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NALOXONE ACCESSIBILITY ACROSS MISSISSIPPI

A Thesis Presented for the

Master of Science

Degree

Department of Pharmacy Administration

Emily Gravlee, PharmD

December 2022

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## ABSTRACT

### **Background/Objectives**

Despite widespread standing orders allowing pharmacies to dispense naloxone under protocol or without a prescription, there is substantial variation in naloxone availability and cost geographically. This study geospatially assessed naloxone availability and cost across community pharmacies within Mississippi. Additionally, this study examined the association of county-level characteristics, including rurality, race, household income, overdose numbers, and percent uninsured, with naloxone availability. This study aims to inform health policymakers about effectiveness of current naloxone standing orders, and to guide potential interventions for improving naloxone accessibility at the community-level.

### **Methods**

This study was a “mystery shopper” telephone census of naloxone availability and cost at all Mississippi pharmacies. Naloxone availability and cost were descriptively analyzed. T-tests were used to detect differences in naloxone availability based on county racial makeup, income, overdose deaths, and percentage uninsured. Chi-square tests were used to detect differences in naloxone availability based on pharmacy type and county rurality.

### **Results**

Overall, there were 591 publicly-available community pharmacies surveyed in Mississippi. Overall, only 36.6% ( $n=216$ ) of Mississippi pharmacies indicated that naloxone was available under state standing order. The mean cost for naloxone nasal spray was \$105.58 (range

\$38.11 to \$229.39). Differences existed in naloxone availability based on pharmacy type ( $X^2(2, N = 591) = 41.09, p < 0.001$ ), but not pharmacy rurality ( $X^2(2, N = 591) = 3.06, p = 0.216$ ). There was no difference in naloxone availability according to county-level measures. Mapping naloxone availability revealed that 16 (19.25%) of 82 Mississippi counties had no naloxone availability at community pharmacies. Almost half ( $n = 30, 46.88\%$ ) of all counties where a pharmacy stocked naloxone nasal spray had naloxone nasal spray available for less than \$100.

### **Implications**

This study demonstrates that, despite lawful availability, naloxone is not widely available across the state of Mississippi. Lack of external drivers of naloxone availability suggest that naloxone availability may be driven by pharmacies. Further studies examining reasons for low naloxone availability, particularly among community pharmacies, should be conducted. Additionally, follow-up analyses of pharmacy pricing for naloxone are warranted.

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## CHAPTER I

### INTRODUCTION

Naloxone is a prescription opioid antagonist that is available as either a nasal spray or injection and is indicated to reverse opioid overdoses.<sup>1</sup> Naloxone has been identified as a life-saving medication for individuals with opioid-use disorder (OUD).<sup>2,3</sup> Forty-seven states have standing orders for naloxone, which means that naloxone can be obtained over-the-counter without a prescription by patients.<sup>4</sup> However, naloxone may not be accessible to patients despite being lawfully available.

Naloxone availability at community pharmacies has been noted to vary widely based on geographic location.<sup>3,5-7</sup> Nationally, previous studies examining the availability of naloxone have found that state or region-wide naloxone availability ranges from around thirty to ninety-five percent.<sup>5,6,8,9</sup> Naloxone costs, which are less frequently reported than availability, vary widely as well. Reported naloxone costs have been found to range from \$119<sup>5</sup> to 166.25<sup>9</sup> for intranasal naloxone formulations, and from \$27 to \$4,500<sup>9</sup> for injectable formulations. Few studies on naloxone availability have been carried out in rural or Southern spaces. A survey study carried out in rural Alabama found that only 104 of 222 surveyed pharmacies stocked naloxone,<sup>8</sup> and a report from the Mississippi Department of Medicaid indicated that of the over 500 beneficiaries with overdose claims only 1.8% of these individuals had prescriptions claims for naloxone.<sup>10</sup>

Lack of insurance may be an additional barrier to uptake for people with OUD.<sup>11-14</sup> More specifically, high rates of uninsured status among this population may mean that naloxone standing orders may be inaccessible due to high out-of-pocket costs. Additionally, disparities in

naloxone availability based on community-level factors, including racial community makeup, average income, and pharmacy setting have been documented.<sup>15-17</sup> An understanding of these factors' impact on naloxone accessibility may be needed to develop appropriate community-driven solutions to naloxone accessibility.

The characterization of naloxone accessibility in Mississippi provides important contextual information in developing targeted community-level public health interventions to reduce the number of opioid-related deaths for people living in Mississippi. Additionally, data from this study may serve as an important health policy tool to assess the effectiveness of current naloxone standing orders on availability, and determine if additional action is needed to improve community-level access.

## CHAPTER II

### LITERATURE REVIEW

#### *Naloxone and Standing Orders*

Naloxone is a prescription opioid antagonist that is available as either a nasal spray or injection and is indicated to reverse opioid overdoses.<sup>1</sup> A 2015 Morbidity and Mortality Weekly Report by the Centers for Disease Control and Prevention (CDC) found that from 1996 to June 2015 layperson-administered naloxone was responsible for 26,463 opioid overdose reversals.<sup>18</sup> Naloxone has been identified as a life-saving medication for individuals with opioid-use disorder (OUD)<sup>2,3</sup>, and has been successfully used by individuals with OUD to treat witnessed opioid overdose. An early pilot study by Seal et al found that after an 8-hour training session on overdose intervention, individuals with OUD successfully used naloxone to treat opioid overdose in 75% of twenty witnessed overdoses over the next six months.<sup>19</sup> In a larger overdose prevention program based in San Francisco 40% of 1,020 naloxone refills provided were provided to participants who stated that they used the previous naloxone dose to treat a witnessed overdose.<sup>20</sup>

Due to potential for life-saving intervention with naloxone, many states have expanded access to this medication through naloxone standing orders. Naloxone standing orders or protocol orders, hereafter referred to as standing orders, authorize pharmacists to supply naloxone to patients without a visit to a prescriber for a prescription.<sup>21</sup> The first standing order for naloxone administration was created in 2007, and sharp uptick in adoption occurred around

2013.<sup>22</sup> Forty-seven states now have standing orders for naloxone.<sup>4</sup> In states that have enacted these measures a 9-11% decrease in opioid-related deaths has been observed.<sup>4</sup> However, naloxone may not be accessible to patients despite being lawfully available.

### ***Naloxone Availability and Cost***

Naloxone availability at community pharmacies has been noted to vary widely based on geographic location.<sup>3,5-7</sup> Nationally, previous studies examining the availability of naloxone have found that state or region-wide naloxone availability ranges from around thirty to ninety-five percent.<sup>5,6,8,9</sup> A study assessing naloxone nasal spray availability in Philadelphia, Pennsylvania found that only one-third of surveyed pharmacies carried the product.<sup>5</sup> A 2019 study of naloxone availability in North Carolina found that around two-thirds of surveyed pharmacies had naloxone available, and that chain pharmacies were significantly more likely than independent pharmacies to carry the medication.<sup>7</sup> Interestingly, this study also noted that naloxone availability was lower for communities where a greater percentage of residents were using public health insurance.<sup>7</sup> A survey of select counties in California found that just over 70% of pharmacies participating in naloxone standing order had naloxone in-stock and available to the patient.<sup>9</sup> In this survey, naloxone availability was noted to be driven predominantly by chain pharmacies<sup>9</sup>, a finding similar to a survey performed in North Carolina.<sup>7</sup> Finally, in a survey of Indiana pharmacies, naloxone availability was noted to be very high, with 92.5% of pharmacies reporting stocking naloxone in 2018.<sup>6</sup>

Despite the number of studies performed to assess naloxone availability, few have been carried out in rural, Southern spaces. A previous survey study carried out in rural Alabama found that only 104 of 222 (47%) surveyed pharmacies stocked naloxone.<sup>8</sup> Low uptake has been found in other Deep South states as well. A report from the Mississippi Department of Medicaid

indicated that of over 500 beneficiaries with overdose claims, only 1.8% of these individuals had prescriptions claims for naloxone.<sup>10</sup> This low uptake may also be compounded by rurality. Sisson et al found that rurality was associated with an increased wait-time compared to non-rural pharmacies to stock requested generic or injectable formulations of naloxone.<sup>8</sup>

Even if naloxone is available via standing orders and in-stock at many pharmacies<sup>4</sup>, it may not be free of charge to patients. Naloxone costs, which are less frequently reported than availability, vary widely as well. Guadamuz et al found that, in Philadelphia, Pennsylvania, costs for naloxone nasal spray ranged from \$119 to \$150.<sup>5</sup> However, a survey of California counties found that naloxone cost ranged from \$44.99 to \$166.25 for intranasal naloxone formulations and from \$27 to \$4,500 for injectable formulations.<sup>9</sup> Notably, these surveys assessed the cash price of naloxone formulations. As such these costs did not account for insurance coverage of naloxone when any portion of costs were paid for under insurance. While insurance policies may cover naloxone cost under state standing orders, lack of insurance coverage may be a great barrier to naloxone uptake for the OUD community.

### ***Naloxone Access Challenges for Individuals Living with OUD***

Along with potential poor naloxone availability in rural spaces, insurance coverage for rural, Southern individuals with OUD may be suboptimal. Data from the United States Census has identified that rural populations are more likely to be uninsured as compared to urban populations.<sup>11</sup> Given that Mississippi has a large rural population<sup>23</sup>, fewer members of the population may be insured, meaning that patients with OUD or their families shoulder out-of-pocket costs for the medication. In fact, the proportion of the uninsured population in Mississippi is 14.5%<sup>11</sup>, above the national average of 10.9%.<sup>12</sup> Aside from rurality, substance use disorder may be another barrier to insurance coverage. Individuals with substance use disorder are more

likely to have limited insurance coverage as compared to other individuals.<sup>13</sup> Data from the 2014-2015 National Surveys on Drug Use and Health found that 28 per 100 individuals with heroin use disorder and 27 per 100 individuals with pain-reliever use disorder were uninsured.<sup>24</sup> More recent data released by Kaiser Family Foundation showed that, in 2019, almost one in five adults with opioid use disorder were uninsured.<sup>14</sup> High rates of uninsured status among this population mean that naloxone may be inaccessible for patients with OUD due to high cost.

Additionally, sociodemographic characteristics of communities may influence the availability of naloxone. Income, race or ethnicity, and rurality all seem to influence the accessibility of naloxone. A recent study by Abbas et al found that neighborhood poverty is associated with lower availability of naloxone among New York pharmacies, but found no difference between availability based on neighborhood racial or ethnic makeup.<sup>15</sup> Despite these findings, the influence of race on naloxone access has been documented. A study of people who inject drugs in Los Angeles and San Francisco, California found that Latinx or African American racial or ethnic background was negatively associated with self-reported receipt of naloxone in the past six months.<sup>16</sup> A separate study examining naloxone access disparities in Southeast Michigan found that non-White status decreased the odds of naloxone access, and that higher income was associated with greater odds of naloxone access.<sup>17</sup>

Poorer naloxone availability<sup>8,10</sup> in rural or Southern spaces is troubling as rural individuals are less likely to have access to community health programs for OUD treatment and may be more likely to experience opioid overdose.<sup>8</sup> A 2018 study describing on-site buprenorphine medication-assisted treatment availability at federally-qualified health centers found that centers in rural areas had about half the odds of providing on-site buprenorphine treatment as compared to those in urban spaces, and that health centers in the South had the

lowest odds of offering buprenorphine treatment for opioid use disorder.<sup>25</sup> In this study, authors found that the odds of federally qualified health centers offering on-site buprenorphine treatment for OUD were 2.69 to 4.29 times more likely in areas outside of the South.<sup>25</sup> Additionally, federal health centers in rural areas had approximately two-thirds the odds of reporting interest in expanding on-site medication assisted treatment for opioid use disorder.<sup>25</sup> Rurality and lack of access to OUD treatment may be particularly damaging in Mississippi where high numbers of opioid prescriptions<sup>26</sup> more frequently place individuals at risk for dependence and overdose. While the national opioid dispensing rate per 100 persons was 51.4 in 2018<sup>27</sup>, opioid dispensing rates for Mississippi ranged from 76.8 per 100 persons in that same year.<sup>26</sup> Additionally, alarming increases in overdose-related deaths among the Southeastern states, including Mississippi, are occurring.<sup>28</sup> While the increase in overdose-related deaths from 2019 to 2020 was 28.9% nationally as of July 2021, the percent change in overdose deaths for Mississippi was an increase of 44.1%.<sup>28</sup> Identifying lapses in naloxone accessibility in this vulnerable area may be beneficial in helping to prevent, or curbing these increases in, overdose-related deaths.

### ***Significance***

The goal of this paper is to better understand naloxone accessibility across Mississippi, and to highlight potential need for further health policy changes to increase naloxone access. The objectives of this paper are to (1) geospatially describe naloxone availability across Mississippi using county-level mapping; (2) assess cost of available naloxone across Mississippi; and (3) examine differences in naloxone availability based on county-level characteristics, including rurality, racial makeup, household income, percent uninsured, and number of county overdoses.



## CHAPTER III

### METHODS

#### *Design*

This study was a “mystery caller” telephone census of Mississippi pharmacies.

#### *Measures*

*Demographic variables.* Demographic variables in this study included pharmacy type, pharmacy county, and pharmacy zip code. Pharmacy type was determined as either a grocery store, chain, or independent pharmacy. A grocery store pharmacy was defined as any pharmacy existing in a larger food product store. This included pharmacies housed within large chain grocers, such as Kroger or Walmart pharmacies. A chain pharmacy was defined as any pharmacy having a presence in more than one state, such as Walgreens or CVS Pharmacies. An independent pharmacy was defined as any pharmacy that did not fall into either of the other categories. Pharmacies were only included in the analysis if they were open-door, publicly available pharmacies. Pharmacy county and zip code were gathered from address data online or in the Hayes 2022 List of Mississippi Community Pharmacies.

*Outcome variables.* Similar to previous studies, availability<sup>8,29</sup> and cash cost<sup>5</sup> of naloxone formulations, including both branded and generic injectable and nasal spray formulations, was assessed. Availability was a dichotomous yes or no variable based on same-day availability at the time of the pharmacy call. Cost was measured in United States dollars. Where naloxone was not readily available for pickup, willingness to order naloxone and time to arrive at the pharmacy setting was assessed. Willingness to order naloxone was a dichotomous yes or no variable. Time

to stock was assessed as the smallest hour-to-stock value provided by the pharmacy. For example, if a pharmacy claims that they can stock naloxone in 1-2 days, then time to stock was recorded as 24 hours.

*Predictor variables.* Predictor variables in this study included neighborhood and pharmacy factors. Neighborhood factors included county-level racial makeup, proportion of households under the poverty line, overdose deaths, rurality, and proportion of the population uninsured. County-level racial makeup was assessed as percent non-white at the county level. Proportion of households under the poverty line was assessed using American Community Survey 2020 data. Data for racial makeup of counties was gathered from 2020 Mississippi Census data. Notably, due to issues in data collection, these estimates are vintage estimates and do not necessarily represent actual Census counts for year 2020.<sup>30</sup> Overdose deaths at the county-level were assessed using the MS Opioid and Heroin Data Collaborative's Provisional Data Report Calendar Year 2020.<sup>31</sup> Rurality was assessed using United States Department of Agriculture Economic Research Service 2010 Rural-Urban Commuting Area (RUCA) zip code-level files, available in Table 1, and were used to create the following categories: Metropolitan (1, 2, 3); Micropolitan (4, 5, 6); and Rural (7, 8, 9, 10).<sup>32</sup> RUCA codes were chosen as they are an estimate of rurality as they were created as an improvement upon other federal measures of rurality, including rural-urban continuum codes, and offer a more accurate depiction of rural areas in the United States.<sup>33</sup> Table 2 provides a summary of all demographic and predictor variables included in the analysis.

**Table 1. Rural-Urban Commuting Codes Categorization and Definitions<sup>32</sup>**

Category	RUCA Code	Description
Metropolitan	1	Metropolitan area core: primary flow within an urbanized area
	2	Metropolitan area high commuting: primary flow 30% or more to an urbanized area
	3	Metropolitan area low commuting: primary flow 10% to 30% to an urbanized area
Micropolitan	4	Micropolitan area core: primary flow within an urban cluster of 10,000 to 49,000 (large urban cluster)
	5	Micropolitan high commuting: primary flow 30% or more to a large urban cluster
	6	Micropolitan low commuting: primary flow 10% to 30% to a large urban cluster
Rural	7	Small town core: primary flow within an urban cluster of 2,500 to 9,999 (small urban cluster)
	8	Small town high commuting: primary flow 30% or more to a small urban cluster
	9	Small town low commuting: primary flow 10% to 30% to a small urban cluster
	10	Rural areas: primary flow to a tract outside a urbanized area or urban cluster

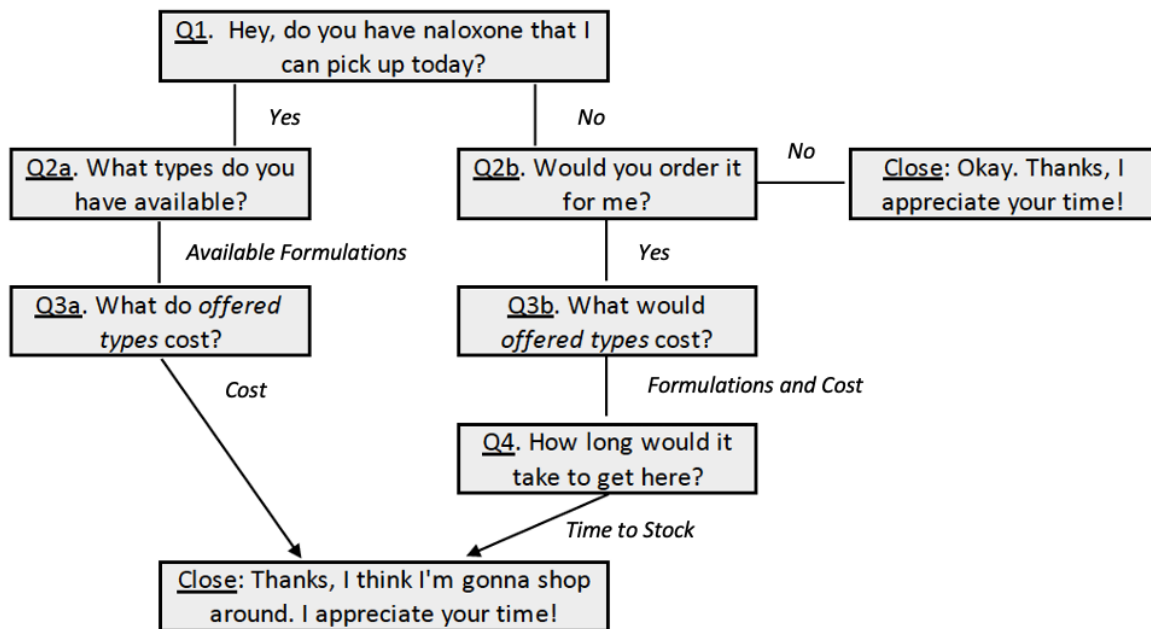
**Table 2. Summary of Variables**

Variable	Levels of Variable	Method of Measure
<b>I. Demographic Information</b>		
Pharmacy Type	Independent Pharmacy Chain Pharmacy Grocery-store Pharmacy	Based on Investigator-Collected Classification
Pharmacy County	County Name	Based on Investigator-Collected Location
Pharmacy Zip Code	County Zip Code	Based on Investigator-Collected Location
<b>II. Outcome Variables</b>		
Naloxone Availability	Naloxone Available Naloxone Unavailable	Survey: Pharmacy Report Question Q1
Naloxone Formulations	Naloxone Nasal Spray Naloxone Injection	Survey: Pharmacy Report Question Q2a and Q3b
Naloxone Cost	Cost in United States Dollars	Survey: Pharmacy Report Questions Q3a and Q3b
Willingness to Order Naloxone	Willing to Order Naloxone Unwilling to Order Naloxone	Survey: Pharmacy Report Question Q2b
Time to Stock Naloxone	Minimum Hours Reported	Survey: Pharmacy Report Question Q4
<b>III. Predictor Variables</b>		
Race	County Percent White County Percent Nonwhite	Based on 2020 Census Data
Proportion of County Population Below Poverty Line	Proportion of County Households Below the Poverty Line	Based on 2020 American Community Survey Data
Overdose Deaths	Number of Overdose Deaths in County in 2020	Based on 2020 Provisional Data Report from Mississippi Opioid and Heroin Data Collaborative
Percent Uninsured	Percent of County Uninsured	Based on American Community Survey Data
Pharmacy Rurality	Metropolitan Micropolitan Rural	Based on Pharmacy Zip Code and 2010 Rural-Urban Commuting Area (RUCA) codes

***Data Collection***

Dr. Gravlee compiled a county-level list of pharmacies using Google searches starting February 2022. In late May, the Hayes 2022 List of Mississippi Community Pharmacies was obtained and used to verify and add to the initial county-level pharmacy list. To ensure completeness of the manually compiled list, Dr. Gravlee cross-checked any county-level lists of

pharmacies created before May with the Hayes list. Additionally, to verify the Hayes list completeness, a manual check of a random 10% sample of counties was performed. Before the pharmacy was called, pharmacy zip code, pharmacy county, and chain, independent, or grocery store status was collected in a data collection form housed within Qualtrics. Each community pharmacy was then contacted by telephone and asked study questions. Study questions and flow are available in Figure 1. When calling a pharmacy, the caller held for up to 15 minutes on the line before hanging up. The caller asked the person who answers the phone, regardless of whether they were a pharmacist or not, the survey questions. If unable to reach anyone at the pharmacy, the caller tried the pharmacist at a different date and time with no more than five attempts made to reach each pharmacy before it was listed as missing from the dataset.



**Figure 1. Study Survey Questions and Flow**

Each pharmacy on the compiled list was called. Study volunteers were recruited from the University of Mississippi Professional Pharmacy Degree Program and Early Entry Program using a flyer and email announcement. Before participating, volunteers completed the Collaborative Institutional Training Initiative (CITI) Social and Behavioral Responsible Conduct of Research Code 1 training. To improve call consistency, volunteers were required to shadow Dr. Gravlee performing at least two calls before they were allowed to call pharmacies on their own. Volunteers were provided a copy of the study protocol, a county-level pharmacy call list, and a link to the Qualtrics data collection form before starting their own calls.

During initial data collection, volunteers were assigned counties from geographically distinct areas to ensure state representativeness in case of unmasking of the secret shopper study. After observations from different regions of the state had been collected volunteers were assigned counties in the alphabetical order in which they were available. Volunteers were allowed preference in how many observations they wanted to collect. For example, they were given a choice between a county with a low versus high number of pharmacies to call, and volunteers were provided a choice to whether they wanted to engage in data collection beyond a single county. After volunteers had completed the county-level pharmacy call list provided to them they were asked to return the completed call log. At this point, volunteers indicated whether they wanted to continue to engage in data collection. If so, they were provided all study materials (copy of the study protocol, county-level pharmacy call list, and link to Qualtrics data collection form) in a new email. On average, each volunteer collected data from approximately 30 pharmacies. Notably, volunteers who were pharmacy students were not allowed to collect data from counties where they had lived or been employed.

### ***Data Management***

Data was collected and entered into a Qualtrics intake form. After data collection, data was transferred from Qualtrics into the Statistical Package of the Social Sciences (SPSS) Version 28 for Mac for cleaning and then to SAS Studio for analysis.

### ***Data Analysis***

Naloxone availability and cost was mapped at a county-level. To assess geographic trends in availability, maps were created to visualize proportion of the population below the poverty line, uninsured status, and opioid overdose deaths. Chi-square tests were used to evaluate differences in naloxone availability by pharmacy type. T-tests were used to evaluate differences in naloxone availability by neighborhood factors. Available naloxone formulations, willingness to order naloxone, time to stock naloxone, and naloxone costs were descriptively analyzed. To protect pharmacies' privacy during the mapping process, naloxone availability per county was reported as an ordinal variable and the denominator of pharmacies per county was suppressed.

## CHAPTER IV

### RESULTS

#### *Pharmacy Descriptive Statistics*

There were 591 publicly available community pharmacies surveyed in Mississippi. The most common type of pharmacy type was independent ( $n=328$ , 55.50%), followed by chain ( $n=147$ , 24.87%), and grocery store pharmacy ( $n=116$ , 19.63%). According to RUCA classifications, most pharmacies were located in metropolitan areas ( $n = 249$ , 42.48%), followed by micropolitan ( $n = 185$ , 31.41%) and then rural ( $n = 155$ , 26.32%) areas. Table 3 shows the breakdown of pharmacy by type and rurality.

**Table 3. Breakdown of Pharmacies by Type and Rurality**

	Metropolitan <i>n</i>	Micropolitan <i>n</i>	Rural <i>n</i>	Total <i>n</i> (%)
Independent <i>n</i> (%)	106 (32.31)	110 (33.54)	112 (34.15)	328 (100)
Chain <i>n</i> (%)	86 (58.50)	38 (25.85)	23 (15.65)	147 (100)
Grocery Store <i>n</i> (%)	57 (49.14)	37 (31.90)	22 (18.97)	116 (100)

#### *Naloxone Availability*

When asked, “Do you have naloxone that I can pick up today?” 36.6% ( $n=216$ ) of surveyed pharmacies indicated that naloxone was available. Among pharmacies that stocked naloxone, the nasal spray was the most commonly-available formulation ( $n=212$ , 98.15%). Overall, 7.41% ( $n=16$ ) of pharmacies with naloxone in stock had the injectable formulation on



hand, and 2.03% ( $n=12$ ) had both the nasal spray and injectable naloxone in stock. The mean cost for naloxone nasal spray was \$105.58 (SD = 35.41, median = \$100.00, range \$38.11 to \$229.39) and the mean cost for the naloxone injection was \$66.62 (SD = 69.27, median = \$37.70, range \$17.00 to \$208.96). Among pharmacies that did not have naloxone in stock but were willing to dispense naloxone ( $n=133$ ), the majority were willing to order naloxone ( $n=101$ , 75.94%). The mean time to stock naloxone nasal spray was 41 hours ( $n=88$ , SD = 38.89) and the mean time to stock the naloxone injection was 28 hours ( $n=12$ , SD = 13.86).

***Differences in Naloxone Availability by Pharmacy Factors***

There were differences in naloxone availability based on pharmacy type ( $X^2 (2, 591) = 41.09, p < 0.001$ ), but not pharmacy rurality ( $X^2 (2, N = 591) = 3.06, p = 0.216$ ) as defined by RUCA metropolitan, micropolitan, and rural classifications (Table 1). Among pharmacy types, independent pharmacies were the least likely type of pharmacy to have naloxone available while chain pharmacies were the most likely pharmacy to have naloxone available. Table 4 contains a breakdown of naloxone availability by pharmacy type. Table 5 examines willingness to order naloxone by pharmacy type.

**Table 4. Naloxone Availability Stratified by Pharmacy Type**

	Independent $n$ (%)	Chain $n$ (%)	Grocery Store $n$ (%)
Naloxone Available $n$	84 (25.61)	67 (45.58)	65 (56.03)
Naloxone Unavailable $n$	244 (74.39)	80 (54.42)	51 (43.97)

**Table 5. Willingness to Stock Among Pharmacies Where Naloxone is Unavailable**

	Independent <i>n</i> (%)	Chain <i>n</i> (%)	Grocery Store <i>n</i> (%)
Naloxone Unavailable and Willing to Stock <i>n</i>	64 (26.23)	22 (27.50)	15 (29.41)
Naloxone Unavailable and Not Willing to Stock <i>n</i>	19 (7.79)	10 (12.50)	3 (5.88)
Willingness to Stock Not Assessed* <i>n</i>	161 (65.98)	48 (60.00)	33 (64.71)

\* Not assessed due to refusal to engage regarding naloxone under standing order

***Differences in Naloxone Availability by Neighborhood Factors***

There were no differences in naloxone availability by county-level proportion below the poverty line ( $t(589) = 1.52, p = 0.128$ ), proportion of the population that is non-white ( $t(589) = 1.71, p = 0.088$ ), proportion of the population that is uninsured ( $t(589) = 0.96, p = 0.336$ ), or number of overdose deaths in the county in 2020 ( $t(589) = -1.65, p = 0.100$ ).

***Naloxone Availability Mapping***

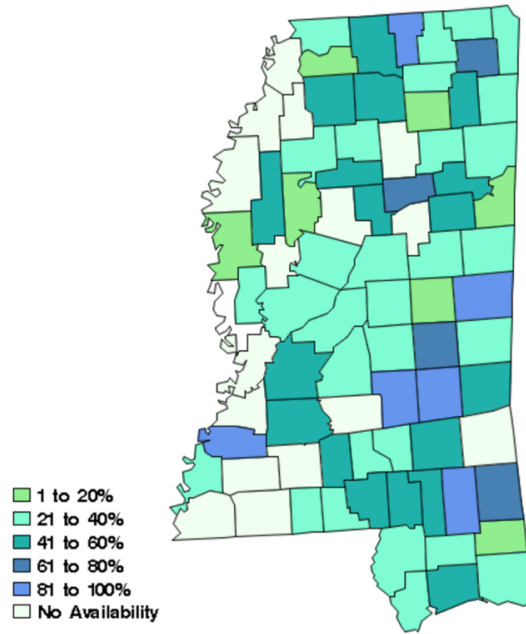
The proportion of pharmacies with naloxone and naloxone nasal spray cost were mapped at a county level (Figures 2, 3). Additionally, the number of pharmacies with naloxone available and the number of overdoses per 10,000 people were mapped to display the density of each factor (Figures 4,5). The proportion of the population that is uninsured, the proportion of the population that is nonwhite, and the proportion of the population that lives below the poverty line were mapped at a county level to visually examine potential geographic patterns in naloxone access and other social determinants of health in Mississippi (see Appendix 1). When mapping naloxone availability across the state, no data for Issaquena County was reported as there are no pharmacies in that county. All other counties contained at least one pharmacy.

Overall, 16 (19.25%) of 82 Mississippi counties had no naloxone availability at community pharmacies. These counties are concentrated along the Western border (Figure 2)

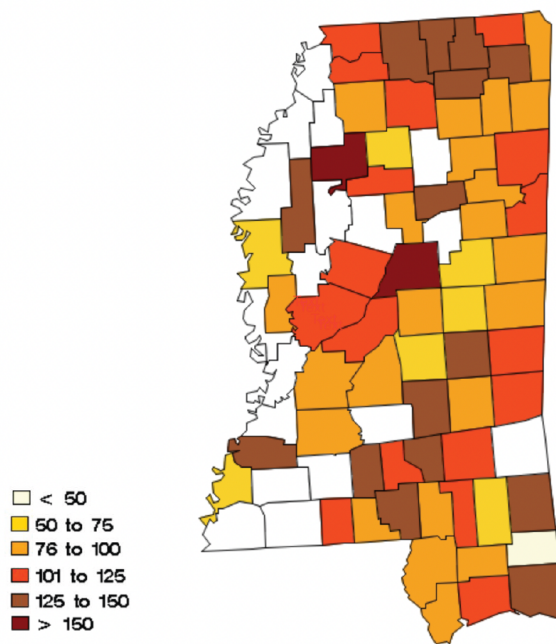
and include the Northwest, Delta, and Southwest portions of the state. There do not appear to be patterns related to naloxone availability related to opioid overdose deaths in the state (Figure 4). Two counties with the highest overdose rates, Hinds and Jackson counties, both have moderate to low naloxone availability (between 41-60% and between 21-40% of community pharmacies stocked naloxone, respectively) at community pharmacies. Other areas of interest near the Southern coast of the state, namely Pearl River County, have low naloxone availability (21-40% of pharmacies stocked naloxone) despite being heavily populated (Figure 4) and experiencing a higher number of overdose deaths than most other counties (Figure 5). Additionally, despite being areas of higher population density close to a metropolitan area, Madison and Rankin counties have a low proportion (21-40% of pharmacies stocked naloxone) of pharmacies stocking naloxone (Figure 2).

### ***Naloxone Nasal Spray Cost Mapping***

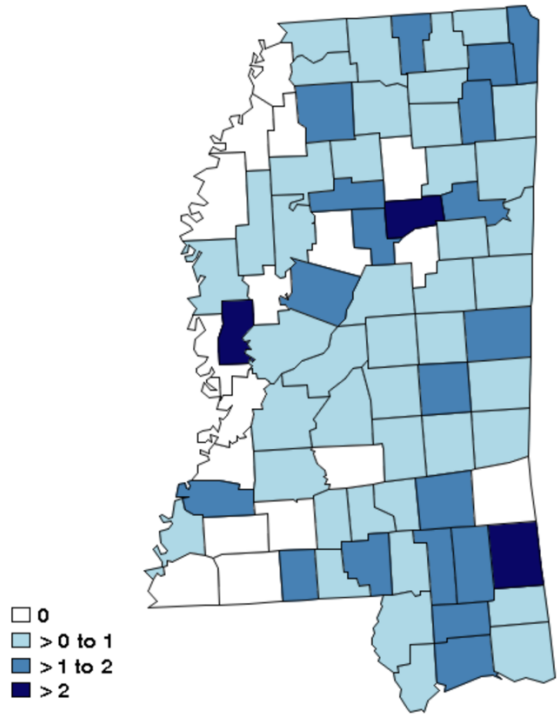
Because of the limited number of pharmacies reporting stock of injectable naloxone ( $n=16$ ), only naloxone nasal spray cost was mapped. For only those counties where naloxone nasal spray was available, the cost of naloxone nasal spray was mapped at a county level (Figure 3). Mapping naloxone cost across the state reveals that quoted costs for naloxone were highest across the Northern border of the state. Despite this finding, this area was not where highest naloxone costs were observed. Naloxone nasal spray costs were quoted to be higher than \$150 in both Attala and Tallahatchie counties. Almost half ( $n=30$ , 46.88%) of all counties where a pharmacy stocked naloxone nasal spray have naloxone nasal spray available for less than \$100.



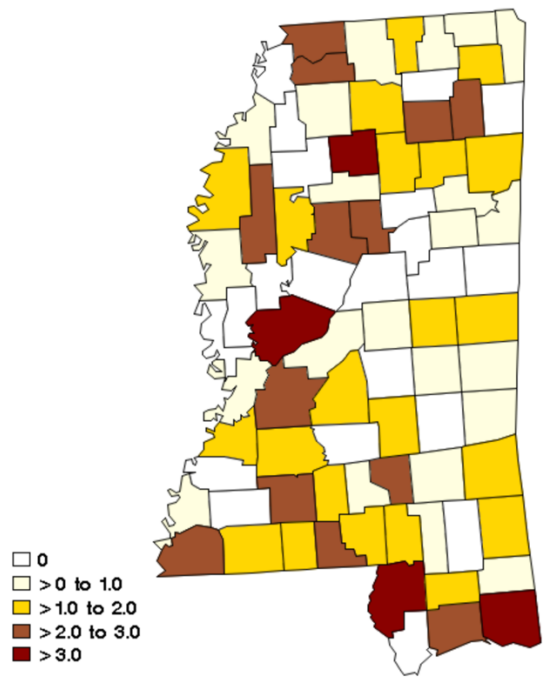
**Figure 2. Proportion of Pharmacies with Naloxone Available in Each Mississippi County**



**Figure 3. Average Cost (USD) of Naloxone Nasal Spray in Each Mississippi County**



**Figure 4. Number of Pharmacies with Naloxone Available per 10,000 People by Mississippi County**



**Figure 5. Number of Overdose Deaths in 2020 per 10,000 People by Mississippi County**

## CHAPTER V

### DISCUSSION

#### *Naloxone Availability and Cost*

While a standing order for naloxone exists across Mississippi, this study shows that less than half of all Mississippi pharmacies make naloxone available for consumers under standing order. The proportion of pharmacies with naloxone available in this census is lower than most others found in literature<sup>34</sup>, and notably even lower than what was found in a study examining naloxone access across community pharmacies within Alabama<sup>8</sup>, a socioeconomically comparable state. This finding highlights the benefit of census methodology when assessing naloxone availability. When we examine access to naloxone at a county level instead of aggregating to the total number of pharmacies in the state, we find almost one-fifth ( $n=16$ , 19.75%) of 81 Mississippi counties containing pharmacies have no naloxone access. This study also suggests that large gaps in naloxone access may be driven by pharmacy mix. Independent pharmacies are the most common type of pharmacies across the state and were also found to be the least likely to have naloxone available for patients wishing for naloxone pickup that day.

The lack of naloxone availability in independent pharmacy settings found in this study aligns broadly with other literature around naloxone availability, which shows that chain pharmacies are more likely than independent pharmacies to have naloxone available.<sup>9,29</sup> There are a variety of reasons that independent pharmacies may have less naloxone than other pharmacy types. To start, independent pharmacies in Mississippi are not required to stock naloxone. Many chain pharmacies have enacted policies or adopted language that encourage

stores to have the medication on-hand.<sup>35,36</sup> CVS claims that nationwide locations have naloxone on hand, and promise naloxone to be available within 1-2 business days.<sup>35</sup> Likewise, Walgreens notes that naloxone is available without a prescription in all its stores across the United States.<sup>36</sup> These corporate positions promote naloxone access in the community. The case of independent pharmacies not stocking naloxone may be what is expected in the absence of such pressure. Other business-related factors may influence the decision of an independent pharmacy to not stock naloxone.<sup>8</sup> For example, lack of perceived demand in the community and fear of product waste both may lead a pharmacist to not stock naloxone. Previous research has found that a small percentage of pharmacists endorsed both expense and lack of patient demand as reasons for not stocking naloxone.<sup>8</sup> The same study also found that 10.5-20.2% of surveyed pharmacists claimed that patients being unable to pay contributed to their decision to not stock naloxone.<sup>8</sup>

Pharmacists' beliefs about naloxone or the people that need it may also influence naloxone availability. While positive attitudes towards naloxone services have been demonstrated in the literature<sup>37</sup>, political atmosphere within studied states may not be representative of attitudes in the Southeastern USA. A study examining pharmacists' attitudes towards naloxone dispensing in Alabama found that 17.3-37.4% of surveyed Alabama pharmacists felt that naloxone dispensing was a useful service to the community, and up to 16.7% felt that naloxone allowed opioid users to continue using at riskier levels than they would without naloxone availability.<sup>8</sup> Potentially, pharmacists' attitudes or misconceptions around naloxone use or users may also be driving decisions to not offer naloxone. Further qualitative studies examining the attitudes of Mississippi pharmacists, and particularly Mississippi independent pharmacists, towards naloxone dispensing under the standing order are warranted.

Mapping of naloxone availability reveals that in the Western portion of the state, including the Delta, Northwest, and Southwest regions, there was lower overall availability of naloxone. Regional disparities in naloxone access, especially in the Western portion of the state, may again be driven by the types of pharmacies which more commonly exist in these areas. For example, in the Northwestern area of the state, which is comprised of Tunica, Coleman, Quitman, and Tallahatchie counties<sup>38</sup>, 91.67% of all pharmacies are independent pharmacies. In the Southwestern portion of the state<sup>38</sup>, 68.97% of all pharmacies are independent pharmacies. However, this narrative does not hold for all of Mississippi. Gaps in naloxone availability also exist at community pharmacies in areas of the state experiencing high overdose deaths and with high population density, for example, in Jackson and Pearl River counties, where only 34.78% and 27.27% of county pharmacies had naloxone available, respectively. Additionally, despite high overdose rates and a variability of pharmacy types around the state capitol, Hinds County had only moderate availability of naloxone (between 41-60% pharmacies stocked naloxone) at community pharmacies. While not in the scope of the current study, a metric for demonstrating naloxone need may be useful to best identify communities where naloxone accessibility interventions would be most beneficial.

Quoted prices and price ranges for naloxone aligned with existing literature, which has demonstrated wide variability in prices geographically.<sup>5,9</sup> Mapping of naloxone costs identified some patterns in naloxone cost across the state. For example, costs for naloxone nasal spray were higher at the Northern border of the state, including Marshall, Benton, Tippah, Prentiss, and Union counties. Of all counties in Mississippi, Tallahatchie and Attala reported the highest costs for naloxone nasal spray, with the average cash cost of naloxone nasal spray in each county



quoted as exceeding \$150. While both of these counties had low naloxone availability under state standing order, there is no clear driver of naloxone nasal spray costs within these areas.

Lack of a clear driver of highly variable costs indicates a need to further explore naloxone cost differences. Given that average wholesale acquisition cost (WAC) for a unit of naloxone nasal spray is ranges from \$110-130 (generally, naloxone nasal spray is packed as two units per package for an average unit cost of around \$55-65)<sup>39</sup>, higher-end estimates of cost provided by pharmacists greatly exceed the anticipated profit margin related to this drug. For example, one pharmacy's quoted cost of \$229.39 represents a markup of roughly 176% for a naloxone package or roughly 353% for a unit dose. Because we see pricing vary substantially post-wholesale, these costs demonstrate pricing choices made by pharmacies themselves. If quoted mean prices are for unit doses of naloxone, markup for naloxone well exceeds the industry post-WAC standard markup of 20%.<sup>40</sup>

Reasons for this high markup are unclear. Notably, costs presented in this study are not necessarily factual prices, but those quoted by pharmacy staff on the phone. It is possible that prices quoted may have been influenced by staff member-specific factors, including attitudes regarding naloxone use or those who use naloxone, which may be a key driver in naloxone access across the state. Regardless of reason for high naloxone markup, further studies examining costs and cost differences for this life-saving medication are needed.

### ***Differences in Naloxone Availability by Key Factors***

This study found differences in naloxone availability based on pharmacy type, which is widely supported by other literature.<sup>8,29,34</sup> Despite previous evidence of rurality disparities in the Southeastern US<sup>8</sup>, this study found no differences in naloxone accessibility by rurality. However, the current finding aligns with a recent meta-analysis which found that there was no significant

difference in naloxone availability without a prescription based on rurality of the pharmacy.<sup>34</sup> This study also failed to find any difference in naloxone availability based on the proportion of the county that was non-white, proportion of the county that was uninsured, the proportion of the county below the poverty line, and number of overdose deaths per county in 2020. These results are partly supported by other literature. A study by Egan et al conducted in North Carolina found that naloxone availability did not differ based on number of opioid overdose death rates in neighborhoods, but did differ based on proportion of individuals with public insurance.<sup>29</sup> Ultimately, these nonsignificant findings, in conjunction with the finding that independent pharmacists are the group least likely to stock naloxone, supports that there is a lack of external influence on naloxone availability within the state. This lack of external influence on naloxone availability suggests that barriers to naloxone access may be driven by internal pharmacist- or pharmacy-related factors.

### ***Limitations***

Limitations of this study include the large number of individuals collecting data, diverse pharmacy staff attitudes towards secret shopper calls, potential bias due to extended period of time over which calls were made, and the use of curated lists to identify pharmacies. Although individuals collecting data were trained and given a script to follow when collecting naloxone availability data, it is likely that deviations existed across calling methods for individuals collecting data due to the secret shopper nature of the study. These differences in call strategy may have influenced pharmacy responses. Additionally, pharmacy staff or pharmacists may have had reservations to assisting secret shoppers with their requests over the phone. For example, a pharmacy employee may feel uncomfortable with answering questions about naloxone over the

telephone or may not want to provide this information to patients with whom they are not familiar. This may have downwardly biased the estimate of naloxone availability across the state.

Secret shopper calls were also conducted over a long period. Although calls were conducted strategically to put geographic distance between sequential call areas, it is possible that receiving calls inquiring about naloxone availability influenced naloxone's availability at other pharmacies. Pharmacists may have informed other stores in their area about this call, or may have spoken with their friends about the request. This could have led to either an upward or downward bias in naloxone availability depending on the attitude of the pharmacy staff towards harm reduction practices, or their comfort in speaking with anonymous patients. Finally, there was difficulty in obtaining a complete pharmacy list for the study, and two approaches were used to obtain a pharmacy call list. While steps were taken to ensure that the list was accurate, there is no way to be certain investigators reached every pharmacy in the state without reviewing state registration documents.

### ***Implications and Conclusions***

This study suggests that, despite lawful availability, naloxone is not widely accessible to patients under Mississippi state standing order. While mapping identifies patterns in naloxone availability, findings from this study suggest that pharmacist or pharmacy-related factors may be drivers of poor uptake of the standing order. Further studies focusing on independent community pharmacists in Mississippi should be conducted to assess reasons for lack of naloxone standing order uptake. Additionally, wide pricing variations and high markup suggest a probe is needed to understand patterns in pricing this life-saving drug.

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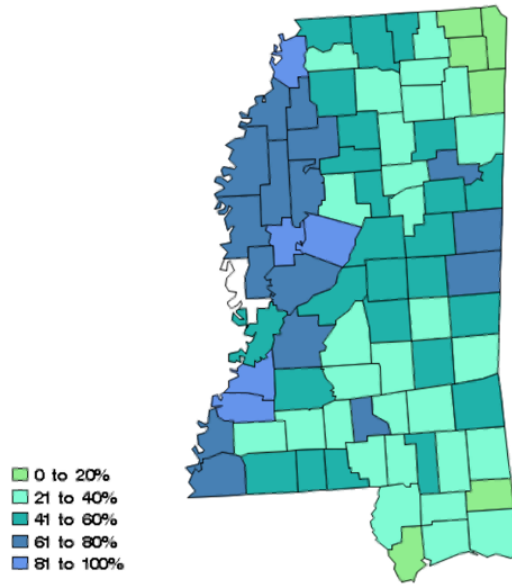
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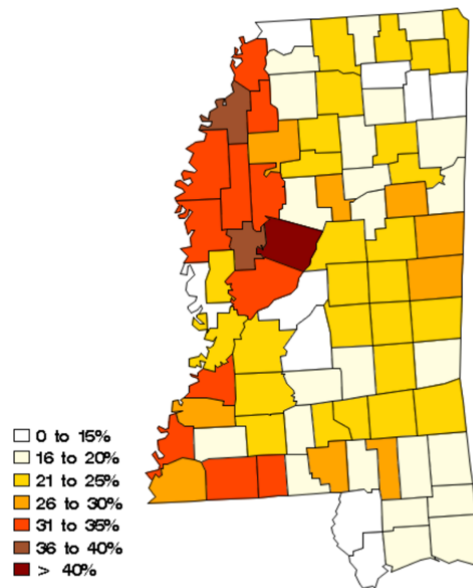
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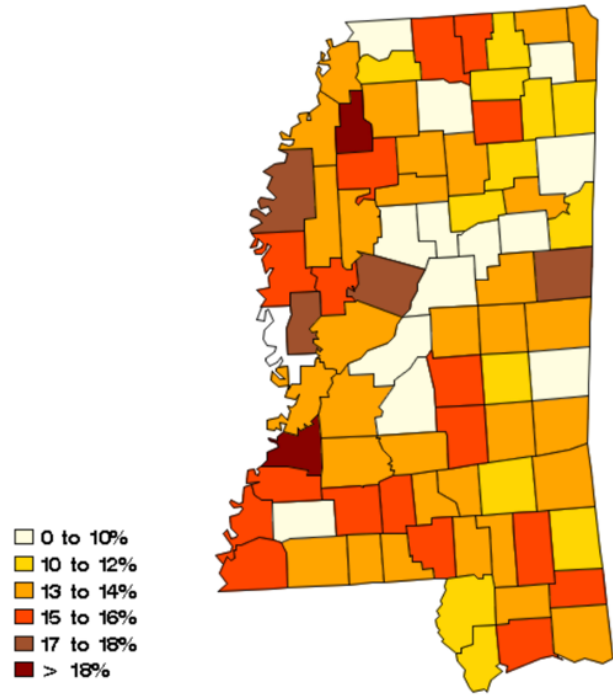
## **APPENDIX**



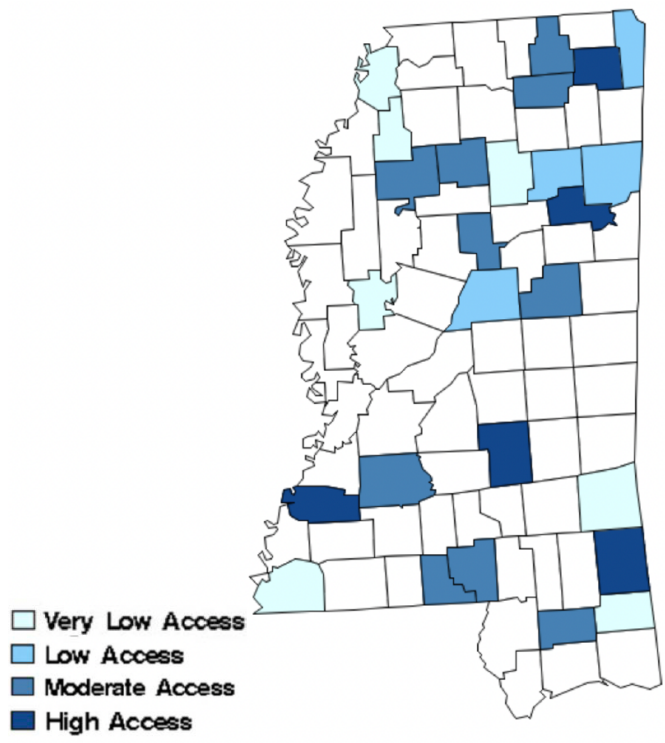
**Figure 6. Proportion of Population that is Non-white for Each Mississippi County**



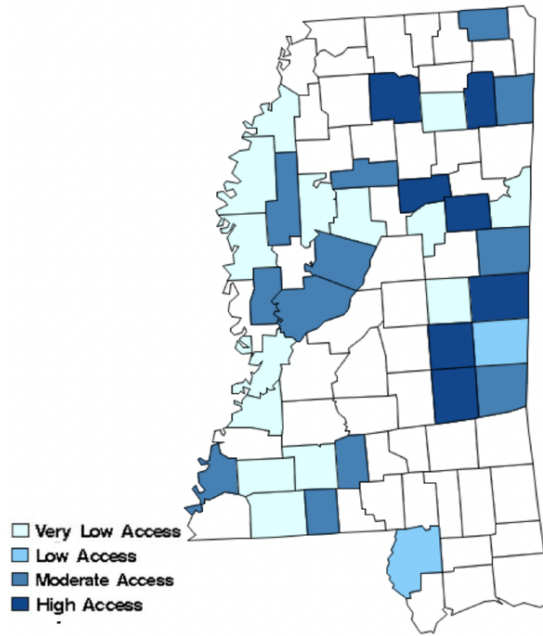
**Figure 7. Proportion of Population Below Poverty Line for Each Mississippi County**



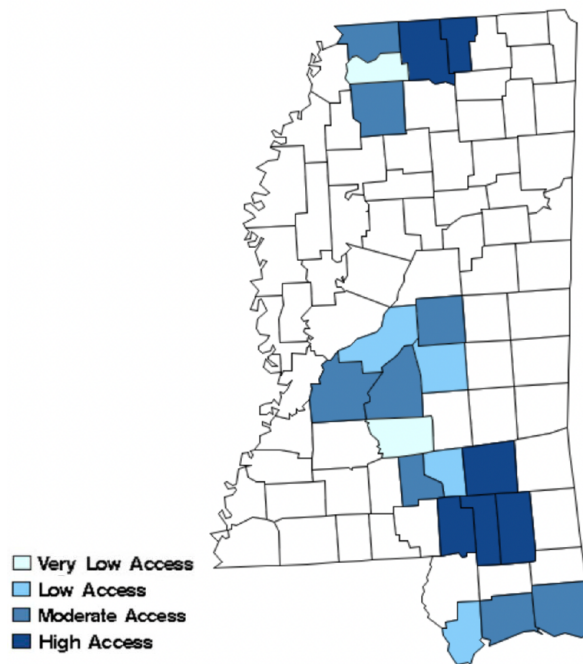
**Figure 8. Proportion of Population Uninsured for Each Mississippi County**



**Figure 9. Naloxone Availability by Quintile Among Rural Mississippi Counties**



**Figure 10. Naloxone Availability by Quintile Among Micropolitan Mississippi Counties**



**Figure 11. Naloxone Availability by Quintile Among Metropolitan Mississippi Counties**

## VITA

Emily Gravlee graduated from the University of Mississippi in 2017 with a Bachelor of Science in Pharmaceutical Sciences and in 2020 with a Doctor of Pharmacy before enrolling in graduate school at the University of Mississippi. She was recognized by the University as a Provost Elite Scholar in 2020 and a University of Mississippi Medical Center Graduate Training and Education Center Robert Smith, MD, Graduate Scholar in 2021.