



PBSS Issue Brief:

Geographic Patterns in Neonatal Abstinence Syndrome and Prescription Opioids in Kentucky

The Rising Issue of NAS

In the wake of the ongoing opioid epidemic, neonatal abstinence syndrome (NAS) has increased sharply nationwide, more than tripling from 2004 to 2013.1 Infants with NAS have longer, more complicated postnatal hospitalizations, with higher risk of low birthweight, significant respiratory complications (including meconium aspiration and respiratory distress syndrome), feeding difficulties, sepsis, and seizures.2 Preventing opioid use disorder among women of childbearing age could help reduce the incidence of NAS,3 and a key strategy for preventing opioid use disorder, not only among women of childbearing age, but for all persons at risk, is to improve the prescribing of opioids for chronic pain. Over-prescribing of opioids has played a major role in the ongoing opioid epidemic in the U.S., and the recent prescribing guideline issued by the Centers for Disease Control and Prevention is aimed at improving prescribing practices.4

Surveillance Data Can Reveal Areas at Increased Risk

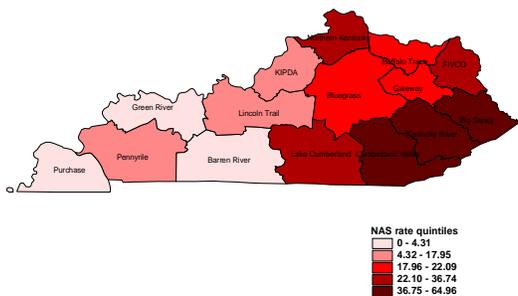
A national surveillance tool for monitoring progress towards more responsible prescribing of opioids in the U.S. is available, and is known as the Prescription Behavior Surveillance System, or PBSS. This system utilizes de-identified, aggregate data from twelve state prescription drug monitoring programs (PDMPs) to calculate a range of controlled substance prescribing indicators at the population level, such as overall rate of opioid prescriptions per 1000 residents, and average dose prescribed. Among these participating PDMPs is the Kentucky All Schedule Prescription Electronic Reporting System, known as KASPER, whose data serves as the focus for this PBSS issue brief. When depicted geographically, PBSS indicators of opioid prescribing behavior can highlight certain regions within a state where opioid prescribing practices may place people at higher risk for opioid use disorder. In this PBSS issue brief, we compare the geographic pattern of NAS rates in the state of Kentucky with the geographic pattern of several PBSS prescribing indicators in the state to demonstrate the relationship between opioid prescribing practices and the risk of NAS.

Geographic Distribution of NAS in Kentucky

Using de-identified NAS data provided by the Kentucky Department for Public Health’s Division of Maternal and Child Health, NAS rates by quintiles were calculated for the period August 2014 through July 2015 for each of Kentucky’s Area Development Districts (ADDs).5 The analysis reveals that the highest NAS rates in Kentucky were concentrated in the southeastern portion of the state (Figure 1).6

Figure 1: Neonatal Abstinence Syndrome Rates per 1,000 Live Births, August 1, 2014 – July 31, 2015.

Rates of NAS per 1,000 live births were lowest in western Kentucky and highest in southeastern Kentucky.

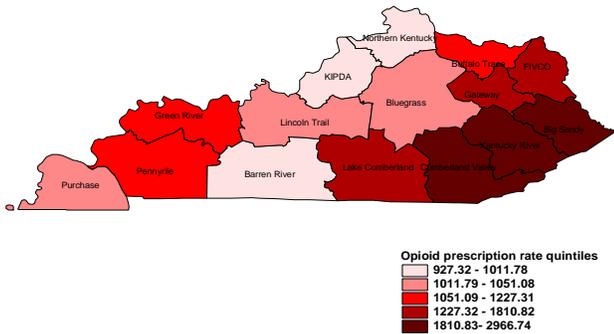


Source: KY Cabinet for Health and Family Services, Department for Public Health, Division of Maternal & Child Health, NAS Surveillance Registry

Geographic Distribution of PBSS Prescribing Indicators in Kentucky

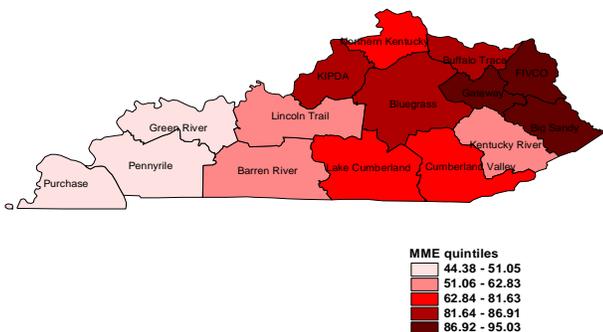
PBSS prescribing indicators for women of childbearing age (aged 17-44) were examined for August 2013-July 2014, the year prior to the NAS data examined, during which time opioid exposure could potentially have adversely affected the developing fetus. The following four measures of opioid prescribing were calculated by quintiles and geographically displayed by ADD: rates of opioid prescribing (Figure 2); average daily opioid dosage in morphine milligram equivalents⁷ (Figure 3); overlapping opioid and benzodiazepine prescriptions⁸ (Figure 4); and opioid prescriptions associated with multiple provider episodes (MPEs⁹) (Figure 5).

Figure 2: Opioid Prescription Rates to Females Aged 17 – 44, per 1,000 Population, August 31, 2013 – July 31, 2014. Rates of opioid prescribing to females aged 17-44 were highest in the same southeastern ADDs that had the highest rates of NAS a year later (see Figure 1).



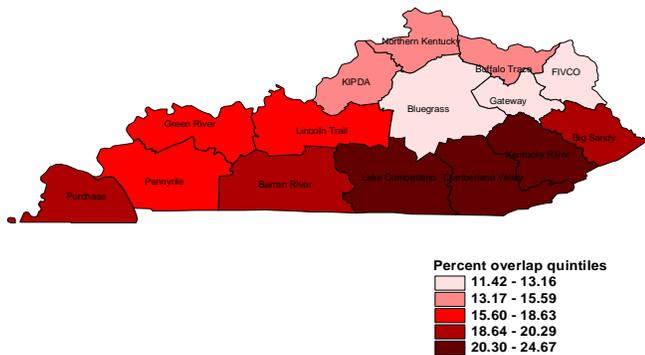
Source: KASPER Data contained in the Prescription Behavior Surveillance System at Brandeis University

Figure 3: Average Daily Opioid Dosage per Patient in Morphine Milligram Equivalents (MME) for Females Aged 17 – 44, August 1, 2013 – July 31, 2014. The average daily opioid dosage was highest in the easternmost ADDs, and NAS rates were relatively high in these same areas the following year (Figure 1). Big Sandy ADD was in the highest quintile for rates of both NAS and average daily opioid dosage.



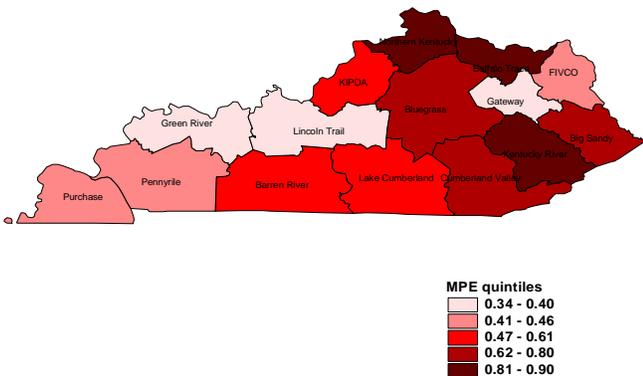
Source: KASPER Data contained in the Prescription Behavior Surveillance System at Brandeis University

Figure 4: Percent of Opioid/Benzodiazepine Prescription Days with Overlapping Opioid and Benzodiazepine Prescriptions, for Females Aged 17 – 44, August 1, 2013 – July 31, 2014. Overlapping opioid and benzodiazepine prescriptions dispensed to females aged 17-44 were highest in the southeastern Kentucky ADDs. Two of these ADDs, Cumberland Valley and Kentucky River, were also in the highest quintile for NAS rates.



Source: KASPER Data contained in the Prescription Behavior Surveillance System at Brandeis University

Figure 5: Percent of Opioid Prescriptions to Females Aged 17 – 44 Associated with Multiple Provider Episodes (MPEs), August 1, 2013 – July 31, 2014. Percent of opioid prescriptions associated with MPEs among females aged 17-44 were highest in eastern Kentucky, with two northeastern ADDs in the top quintile. Kentucky River ADD was in the highest quintile for both opioid prescriptions associated with multiple provider episodes and NAS rate.



Source: KASPER Data contained in the Prescription Behavior Surveillance System at Brandeis University

Correlation between High Rates of NAS and Risky Prescribing Practices

Comparison of geographic distributions of NAS rates with opioid prescribing rates (Figure 1 vs Figure 2), reveals a high degree of similarity, with both rates being highest in three southeastern ADD areas of Cumberland Valley, Kentucky River, and Big Sandy. These overlapping geographic patterns are suggestive of a close association between NAS and high opioid prescribing rates the preceding year among women of childbearing age. Comparison of NAS rates with average daily opioid dosing, percentage of overlapping opioid/benzodiazepine prescriptions, and percent of opioid prescriptions associated with a multiple provider episode reveal a lesser degree of geographic overlap compared to opioid prescribing rates, but does reveal a general pattern of higher rates of these prescribing behaviors in the eastern half of the state, where NAS rates also tend to be higher.

A Path Forward

Overall, these similar geographic patterns are suggestive of a general association between risk of NAS and risky opioid prescribing behaviors and highlight the importance of improving opioid prescribing practices in order to decrease the risk of opioid use disorder among women of childbearing age.¹⁰ The Kentucky Administrative Regulation establishing Professional Standards for prescribing and dispensing controlled substances ([201 KAR 9:260](#)), and the CDC's Guideline for Prescribing Opioids for Chronic Pain are important tools which can be used by providers to improve opioid prescribing practices. Academic detailing, a proven method for increasing provider knowledge and enhancing implementation of opioid prescribing best practices, could be emphasized in the response to the opioid epidemic in Kentucky, particularly in those areas of the state where risky opioid prescribing practices are most evident.¹¹ Ongoing surveillance of PBSS opioid prescribing indicators and NAS rates in Kentucky could serve to assess the impact of such interventions, including the long term impact of Kentucky's recent comprehensive prescription drug abuse legislation (HB1),¹² which includes measures designed to improve opioid prescribing practices in the state.¹³

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About PBSS. The Prescription Behavior Surveillance System (PBSS) provides epidemiological analyses of de-identified data from state prescription drug monitoring programs to help target and evaluate interventions aimed at reducing prescription drug abuse and diversion. For further information, see the PBSS webpage at <http://www.pdmpassist.org/content/pbss>.

Endnotes

- ¹ Veeral N. Tolia et al., Increasing Incidence of the Neonatal Abstinence Syndrome in U.S. Neonatal ICUs, *N Engl J Med* 2015; 372:2118-2126, May 28, 2015, DOI: 10.1056/NEJMsa1500439, <http://www.nejm.org/doi/full/10.1056/NEJMsa1500439>; Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012 Patrick SW, Davis MM, Lehman CU, Cooper WO. *J Perinatol*. 2015 Aug;35(8):667. doi: 10.1038/jp.2015.63. <http://www.ncbi.nlm.nih.gov/pubmed/26219703>
- ² Patrick SW, Davis MM, Lehman CU, Cooper WO, Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009-2012, *Jour of Perinatology* (2015), 35, 650-655
- ³ Implementation of a Statewide Surveillance System for Neonatal Abstinence Syndrome — Tennessee, 2013 *Morbidity and Mortality Weekly Report (MMWR)*, February 13, 2015 / 64(05);125-128, <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6405a4.htm>
- ⁴ Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1–49. DOI: <http://dx.doi.org/10.15585/mmwr.rr650>

⁵ Kentucky is divided into 15 regions known as Area Development Districts (ADD). These ADDs provided a wide variety of services to the counties they serve such as Workforce and Economic Development, Healthcare and Aging Services, etc. Each ADD is comprised of a group of counties.

⁶ NAS cases reported here may include drugs besides opioids; poly-substance use is common among mothers of NAS-affected infants. Women of childbearing age are at risk for newborns with NAS even if they take opioids as prescribed or as part of medication-assisted treatment for opioid use disorder, see Jones, H.E., et al., Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on the neonatal abstinence syndrome, *Drug and Alcohol Dependence*, Volume 79, Issue 1, 1 July 2005, pp. 1–10, <http://www.sciencedirect.com/science/article/pii/S0376871605000189>.

⁷ Daily morphine milligram equivalents (MMEs) is the daily dosage of morphine that would provide an equal amount of analgesia as the daily dosage of the opioid. Mean daily dosage is calculated for state residents in the PDMP that have an opioid prescription in a given quarter and refers to MMEs per day prescribed (total number of MMEs prescribed divided by the total number of prescription days). For definitions of PBSS measures, see

<http://www.pdmpexcellence.org/sites/all/pdfs/Definitions%20of%20PBSS%20Measures.pdf>. Higher daily opioid dosages are associated with increased risk of opioid use disorder; see Kobus et al. Correlates of higher dose opioid medication use for low back pain in primary care, *J Pain*. 2012 Nov; 13(11): 1131–1138, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3641146/>

⁸ Percentage of overlapping prescriptions is calculated as the number of days with at least one prescription in both opioid and benzodiazepine classes divided by the total number of prescription days for the opioid class; see <http://www.pdmpexcellence.org/sites/all/pdfs/Definitions%20of%20PBSS%20Measures.pdf> for additional methodological details. Benzodiazepine exposure may result in longer duration of NAS symptoms, Coghlan, D. et al., Neonatal abstinence syndrome, *Irish Medical Journal*, 1999, <http://europepmc.org/abstract/med/10360095>.

⁹ A multiple provider episode is defined for this report as use of five or more prescribers and five or more pharmacies within three months – an indicator of possible controlled substance misuse, abuse or diversion. Rates are calculated by drug class for those receiving a prescription in the drug class and are averaged over four quarters to obtain an annual rate. Note that the threshold used here was assigned by PBSS for the purpose of obtaining population estimates only.

¹⁰ States and localities with higher opioid prescribing rates may be at greater risk for adverse opioid-related health outcomes, *MMWR*, Vital Signs: Variation Among States in Prescribing of Opioid Pain Relievers and Benzodiazepines — United States, 2012, <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6326a2.htm>.

¹¹ Kattan JA, Tuazon E, Paone D, Dowell D, et al., “Public Health Detailing-A Successful Strategy to Promote Judicious Opioid Analgesic Prescribing, *Am J Public Health*, 2016; 106: 1430-1438

¹² With legislation that took effect in July 2012 (HB1), Kentucky became one of the first states to require prescribers to register and utilize the Prescription Drug Monitoring Program. Since the requirement went into effect, Kentucky has experienced significant declines in the number of opioid and benzodiazepine prescriptions, and in the rate of multiple provider episodes. Kentucky prescribers also report more frequent discussions with patients regarding their PDMP reports and treatment with controlled substances. For details on these and other outcomes of the legislation, see Patricia R. Freeman, et al., Kentucky House Bill 1 Impact Evaluation, 2015, <http://www.chfs.ky.gov/NR/rdonlyres/8D6EBE65-D16A-448E-80FF-30BED11EBDEA/0/KentuckyHB1ImpactStudyReport03262015.pdf>

¹³ In Kentucky’s recently approved budget for FY17, 2.5 million dollars were allocated to Kentucky’s Justice and Safety Cabinet for the purpose of addressing the increasing residential treatment for pregnant woman to decrease the number of infants born opiate exposed who were at risk of neonatal abstinence syndrome (NAS) or Neonatal Opiate Withdrawal (NOW). The Department for Behavioral Health, Developmental and Intellectual Disabilities (under the Cabinet for Health and Family Services) is partnering with the Office of Drug Control Policy (ODCP) in the Justice and Public Safety Cabinet to solicit proposals for funding from programs interested in serving these woman and infants. Priority will be given to programs that utilize evidence based practices such as medication assisted treatment (MAT), geographically underserved areas, and programs that demonstrate a plan for sustainability. Funds were made available to selected programs in September 2016.

¹⁴ *PBSS Issue Brief: Geographic Patterns in Neonatal Abstinence Syndrome and Prescription Opioids in Kentucky*. Frankfort, KY: Kentucky Cabinet for Health and Family Services, Office of the Inspector General, Department for Public Health; Brandeis University, Institute for Behavioral Health; Centers for Disease Control and Prevention, Division of Unintentional Injury Prevention, 2017.

This study was determined to be exempt from review by the Kentucky Cabinet for Health and Family Services Institutional Review Board.