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A Note to the Reader:

In some cases (particularly in looking at data at the regional level), the counts included in this report are small and therefore may be statistically unreliable. Therefore, readers should interpret all findings with caution. We especially encourage caution in interpreting findings and comparing differences across regions.

If you have questions about particular data points or need assistance in interpreting the data, please contact Angela M. Miller, PhD, MSPH.

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Executive Summary

Since the early 2000s, the use of opioid pain relievers in the US and Tennessee has increased rapidly. Accompanying this increase in drug use has been a ten-fold increase in the incidence of Neonatal Abstinence Syndrome (NAS), a condition in which an infant experiences withdrawal from opioid substances the mother took during pregnancy. In an effort to monitor the extent of the rise in NAS cases, the Tennessee Department of Health established NAS as a reportable condition, effective January 1, 2013.

Since NAS reporting began, there have been over 4,000 reports of NAS cases to the surveillance system. While more infants were diagnosed with NAS in 2016 than in previous surveillance years, the case rate, relative to the number of births, did not change significantly. A majority of cases continue to come from East Tennessee, where opioid drug use is high.

Over 70% of mothers who delivered babies with NAS in 2016 were taking at least one medication prescribed to them by a health care provider, either alone or in conjunction with an illegally obtained substance. The percentage of women reporting only prescription medication use has steadily increased over the last several years. In 2015, nearly half of women reported taking only prescription medications during pregnancy, with 81% of those being on medication-assisted treatment (MAT). In comparison, 52.5% of women reported only prescription drug use in 2016, with 86.1% of those on MAT.

While the count of NAS cases remains high, we are somewhat reassured that the rate is not increasing significantly. This may indicate that the NAS epidemic is reaching a plateau; additional time will be needed to determine this with certainty.

The patterns of exposure highlight continued opportunity for primary prevention of NAS—preventing substance misuse/abuse among women of childbearing age, and preventing an unintended pregnancy among women at risk of misusing/abusing substances. Additionally, the findings underscore the continued need for substance abuse treatment resources in Tennessee.
Introduction

Neonatal Abstinence Syndrome (NAS) is a condition in which an infant undergoes withdrawal from a substance to which he or she was exposed in-utero. The most common substances causing NAS are the opioid class of drugs, which includes morphine and heroin, as well as opioid pain medications and medication-assisted treatment such as buprenorphine and methadone. NAS can occur when a pregnant woman takes prescription medications prescribed to her, an illicit drug, or a prescription medication written for someone else but diverted to her.

Since the early 2000s, the incidence of NAS in Tennessee has increased by 10-fold, far exceeding the national increase (3-fold over the same time period). A sub-cabinet working group focused on NAS was convened in 2012, consisting of Commissioner-level representation from the Departments of Health, Children's Services, Mental Health and Substance Abuse Services, Medicaid (TennCare), Safety and the Children's Cabinet. This group has focused on aligning efforts across state agencies, with a focus on upstream (primary) prevention strategies.

In 2013, Tennessee became the first state in the nation to require reporting of NAS for public health surveillance purposes. Providers are required to report all diagnoses of NAS within 30 days of diagnosis. The data in this report reflect reporting to this surveillance system for CY2016.
Statewide Data

### Highlights: Statewide Reporting
- There has been a non-statistically significant increase in number of NAS cases as a percentage of live births since surveillance began in 2013.
- In CY 2016, more males were diagnosed with NAS than females.
- In CY 2016, most NAS cases were reported by the baby's birth hospital.

### Case Reports

During CY2016, providers reported 1,068 cases of NAS to the surveillance portal. An additional 52 cases of infants with *in-utero* drug exposure but no clinical signs of withdrawal were also reported; these infants are not included in this analysis as clinical withdrawal is the definitive characteristic of NAS.

The majority of cases (84.1%; n=898) were reported by the baby's birth hospital, and 15.9% (n=170) were reported after the baby was transferred to another facility.

Reported cases of NAS were more likely to be male than female (53.7% versus 46.3%; p=0.02).

The Tennessee Department of Health (TDH) requires that all cases of NAS be reported within 30 days of diagnosis. In 2016, the average of length of time between the date of birth and date of reporting was 24.9 days (range 0-375 days), with 74.2% of cases being reported within 30 days of birth.

### Number and Rate of Cases by Month of Birth

In 2016, there were 1,068 cases of NAS, an increase from 1,049 cases in 2015 (See Technical Note) and 1,034 cases in 2014 (Figure 1). In 2016, NAS cases represented 1.31% of all live births in Tennessee, an increase of 12.0% since surveillance began in 2013\(^1\). This increase was not statistically significant (p=0.07).

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\(^1\) Rates published in this report are calculated using 2015 live births as the denominator.
Figure 1: Number of Cases of Neonatal Abstinence Syndrome as a Percentage of Live Births, Tennessee 2013-2016.
Source of Exposure for NAS Infants

### Highlights: Source of Exposure

- Since 2013, there has been a statistically significant increase in exposure to prescribed drugs.
- In CY2016, 80% of infants with NAS were exposed to at least one prescription medication, with or without concomitant exposure to an illicit drug.
- In CY2016, 70% of infants with NAS were exposed to medication-assisted treatment (MAT) for substance use disorders.

### Source of Exposure

Effective January 1, 2016, the response categories for exposure were changed, therefore limiting the ability to examine changes for individual substances over time. However, the distribution of exposures available for 2016 is displayed adjacent to the exposure categories with which they most closely aligned in 2015 (Table 1). Individual cases could have been exposed to multiple substances. Therefore, the sum of cases reported in Table 1 is greater than the number of NAS cases reported.

Consistent with previous years’ data, the proportion of infants exposed to medications used to treat substance use disorders (supervised replacement therapy; medication assisted treatment) has continued to increase (58.9% in 2015 vs. 69.4% in 2016). In 2016, 27.2% of infants were exposed to diverted prescription opioid medications, and 11.2% were exposed to diverted prescription non-opioid medications. Twenty three cases were reported as having been exposed to other substances, including tobacco (n=10) and alcohol (n=6). All cases with an ‘other’ exposure were also exposed to either prescription drugs and/or illicit substances.

When categorized into mutually exclusive categories of exposure, 79.7% of NAS infants were exposed to at least one prescription medication: 52.5% of cases were exposed to prescription medications only, and 27.2% percent of infants were exposed to a mix of prescription and illicit or diverted drugs. Nineteen (19.4%) percent were exposed only to illicit or diverted drugs. The remainder (0.9%) had no known exposure, or exposure information was not reported.

Since 2013, there has been a statistically significant increase in the percentage of NAS cases exposed only to prescription medications (p<0.01; Figure 2). There was also a
statistically significant decrease in the proportion of cases exposed to illicit drugs or diverted medications \( (p=0.03) \). The percentage of cases exposed to both prescription medications and illicit drugs remains unchanged \( (p=0.125) \).

Among the 561 cases exposed to only prescription medications, 86.1% \( (n=483) \) were exposed to medication assisted treatment for the mother’s substance use disorder. Thirty-nine percent \( (39.0\%; n=80) \) were exposed to legally prescribed opioid pain relievers, and 19.7% \( (n=57) \) were exposed to legally prescribed non-opioid medications.

Table 1: Reported Non-mutually Exclusive Sources of Exposure for Neonatal Abstinence Syndrome Cases, Tennessee 2015-2016

<table>
<thead>
<tr>
<th>Source</th>
<th>2015 # Cases</th>
<th>% Cases</th>
<th>Source</th>
<th>2016 # Cases</th>
<th>% Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supervised replacement therapy</td>
<td>612</td>
<td>58.9</td>
<td>Medication Assisted Treatment</td>
<td>740</td>
<td>69.4</td>
</tr>
<tr>
<td>Supervised pain therapy</td>
<td>106</td>
<td>10.2</td>
<td>Legal prescription of an opioid pain reliever</td>
<td>110</td>
<td>10.3</td>
</tr>
<tr>
<td>Therapy for psychiatric or neurological condition</td>
<td>86</td>
<td>8.3</td>
<td>Legal prescription of a non-opioid</td>
<td>90</td>
<td>8.4</td>
</tr>
<tr>
<td>Prescription substance without a prescription</td>
<td>343</td>
<td>33</td>
<td>Prescription opioid without prescription</td>
<td>290</td>
<td>27.2</td>
</tr>
<tr>
<td>Non-prescription substance</td>
<td>224</td>
<td>21.6</td>
<td>Non-opioid prescription without a prescription</td>
<td>120</td>
<td>11.3</td>
</tr>
<tr>
<td>No known exposure but clinical signs consistent with NAS</td>
<td>5</td>
<td>0.5</td>
<td>Heroin</td>
<td>40</td>
<td>3.8</td>
</tr>
<tr>
<td>No response</td>
<td>51</td>
<td>4.9</td>
<td>Other non-prescription substance</td>
<td>189</td>
<td>17.5</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
<td>No known exposure but clinical signs consistent with NAS</td>
<td>9</td>
<td>0.8</td>
</tr>
<tr>
<td>No response</td>
<td>0</td>
<td>0</td>
<td>No response</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
<td>Other</td>
<td>23</td>
<td>2.2</td>
</tr>
</tbody>
</table>
Table 2: Derivation of Mutually Exclusive Categories of Exposure from Individual Exposures

<table>
<thead>
<tr>
<th>Prescription Medications Only</th>
<th>Illicit Drugs or Diverted Medications Only</th>
<th>Combination of Prescription Medications and Illicit Drugs/Diverted Medications</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to one or more of the following <strong>ONLY</strong>:</td>
<td>Exposure to one or more of the following <strong>ONLY</strong>:</td>
<td>At least one medication from “Prescription Medications Only” <strong>AND</strong> At least one substance from “Illicit Drugs or Diverted Medications Only”</td>
<td>“No known source of exposure but clinical signs consistent with NAS” was selected at time of report <strong>OR</strong> No exposure options were selected at time of report</td>
</tr>
</tbody>
</table>
|   • Medication Assisted Treatment (MAT) |   • Prescription opioid medication obtained without a prescription | | }
The increase in exposure to prescription medications only was statistically significant (p<0.01), as was the decrease in exposure to illicit substances only (p=0.03). There was no statistically significant change in exposure to a combination of prescription medications and illicit drugs (p=0.125).
Regional Data

<table>
<thead>
<tr>
<th>Highlights: Regional Trends for NAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Rates of NAS increase when moving from west to east across Tennessee.</td>
</tr>
<tr>
<td>• Patterns of exposure source vary by urban versus rural region status.</td>
</tr>
</tbody>
</table>

**NAS Incidence by Region**

In 2016, rates of NAS varied by health department region. Rates of NAS are lowest in West Tennessee and increase in an easterly fashion. There has been some annual variation in the case rate by region, but time trends were statistically significant only for the Upper Cumberland and South East Health Regions (Figure 3). Previous reports of NAS showed the East and Northeast Health Regions and Sullivan County as bearing the greatest burden of NAS. It now appears that NAS rates in the East Health Region have decreased each year, while rates in surrounding counties have either increased or remained relatively unchanged (Figure 4-7).

**Exposure Source by Region**

There also appears to be geographic variation in the substance causing NAS (Figure 8). Compared to previous surveillance years, exposure to prescription medications has become more prevalent, being the primary source of exposure in all of the rural health department regions. Of the metro regions, prescription medications were also the primary source of exposure, except in Shelby, Knox and Hamilton Counties, where a mix of prescription medications and illicit drugs were most prevalent.

Exposure to medication assisted treatment (MAT) is distributed somewhat evenly across the state, though prevalence tends to be higher in East Tennessee (Figure 9). Use of legally obtained opioid medications is more common in Middle and West Tennessee, with legally obtained non-opioid medications more common in East Tennessee (Figure 10). Exposure to diverted substances is distributed evenly across the state, with exposure to diverted opioid medications more common than diverted non-opioid medications. There was a higher proportion of NAS cases exposed to diverted opioids in Knox County (Figure 11). Though a small number of cases (n=40) were exposed to heroin, use of heroin is most common in
urban areas, and the surrounding counties (i.e., Davidson County and neighboring Mid-Cumberland Health Region (Figure 12).
Figure 3: Annual Neonatal Abstinence Syndrome Case Rate by Tennessee Health Region, 2013-2016. Trends were statistically significant only for Upper Cumberland and South East Health Regions.
Figure 4: Rate of NAS Cases by County, 2013.

Figure 5: Rate of NAS Cases by County, 2014.
Figure 6: Rate of NAS Cases by County, 2015.

Figure 7: Rate of NAS Cases by County, 2016.
Figure 8: Distribution of Mutually Exclusive Sources of Exposure by Health Region for Neonatal Abstinence Syndrome Cases, Tennessee 2016.
Figure 9: Prevalence of Exposure to Medication Assisted Treatment among NAS Cases by Region, 2016.

Figure 10: Prevalence of Exposure to Legally Obtained Prescription Medications among NAS Cases by Region, 2016.

Figure 11: Prevalence of Exposure to Diverted Prescription Medications among NAS Cases by Region, 2016.

Figure 12: Prevalence of Exposure to Illicit Drugs among NAS Cases by Region, 2016.
Non-Residential NAS Cases

**Highlights: Non-Residential NAS Cases**

- In CY2016, Tennessee hospitals reported 118 NAS cases in which the infant was from another state.
- The majority (64.4%) of non-residential NAS cases were from Virginia.

Effective July 1, 2014, reporting hospitals were asked to report cases of NAS treated at Tennessee hospitals that were residents of states that border Tennessee. These states include Alabama, Arkansas, Georgia, Kentucky, Mississippi, Missouri, North Carolina and Virginia.

In 2016, 118 cases of NAS from other states were treated in Tennessee. The distribution of out of state cases, by maternal state of residence, is shown in Table 3.

Less than half (46.6%, n=55) of out of state NAS cases were born in Tennessee (for example, the baby's mother was from North Carolina but delivered in Tennessee). The majority were born in out of state hospitals and transferred to a Tennessee hospital for care (for example, the baby was born in Virginia but transferred to Tennessee for care).
Table 3: State of Residence for Non-Resident Cases of Neonatal Abstinence Syndrome Reported in Tennessee, 2016

<table>
<thead>
<tr>
<th>State</th>
<th>No. of Cases</th>
<th>% of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Arkansas</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Georgia</td>
<td>15</td>
<td>12.7</td>
</tr>
<tr>
<td>Kentucky</td>
<td>10</td>
<td>8.5</td>
</tr>
<tr>
<td>Mississippi</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Missouri</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>North Carolina</td>
<td>8</td>
<td>6.8</td>
</tr>
<tr>
<td>Virginia</td>
<td>76</td>
<td>64.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>118</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>
Conclusion

Since becoming a reportable condition in 2013, the proportion of births affected by Neonatal Abstinence Syndrome each year has not changed significantly. From 2002 to 2013, the rate of NAS increased 10 fold, as measured by Hospital Discharge Data. The rate measured by surveillance data has not shown a statistically significant increase over the four years since surveillance began.

While the count of NAS cases remains high, we are somewhat reassured that the rate is not increasing significantly. This may indicate that the NAS epidemic is reaching a plateau; additional time will be needed to determine this with certainty.

Since 2013, there has been a shift in the exposure sources associated with NAS, with more mothers of NAS infants taking medications prescribed by a provider. That nearly 70% of mothers of all NAS infants were receiving medication assisted treatment is suggestive that women with a history of substance use disorder are becoming more engaged with medical providers before and during pregnancy.

The patterns of exposure (with nearly 80% of cases being exposed to at least one substance prescribed by a healthcare provider) highlight opportunities for primary prevention. Healthcare providers should explore non-opioid treatment modalities in women of childbearing age, and should promote effective contraceptive methods to prevent unintended pregnancies among women who use opioids.

Acknowledgements

The Tennessee Department of Health would like to acknowledge the reporting hospitals and providers across the State of Tennessee, the NAS Sub-Cabinet Working Group and TDH Staff.
Technical Notes

1. At publication of the 2015 Neonatal Abstinence Syndrome Surveillance Annual Report, 1,039 cases with a birth year of 2015 had been reported. After publication of the 2015 report, an additional 10 cases were reported and are included here.

2. All rates for 2016 were calculated using the 2015 Birth Statistical File.

Suggested Citation

This report was prepared by Angela M. Miller, PhD, MSPH, Morgan McDonald, MD and Michael Warren, MD, MPH.