

Brief Report

Prescription Filling Patterns of Evidence-Based Medical Therapies for Heart Failure During the COVID-19 Pandemic in the United States

MUTHIAH VADUGANATHAN, MD, MPH,¹ DIANE LI, BA,² JEROEN VAN MEIJGAARD, PHD,² AND HAIDER J. WARRAICH, MD^{1,3}

Boston, Massachusetts; and Santa Monica, California

ABSTRACT

Background: Maintaining a steady medication supply during a public health crisis is a major health priority. We leveraged a large U.S. pharmacy-claims database to understand the use of evidence-based therapies in heart failure (HF) care during the coronavirus disease-2019 (COVID-19) pandemic.

Methods: We analyzed 27,027,650 individual claims from an all-payer pharmacy-claims database across 56,155 chain, independent and mail-order pharmacies in 14,164 zip codes in 50 states. Prescriptions dispensed (in 2-week intervals) of evidence-based HF therapies in 2020 were indexed to comparable timeframes in 2019. We normalized these year-to-year changes in HF medical therapies relative to those observed with a stable basket of drugs.

Results: Fills of losartan, lisinopril, carvedilol, and metoprolol all peaked in the weeks of March 2020 and demonstrated trajectories thereafter that were relatively consistent with the reference set of drugs. Fills of spironolactone (+4%) and eplerenone (+18%) showed modest trends toward increased relative use during 2020. Fills of empagliflozin (+75%), dapagliflozin (+65%) and sacubitril/valsartan (+61%) showed striking longitudinal increases throughout 2020 that deviated substantially from year-to-year trends of the overall basket of drugs. For all 3 therapies, fills of all quantity sizes increased relatively throughout 2020. For both generic and brand-name therapies, prescription fill patterns from mail-order pharmacies increased substantially over expected trends beginning in March 2020.

Conclusion: Prescription fills of most established generic therapies used in HF care were maintained, whereas those of sacubitril/valsartan and the sodium-glucose cotransporter-2 inhibitors steeply increased during the COVID-19 pandemic. These nationwide pharmacy claims data provide reassurance about therapeutic access, during a public health crisis, to evidence-based medications used in HF care. (*J Cardiac Fail* 2021;27:1280–1284)

Key Words: COVID-19, generic, heart failure, prescription fills, guideline-directed medical therapy.

Maintaining a steady medication supply during a public health crisis is a major health priority. Patients with

chronic medical conditions such as heart failure (HF) face heightened risks with coronavirus disease 2019 (COVID-19),¹ but the pandemic may have indirect consequences, even for noninfected individuals whose routine medical care and therapeutic access are disrupted.² Uncertainties regarding the safety of angiotensin-converting enzyme inhibitors (ACEis) and angiotensin receptor blockers (ARBs) have further complicated routine HF care.³ However, in parallel with this global disruption, discovery science and care innovation in HF accelerated in 2020, and there is growing support for the initiation and maintenance of multidrug regimens to slow disease progression in HF with reduced ejection fraction. We leveraged a large U.S. pharmacy-claims database to understand the use of

From the ¹*Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, Massachusetts;* ²*GoodRx, Santa Monica, California and* ³*Department of Medicine, VA Boston Healthcare System, Boston, Massachusetts.*

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Reprint requests: Muthiah Vaduganathan, MD, MPH, Brigham and Women's Hospital Heart & Vascular Center and Harvard Medical School, 75 Francis Street, Boston, MA 02115. Tel: (617) 525-7053; Fax: (617) 264-5265. E-mail: mvaduganathan@bwh.harvard.edu

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evidence-based therapies in HF care before and during the COVID-19 pandemic.

Methods

We analyzed data from an all-payer pharmacy-claims database across 56,155 chain, independent and mail-order pharmacies in 14,164 zip codes in 50 states.⁴ Prescriptions dispensed (in 2-week intervals) of evidence-based HF therapies in 2020 (December 29, 2019, to December 26, 2020) were indexed to comparable timeframes in 2019 (December 30, 2018, to December 28, 2019). Only complete 2-week intervals were included, and each period began on a Sunday and ended on a Saturday. To further reduce noise due to short-term trends and cyclical seasonal variations and to address potential unobserved changes in the number of people covered in these pharmacy claims data (the denominator), we normalized these year-to-year changes in HF medical therapies relative to those observed in a reference set of 859 drugs used in general medical practice and that excludes seasonal drugs (eg, oseltamivir). Data are presented as percentage deviation from the expected year-to-year trends seen with this stable basket of drugs.

Prescriptions of brand-name therapies were further evaluated by quantity of fills (<28 tablets, 28–60 tablets, >60 tablets). Finally, prescription fill patterns were characterized on the basis of pharmacy type (mail-order or retail). Using the National Council for Prescription Drug Programs dataQ Pharmacy Database, we applied a broad definition of mail-order pharmacies and considered any pharmacy that self-identified as such based on Primary, Secondary, and Tertiary Provider Type Code. To better understand shifts in pharmacy activity in relation to the COVID-19 pandemic, we additionally summarized the overall percentage deviation from the expected year-to-year trends from the week the World Health Organization declared COVID-19 a global pandemic (March 11, 2020) and the U.S. declared a national emergency (March 13, 2020) until the end of the study period. Analyses were performed using R Software, version 3.6.1 (Vienna, Austria).

Results

In 2019 and 2020, we evaluated 27,027,650 individual claims for 9 therapies across 6 classes used in HF management: lisinopril, losartan, metoprolol (immediate-release or

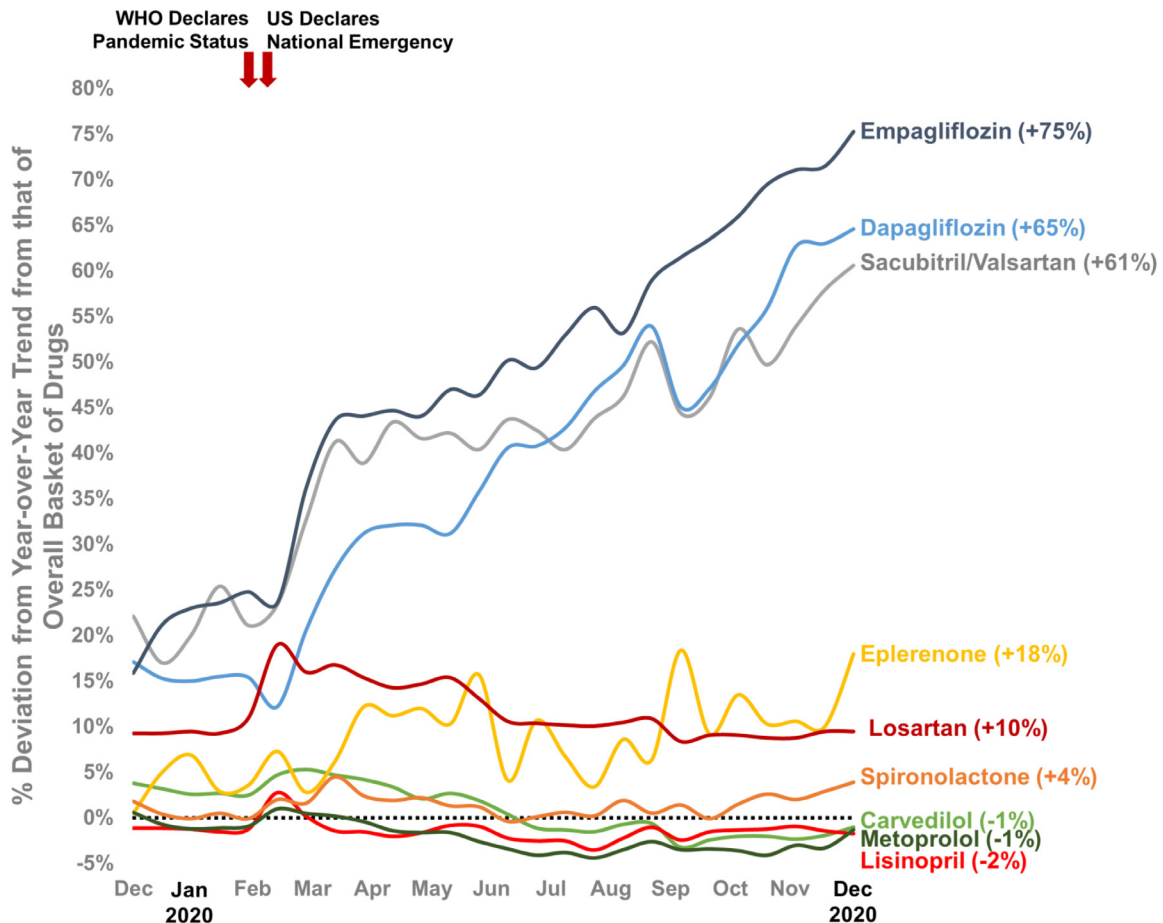


Fig. 1. Relative prescription fills of evidence-based therapies used in heart failure care in 2020 in the United States. Prescription fills (in 2-week intervals) in 2020 were first indexed to 2019. These year-to-year changes were then normalized relative to those observed with a reference set of drugs. The percentages displayed in the figure represent deviation from the expected year-to-year trends seen with the reference set of drugs. WHO, World Health Organization.

extended-release), carvedilol (immediate-release or extended-release), spironolactone, eplerenone, dapagliflozin, empagliflozin, and sacubitril/valsartan.

Fills of losartan, lisinopril, carvedilol, and metoprolol all peaked in the weeks of March 2020 and demonstrated trajectories thereafter that were relatively consistent with the reference set of drugs for the remainder of 2020 (deviating <10% above or below expected trends) (Fig. 1). Fills of spironolactone (+4%) and eplerenone (+18%) showed modest trends toward increased relative use during 2020.

Fills of empagliflozin (+75%), dapagliflozin (+65%) and sacubitril/valsartan (+61%) showed striking longitudinal increases throughout 2020 that deviated substantially from the year-to-year trends of the reference set of drugs (Fig. 1). For all 3 therapies, fills of all quantity sizes increased relatively throughout 2020. For dapagliflozin and empagliflozin, fills <28 tablets (+259% and +131%, respectively) showed the greatest deviation from the expected trend, whereas for sacubitril/valsartan, fills >60 tablets (+116%) showed the greatest deviation.

For all 9 therapies sampled, the prescription-fill patterns from mail-order pharmacies increased over expected trends beginning in March 2020 (Fig. 2). These trajectories generally plateaued for generic therapies but continued to

increase through the end of 2020 for brand-name therapies (dapagliflozin, empagliflozin and sacubitril/valsartan). From the week of March 8, 2020 (the week the World Health Organization declared pandemic status and the U.S. declared a national emergency), to the end of 2020, prescription fills of both brand-name therapies (range +112% to +173%) and generic therapies (range +59% to +81%) from mail-order pharmacies showed substantial deviation from expected trends (Table 1). At retail pharmacies, prescription fills for generic therapies remained relatively stable compared with the reference set of drugs (deviating <10% above or below expected trends), whereas prescription fills for brand-name therapies increased relative to expected trends (range +39% to +46%).

Discussion

These nationwide pharmacy-claims data suggest that prescription fills of most established generic components of medical therapies used in HF care were maintained at use patterns consistent with that of many other common therapies during the COVID-19 pandemic. In contrast, the use of newer brand-name therapies (sacubitril/valsartan and the sodium-glucose co-transporter-2 inhibitors) showed steep

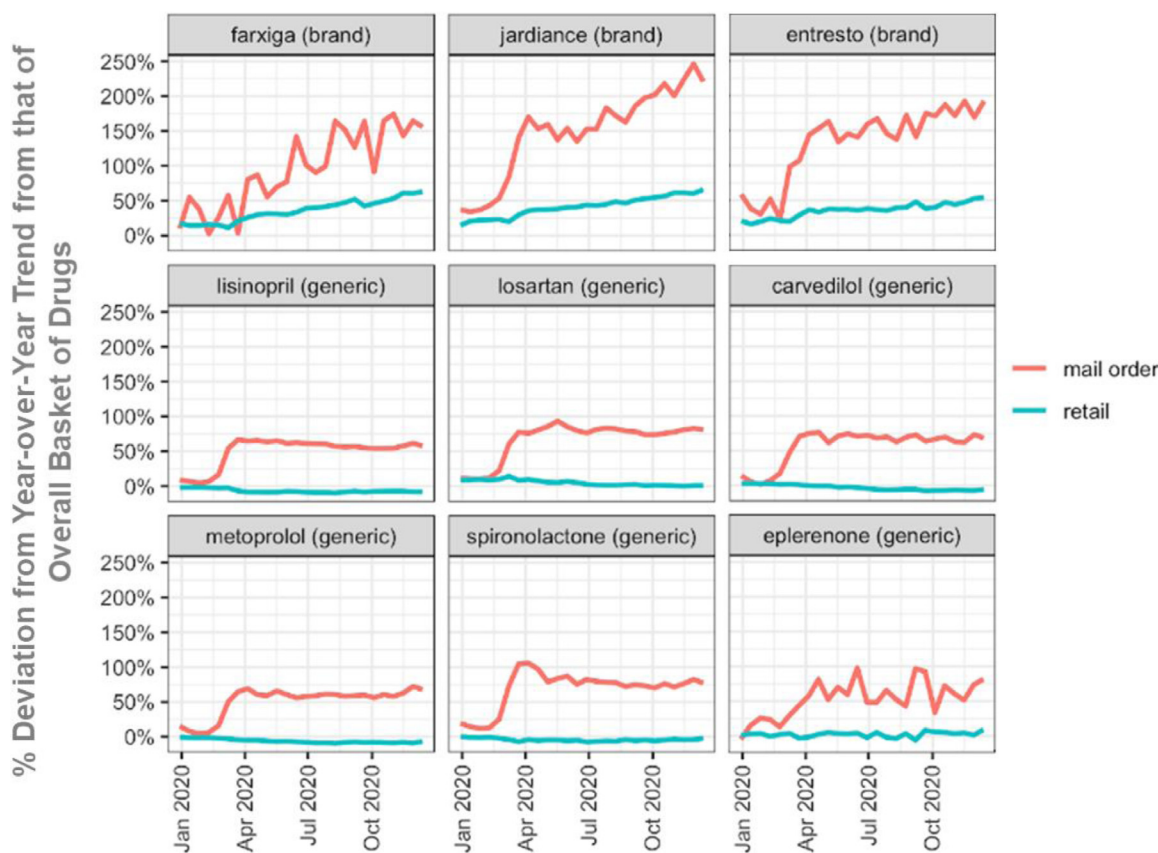


Fig. 2. Relative prescription fills of evidence-based therapies used in heart failure care at mail order and retail pharmacies. Prescription fills (in 2-week intervals) in 2020 were first indexed to 2019. These year-to-year changes were then normalized relative to those observed with a reference set of drugs. The percentages displayed in the figure represent deviation from the expected year-to-year trends seen with the reference set of drugs. Pharmacy type (mail-order or retail) was based on self-identified designation in the National Council for Prescription Drug Programs dataQ Pharmacy Database.

Table 1. Prescription Fill Patterns of Evidence-Based Therapies Used in Heart Failure Care During the COVID-19 Pandemic by Pharmacy Type

	Average 2-week Prescription Fill % Deviation from Expected Trend (March 8, 2020–December 26, 2020)	
	Mail-order Pharmacy	Retail Pharmacy
Brand-name therapies		
Sacubitril/valsartan	+154.5%	+39.1%
Dapagliflozin	+111.8%	+40.1%
Empagliflozin	+172.7%	+45.7%
Generic therapies		
Carvedilol*	+67.9%	−4.0%
Eplerenone	+62.0%	+2.6%
Lisinopril	+59.4%	−7.9%
Losartan	+78.9%	+3.7%
Metoprolol*	+60.6%	−7.3%
Spironolactone	+80.6%	−5.2%

Note: Expected trends are estimated based on a reference set of 859 drugs used in general medical practice, excluding seasonal drugs. COVID-19, coronavirus disease-2019.

*Includes both immediate-release and extended-release formulations.

deviation from expected trends, with increasing use throughout 2020. Prescription fills for all therapies from mail-order pharmacies increased early as the COVID-19 pandemic evolved with initial lockdown phases.

Similar to observations of other therapies,⁵ ACEis, ARBs and β-blockers showed slight inflections in relative use in March 2020, which may represent stockpiling behavior in anticipation of the impending global pandemic and the easing of restrictions to allow early and flexible prescription fills.⁶ ACEi/ARB use was otherwise relatively stable, suggesting limited perturbations resulting from initial safety concerns that were voiced related to their use during the COVID-19 pandemic.³ Prompt multisociety guidance and reassuring signals from interval trials may have supported their continued use.^{7,8}

Marked relative increases in the use of newer medical therapies provide reassurance that patients with HF and cardiometabolic illnesses are able to access latest advances in medical therapies, even during a public health crisis. Mail-order pharmacies may have facilitated continued therapeutic access, even during lockdown phases. Restructuring of HF care with virtual-care pathways may have facilitated this uptake without necessitating in-person visits. Increasing awareness of best practices in HF care and emerging supportive trial evidence and regulatory labels may have also contributed.

Limitations

These findings should be considered in the context of the study’s limitations. We relied on pharmacy-claims information and did not have access to patient-level characteristics. As such, we were unable to track whether therapies were titrated, continued or discontinued in individual patients. Similarly, we could not distinguish between new versus refill prescriptions. Although it is challenging to ascertain definitively the denominator of persons eligible for a

prescription, we did attempt to normalize these observations to trajectories of fill patterns of more than 800 common therapies. Strong divergence of certain medical therapies used in HF care from these expected patterns suggests that a large influx of covered persons is unlikely to be responsible for this growth in prescription numbers. Importantly, however, aside from sacubitril/valsartan, many of these therapies are indicated and commonly used in other medical conditions, and we cannot definitely attribute their prescription to HF care. We intentionally attempted to be inclusive in our analysis and included both immediate-release and extended-release formulations of a given therapy (for instance, metoprolol tartrate and metoprolol succinate), even though evidence may support 1 formulation preferentially. We excluded combination therapies for analytic purposes. Finally, this report does not characterize prescription fill patterns in relation to regional COVID-19 disease activity, given the challenges in attributing prescription fills to a particular region. Mail-order pharmacies may be physically located in 1 geographic region, but prescriptions are often filled nationwide.

Conclusion

These contemporary data, encompassing a large U.S. pharmacy catchment area and more than 27 million claims, provide reassurance about therapeutic access to evidence-based medications used in HF care during the COVID-19 pandemic.

Disclosures

This work represented an academic collaboration with GoodRx. The study was unfunded, and no compensation was received. These analyses are based on a representative sample of claims in the U.S. and are not based on GoodRx transactions. The manuscript was drafted by the first author and revised based on input by all coauthors.

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