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Issue Brief:
Assessing the impact of formulary exclusion on healthcare costs and outcomes for patients on therapy for certain chronic conditions

May 2023

Introduction

Delaying, changing, or stopping therapy for a medicine due to a formulary exclusion can impact a patient's health. This issue brief employs a claims-based approach to evaluate the impact on adverse events and out-of-pocket (OOP) costs for patients who were previously stable on therapy but whose plan stopped coverage due to a formulary exclusion by their pharmacy benefit manager (PBM).[a] This brief focuses on 2 therapeutic areas as case studies to compare the change in a patient's health before and after the formulary exclusion was implemented. This brief also assesses whether the impact of formulary exclusions is equitably distributed or if the outcomes disproportionately affect certain population segments. The brief highlights the negative impact formulary exclusion has on patients and shows that PBMs have cause to reconsider their formulary exclusion methodology to ensure health outcomes are prioritized, and patients previously stable on therapy can remain on therapy.

Background

In recent years, PBM formulary exclusions have drastically increased in the commercial market

Pharmacy benefits are typically managed through PBMs on behalf of their clients, the plan sponsors. Due to consolidation, 3 of the largest PBMs (CVS Caremark, Express Scripts, and OptumRx) process more than 80% of retail prescriptions.[1]

The PBMs develop formularies, which are a list of medicines for which the plan sponsor will provide reimbursement. The initial intent of formularies was to incentivize the use of the least costly medication that was also safe and effective for a particular medical condition.[2] However, in the last 10 years or so, PBMs have begun excluding medicines from formularies to gain further leverage in contract negotiations with biopharmaceutical manufacturers.

The pace of formulary exclusions has accelerated at an astonishing rate. An Xcenda analysis found that in 2022, 1,156 unique prescription medicines were excluded from the standard formularies of at least 1 of the 3 largest PBMs, a 961% increase from 2014, when 109 medicines were excluded.[3] From 2014 to 2022, the number of medicines excluded by 1 or more PBMs increased by an average of 34% per year.

Historically, PBM exclusions have focused on medicines with generic equivalents or classes where multiple products have been shown to achieve similar clinical outcomes. The Xcenda analysis found that PBMs often exclude medicines for conditions where it is important for patients and physicians to have multiple treatment options, such as oncology, cardiovascular, and autoimmune disorders. In fact, the analysis found that 547 (47.3%) of the formulary exclusions were single-source drugs with no generic equivalents.

The Inflation Reduction Act (IRA) may result in more restrictive plan formulary management for the Medicare population

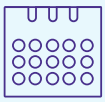
The IRA shifts payment responsibilities in the Part D catastrophic phase away from the federal government (80% to 20%) and toward plans (15% to 60%) and manufacturers (0% to 20%). The 4-fold increase in plan liability under the IRA may lead plans to seek ways to offset their increased costs.

[a] This study does not assess the impact of utilization management techniques (eg, prior authorization or step therapy), which can also result in similar adverse access issues as a formulary exclusion.

The IRA also limits base beneficiary premium increases starting in 2024. Faced with the limited ability to raise revenue via premiums to offset greater drug expenses, plans will likely increase their cost-control measures for drugs typically used by high-cost patients. Such efforts may include adding or imposing stricter utilization management measures (eg, prior authorization, step therapy) and tighter formulary management.

Formulary exclusions can have detrimental impacts on shared decision making, patient access, and outcomes

Excluding a drug means the insurer will not reimburse any portion of its cost, leaving the patient to pay the product's full price. This burden presents an insurmountable financial barrier for many patients. As a result, formulary exclusions lead directly to disruptions with treatment regimens, as physicians must review the patient's plan formulary for another medication. This disruption, also referred to as *non-medical switching* or *PBM prescribing*, can occur when plans or PBMs exclude a medication from their formulary or adversely increase the cost-sharing tier, thus forcing stable patients and their physicians to switch to an alternative medication for non-clinical reasons. The impact of these switches can be minimal for some patients; however, for those with complex and clinically challenging diseases, the consequences can be disastrous and life threatening.



"It can take 1 to 2 years to get many of our patients stabilized on a medication. To just arbitrarily stop that medication and switch to another, and then expect the patient to do as well is just wishful thinking."[4]

– Madelaine A. Feldman, MD, president of the Coalition of State Rheumatology Organizations and clinical assistant professor of medicine at Tulane University School of Medicine

Another negative consequence of formulary exclusions is the insertion of the payer between the physician and patient in the treatment decision. The removal of a treatment interrupts thoughtful, shared decision making and individualized care between the doctor and patient.

Furthermore, having to switch to their PBM's preferred formulary therapy may be accompanied by increased risk of worse health outcomes for patients. A 2016 literature review identified 20 empirical studies that evaluated how the drug-exclusion policies affected patients.[5] Of the 20 studies reviewed by the authors, 6 (28.6%) were reported to have had a negative impact, including increased glycated hemoglobin (A1C) levels (for diabetes), increased incidence of acute care events (for psychotic disorder), and increased frequency and severity of symptoms and side effects (for gastroesophageal reflux disease and hypertension).

Other studies have also shown negative consequences of formulary exclusions. A 2020 commercial claims analysis showed that claim rejections due to formulary restrictions led to a week-long delay in receiving antiepileptic treatment among patients with focal seizure compared to patients with an initially approved claim.[6] Additionally, a 2010 commercial claims analysis on smoking cessation (SC) treatment showed that only 15.3% of patients filled an SC treatment prescription in the 6 months after facing a rejected claim for varenicline, the newest SC treatment at the time, due to lack of coverage.[7]

Methods

To measure the impact of formulary exclusions on patient outcomes and costs, we identified treatments under 2 therapeutic areas, cardiovascular and gastrointestinal, to serve as case studies. These therapeutic areas were selected as case studies since they encompass common and often costly chronic conditions among patients within the United States (US),[8,9] and each include a therapy that was excluded by at least 1 of the 3 largest PBMs in recent years (between 2016 and 2021). We restricted the analysis to therapies that were on the market for at least a year before PBM exclusion.

We measured pre- and post-outcomes (ie, inpatient hospitalization and outpatient emergency department [ED] visits) and per-member-per-month (PMPM) OOP drug costs for patients through longitudinal commercial claims in the US. Average hospitalizations and ED visits were measured for patients who had at least 1 adverse event; changes in average OOP costs were assessed for patients who were adherent to the therapy in both the pre- and post-periods.[b] The analysis also accounted for patients with outlying values in adverse events and costs.[c]

[b] Patients were identified as adherent if they had at least 60 days on therapy both pre-formulary exclusion and post-formulary exclusion.
[c] Outliers at the top end of the distribution for adverse events or costs were winsorized at the 90th and 99th percentiles, respectively.

To be included in the analysis, patients had to be enrolled in a plan associated with a PBM of interest during the 6 months prior and 6 months after the date of formulary exclusion. Additionally, patients were required to have 60 or more days' supply of the product during the 6-month period prior to the formulary exclusion to ensure they were stable on therapy.

Patients utilizing the therapies indicated for each of the therapeutic areas were not further restricted based on diagnosis criteria since formulary exclusions are typically indication agnostic. Additionally, the findings are stratified based on patient age, gender, geography, and a measure of the patient's clinical risk, as defined by the Charlson comorbidity index (CCI).[10]

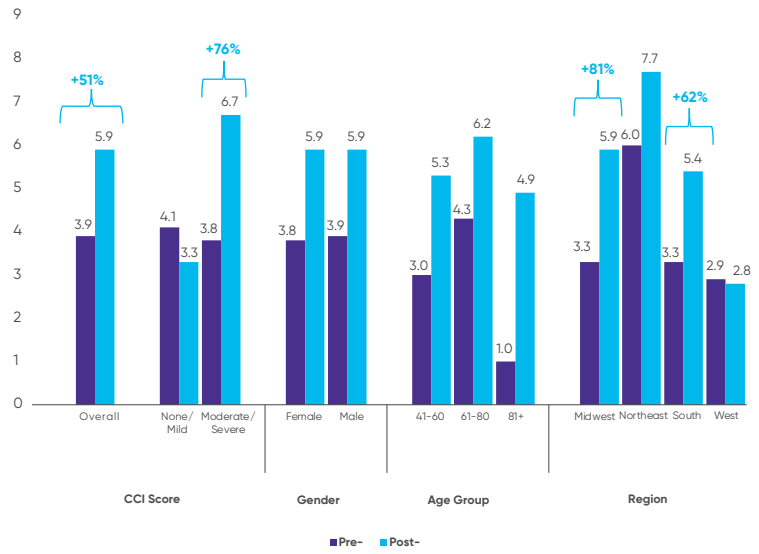
Results

Case Study: Cardiovascular Therapy

We assessed 775 commercial patients utilizing a therapy primarily indicated for treatment of a cardiovascular condition. The therapy was excluded by 1 of the 3 major PBMs in 2017. Overall, commercial patients treated with the cardiovascular therapy had higher rates of hospitalization (+51%) during the 6-month period, post-formulary exclusion, relative to the 6-month period prior to the exclusion (**Figure 1**). Patients with moderate or severe clinical risk were more likely to experience an increase in hospitalizations post-exclusion (+76%) compared to those with mild risk or no comorbidities. Geography was also associated with the likelihood of patients experiencing an increase in adverse events post-formulary exclusion. Patients in the South and Midwest had the largest increase in hospitalizations (+62% and +81%, respectively).

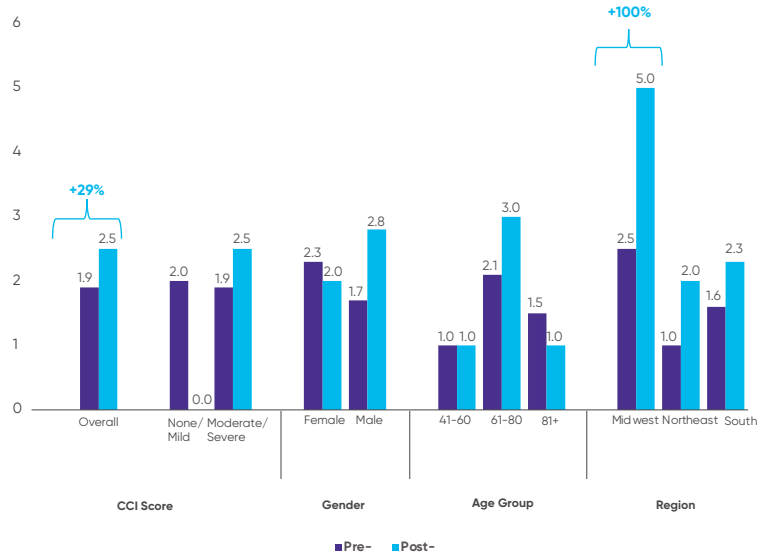
Like the findings for inpatient hospitalizations, commercial patients treated with the cardiovascular therapy had higher rates of outpatient ED visits (+29%) during the 6-month period, post-formulary exclusion, relative to the 6-month period prior to the exclusion. The increase in ED visits was attributable to patients with moderate to severe clinical risk. Moreover, ED visits doubled for patients residing in the Northeast and Midwest (**Figure 2**).

Figure 1. Average number of hospitalizations during 6-month period, pre-and post exclusion, among cardiovascular patients experiencing at least 1 hospitalization



Key: CCI – Charlson comorbidity index.

Figure 2. Average number of ED visits during 6-month period, pre- and post-exclusion, among cardiovascular patients experiencing at least 1 ED visit



Key: CCI – Charlson comorbidity index; ED – emergency department.
Note: West is excluded due to lack of sufficient sample size.

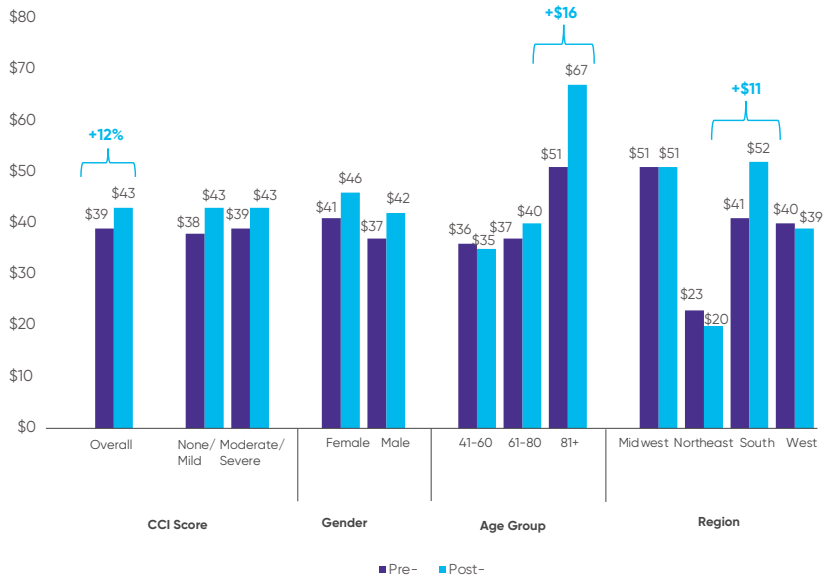
Results (cont'd)

Among patients who were adherent to the therapy during the 6-months before and 6-months after the formulary exclusion, PMPM OOP costs for the therapy rose from $39 prior to the exclusion to $43 post-exclusion (+12%), representing an annual increase of $48. Older patients and patients living in the South were likely to have the largest impacts on OOP costs, experiencing annual increases of $192 ($16 PMPM) and $132 ($11 PMPM), respectively (**Figure 3**).

Case Study: Gastrointestinal Therapy

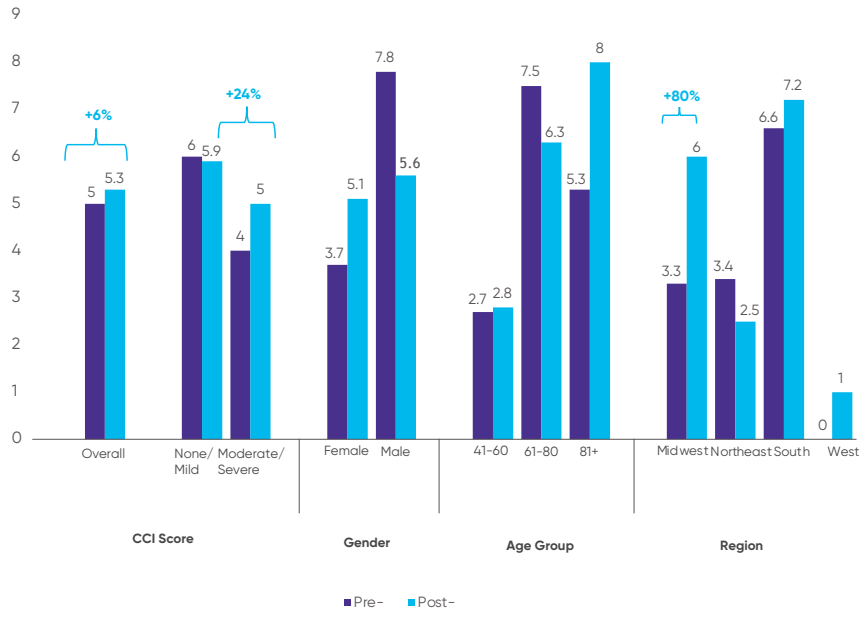
We assessed 174 commercial patients utilizing a therapy primarily indicated for treatment of a gastrointestinal condition. The therapy was excluded by each of the 3 major PBMs at some point between 2016 and 2021. Overall, patients experienced a 6% increase in inpatient hospitalizations during the 6-month period after the formulary exclusion relative to the 6-month period prior to the exclusion (**Figure 4**). Patients with moderate to severe clinical risk were more likely to experience an increase in hospitalizations (+24%) as were patients residing in the Midwest (+80%).

Figure 3. Average OOP costs PMPM during 6-month period, pre- and post-exclusion, among cardiovascular patients who remained adherent to therapy



Key: CCI – Charlson comorbidity index; OOP – out-of-pocket; PMPM – per member per month.

Figure 4. Average number of hospitalizations during 6-month period, pre- and post exclusion, among gastrointestinal patients experiencing at least 1 hospitalization



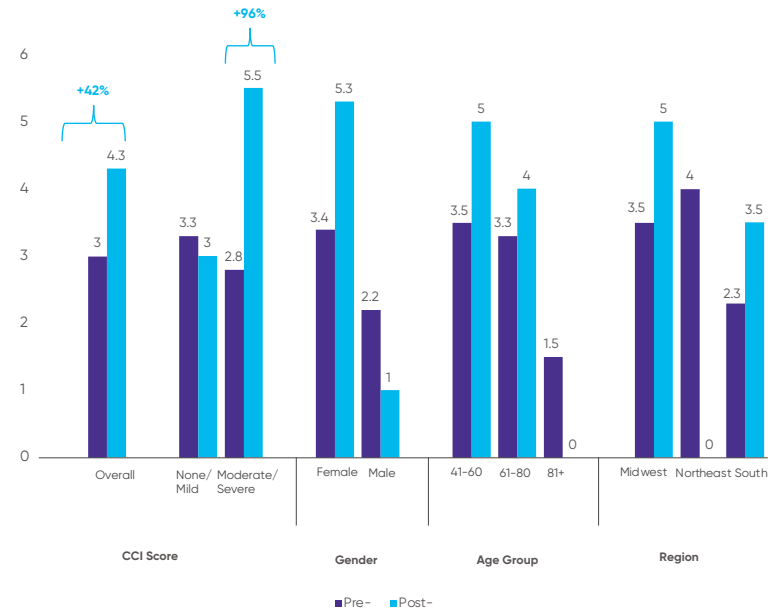
Key: CCI – Charlson comorbidity index.

Results (cont'd)

Outpatient ED visits increased by 42%, on average, during the 6 months prior and the 6 months post-formulary exclusion for patients overall. Patients with the highest clinical risk (ie, moderate to severe) were more likely to experience a larger increase in ED visits compared to their lower-risk counterparts. In fact, ED visits increased nearly two-fold, from 2.8 visits during the period prior to formulary exclusion compared to 5.5 visits during the period following the exclusion for these patients (**Figure 5**).

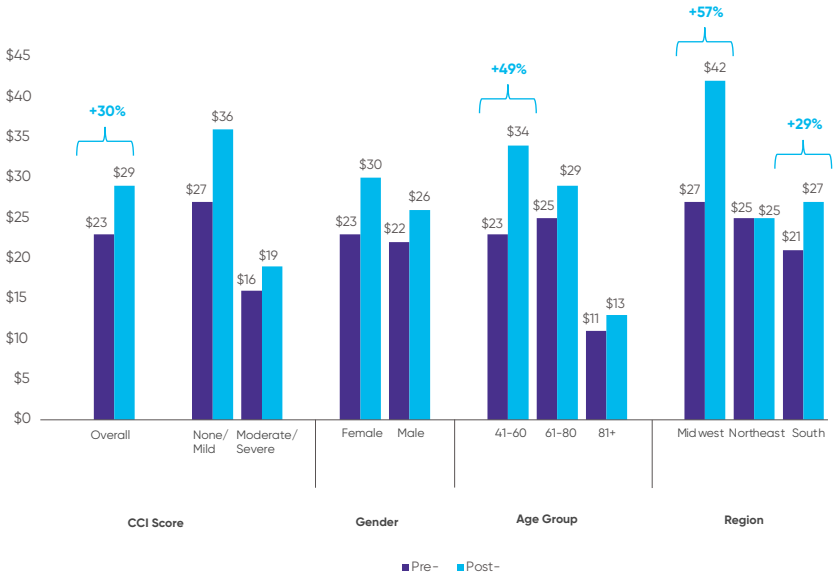
Among patients who were adherent to the gastrointestinal therapy in the 6-month period prior to the exclusion and during the 6-month period post-formulary exclusion, PMPM OOP costs for the therapy increased $6 from $23 to $29 (+30%), representing an annual increase of $72. Patients in the Midwest and South experienced larger increases in OOP costs (+57% and +29%, respectively) compared to those in the Northeast. Moreover, patients in the younger age bracket of 41 to 60 years were more likely to have larger increases in OOP costs (+49% or $11 PMPM), translating to an estimated annual increase of $132 (**Figure 6**).

Figure 5. Average number of ED visits during 6-month period, pre- and post-exclusion, among gastrointestinal patients experiencing at least 1 ED visit



Key: CCI – Charlson comorbidity index; ED – emergency department.
Note: West is excluded due to lack of sufficient sample size.

Figure 6. Average OOP costs PMPM during 6-month period, pre- and post-exclusion, among gastrointestinal patients who remained adherent to therapy



Key: OOP – out-of-pocket; PMPM – per member per month.
Note: West is excluded due to lack of sufficient sample size.

Conclusion

The case studies on the cardiovascular and gastrointestinal therapies indicate that on average, patients with chronic illnesses who are stable on a therapy experience an increase in both adverse health outcomes and OOP costs after a PBM excludes the therapy from their plan formulary. Patients with moderate to severe clinical risk are especially vulnerable to an increase in hospitalizations and ED visits, as are patients living in the southern and midwestern regions of the US.

The findings are limited to the top 3 PBMs and the additional patient inclusion criteria detailed in the analysis. As a result, the sample size is limited in comparison to the total number of patients on cardiovascular and gastrointestinal therapies in the US. Lastly, the study tracked hospitalizations and ED visits for patients 6 months pre- and post-PBM exclusion date and, as a result, any long-term adverse events that lead to hospitalizations and ED visits may not be captured.

The case studies indicate that, on average, patients with chronic illnesses who are stable on a therapy experience an increase in both adverse health outcomes and OOP costs after a PBM excludes the therapy from their plan formulary.

Formulary exclusions implemented by the 3 largest PBMs have increasingly affected commercially insured patients, with a 34% per-year increase in the number of medicines excluded since 2014. With the potential for Medicare Part D reforms under the IRA to induce plans to offer more narrow formularies, the negative consequences of formulary exclusions, particularly in terms of impacts on patient health outcomes, may become even more widespread.

To address these adverse impacts to patients, both Congress and the Centers for Medicare & Medicaid Services (CMS) can take actions to counteract PBM formulary exclusions and, thereby, reduce the negative consequences of treatment disruption. Congressional oversight into PBM practices, including formulary exclusions, can lead to enforcement actions to safeguard patient access to therapies and provider choice. CMS's continued review of Medicare Part D formularies to ensure that beneficiaries have access to a broad range of medically appropriate drugs will be a critical factor to mitigating potentially tighter formulary management resulting from increased plan liabilities under the IRA.

PBM formulary exclusions have important real-word implications. Not only do they inhibit provider choice and increase patient OOP costs for certain chronic illnesses, but they are also associated with an increased rate of hospitalizations and ED visits, particularly for patients with higher clinical risk. Counteracting PBM formulary exclusions is critical to safeguarding patient access and affordability, and maintaining health outcomes.

References: 1. Fein A. The top pharmacy benefit managers of 2021: The big get even bigger. April 5, 2022. Accessed February 8, 2023. https://www.drugchannels.net/2022/04/the-top-pharmacy-benefit-managers-of.html. **2.** Kelly D. A brief history of drug formularies and what to expect in 2019. CoverMyMeds. December 18, 2018. Accessed February 7, 2023. https://www.covermymeds.com/main/insights/articles/a-brief-history-of-drug-formularies-and-what-to-expect-in-2019/ **3.** Xcenda. Skyrocketing growth in PBM formulary exclusions continues to raise concerns about patient access. May 2022. Accessed February 7, 2023. https://www.xcenda.com/-/media/assets/xcenda/english/content-assets/white-papers-issue-briefs-studies-pdf/xcenda_pbm_exclusion_may_2022.pdf. **4.** Volansky R. Formulary exclusions, non-medical switching jeopardize disease control, patient trust. *Healio Rheumatology*. December 14, 2020. Accessed February 8, 2023. https://www.healio.com/news/rheumatology/20201214/formulary-exclusions-nonmedical-switching-jeopardize-disease-control-patient-trust. **5.** Chambers JD, Rane PB, Neumann PJ. The impact of formulary drug exclusion policies on patients and healthcare costs. *AJMC*. August 16, 2016. Accessed February 8, 2023. https://www.ajmc.com/view/the-impact-of-formulary-drug-exclusion-policies-on-patients-and-healthcare-costs. **6.** Mehta D, Davis M, Epstein AJ, et al. Impact of formulary restrictions on antiepileptic drug dispensation outcomes. *Neurol Ther*. 2020;9:505-519. Accessed February 7, 2023. doi:10.1007/s40120-020-00195-3. **7.** Zeng F, Chen CI, Mastey V, Zou KH, Harnett J, Patel BV. Utilization management for smoking cessation pharmacotherapy: varenicline rejected claims analysis. *Am J Manag Care*. 2010;16(9):667-674. Accessed February 7, 2023. https://www.ajmc.com/view/ajmc_10sep_zeng_667to674. **8.** Global Burden of Cardiovascular Diseases Collaboration. The burden of cardiovascular diseases among US states, 1990-2016. *JAMA Cardiol*. 2018;3(5):375-389. Accessed April 12, 2023. doi:10.1001/jamacardio.2018.0385. **9.** Peery AF, Crockett SD, Murphy CC, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: Update 2021. *Gastroenerology*. 2022;62(2):621-644. Accessed April 12, 2023. doi:10.1053/j.gastro.2021.10.017. **10.** Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-83. Accessed April 12, 2023. doi:10.1016/0021-9681(87)90171-8

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