an association with age in that people over 65 are at risk, and the risk increases even further at age 85 and older. Despite the lack of a full understanding of the causes of the disease, there is evidence that the buildup of amyloid plaque between brain cells and tangles inside cells – twisted fibers of a protein called tau – are two important contributing factors.

There are a number of existing drugs on the market that treat Alzheimer's disease symptoms, including donepezil (Aricept and generics), rivastigmine (Exelon and generics), galantamine (Reminyl and generics), and memantine (Ebixa and generics). These drugs do not cure Alzheimer's disease, nor stop it from getting worse. Rather, they are known as cognitive enhancers – helping to treat the cognitive symptoms of the disease. These drugs vary in cost but average about $5 per day or less (or approximately $2,000 per year).

Pharmaceutical manufacturers have tried for decades to develop drug therapies to address the progression of Alzheimer's disease, but with little success. More than 200 experimental therapeutic agents have been assessed in failed or abandoned investigational programs over the years, all of which have failed to produce any meaningful effect on disease progression.*

In June 2021, the United States Food and Drug Administration (FDA) approved Biogen's Alzheimer's drug called Aduhelm (aducanumab), the first new Alzheimer's treatment in nearly two decades. However, this approval came with a backdrop of significant controversy. An independent advisory panel recommended that the FDA not approve Aduhelm on the basis of several concerns. Following the FDA decisions, three of the 11 members of the panel resigned. Furthermore, the FDA commissioner has invited an independent investigation into the relationship between the agency staff and the drug manufacturer.

More than 200 experimental therapeutic agents have been assessed in failed or abandoned investigational programs over the years.

Three major concerns have been noted with Aduhelm – efficacy, safety, and cost. The efficacy concerns are based on the fact that Aduhelm was approved on a surrogate endpoint (an endpoint that does not represent a direct benefit but rather predicts clinical benefit) – amyloid beta plaque reduction. While the plaque is an important aspect of the disease, it is not clear whether the reduction will result in a clinical benefit for the patient.

* Konstantina G. Yiannopoulou, Aikaterini I. Anastasiou, Venetia Zachariou, and Sygkliti-Henrietta Pelidou, "Reasons for Failed Trials of Disease-Modifying Treatments for Alzheimer Disease and Their Contribution in Recent Research," Biomedicines 2019; 7(4):97, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6966425/.

The safety concerns are based on the fact that Aduhelm has been shown to cause significant side-effects, including brain swelling and microbleeds in up to 40 per cent of patients taking the drug. Those safety concerns demand close monitoring of these patients throughout their treatment process.

Finally, the price of Aduhelm, at US$56,000 per year, is a significant issue for payors, when combined with a very large eligible population (up to six million U.S. residents). While the drug was only tested in early-stage Alzheimer's patients, the drug was approved for all patients regardless of disease status. With the current list pricing, the U.S. Medicare program could spend up to $57 billion a year on this drug alone, which is more than the entire Medicare Part B spends on all drugs combined. Some payors have already stated they won't cover Aduhelm, with the Department of Veterans Affairs citing insufficient evidence and concerns around safety.*

Aduhelm has yet to be approved by Health Canada, and given the significant concerns noted, it remains to be seen how Canadian payors – public and private – will embrace the product on their formularies. It is clear that the unmet need for patients with Alzheimer's disease is quite high, but what is not clear is to what degree Aduhelm meets that need or, alternatively, represents a false hope.

Psychedelics for mental health

The COVID-19 pandemic has exacerbated an already growing incidence of mental health challenges in Canada and internationally. The dynamics of some of those mental health issues are illustrated in the HBM+ claims data, which is discussed in a previous section. Traditional pharmacotherapy-based regimens for the treatment of anxiety, depression, and other mental health issues have had limited effectiveness for many patients with up to one-third responding sub-optimally. This limited effectiveness combined with low adherence has resulted in many patients unable to achieve effective management of their mental health conditions.

* Ed Silverman and Damian Garde, "Veterans Affairs declines to cover Biogen's Alzheimer's drug over effectiveness, safety concerns," Stat, August 11, 2021, https://www.statnews.com/pharmalot/2021/08/11/alzheimers-aduhelm-drug-veterans-affairs/.

With this as a backdrop, a host of new and novel therapeutics has recently started to appear on the landscape, including a category called psychedelics. These therapeutics have been increasingly investigated for treating conditions such as major depressive disorder, severe anxiety, and substance abuse. One of those psychedelics is Ketamine, first approved in Canada and the United States as a general anesthetic in the 1970s. Over the years, it gained a reputation as a recreational "party drug." However, in recent years, a small but growing body of research has shown utility in using it as a fast-acting treatment for depression. Nevertheless, it does come with a significant amount of controversy, including limited research on effectiveness, as well as safety concerns such as addiction and psychosis. There is also the question of cost, with annual treatment costing up to $5,000, and typically no coverage through either public or private drug plans.

Other psychedelics currently being tested include MDMA (Methylenedioxymethamphetamine) – commonly known as ecstasy or molly. When combined with psychological counselling, MDMA has been shown in a phase III clinical trial to improve outcomes for patients with post-traumatic stress disorder (PTSD).*

Psilocybin, a psychoactive ingredient found in some mushrooms, is another psychedelic going through a number of clinical trials and showing promise. A study published in the New England Journal of Medicine in 2021 showed some benefits of psilocybin in treatment of major depressive disorder.** While the exact mechanism of action of psilocybin is unknown, the study showed promising results favouring psilocybin therapy over an antidepressant (escitalopram). As a result of the promising findings, the FDA has granted psilocybin "breakthrough" therapy designation which is meant to accelerate the drug development and review process.

* J.M. Mitchell, M.Bogenschutz, A. Lilienstein, et al., "MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study," Nat Med 27, 1025–1033 (2021), https://www.nature.com/articles/s41591-021-01336-3.

** Robin Carhart-Harris, et al., "Trial of Psilocybin versus Escitalopram for Depression," New England Journal of Medicine, April 2021, https://www.nejm.org/doi/full/10.1056/NEJMoa2032994.

Finally, esketamine (Spravato) was approved by the FDA in 2019 and by Health Canada in 2020 for treatment-resistant depression. It was the first psychedelic treatment approved for a psychiatric disorder and offers promise for treatment of depression for a population of patients that have traditionally struggled to achieve effective control with antidepressants. Esketamine has a significantly higher price tag – ranging on average from $20,000 to $30,000 for a year of treatment – compared to traditional antidepressant therapies.

While still relatively early in terms of the body of supportive research, psychedelics are an interesting area to watch and are likely to lead to an abundance of new treatment options for patients in the coming years.

Gene therapies

Recent advances in research and drug development have led to gene therapies as a paradigm for the treatment of many diseases, including cancer, blindness, heart disease, and others. Gene therapy involves changing a patient's genetic makeup to treat or cure a disease. Over 300 gene therapies are currently in the development pipeline, and expectations are high that these therapies will unlock new highly effective ways of treating diseases. Four gene therapies have now been approved in Canada (Table 5.7), with the most recent approval in early 2021.

TABLE 5.7 | Gene therapies approved in Canada

Gene Therapy	Indications	Approval Date
Kymriah	B-cell Acute Lymphoblastic Leukemia (ALL) and Relapsed or Refractory Large B-cell Lymphoma (LBCL)	May 2019
Yescarta	Relapsed or Refractory LBCL	November 2019
Luxturna	Inherited Retinal Dystrophy	October 2020
Zolgensma	Spinal Muscular Atrophy (SMA)	February 2021

While incredibly exciting from a treatment perspective, gene therapies introduce new affordability challenges for public and private drug plans. Unlike most chronic disease drugs, gene therapies are one-time treatments with price tags that typically exceed $1 million, or in the case of Zolgensma, almost $3 million per treatment. HBM+ has developed a gene therapy strategy; the core elements were outlined in the 2020 HBM+ Drug Trends and Strategic Insights report. Since that report was published, important developments have occurred; specifically a number of provincial governments across the country have opened up access to Zolgensma and Luxturna on a "case-by-case" basis. This interim measure allows any individual suffering from the disease states treated by these gene therapies to apply for access, regardless of the person's public or private drug plan eligibility. This is expected to be an interim measure until the provinces can make more definitive decisions around the exact placement of gene therapies on public drug plans. HBM+ is actively monitoring these developments and will be ready to implement its gene therapy strategy in line and coordinated with the outcome of provincial program decisions.

Biosimilars pipeline

Since their arrival in the Canadian market in 2015, biosimilars have been an important element of an effective drug plan sustainability strategy. The recent arrival of the five Humira biosimilars has reinvigorated the important discussions around the role of biosimilars and the most effective ways to achieve the associated savings.

Looking forward, the biosimilar pipeline continues to be rich in new molecules that will further drive savings to drug plans. It is important to recognize that some or perhaps all of the biosimilars in the pipeline are dependent on the outcomes of legal patent challenges, clinical trials, and manufacturing efforts. Consequently, the exact timing and commercialization of these biosimilars is uncertain, but Table 5.8 provides some indicative timing of when new biosimilars are expected in the Canadian market.

TABLE 5.8 | Biosimilar drug pipeline

Biosimilar Details	Therapeutic Area	Expected Biosimilar Availability or Phase of Development
Ranibizumab (biosimilar to Lucentis)	Ophthalmology	Currently under Health Canada review (since May 2021)*
Natalizumab (biosimilar to Tysabri)	Immunosuppressant	2021-2022
Omalizumab (biosimilar to Xolair)	Respiratory Agent	2021-2022
Aflibercept (biosimilar to Eylea)	Ophthalmology	Late-phase development
Tocilizumab (biosimilar to Actemra)	TNF Blocker	Late-phase development
Ustekinumab (biosimilar to Stelara)	TNF Blocker	Late-phase development

* As of August 2021

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