Industry Trend Report in Pharmacy Quality 2021

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PQS

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LETTER FROM THE CEO

In 2021, we continued to witness how our world, communities and individual lives have changed due the pandemic. For healthcare providers in particular, the realities and stresses have likely been unimaginable. While we all long to have the pandemic be something of the past, taking a step back we can appreciate just how nimble healthcare can be as we look at how access and utilization have changed, and how rapidly new knowledge has been disseminated to influence prescribing patterns and services.

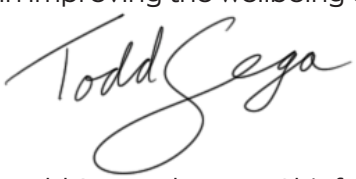
For the PQS 2021 Trend Report in Pharmacy Quality, we continued to focus on reviewing information and reflections to foster a common language across various healthcare providers. We aim to align payers and providers on areas of opportunity and to serve as a foundation for how they can bring higher quality and improved outcomes to the patients they collectively serve.

As a reminder, PQS has alternated the focus for the trends each year. One year we cover quantitative quality and utilization trends across large populations and in the next year we focus on qualitative perceptions of change, value-based reimbursement models between payers and providers, and consumer perceptions of pharmacist-provided services.

In last year's Trend Report, we provided insights on consumer perceptions, comfort and likelihood to engage with community pharmacies for COVID-19 testing and treatment. In this year's Trend Report, we covered how those perceptions likely factored into the impact on prescription claim utilization and access to community pharmacies throughout last year. We have identified unique utilization trends and patterns based upon stay-at-home orders and key emergency use authorizations by government agencies such as the Centers for Disease Control (CDC). We also analyzed secondary effects of medication utilization due to access to care disruptions and how supply changes were supported to allow patients to obtain greater amounts of medication to limit the need for healthcare interactions. Unique trends for antibiotic utilization were also observed, likely due to social distancing, restricted public gatherings and increased mask wearing.

Despite large shifts and spikes in general and specific medication utilization patterns, one fact remains steady and true: the role of public health and that of community pharmacy in protecting and supporting the health of our communities is paramount and must stay relevant. For public health, partnerships between nations and with private sector entities must continue to progress. For pharmacy, new roles and partnerships have expanded and emerged. We look forward to monitoring pandemic-influenced evolutionary shifts and supporting the advancement of pharmacy in healthcare.

I hope you enjoy our 2021 Trend Report and that it serves as a source of inspiration for you to continue innovating on quality improvement. The dedication of payers and providers during this challenging time, and going above and beyond every day to serve their patients, has been inspiring. We at PQS are honored to support you in improving the wellbeing of your communities, one measure at a time.



Todd Sega, PharmD, Chief Executive Officer

INTRODUCTION

Each year, the PQS Trend Report is produced to educate the marketplace and inform healthcare payers, pharmacy providers and life science organizations on trends and changes the marketplace is making to improve quality. Given the unique circumstances presented at the end of 2019 and throughout 2020, this report highlights prescription trends specifically related to the COVID-19 public health emergency (PHE) and associated mitigation approaches that may have impacted pharmacy and medication utilization patterns.

The data we analyzed is based upon retrospective prescription claims analysis, from a subset of health plans and pharmacy benefit managers, representing total patient counts of approximately 25.4M and 27.1M, from 2019 and 2020 respectively. Prescription claims were associated with Medicare Advantage Prescription Drug Plans (MAPD) and standalone Prescription Drug Plans (PDP) lines of business. Given that 2020 was a year unlike any other, it was not appropriate to compare to previous year's data. Instead, this analysis evaluates the change in weekly prescription claims volume, from baseline, based on date of service and number of claims for 2020 (2019 change also included).

CHAPTER 1

Changes in Pharmacy Utilization

BACKGROUND: In response to the national COVID-19 Public Health Emergency (PHE) in March 2020, the Centers for Medicare & Medicaid Services (CMS) issued temporary regulatory waivers and new rules to equip Medicare Advantage (MA) and Part D plans with the flexibility needed to provide access to care and prescription medications for beneficiaries affected by the pandemic.[1] These flexibilities included extended days' supply, relaxed "refill-too-soon" edits, and increased options for prescription home delivery.

As in-person appointments and activities were reduced due to COVID-19 restrictions, patients may have opted for extended days' supply or used low- or no-contact pickup or delivery methods. This chapter explores trends in pharmacy utilization, days' supply, and mail order use throughout calendar year 2020.

OVERALL CONSIDERATIONS: The figures included represent the week-over-week change in prescription claims, compared to baseline, of the calendar year. Baseline is considered week three of the calendar year (unless otherwise noted) to minimize the impact of prescription claims variability due to health care coverage changes, associated with the start of the new calendar year, and not covid-19 related. Where applicable, previous year pharmacy utilization was also included for reference.

Across several graphs, vertical lines are used to illustrate significant national events that occurred related to the COVID-19 pandemic. Beginning in late 2019 and early 2020, news reports relayed details about a mysterious illness and lock-down in Wuhan, China. The first cases of COVID-19 infections were reported in the United States in January 2020. On March 11, 2020 the World Health Organization (WHO) declared COVID-19 a pandemic. Subsequently, the United Stated declared COVID-19 a national Public Health Emergency (PHE) on March 13, 2020. As regional outbreaks occurred, many hospitals were overwhelmed with COVID-19 patients causing a personal protective equipment (PPE) shortage in these healthcare settings. Schools ceased in-person instruction, employees began to work from home, restaurants closed to indoor dining, mask mandates and social distancing were enacted. As individuals were kept from traveling or leaving their homes except for "essential" functions, numerous people were laid off from their jobs due to the PHE and subsequent restrictions. These factors contributed to peak job loss in April 2020, with a record 14.7% unemployment rate. A significant proportion of these newly unemployed individuals lost access to their employee-sponsored health insurance (ESI).[2]

To boost the flailing economy Congress passed the Coronavirus Aid, Relief, and Economic Security Act (CARES) on March 27, 2020. The CARES Act increased unemployment benefits and financial assistance to Americans, and also established the Paycheck Protection Program that provided forgivable loans for small business. In the middle of May 2020, the first "flattening" of the COVID-19 surge appeared.

However, by July 2020, the US reported record numbers of COVID-19 cases and deaths. In early December 2020, two COVID-19 vaccines were approved for Emergency Use Authorization (EUA) by the FDA which led to vaccinations for healthcare workers and high-risk individuals in early 2021.

As noted in the following graphs, specific national events occurred in 2020 that appear to have potentially impacted pharmacy utilization.

CHAPTER 1

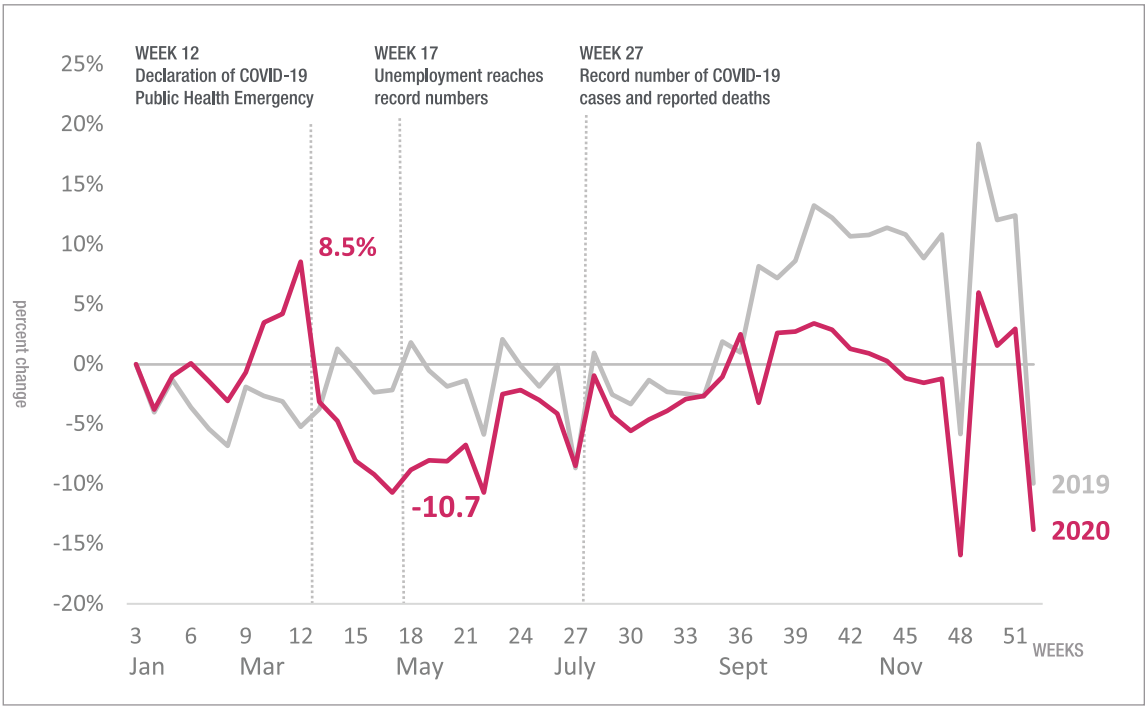
Key Highlights

- At or around the time of the declaration of the PHE, there appears to be a significant increase in the overall volume of prescription claims, but this increase was not typically sustained throughout 2020.
- There was an initial spike in volume of prescription claims for chronic* medications in early 2020, by May the pattern appears to align closely with the previous year.
- There was increased utilization of pharmacy claims written for 90 days' supply.
- There was sustained use of 90 days' supply throughout 2020, identified by peaks in prescription claims every 12 weeks.

**Chronic medication categories were based on the PQA PDC-DR, PDC-STA and PDC-RASA measures and associated medication value sets*

OBSERVATION: There was increased pharmacy utilization for all prescription claims, starting at week 9 and reaching a peak at week 12, with a significant decrease after week 12 which led to low utilization through the remainder of 2020.

CHANGE IN ALL CLAIMS PHARMACY UTILIZATION*



**Pharmacy utilization was defined as the change in weekly prescription claims volume, from baseline, based on date of service and number of claims.*

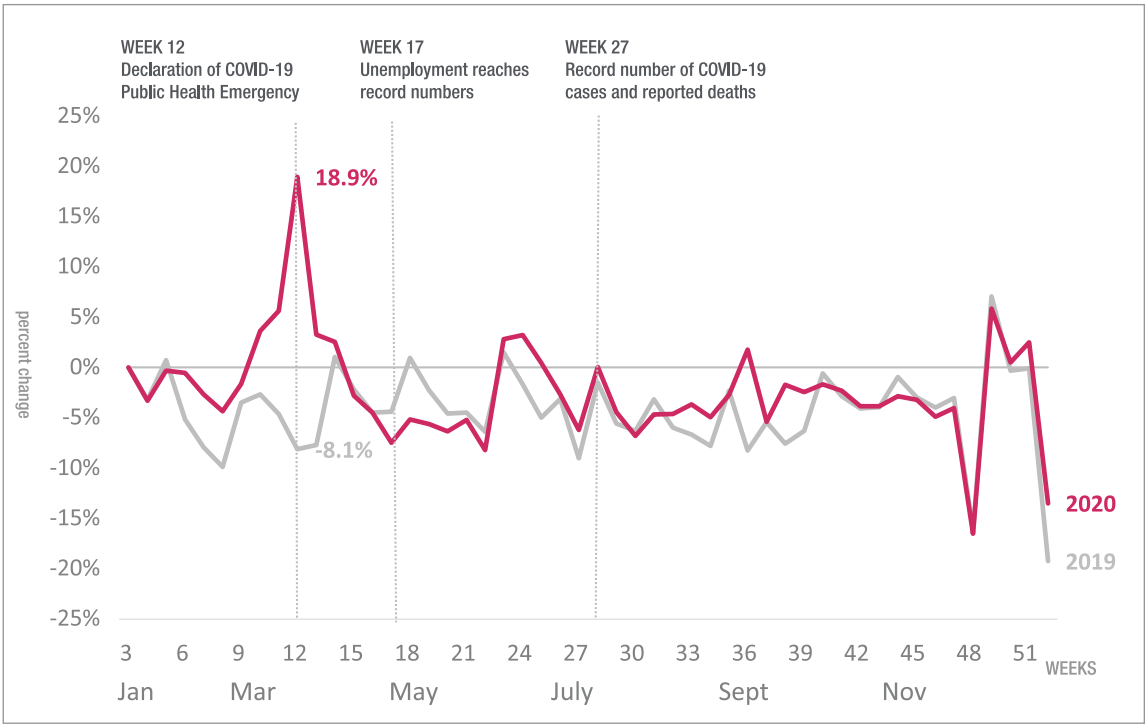
This analysis evaluated change in overall pharmacy utilization from baseline. Pharmacy utilization was defined as the change in weekly prescription claims volume, from baseline, based on the date of service and number of claims for the calendar year.[1]

In early 2020, there was significant increase in overall pharmacy utilization, likely related to concern about continued access to medications early in the PHE. An 8.5% increase in pharmacy utilization, compared to baseline, is noted near week 12. However, pharmacy utilization drops sharply between weeks 12-18 and decreased pharmacy utilization is sustained throughout the rest of 2020.

The observed decrease in pharmacy utilization is likely multifactorial: increased utilization of 90+ days' supply, decreased in-person provider encounters, a lag in provision of telehealth visits, and increased use of mail order or medication synchronization programs may all have contributed. Likewise, for individuals with discontinued employment during the pandemic, the loss of employer sponsored insurance (ESI) may also decrease overall pharmacy utilization. However, it it less likely to be a significant contributor to the Medicare population.[2] Although depressed overall, there may be a seasonal component impacting the pattern of pharmacy utilization based on comparison of trends between 2019 and 2020.[3]

OBSERVATION: There was substantial increase in pharmacy utilization of chronic* medication prescription claims between weeks 9-12, with stabilization starting near week 21 that was sustained through the end of 2020.

CHANGE IN PHARMACY UTILIZATION OF CHRONIC* MEDICATION PRESCRIPTION CLAIMS



**The figure represents the general trend for chronic medication pharmacy utilization across all three chronic medication classes as there was no notable difference between the three unique chronic medication classes evaluated.*

This analysis evaluated the change in weekly prescription claims volume for chronic medications, compared to baseline (week 3). Chronic medications were identified as diabetic medications (excluding insulin), statin medications and renin angiotensin system antagonists. Any prescription claim including an NDC from an identified chronic medication drug class was counted in this analysis.

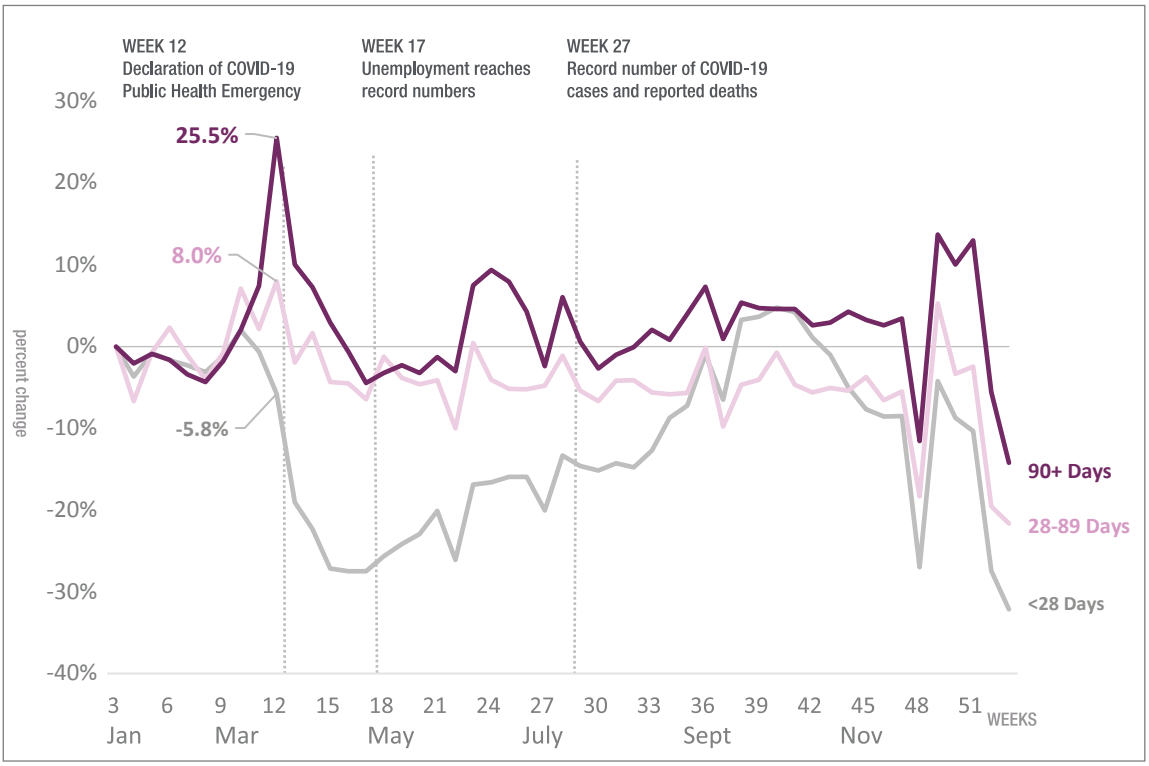
When looking at pharmacy utilization for chronic medication prescription claims, a similar pattern was seen across all three different medication classes.

Chronic medication pharmacy utilization begins to increase at week 9 and peaks near week 12, then drops precipitously between weeks 12-21. Normalization of pharmacy utilization for chronic medications is noted from week 21 throughout 2020.

Potential factors or causes for stable utilization of chronic medications through the second half of 2020 include less need for in-person provider appointments to continue established care during the pandemic, transition to mail order and increased use of 90 days' supply.

OBSERVATION: There was increased utilization of prescription claims written for 90+ days' supply and a decrease in utilization of prescription claims for < 90 days' supply.

CHANGE IN OVERALL PHARMACY UTILIZATION BY DAYS' SUPPLY



"Our pharmacy dealt with various changes during the pandemic. With stay-at-home orders in effect, our customers wanted less in-person contact which led to prescribers sending in more 90-day supply prescriptions." – *Quan Tran, Raley's*

Overall pharmacy utilization for prescription claims written for 90+ days' supply was up 25.5% by week 12 of 2020, near the declaration of the PHE. This was followed by a steady decline through week 17 (mid-April). At the same time, prescriptions written for 28-89 days' supply were up 8.0%, while those with less than 28 days' supply were down 5.8%. Overall, 90+ days' supply claims appear to have sustained elevations demonstrated across most of the weeks in 2020.

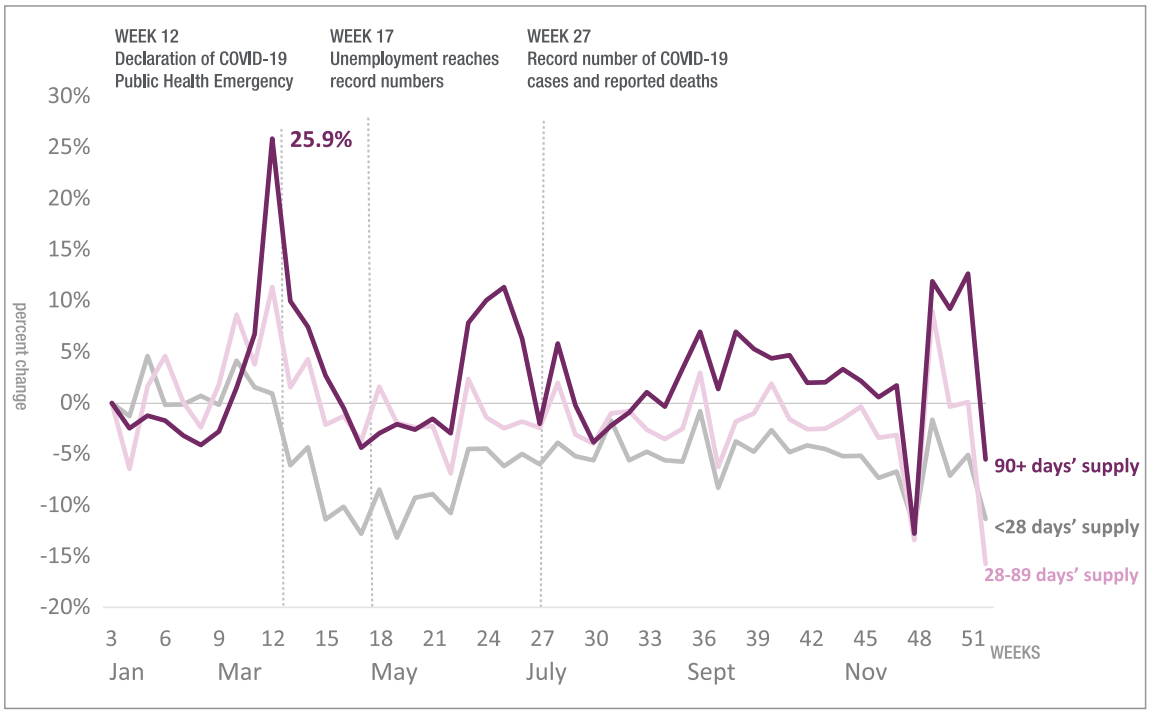
The decrease in prescription claims for less than 28 days' supply could potentially align with the observed decrease in provider visits during this time frame. Significantly fewer acute care visits contributed to lower acute prescriptions written (<28 days). This shift may indicate a pattern by prescribers to transition from shorter to longer days' supply during the timeframe. Mehrotra et al. found total ambulatory care visits had already decreased by 43% for those with Medicare compared to baseline at the time of these peak prescription claim volumes. Additionally, they note telemedicine peaked at 13.9% relative to baseline the week of April 12 for all patient populations.[4]

These findings are similar to a report stating that the share of 90-day prescriptions dispensed at retail pharmacies grew, from 19.8% in the first week of January to 23.9% in the first week of June, a few months after the initial stay-at-home order was issued. These trends then dropped to 22.9% by early August.[5]

OBSERVATION: There was increased utilization of prescription claims written for 90+ days' supply and a decrease in utilization of prescription claims for < 90 days' supply.

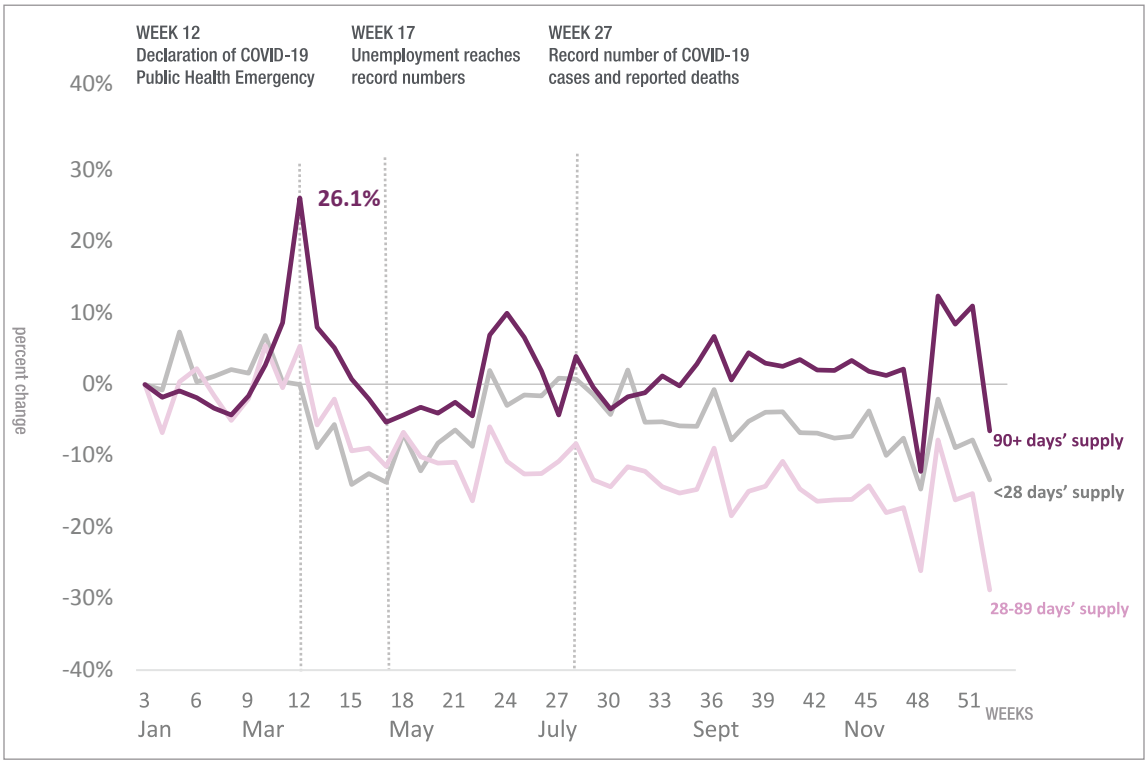
CHANGE IN OVERALL PHARMACY UTILIZATION FOR DIABETIC MEDICATION PRESCRIPTION CLAIMS BY DAYS' SUPPLY

↑25.9% for diabetes



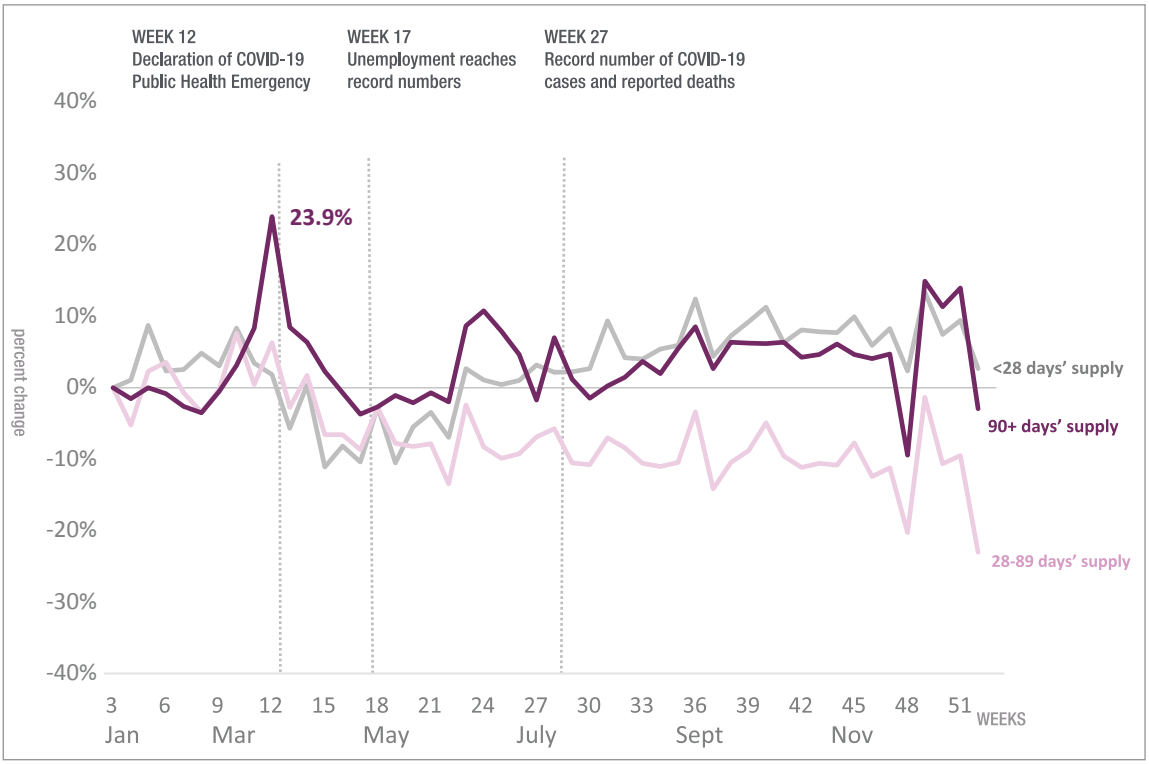
CHANGE IN PHARMACY UTILIZATION FOR RENIN ANGIOTENSIN SYSTEM ANTAGONIST (RASA) PRESCRIPTION CLAIMS BY DAYS' SUPPLY

↑26.1% for RAS antagonists



CHANGE IN PHARMACY UTILIZATION OF STATIN MEDICATION PRESCRIPTION CLAIMS BY DAYS' SUPPLY

↑23.9%
for statins



This analysis evaluated the change in weekly prescription claims volume, compared to baseline, by days' supply (<28, 28-89, and 90+) for medications used in the three Medicare Part D Star Ratings adherence measures in 2020. The medication classes included diabetes medications (except insulin), statins, and renin angiotensin system antagonists.

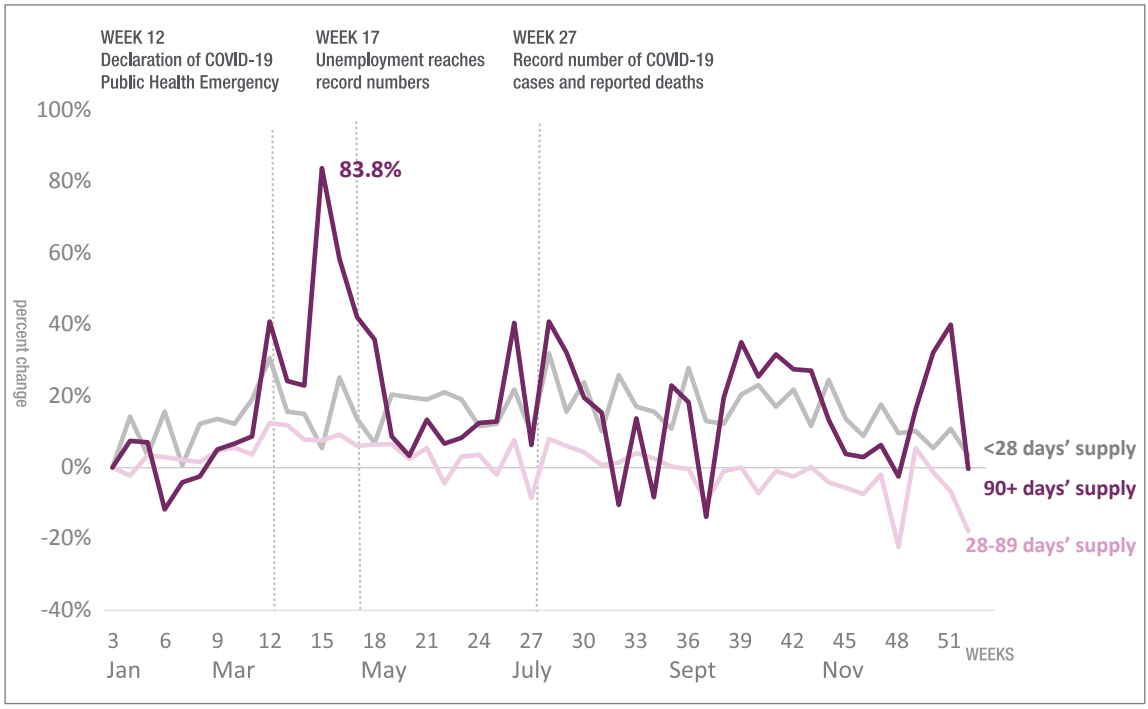
After the COVID-19 national emergency was declared and the first stay-at-home order was issued (week 12; mid-March), there was a marked increase in 90+ days' supply for medications in CMS' Medicare Part D Star Ratings system adherence measures for diabetes, high blood pressure (renin-angiotensin system [RAS] antagonists), and high cholesterol (statins).

The marked rise in extended days' supply prescription claims may subsequently inflate observed Medicare Part D adherence measure rates, which would be reflected in the 2022 Medicare Part D Star Ratings. This would align with the Evernorth 2020 Drug Trend Report, which reported higher adherence to medications for diabetes (5.0% increase), high blood pressure (3.2% increase), and high cholesterol (3.3% increase).[6]

Adherence Star Ratings using data during the pandemic will need to be evaluated for potential impact related to changes in prescribing for extended days' supply.

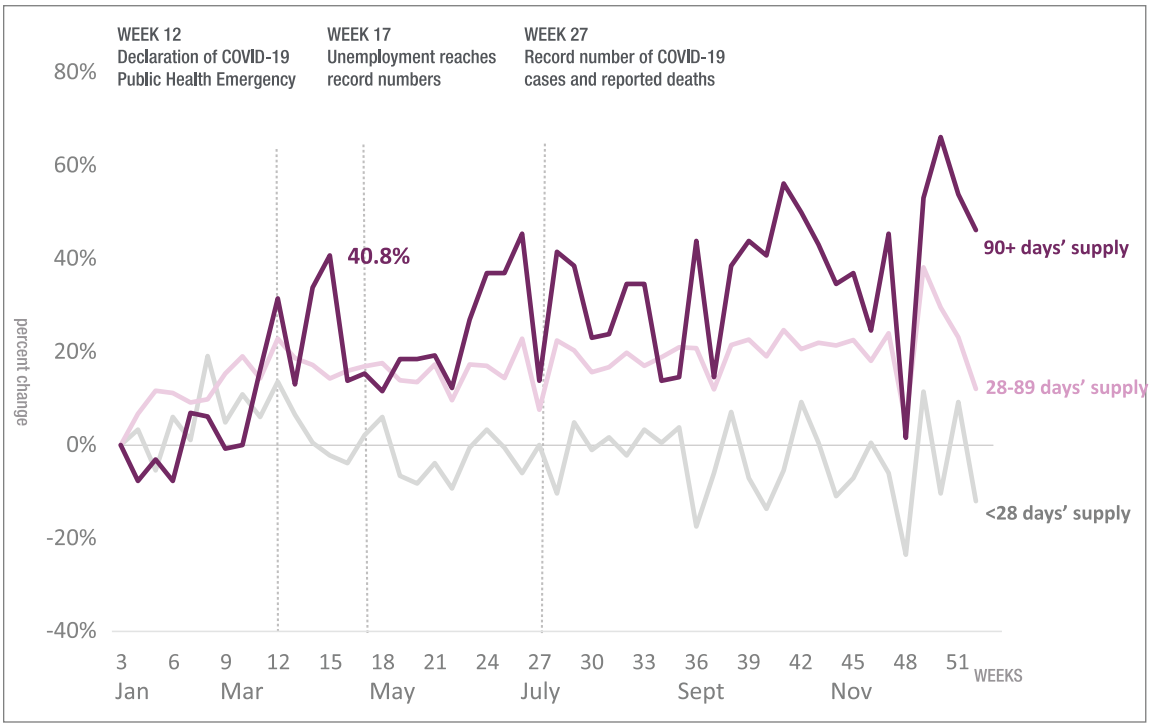
OBSERVATION: There is significant shift in volume of 90+ days' supply prescriptions, from baseline, for medications used to treat multiple sclerosis and rheumatoid arthritis.

CHANGE IN PHARMACY UTILIZATION FOR MULTIPLE SCLEROSIS MEDICATION PRESCRIPTION CLAIMS BY DAYS' SUPPLY



"Chronic medications are usually a high priority in our pharmacy and especially within the Medicare population. For our pharmacy, though, specialty medications are also a high priority. The patients taking a Multiple Sclerosis medication needed their medications now more than ever. They began needing more medication on hand than what is typically expected."
– Amy Amond, Giant Eagle

CHANGE IN PHARMACY UTILIZATION FOR RHEUMATOID ARTHRITIS MEDICATION PRESCRIPTION CLAIMS BY DAYS' SUPPLY



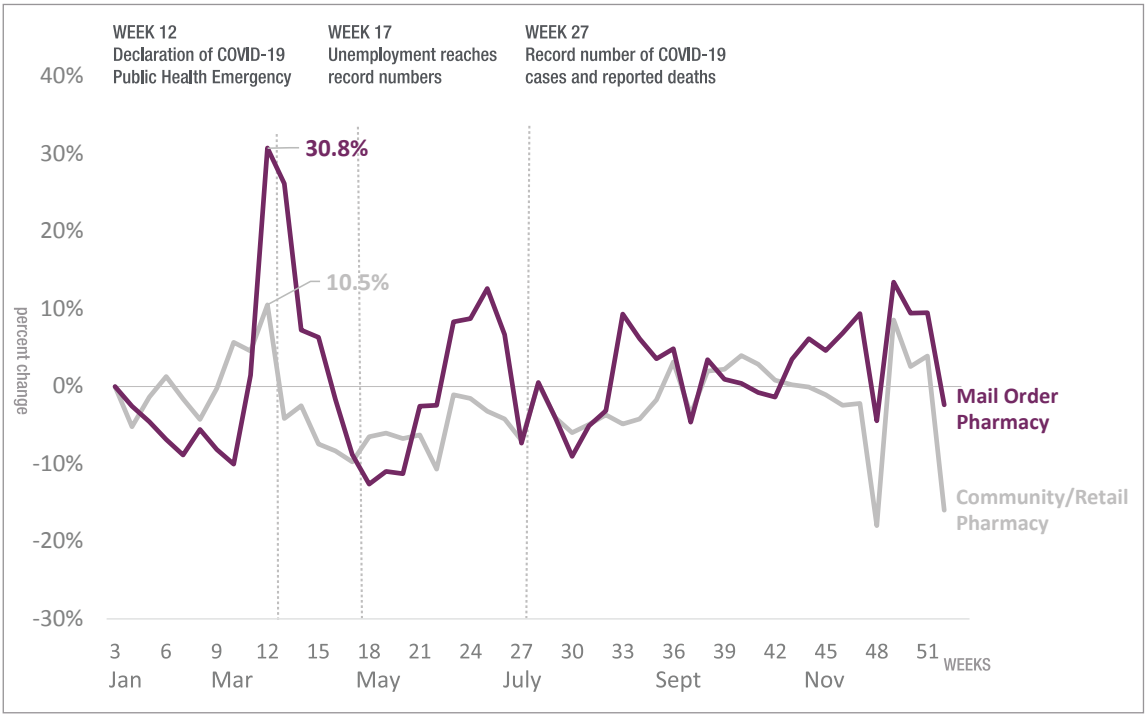
These figures display the change in weekly prescription claims volume, from baseline, by days' supply (<28, 28-89, and 90+) for medications used to treat multiple sclerosis and rheumatoid arthritis in 2020. The medication classes included non-infused biologic medications used to treat rheumatoid arthritis and non-infused disease modifying agents for multiple sclerosis.

Similar to the increase in 90+ days' supply for all prescription claims, there was an increase in 90+ days' supply for medications used for Multiple Sclerosis and Rheumatoid Arthritis. However, the increase in 90+ days' supply for MS/RA claims appears a few weeks later than that seen with all prescription claims.

The delay for individuals to shift to a 90+ days' supply for these specialty medications may be related to the ability to access specialty care providers during the pandemic. This increase in prescription claims for 90+ days' supply may also be related to changes/exemptions in benefit design during the pandemic that that allowed 90 day fills for specialty products and/or waived patient out of pocket costs for specialty medications.[7]

OBSERVATION: Pharmacy utilization place of service shifted from community/retail to mail order near the declaration of the PHE, with continued peaks of mail order utilization every subsequent 12 week internal, which aligns with the identified shift to 90+ day supply.

OVERALL PHARMACY UTILIZATION BY PLACE OF SERVICE (MAIL ORDER PHARMACY VS. COMMUNITY PHARMACY)



This analysis evaluated the change in weekly prescription claims volume, from baseline, by place of service. Place of service was identified as either mail order pharmacy or community/retail pharmacy. NCPDP's primary provider type code was used to identify place of service.

Use of mail order pharmacy was up 30.8% from baseline (week 3), compared to 10.5% for community/retail pharmacy settings. Throughout the remainder of 2020, mail order pharmacy remained a popular choice, with a greater percent change in utilization than community/retail in 30 out of the 51 weeks reported. Fluctuations (peaks and drops) in pharmacy utilization place of service seem to coincide with the shift to 90 days' supply, with elevated peaks occurring approximately every 12 weeks.

Plans may have relaxed limitations on prescription delivery for retail pharmacies that chose to offer those mail or home delivery services. Many pharmacies responded early in the pandemic by providing free delivery to members. With stay-at-home orders and in the absence of a vaccine, members may have been eager to leverage ways to access medications without entering the pharmacy.

According to a press release from *Wall Street Journal*, mail order prescriptions increased by 21% during the last week in March 2020 compared to the previous year.[8] Similarly, CoverMyMeds reported an increase in patient utilization of mail order from 18% (December 2019) to 25% (May 2020) in their 2021 Medication Access Report based on a patient survey of 1,000 responses across the US.[9]

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CHAPTER 2

Utilization Patterns Among Hypothesized Treatments for COVID-19

BACKGROUND: As mentioned in Chapter 1, the United States government and regulatory bodies had a multifaceted response to the COVID-19 PHE. Across several graphs, vertical lines illustrate significant national events related to the COVID-19 pandemic that may have influenced patterns of prescription utilization. In addition to key national events, medication specific events that may have contributed to modified pharmacy utilization are noted where applicable. Medication shortages and access issues, the rapid evolution of scientific evidence for treatment and/or prevention of COVID-19, and relaxed prescribing restrictions likely had a significant impact on utilization in four key medication groups (albuterol, hydroxychloroquine, azithromycin+ hydroxychloroquine and dexamethasone) throughout the pandemic.

As previously noted by Dr. Bookwalter in *Drug Shortages Amid the COVID-19 Pandemic*, *"The spread of COVID-19 to the level of a global pandemic impacted the acquisition of raw material and caused manufacturing shutdowns around the world." She continues on to say, "With factory doors closed and COVID-19 a global threat, supplies start to run low. Not knowing when and where the next COVID-19 surge will occur, everyone is trying to be prepared. Pharmacies prepare by managing the inventory of critical drugs required for providers to adequately treat the virus."* [1]

Chapter 2 of the PQS Trend Report, evaluated pharmacy utilization for unique medications identified as likely to have modified utilization in 2020, based on the hypothesized roll in COVID-19 treatment or prevention. The figures provide the week-over-week change in prescription claims, compared to baseline, by specific medication. The analysis starts at week 3 (baseline) of the year to minimize the impact of prescription claims variability due to health care coverage changes. The variability was likely due to health care coverage changes which were associated with the start of the new calendar year and not COVID-19 related. Where applicable previous year pharmacy utilization is also included for reference.

"As soon as evidence surfaces to support a potential treatment, pharmacies begin procuring the drug, and global demand starts to increase. Some drugs that have been in high demand in association with COVID-19 include albuterol metered-dose inhalers (MDIs), azithromycin, hydroxychloroquine and chloroquine, and sedation medications."
– Dr. Bookwalter

CHAPTER 2

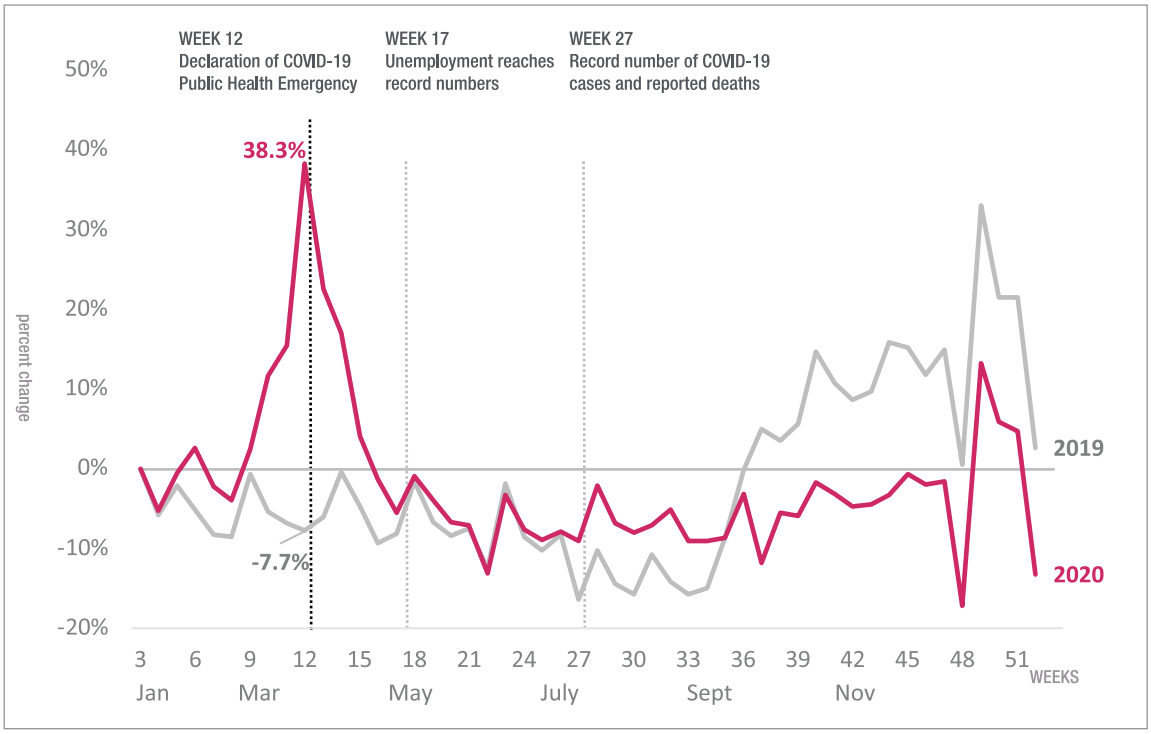
Key Highlights

- Albuterol, hydroxychloroquine, and azithromycin + hydroxychloroquine utilization peaked near the time of the declaration of the public health emergency.
- Increased hydroxychloroquine utilization was sustained throughout most of 2020.
- Overall utilization of hydroxychloroquine was markedly increased in 2020, for patients with and without prior use.
- Prescription claims for hydroxychloroquine, although increased overall, tended to be written for shorter days' supply more than 90+ days' supply.
- There was an increase in utilization of combination hydroxychloroquine and azithromycin in 2020.
- Dexamethasone utilization increased in the last half of 2020.

OBSERVATION: Albuterol utilization peaked near the declaration of the PHE (weeks 12) with substantial drop in utilization between weeks 12 thru 17 levels. Lower utilization was sustained throughout most of 2020.

CHANGE IN OVERALL ALBUTEROL* UTILIZATION IN 2020

WEEK 12
First FDA alert on albuterol shortage



levalbuterol included in analysis

This analysis evaluated the change in week-over-week prescription claims, from baseline, for albuterol and levalbuterol in 2020 (previous year included for reference).

Reports indicate that albuterol was one of the most widely obtained COVID-19 relevant drugs prior to the pandemic.[2] The current analysis indicates an almost 40% increase in prescription claims for albuterol in 2020. This may be related to previous albuterol users with general concern about access to medications or loss of employment that would make acquiring the medication more difficult. Increased utilization of albuterol may also be related to the hypothesis that its use may provide symptomatic relief in COVID-19 infections.

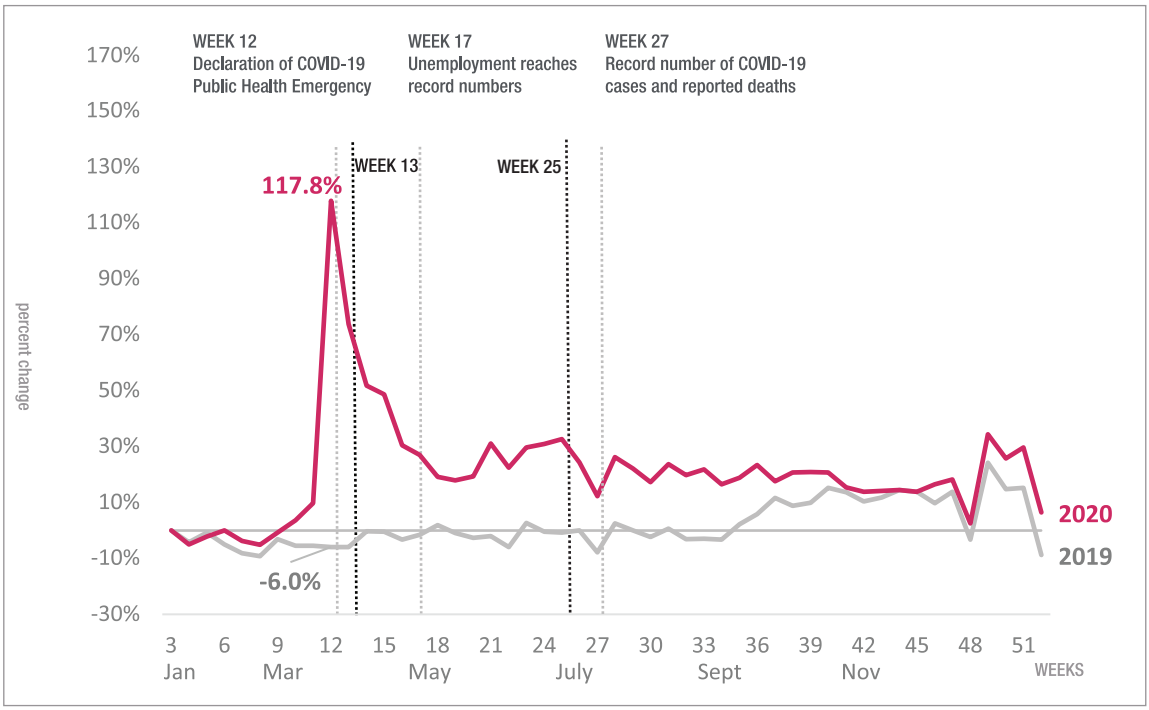
Although spikes in utilization are seen in early 2020, pharmacy utilization of albuterol drops sharply near week 13 and is depressed throughout most of 2020. The observed decrease is likely multifactorial: increased utilization of 90+ days' supply, decreased in-person provider encounters, a lag in the provisions of telehealth visits, and increased use of mail order or medication synchronization programs may all have contributed. For individuals with discontinued employment during the pandemic, the loss of employer sponsored insurance (ESI) may also decrease overall pharmacy utilization. However, it it less likely to be a significant contributor to the Medicare population.[3] Finally, in Spring 2020, albuterol shortages were first reported, which lasted throughout the year and likely contributed to the decreased utilization seen through most of 2020.[4]

OBSERVATION: Change in overall utilization of HCQ was increased throughout 2020.

CHANGE IN OVERALL HYDROXYCHLOROQUINE (HCQ) UTILIZATION IN 2020

WEEK 13
Approval for HCQ use in COVID-19

WEEK 25
EUA for HCQ retracted by FDA



This analysis evaluated the change in week-over-week prescription claims, compared to baseline, for hydroxychloroquine in 2020 (previous year included for reference).

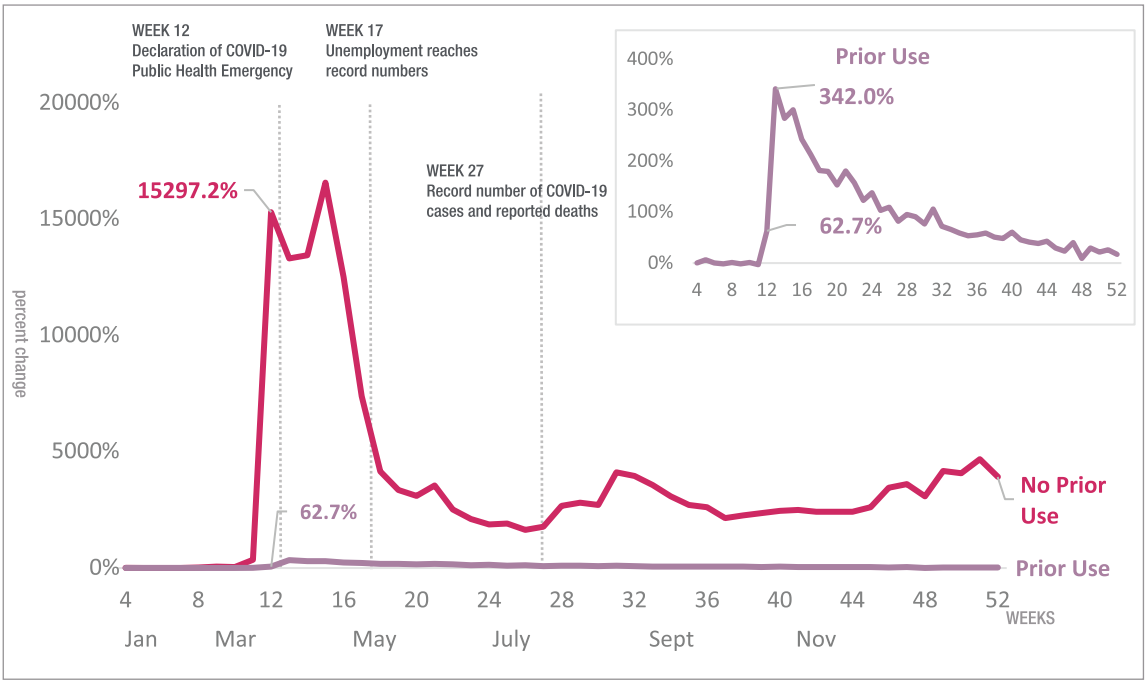
In early March 2020, the FDA approved hydroxychloroquine emergency use authorization (EUA) for COVID-19 treatment based on data available at the time. Of note, HCQ dosing for COVID-19 in 2020 was unclear. However, this EUA was subsequently revoked by the FDA in June 2020, citing a lack of efficacy or improved mortality data.[5]

There was a significant spike in HCQ utilization in March 2020, related to the FDA EUA and increased demand for "on-hand" HCQ by individuals. Utilization of HCQ dropped precipitously around April, and continued to taper off, reaching previous year utilization levels near the end of 2020. Residual elevations in claims for HCQ can be seen throughout most of 2020, likely as individuals continue to believe in potential benefit of the medication, regardless of lack of evidence to support use. Also, several plans commented there were concerns of potential shortages of HCQ for their members stabilized on the medication for rheumatoid arthritis. Plans addressed this by adjusting copays for branded products, to ensure access for those who could not afford brand copays. This also may have contributed to sustained elevated utilization of HCQ throughout most of 2020.

In Spring 2020, there was a drop in HCQ utilization which is likely related to updated information about the safety and efficacy of HCQ in COVID-19 and the subsequent reversal of the FDA EUA approval for use in COVID-19 in June 2020. Another consideration related to lower pharmacy utilization is that many individuals lost access to their employer sponsored insurance (ESI) in early 2020, which could manifest into an inability to afford necessary medications while unemployed and without ESI.[3] However, loss of ESI is unlikely to have a significant impact on the Medicare population being evaluated.

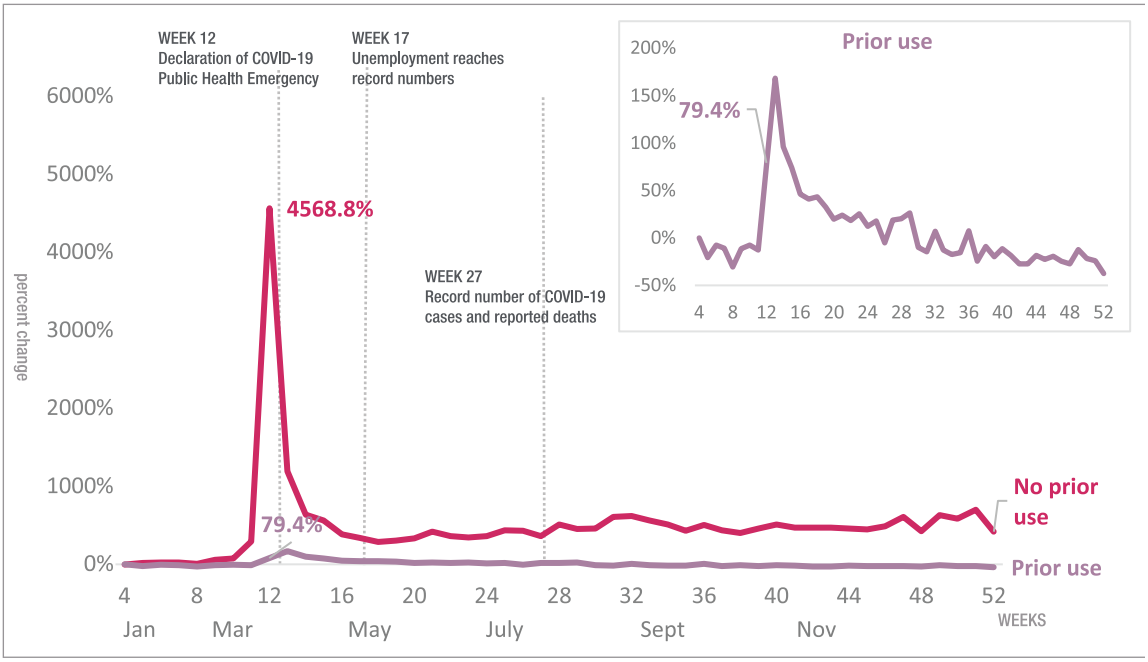
OBSERVATION: There was an overall increase in utilization for HCQ for those with prior use and those without prior use.

CHANGE IN HYDROXYCHLOROQUINE UTILIZATION FOR CLAIMS WITH ≤ 14 DAYS' SUPPLY (prior use* vs. no prior use)

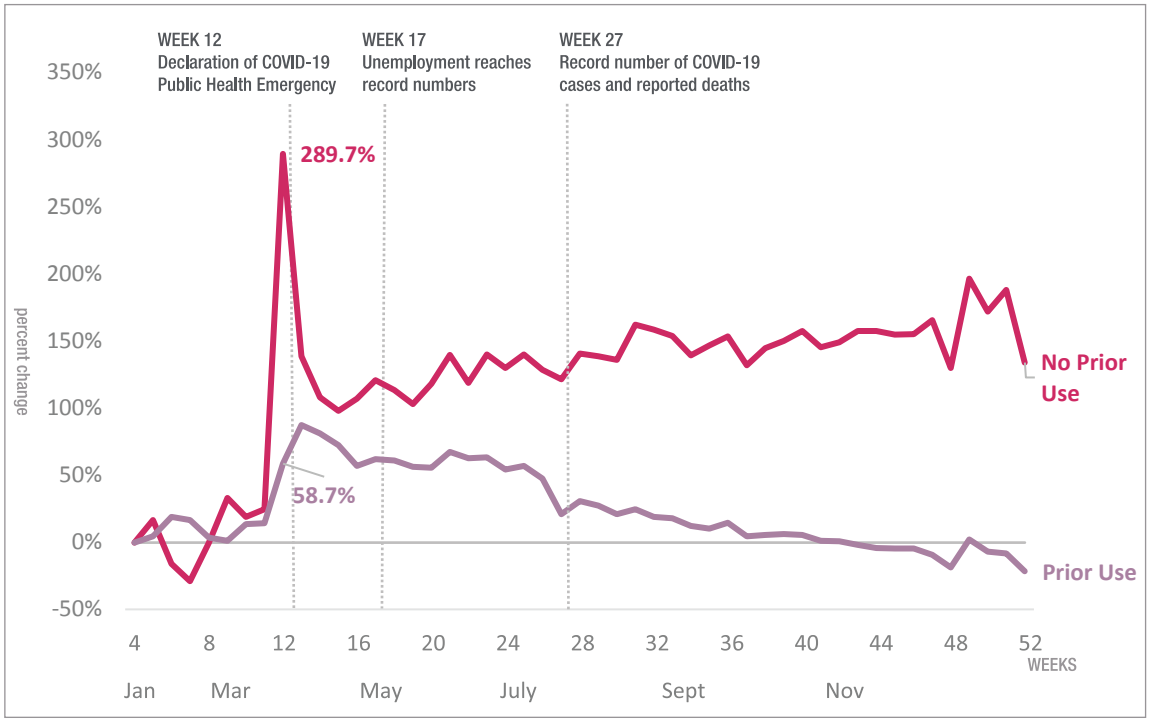


**Prior use is defined as any individual having at least one claim for HCQ from January 2019 through January 2021. Individuals without any claims for HCQ from January 2019 through January 2021 were counted in No Prior Use.*

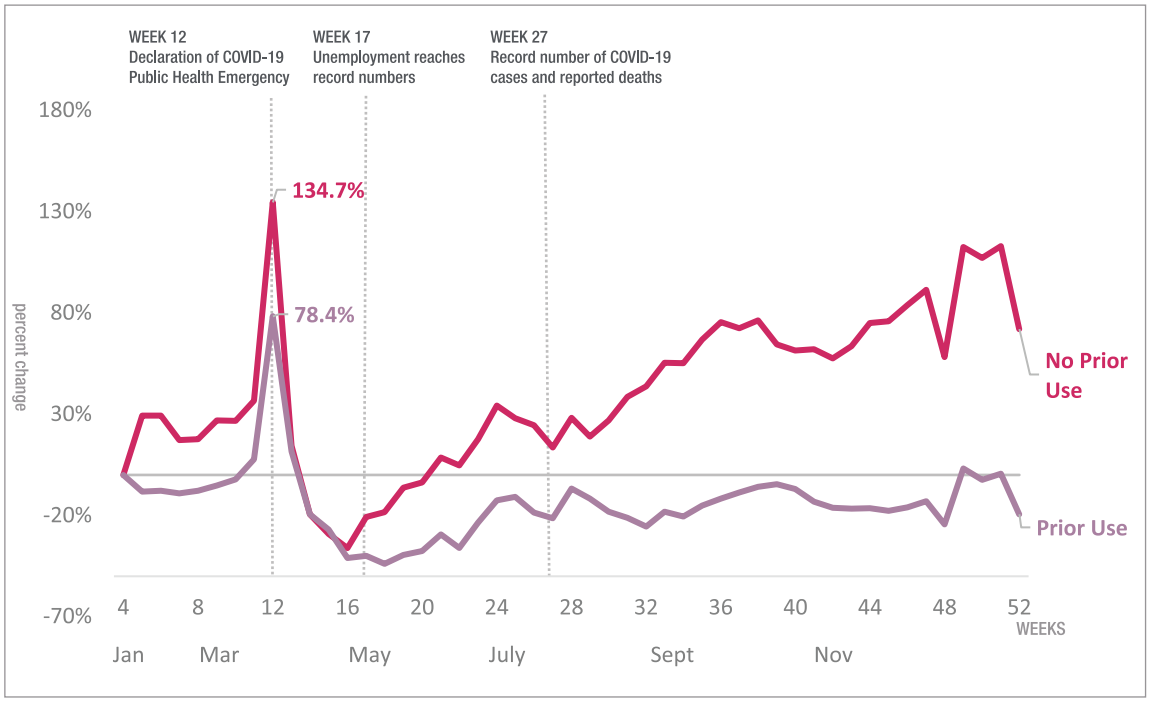
CHANGE IN HYDROXYCHLOROQUINE UTILIZATION FOR CLAIMS WITH 15-27 DAYS' SUPPLY (prior use* vs. no prior use)



CHANGE IN HYDROXYCHLOROQUINE UTILIZATION FOR CLAIMS WITH 28-89 DAYS' SUPPLY (prior use* vs. no prior use)



CHANGE IN UTILIZATION OF HYDROXYCHLOROQUINE CLAIMS WITH 90+ DAYS' SUPPLY (prior use* vs. no prior use)



This analysis evaluated the change in weekly prescription claims volume, from baseline, for hydroxychloroquine by various days' supply (≤ 14, 15-27, 28-89, and 90+).

There was a lack of consensus around appropriate dosing of HCQ for COVID-19, so various days' supply considerations were evaluated. Prescription claims with prior use were compared to claims without prior use, to assess likely "new starts" of hydroxychloroquine treatment in 2020. "Prior use" is defined as any individual having at least one claim for HCQ from January 2019 through January 2021. Individuals without any claims for HCQ from January 2019 through January 2021 were counted in No Prior Use.

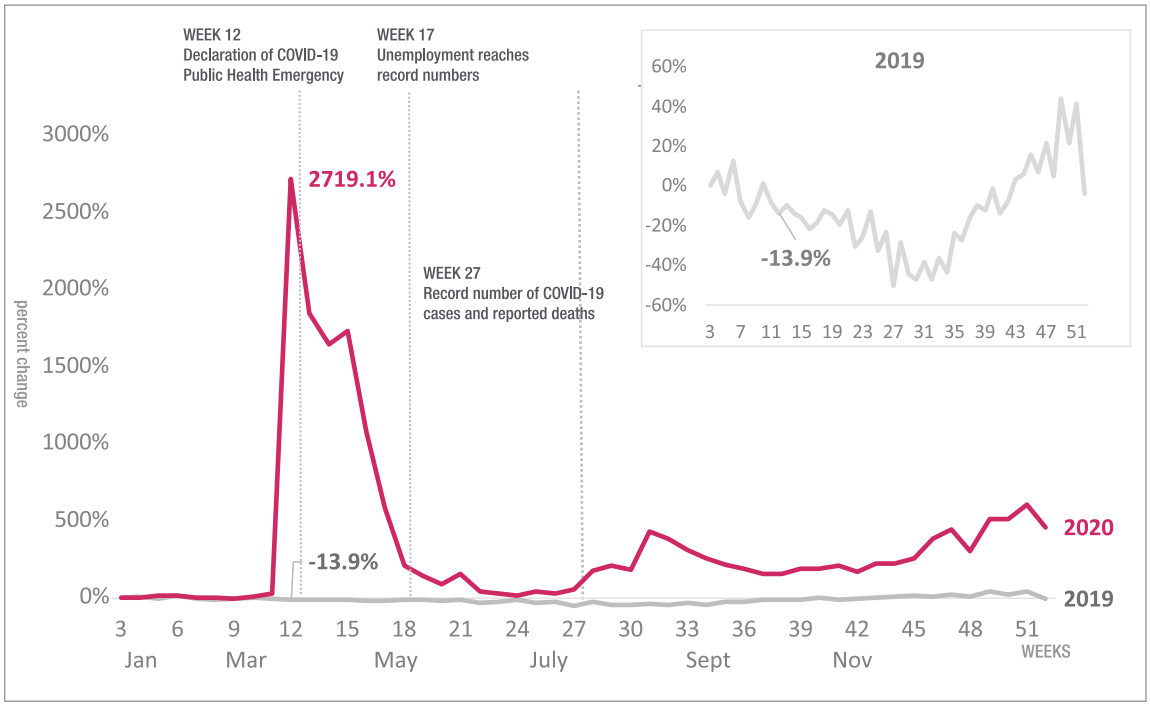
There was an overall increase in the volume of prescription claims for HCQ for those with no prior use across all days' supply, with significant increases seen in claims written for ≤28 days' supply. This indicates that shorter courses of therapy tended to be used for new HCQ prescriptions.

Increased utilization was also seen for new HCQ claims written for ≥28 days' supply, but these were much smaller than those identified in the ≤ 28 days' supply group. Also, utilization was increased in those with prior utilization of HCQ. Notably, the utilization pattern appears similar between the prior use and no prior use group, particularly near week 12, when the EUA for HCQ was approved. A continued gradual increase in new HCQ utilization for 90+ days' supply is observed for both groups throughout 2020. This may be related to increased provider visits (both in person and virtual) beginning in mid-2020, relaxed clinical edits for HQC by payers, and potential concerns about continued access to treatment. Additionally, utilization of medications used for rheumatoid arthritis and lupus, both conditions that hydroxychloroquine is approved for use, tend to increase in the spring and winter and is demonstrated by the trend.[6,7]

Overall, HCQ utilization spiked near the declaration of the PHE (weeks 12) for all categories evaluated and then dropped near week 16. The utilization of HCQ had a significant spike in March 2020, likely related to the FDA EUA and increased demand for "on-hand" HCQ by individuals. Residual elevations in claims for HCQ can be seen throughout most of 2020, likely as individuals continue to believe in potential benefit of the medication, regardless of lack of evidence to support use and the removal of EUA from FDA in June 2020.

OBSERVATION: There was significant increase in combined use of azithromycin + hydroxychloroquine at the time of the PHE. Elevated utilization was sustained throughout 2020.

CHANGE IN OVERALL UTILIZATION OF AZITHROMYCIN + HYDROXYCHLOROQUINE



This analysis evaluated the change in weekly prescription claims volume for combined azithromycin + hydroxychloroquine use, from baseline, in 2020 (previous year included for reference).

Azithromycin + hydroxychloroquine prescription claims were identified by the following process:

1) Identification of unique patients, by week, that had at least one hydroxychloroquine fill in the calendar year(s).

2) Identification of unique patients, by week, that had at least one azithromycin fill during the same week and year as hydroxychloroquine, in the calendar year(s).

This identified combined use of hydroxychloroquine and azithromycin based on the numerical week of the year. It does not indicate that that the combined use was within +/- seven days of each other on a rolling basis. For example, a hydroxychloroquine claims on January 4, 2020 (week 1) and an azithromycin claim on January 5, 2020 (week 2) would not be counted. The change in utilization is based on percent difference from baseline (week 3) of the year.

There was an increase in overall azithromycin + hydroxychlorquine utilization around week 12 of 2020, that declined rapidly to previous utilization rates near week 22.

There was speculation that azithromycin has anti-inflammatory properties that could reduce cytokine levels and prevent progression of COVID-19, but subsequent research did not support this hypothesis.[8]

OBSERVATION: utilization for dexamethasone was increased beginning in July 2020 and sustained through most of 2020.

CHANGE IN OVERALL UTILIZATION OF DEXAMETHASONE

WEEK 26
Recovery trial preliminary report

WEEK 36
WHO Treatment Guidance Issued

This analysis evaluated the change in weekly prescription claims for dexamethasone, from baseline, in 2020 (previous year included for reference).

The utilization of dexamethasone for 2020 appears unremarkable until mid-2020 when evidence began to support use of the dexamethasone to reduce mortality in COVID-19 patients receiving respiratory support (oxygen or ventilation).[9] In Sept. 2020 the WHO issued interim guidance on the use of dexamethasone for the treatment of COVID-19. The guidance recommended:

1) Corticosteroids be given orally or IV for the treatment of patients with severe and critical COVID-19.

2) Against the use of corticosteroids in treatment of patients with non-severe COVID-19, unless the patient is already taking the medication for another condition.[10]

Utilization patterns seem to indicate that use of dexamethasone increased, likely in a population of patients not necessarily recommended to use the product. Those with severe or critical COVID-19 illness would likely be hospitalized and would not receive the prescription from the community or retail pharmacy. This likely indicates that prescribing of dexamethasone, outside of standards of care and recommendations from WHO, increased in late 2020.

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CHAPTER 3

Medication Utilization Patterns Impacted by COVID-19

BACKGROUND: Chapter 3 of the PQS Trend Report broadly evaluates utilization patterns of medication classes likely indirectly impacted by the COVID-19 pandemic. An environmental scan identified three key medication classes for additional scrutiny; anticoagulants, antidepressants and antibiotics. An increased risk for blood clots with COVID-19 infection, coupled with updates to atrial fibrillation treatment guidelines in 2019, supported closer examination of anticoagulants. Likewise, efforts to mitigate the pandemic's impact on mental health encouraged closer evaluation of antidepressant utilization patterns. Lastly, with public health safety measures implemented to decrease transmission of diseases, antibiotic utilization patterns were evaluated.

The figures included in Chapter 3 represent the week-over-week change in prescription claims compared to baseline. The analysis starts at week 3 (baseline) of the year to suppress the inclusion of prescription claims variability likely due to health care coverage changes associated with the start of the new calendar year and not COVID-19 related. Where applicable, previous year pharmacy utilization is also included for reference.

CHAPTER 3

Key Highlights

- Near the time of the declaration of the PHE, there is an isolated increase in antidepressant[1] utilization followed by a sustained decrease.
- In 2020, DOACs[2] and warfarin experienced peak utilization near the declaration of the PHE; after hitting the peak, warfarin demonstrated a steady overall decrease in utilization, while DOAC utilization remained consistent.
- Starting in early spring 2020, there is a sharp decrease in antibiotic[3] utilization.

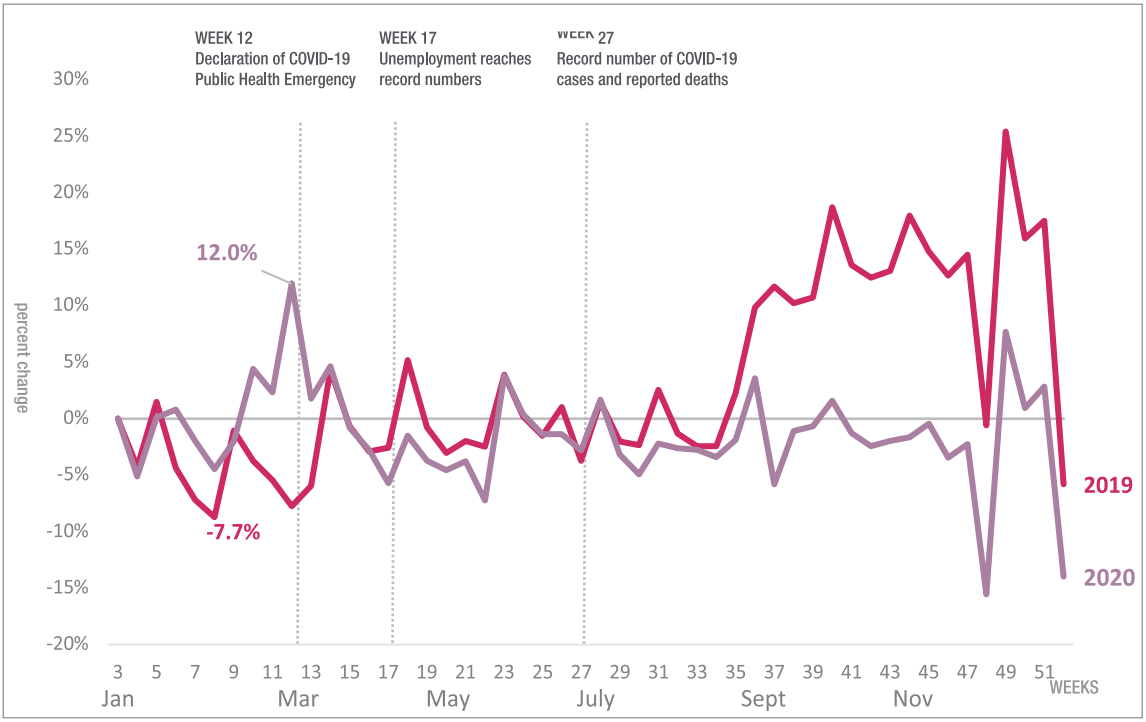
[1]*Antidepressant classes include selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs)*

[2]*DOACs include apixaban, rivaroxaban, edoxaban, and dabigatran*

[3]*Antibiotic classes include cephalosporins, fluoroquinolones, tetracyclines, macrolides, and penicillins*

OBSERVATION: Antidepressant utilization peaked near the declaration of the COVID-19 PHE, then dropped and maintained depressed utilization rates throughout the rest of 2020.

CHANGE IN OVERALL ANTIDEPRESSANT UTILIZATION



This analysis evaluated the change in weekly prescription claims volume, compared to baseline, for antidepressants in 2020. The medication classes included are selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs).

In April 2020, Express Scripts published the *America's State of Mind Report* stating that the number of prescriptions filled per week for antidepressants increased 14.8% between February 16 and March 15, 2020. Additionally, their data showed 78% of prescriptions filled for mental health medications, defined as treatments for depression, anxiety, and insomnia, during the week of March 15, 2020 were new prescriptions.[1] In March 2021, an updated report showed an overall increase of 7.9% in antidepressant utilization between 2019 and 2020. Furthermore, 32.1% of people taking antidepressants in 2020 had no history of antidepressant use six months prior to their first antidepressant prescription in 2020.[2] These reports suggest the scale of the pandemic's impact on mental health indicating a need to further analyze antidepressant prescription claims.

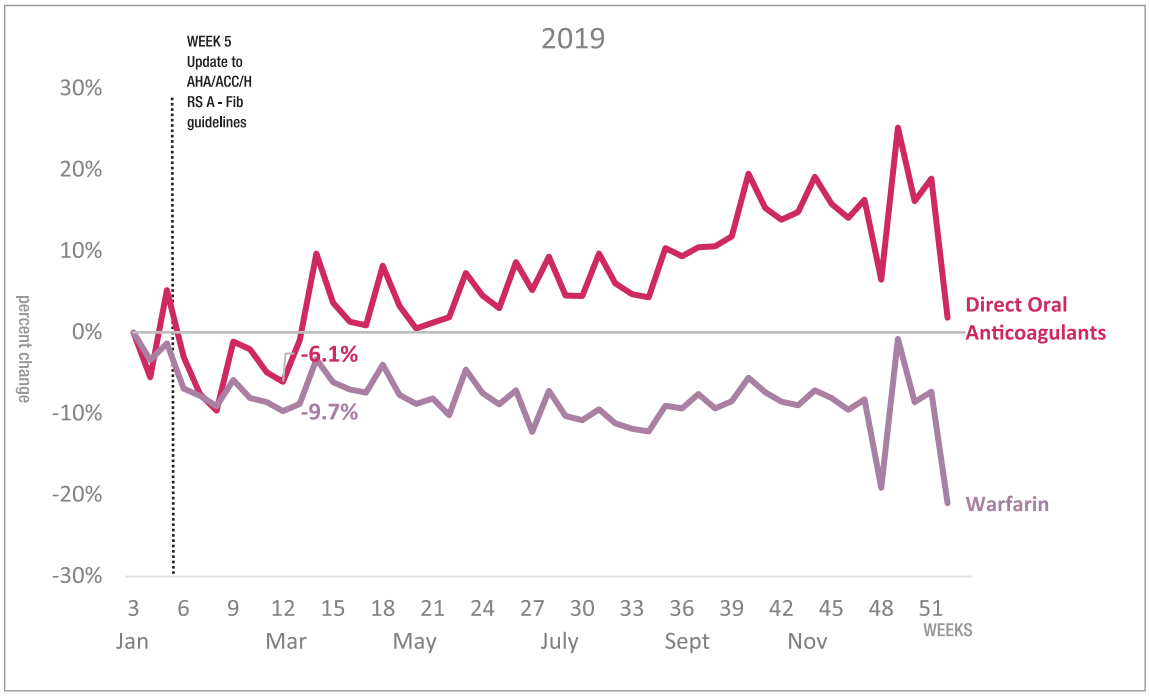
Evaluating the change in antidepressant utilization, an almost 12% increase in prescription claims from baseline is noted near the beginning of the COVID-19 PHE.

This initial peak at week 12 coincides with the 14.8% increase in antidepressant utilization between February 16 and March 15, 2020 reported in the *America's State of Mind Report*.[1] After the initial peak, there are subsequent peaks of prescription claims approximately every 90 days. The observed decrease in pharmacy utilization may be due to increased utilization of 90+ days' supply.

Furthermore, CMS data shows that, between March 2020 and October 2020, beneficiaries have decreased utilization of primary, preventative, and mental health care visits due to the COVID-19 PHE.[3] Compared to the previous year's data, CMS noted a 22% decline in mental health service utilization in adults aged 19-64. A decrease in routine appointments with mental health prescribers could result in decreased prescriptions. Even though policies were implemented requiring modified and flexible insurance coverage of mental health services in 2020,[4] the current analysis does not indicate that these changes increased utilization of antidepressants.

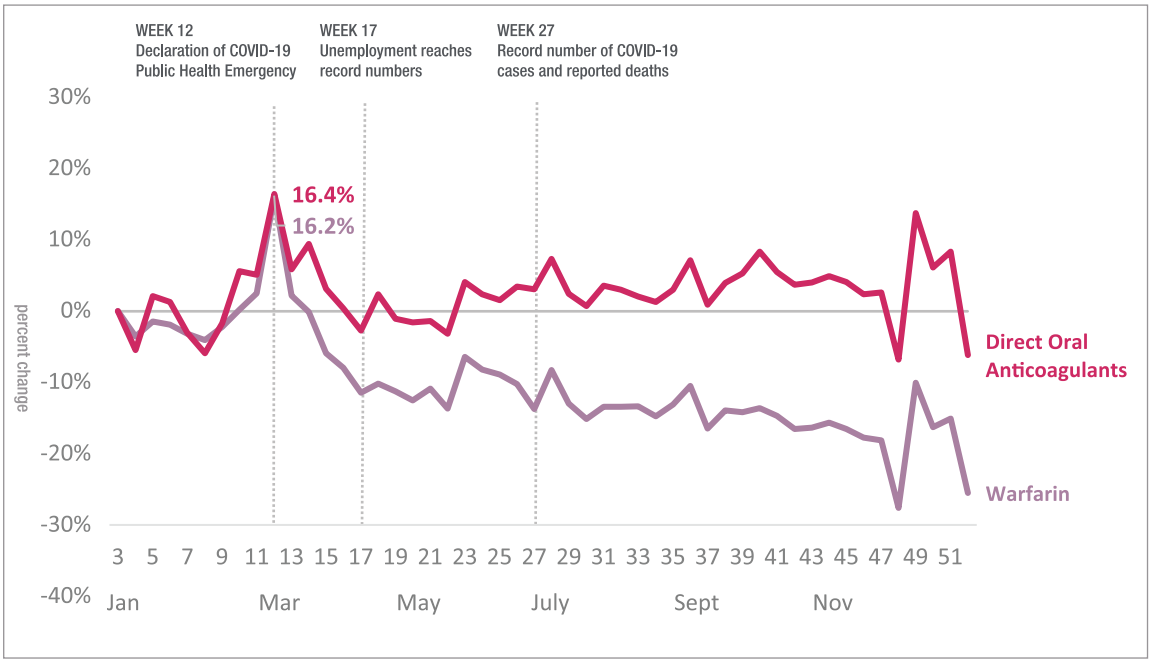
OBSERVATION: During 2019, direct oral anticoagulants (DOAC) utilization steadily increased while warfarin utilization decreased.

CHANGE IN DOACS AND WARFARIN UTILIZATION DURING 2019



OBSERVATION: During 2020, DOAC and warfarin utilization peaked near the declaration of the COVID-19 PHE. While warfarin utilization dropped throughout the rest of the year, DOAC utilization remained fairly consistent.

CHANGE IN DOACS AND WARFARIN UTILIZATION DURING 2020



The analyses evaluated the change in weekly prescription claims volume, compared to baseline (week 3), for warfarin and direct-acting oral anticoagulant (DOAC) medications in 2019 and 2020.

In January 2019, the American Heart Association/American College of Cardiology/ Heart Rhythm Society (AHA/ACC/HRS) Atrial Fibrillation guidelines were published and recommend DOACs over warfarin in patients with atrial fibrillation.[5]

Furthermore, a recent study found an increase in anticoagulant sales globally. On average, anticoagulant sales increased annually by 6%, including a 26% increase in direct oral anticoagulants (DOACs) and an 8% decrease in warfarin. Not only was an annual increase noted, the data also represented an increase in DOACs during March 2020. This led authors to speculate that patients who require chronic DOAC use could have hoarded medications in the early months of the COVID-19 pandemic.[6]

In 2019, there was sustained, gradual increase in DOAC utilization and decreased warfarin utilization. This suggests a shift towards increased initiation of DOACs as first line treatment of anticoagulation disorders and atrial fibrillation, and perhaps a trend to convert from warfarin to DOACS in patients on existing anticoagulation therapy.

The update to the AHA/ACC/HRS Atrial Fibrillation guidelines in early 2019, strongly recommending the use of DOACs over warfarin for atrial fibrillation, could have contributed to the difference in warfarin and DOACs utilization seen in the graph above.[5]

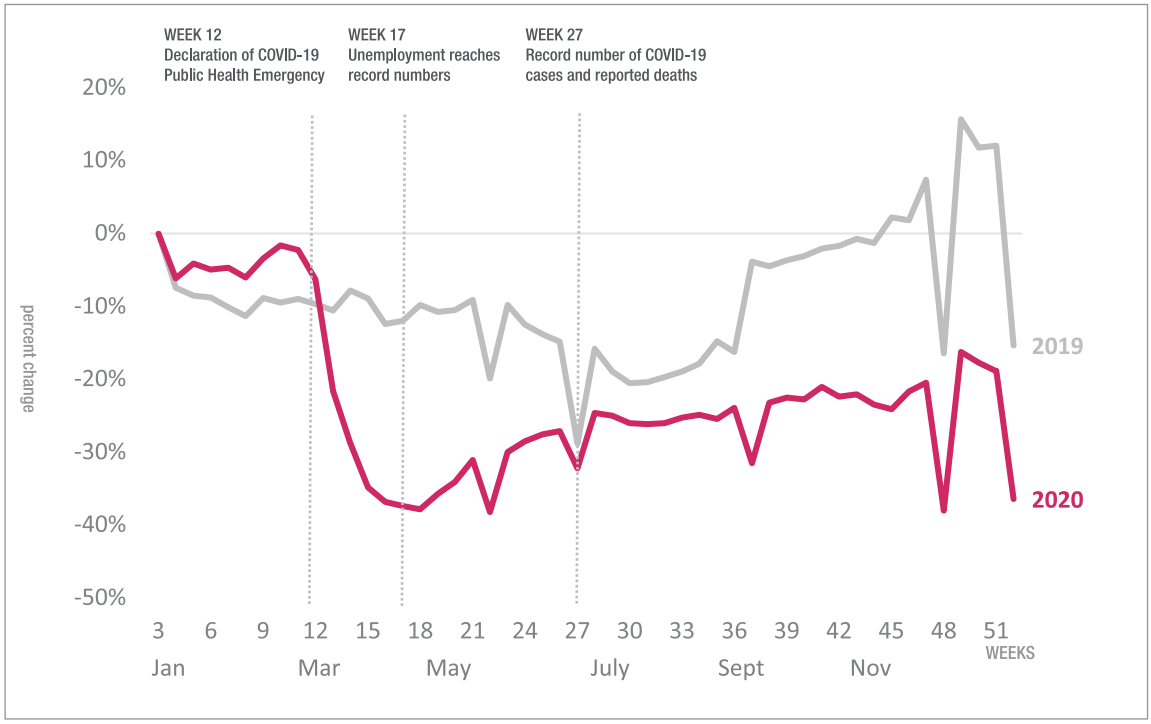
In 2020, peak utilization of both DOACs and warfarin occurred near the declaration of the COVID-19 PHE. Following peak utilization, DOACs experienced a minor change in utilization throughout the rest of the year, while warfarin experienced a steady decline in utilization from baseline. A recent study evaluating anticoagulant global sales trends demonstrated an increase in anticoagulant sales in 2020 and specifically an increase in DOAC sales in March 2020, which coincide with the prescription claims analyses above.[6]

Increased utilization of anticoagulants can be explained in part by initial COVID-19 studies which indicated an increased risk of thromboembolism (TE), including venous thromboembolism (VTE), in patients with COVID-19.[7] While initial studies focused on rates of occurrence, newer studies led to the recommendation that anticoagulation therapy should be utilized in hospitalized COVID-19 patients[8], which may relate to the increased outpatient utilization trends found.

An additional consideration for correlating decreased utilization of warfarin with increased utilization of DOACs is warfarin therapy's requirement for frequent lab testing of the international normalized ratio (INR). Historically, patients on warfarin therapy would require in-person visits to laboratory centers, physician offices, or health systems to monitor their INR. With the PHE and increased "stay at home" orders across the country, a shift to DOAC use is reasonable, as the requirement for in-person monitoring isn't needed.

OBSERVATION: Decreased overall antibiotic prescription claims near the declaration of the COVID-19 PHE, with continued depression throughout 2020.

CHANGE IN OVERALL ANTIBIOTIC PRESCRIPTION UTILIZATION



This analysis evaluated the change in weekly prescription claims volume, compared to baseline, for antibiotics in 2020.

Lastly, with public health measures including social distancing, mask-wearing and sanitizing efforts, impact on antibiotic utilization patterns were evaluated as decreased use of antibiotics was expected. Recent available data demonstrate a 10% decrease in adult primary care visits. Decreased healthcare provider visits reduce the opportunity to prescribe antibiotics,[9] which is apparent when evaluating the change in overall antibiotic prescription utilization for 2020.

Additionally, overall infection rates were low in 2020. The CDC reported 1,316 positive flu cases between September 2020 and January 2021; during the same period the previous year, the CDC reported approximately 130,000 cases.[10]

Additional data shows that the number of physician visits during the last three months of 2020 was 5% to 6% lower than the average amount of visits from during those respective months in 2016 to 2019. Furthermore, the data shows an overall 10% decrease in volume of adult primary care visits in 2020.

A reduction in physician office visits decreased opportunities for prescribers to issue antibiotic prescriptions and likely contributed to the observed decrease in overall antibiotic utilization in 2020.[9]

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